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EDITORIAL

Dear Colleagues,

This issue of *European Eye Research* brings together a collection of 13 original articles and 4 case reports that examine current clinical trends, surgical considerations, and diagnostic innovations across various subspecialties of ophthalmology.

The perspectives of ophthalmologists regarding surgical loupes reveal important insights into magnification choices and clinical utility. Clinical competence in eye drop self-administration is evaluated among healthcare professionals, highlighting practical challenges that underscore the critical need for structured patient education. The role of family physicians in neonatal vision screening is evaluated in terms of practice patterns, knowledge levels, and awareness regarding early pediatric eye evaluations.

Pediatric and developmental eye care is explored through investigations of the frequency and clinical features of microtropia identified during preschool screenings, alongside evaluations of the macular and optic disc microvascular circulation in children who have undergone pediatric cataract surgery. The impact of keratoconus is assessed using specific emotional and functional questionnaire subscales among patients managed with or without surgery. An article from a tertiary eye bank examines how the rise of lamellar keratoplasty has influenced tissue processing, donor trends, and modern eye banking.

Peripapillary microvasculature and retinal nerve fiber layer thickness during both the active and quiescent phases of intermediate uveitis are evaluated. Another original article also reviews systemic inflammatory markers in retinal venous occlusions, as well as the microvascular and morphological choroidal differences associated with hypertensive retinopathy.

The influence of corneal suture removal timing on postoperative astigmatism following phacoemulsification is analyzed to optimize early visual rehabilitation. In addition, other articles detail the clinical characteristics, device prescription patterns, and quality-of-life profiles of patients managed in low-vision units, as well as the anatomical and morphological predictors of visual outcomes following advanced macular hole surgery.

Finally, this issue also features a series of instructive case reports highlighting rare clinical entities and unusual presentations, including hydrochlorothiazide-induced bilateral acute angle-closure glaucoma, orbital and craniofacial involvement of an aneurysmal bone cyst, the spontaneous closure and reopening of idiopathic full-thickness macular holes, and spontaneous bleeding from a concealed deep orbital hemangioma following a routine screening examination.

Together, these original investigations and case presentations offer valuable perspectives that enrich our understanding of contemporary ophthalmology and inform future clinical care.

We hope you enjoy reading and sharing this issue.

European Eye Research is proud to grow with you—our readers, valued authors, dedicated reviewers, and everyone who contributes to advancing the field of ophthalmology.

Sincerely,

Melis Palamar, MD

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Perspectives on the use of surgical loupes among ophthalmologists in Turkey: A national survey study

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Abstract

Purpose: To investigate the use of surgical loupes in the clinical practice of Turkish ophthalmologists and to understand their perspectives on the use of surgical loupes.

Methods: This descriptive study was conducted between April and May 2024 and comprised 106 ophthalmologists who completed the survey. A link to a questionnaire, in which demographic characteristics as well as loupe usage patterns and perspectives were evaluated, was sent to the members of the Turkish Ophthalmology Association through email, WhatsApp, and Instagram. Google Forms was used to collect survey responses.

Results: 44.5% of participants felt loupes improve surgery, and 45% were undecided. 54.8% found loupes useful for surgical residency training, while only 7.5% disagreed. Nonetheless, only 14% made a purchase. The loupe was mainly used in oculoplastic procedures such as dacryocystorhinostomy (60%), nasolacrimal duct surgeries (66%), and ptosis repair (60%). The most cited benefits were as follows: The magnification of the image (73.6%), the improved recognition of anatomical structures (66%), enhanced visual acuity (30.2%), and improved posture and ergonomics (22.6%). The most common reasons for not purchasing a loupe were lack of need in clinical practice (68%) and high cost-performance ratio (20.9%). While 39 (36.8%) of respondents reported no negative experiences using a loupe, the most common issues cited were discomfort (20.8%), difficulty with adjustments (17.9%), and limited depth perception (12.3%).

Conclusion: The loupe is an auxiliary instrument known to be helpful in varying surgeries, including oculoplastic surgery. This study is the first to explore the perspectives on the use of loupes among ophthalmologists in Turkey and to examine the advantages, limitations, and obstacles to their use.

Keywords: Oculoplastic surgery, Ophthalmology, Residency training, Surgical instruments, Surgical loupes, Turkish ophthalmologists

Loupes are surgical tools that magnify vision 2×–8×. They consist of binocular magnifying lenses attached to frames such as conventional safety spectacles. The use of surgical loupes has been reported in a variety of specialties, including dermatology, neurosurgery, cardiothoracic surgery, otolaryngology, plastic surgery, and maxillofacial surgery.[1-3] Ophthalmologists are reported to use surgical loupes less frequently, as they use microscopes to provide the higher magnifications required for certain microsurgical procedures.[4] Despite their comparatively lower frequency of use, surgical loupes have distinct advantages over surgical microscopes, including enhanced flexibility, portability, and cost-effectiveness. Moreover, surgical loupes allow closer access to the surgical area, expanded

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orientation, and swift adjustments in the viewing angle and position within the surgical field through head and neck changes during surgery.[1]

In studies regarding the utilization of surgical loupes in ophthalmology, the usage rates of oculoplastic surgeons were reported as 80.9%,[5] 95%,[4] and 55%.[6] Considering regional disparities in the purchasing power of surgical loupes, it is expected that loupe usage rates, doctors' priorities, and perceptions may vary. Given the scarcity of studies on the use of surgical loupes in the field of ophthalmology and their direct impact on ergonomics, the present study aimed to address this gap through a national survey. The primary goal was to investigate and elucidate usage patterns and perceptions regarding the application of surgical loupes among ophthalmologists in Turkey.

Materials and Methods

The questionnaire used in this study was developed drawing upon the literature, particularly the studies by Wei and Wu[4] and Hunt *et al*.[3], which examined the use of surgical loupes in ophthalmology and dermatology, respectively. The items were contextually adapted and refined by the authors. To assess the clarity, comprehensibility, and face validity of the instrument, a pilot test was conducted with 15 ophthalmologists. Participants evaluated each item individually in terms of wording, understandability, and relevance to clinical practice. The questionnaire included multiple-choice questions (some permitting multiple selections) to collect demographic information and assess patterns of surgical loupe usage, as well as Likert-type questions using a five-point scale to evaluate participants' awareness, perceptions, and attitudes regarding the use of surgical loupes. No total or composite score was calculated. As each question was reviewed separately and no psychometric analysis was performed in this descriptive questionnaire, further validation procedures were not deemed necessary. Minor revisions were made based on the feedback obtained during the pilot testing to finalize the questionnaire (Appendix 1).

All participants provided informed consent before the commencement of the surveys. For this study, which was prepared in accordance with the principles of the Declaration of Helsinki, ethical approval (decision number 54) was received from the Kayseri City Hospital Clinical Research Ethics Committee (April 18, 2024).

This cross-sectional descriptive study included ophthalmologists registered with the Turkish ophthalmological association (TOD) as of 2024, representing a total population of 4,313 individuals. The minimum required sample size was calculated using G*Power software (version 3.1), assuming an effect size of 0.3, 80% statistical power, a margin of error of 5%, and a confidence interval of 95%, yielding 108 participants.

Participants were selected using a simple random sampling method from the TOD registry. Individuals without available contact information and resident physicians were excluded. The questionnaire prepared through Google Forms was distributed to eligible participants through email, WhatsApp, and Instagram. A total of 300 ophthalmology specialists were invited to participate in the study. A reminder e-mail was dispatched to them 2 weeks later, and 115 responses were received, giving an overall response rate of 38.3%. Following the exclusion of nine questionnaires deemed incomplete or invalid, a total of 106 complete responses were included in the final analysis.

Statistical Analysis

The Kolmogorov–Smirnov test was used to analyze the distribution of variables. For group comparisons, the Kruskal–Wallis test or the Mann–Whitney U test was used. For categorical values, the Chi-squared test or Fisher's exact test was used. Descriptive statistics included mean ± standard deviation, median, frequencies, and ratios. A $p<0.05$ was considered statistically significant, and statistical analyses were performed using the Statistical Package for the Social Sciences for Windows version 22.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 106 ophthalmologists participated in the survey and provided valuable information evaluating their experiences and opinions about surgical loupes. The average age of the participants was 36.99±8.82 years, and their experience was 8.43±8.20 years as a specialist. 57.5% worked in academic hospitals, 19.8% in public hospitals, 16% in private hospitals, and 6.6% in private clinics providing outpatient services. In addition, 67(63.2%) of the ophthalmologists who completed the survey were male, and 39 (36.8%) were female.

The questionnaire highlighted the main benefits of using loupes. The most cited benefits were magnification of the surgical field (73.6%), improved recognition of anatomical structures (66%), improved visual acuity (30.2%), and improved posture and ergonomics (22.6%) (Table 1). A total of 44.3% of respondents felt that loupes improved surgical performance, while 45% were undecided. In addition, 54.8% of participants felt that loupes were useful

for surgical training during residency, with only 7.5% disagreeing. While most participants believed that loupes should be provided free of charge during residency, many were undecided about whether residents should purchase them themselves during training (Table 2).

Despite the perceived benefits, only 14% of respondents said they had purchased loupes. Of those who had purchased them, a significant 73.33% stated that their purchase was made during their specialization training. When examining the specific procedures in which loupes were used, the following trends emerged: usage was most common in dacryocystorhinostomy (66%), followed by nasolacrimal duct and punctum surgery (60%), ptosis repair (60%), trichiasis (60%), ectropion and entropion surgery (53.3%). In addition, 53.3% of respondents performed blepharoplasty using loupes. Of the loupe owners, 66% revealed that they used 2.5× magnification, indicating its popularity with users. A smaller subgroup of 20% chose 3.5× magnification. It is worth noting that none of the respondents reported using a 4.5× magnification. Two of the ophthalmologists (13.3%) stated that they were unaware of the magnification of their loupe. These results highlight the prevalence of 2.5× magnification in surgical practice but also indicate a lack of knowledge of the options available.

Table 1. Perspectives on loupe use

Question / Response	%
Perceived benefits of loupe use	
Magnification of the surgical field	73.6
Improved recognition of anatomical structures	66.0
Improved visual acuity	30.2
Better posture and ergonomics	22.6
Provides eye protection	19.8
Improved comfort while operating	16.0
No perceived benefit	5.7
Reasons for not purchasing a loupe	
Perceived lack of need in clinical practice	68.0
Cost-performance concerns	20.9
Had no thought of its use before	18.8
Would be beneficial too infrequently	10.7
Requires long time to adjust	3.3
Negative experiences associated with loupe use	
Had not experienced any adverse situations	36.8
Discomfort	20.8
Difficulty with adjustment	17.9
Reduced depth perception	12.3
Headache	5.7
Eye soreness	4.7
Fatigue	3.8
Possible contamination	2.8

The results further revealed significant barriers to adoption. The most common reasons for not purchasing a loupe were a perceived lack of need in clinical practice (68%) and concerns regarding the cost-performance ratio (20.9%). In terms of negative experiences associated with loupe use, 39 respondents (36.8%) said they had not experienced any adverse situations. Of those who reported problems, discomfort was the most common (20.8%), followed by difficulty with adjustment (17.9%) and reduced depth perception (12.3%) (Table 1).

Discussion

Due to the rapid progress in device technology, surgical loupes have emerged as an important tool in contemporary surgery in different medical disciplines.[1,3,7] While numerous publications have examined the use of surgical loupes across various medical fields and explored physicians' perspectives on their effectiveness, few studies specifically focused on their application in ophthalmology.[4-6] Since two studies were conducted in the USA and one in Saudi Arabia, it was important to examine whether these

Table 2. Survey responses on the perceived benefits, impact on surgical performance, and availability of surgical loupes during residency

Questions	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)
Do you believe that loupes are beneficial for surgical training during residency	27.4	27.4	34.0	3.7	7.5
Do you think using a loupe improves surgical performance?	24.0	20.0	45.0	6.0	5.0
Do you think loupes should be provided free of charge during residency?	34.0	15.1	28,3	6.6	16.0
Do you think residents should purchase surgical loupes during their specialty training?	6.6	9.4	47.2	17.0	19.8

*Rating on a scale from 1 to 5 (1=Definitely 3=Undecided 5=Not at all)

findings applied to other regions of the world. Therefore, this study revealed the perspectives on the use of surgical loupes among ophthalmologists in Turkey and filled an important gap in the existing literature. We analyzed the usage patterns, attitudes, and challenges faced by ophthalmologists using surgical loupes, highlighting both the practical benefits and the limitations.

Our questionnaire inquired about the main benefits of using a loupe in surgical applications. Many respondents emphasized that loupes increase the magnification of the surgical field, allowing better recognition of anatomical structures. However, a smaller number of respondents (30.2%) reported that these magnification tools contribute to improved visual acuity during procedures. Some respondents (22.6%) also pointed out the advantages of improved posture and ergonomics, indicating that loupes may help mitigate physical strain during surgery. While our study indicates that the contribution of loupes to ergonomics is comparable to the rates found in other studies involving ophthalmologists, this rate may vary according to different specialties.[4-6] A randomized controlled trial among dental students showed that early use of these tools improved posture and encouraged healthier work habits.[8] Furthermore, one survey revealed that 89% of dental and health students recognized the ergonomic benefits of surgical loupes.[9] Recent findings from a randomized controlled trial have highlighted the remarkable benefits of using loupes in various surgical procedures across different specialties. Participants demonstrated notably reduced head inclinations ($p<0.001$), a substantial decrease in neck muscle activity ($p<0.05$) and lower neck discomfort ($p<0.01$).[10] One of the main factors behind the perception of limited ergonomic benefits of loupes among ophthalmologists is the unavoidable comparison with operating microscopes. The advanced ergonomic features and visualization capabilities of surgical microscopes may overshadow the benefits of loupes in this specific field. Nevertheless, despite the high prevalence of neck and back pain reported among ophthalmologists,[11] both studies investigating this issue found no significant association between surgical loupe use and these complaints.[5,6]

In addition, a considerable proportion of respondents (44.5%) believed that the use of loupes improves overall performance in surgical practice. Some respondents (45%) were undecided about the effectiveness of these tools, indicating that further research is needed to fully understand the impact of loupes in real-world settings. An experimental study showed that the use of loupes or surgical microscopes during microsurgery significantly improves performance and reduces complication rates. As a result, the study concluded that these tools should be considered essential in such procedures.[7] In a randomized prospective study of the surgical treatment of basal cell carcinoma of the face, the use of the loupe was shown to provide better tumor margin assessment and histological clearance.[12] A study in the field of urology has shown that application of intraoperative magnification tools during sperm retrieval significantly enhances the success rate of sperm extraction in men with non-obstructive azoospermia and testicular volumes of 10 mL or less.[13] These instruments have been shown to reduce the likelihood of positive surgical margins in radical prostatectomy when used at a magnification of 4.3× compared to 2.5×.[14] Nevertheless, the 2.5× magnification level continues to be the most preferred choice among urologists.[15] Our study, along with other studies conducted with ophthalmologists, also found that 2.5× was the favored option.[4-6] This similarity across specialties (dental trainers, trainees,[16] and maxillofacial surgeons[17]) demonstrates the practicality and broad relevance of 2.5× magnification in such surgical procedures. Given its primary use in oculoplastic surgery as an alternative to the operating microscope, this magnification may be considered sufficient.

In the present study, participants reported several negative experiences related to magnifying loupes. Discomfort was the most frequently reported problem (20.8%), followed by difficulty adjusting (17.9%) and reduced depth perception (12.3%). These negative effects may explain the preference for 2.5× magnification, as this level appears to strike a balance between ergonomic comfort and sufficient visual enhancement. In support of this, Du *et al*.[18] reported that stereo acuity and depth perception were reduced when looking through a magnifying loupe or microscope, and these effects were more pronounced with increasing magnification. Moreover, they found that even familiarity with magnifying equipment did not make a difference in stereo acuity.

One striking finding from our study is that the purchase rate of loupes was significantly lower than in previous studies,[4-6] with only 14% of participants reporting that they have made a purchase. In addition, key barriers to adoption were identified, including a perceived lack of need in clinical practice (68%) and concerns regarding the cost-performance ratio (20.9%). However, only 7.5% of respondents disagreed with the statement that the use of loupes would be useful during residency. Various factors could be responsible for this outcome. First, financial limitations may influence the availability of surgical tools

like surgical loupes and perspectives on their use. The limited availability of operating microscopes in resource-constrained settings is a well-documented challenge.[19] In such settings, surgical loupes are often more accessible within the healthcare system due to their lower cost and distinct advantages, making them a viable alternative to operating microscopes. In contrast, in countries facing certain socio-economic challenges, such as Turkey, surgical microscopes are often more readily available than surgical loupes due to a centralized purchasing system. This disparity may result from the classification of loupes as instruments designed for individual use and the prioritization of formal cost-effectiveness assessments in hospital purchasing decisions.[20] A recent study examining the financial and logistical factors that influence loupe use among endodontists in Turkey revealed significantly lower usage rates compared to existing literature. The authors suggested that this low adoption rate may be linked to high patient volume, constraints in clinical practice, limited resources, and costs associated with acquiring and maintaining equipment.[21] Second, focusing exclusively on oculoplastic surgeons could have yielded higher rates of reported surgical loupe usage and adoption, given their greater dependence on these tools. However, by including general ophthalmologists from various subspecialties, our study provides a more comprehensive view of loupe usage patterns in ophthalmology.

While most respondents supported providing surgical loupes free of charge during residency, opinions were more varied concerning requiring residents to purchase loupes themselves. Since previous studies show that early access to loupes increases familiarity and adoption,[6,9] it is reasonable to recommend that residency programs facilitate loupe access, either by providing them or by offering subsidies.

A notable limitation of this study is its reliance on electronic survey methodology. While this approach facilitates access to a wider audience, including ophthalmologists in different regions of Turkey and varying institutions, it also presents some inherent challenges. A significant number of methodological reviews have drawn attention to the risk of bias in survey-based research when response rates are low or when participants voluntarily participate in the study.[22,23] Therefore, a major drawback is the potential for sample bias due to the exclusion of ophthalmologists who may not have access to or chose not to participate in the electronic survey. This situation has the potential to compromise the representativeness and evaluation of the sample at the national level. Consequently, more comprehensive studies involving a broader portion of the ophthalmologist population in Turkey are required to better evaluate and generalize these findings.

Conclusion

The primary strength of this study is that it focuses on the use of loupes within a single country, which serves as a valuable example for developing countries, an issue that has been relatively under-researched in previous studies. These findings reveal the varying perceptions of surgical loupes among the ophthalmologists who participated in our survey and highlight their potential benefits as well as barriers that hinder wider adoption. Based on the results of this study and the evidence from previous research, we suggest the incorporation of surgical loupes as a useful tool for ophthalmologists to improve surgical precision and outcomes.

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Ethics Committee Approval: This study was approved by The Kayseri City Hospital Clinical Research Ethics Committee (Decision number 54; April 18, 2024).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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APPENDIX

Perspectives on the use of surgical loupes among ophthalmologists in Turkey: A national survey study

Dear Ophthalmologist,

This study, titled "perspectives on the use of surgical loupes among ophthalmologists in Turkey: A national survey study" has been designed to investigate the impact of surgical loupe use. The results obtained from your responses will make it possible to assess the effect of surgical loupe use. For this reason, it is of great importance that you answer all questions completely and honestly.

Thank you for completing this survey.

☐ I agree to participate in the study.

1. Demographic Information

1.1. Sex

☐ Female
☐ Male

1.2. Age: _____

1.3. Years of experience as a specialist: _____

1.4. What is the type of clinic you currently work at?

☐ Academic hospital
☐ Public hospital
☐ Private hospital
☐ Private clinics providing outpatient service

2. Surgical Loupe Use Status

2.1. Is there a surgical loupe provided by your clinic that is available for shared use?

☐ Yes
☐ No

2.2. Do you have your own surgical loupe? (If your answer is "no," please skip the remaining questions and proceed directly to Question 1 of Section 3.)

☐ Yes
☐ No

2.3. How many years have you been using a surgical loupe?

☐ <5 years
☐ 5-10 years
☐ >10 years

2.4. When did you purchase your surgical loupe?

☐ During their specialization training.
☐ After becoming a specialist
☐ Other: _____

2.5. What magnification ratio do you use?

☐ 2.5x
☐ 3.5x
☐ 4.5x
☐ No idea

2.6. How often do you use a surgical loupe during the surgical procedures you perform?

☐ Always
☐ Often (approximately 75% of surgeries)
☐ Sometimes (approximately 50% of surgeries
☐ Rarely (approximately 25% of surgeries)
☐ Never

2.7. In which surgical procedures do you use a surgical loupe? (Multiple selections allowed)

☐ Chalazion surgery
☐ Ptosis repair
☐ Orbital tumor excision and biopsy
☐ Orbital fracture surgeries
☐ Laser surgeries
☐ Botox procedures
☐ Enucleation, evisceration, exenteration
☐ Nasolacrimal duct and punctum surgery
☐ Dacryocystorhinostomy
☐ Trichiasis
☐ Ectropion and entropion surgery
☐ Orbital decompression surgeries
☐ Blepharoplasty
☐ Jones tube implantation
☐ Other surgeries

3. Perspectives on loupe use

3.1. Which factor(s) influenced your decision not to purchase a surgical loupe? (Please do not answer this question if you have already purchased or currently use a surgical loupe)

☐ I did not feel a need for it in my own practice
☐ I think it would be useful only very rarely
☐ Cost-performance concerns
☐ Requires long time to adjust
☐ Had no thought of its use before
☐ Other

3.2. Are you considering purchasing a surgical loupe? (Please do not answer this question if you have already purchased or currently use a surgical loupe.)

☐ 1 (Definitely yes)
☐ 2
☐ 3 (Undecided)
☐ 4
☐ 5 (Not at al)

3.3. In your opinion, what are the advantages of using a surgical loupe? (Multiple selections allowed)

☐ Magnification of the surgical field
☐ Provides eye protection
☐ Better posture and ergonomics
☐ Improved comfort while operating
☐ Improved patient care quality
☐ Improved recognition of anatomical structures
☐ Improved visual acuity
☐ No perceived benefit
☐ Other: _____

3.4. What negative experiences have you had with the use of a surgical loupe?

☐ Headache
☐ Eye soreness
☐ Fatigue
☐ Vertigo
☐ Reduced depth perception
☐ Discomfort
☐ Difficulty with adjustment
☐ Possible contamination
☐ Other: _____
☐ Had not experienced any adverse situations

3.5. Do you think using a loupe improves surgical performance? (Please rate on a scale of 1–5)

☐ 1 (Definitely yes)
☐ 2
☐ 3 (Undecided)
☐ 4
☐ 5 (Not at all)

4. Education and Future Perspectives

4.1. Do you believe that loupes are beneficial for surgical training during residency? (Please rate on a scale of 1–5)

☐ 1 (Definitely yes)
☐ 2
☐ 3 (Undecided)
☐ 4
☐ 5 (Not at all)

4.2. Do you think residents should purchase surgical loupes during their specialty training? (Please rate on a scale of 1–5)

☐ 1 (Definitely yes)
☐ 2
☐ 3 (Undecided)
☐ 4
☐ 5 (Not at all)

4.3. Do you think loupes should be provided free of charge during residency? (Please rate on a scale of 1–5)

☐ 1 (Definitely yes)
☐ 2
☐ 3 (Undecided)
☐ 4
☐ 5 (Not at all)

5. If you have any additional comments or suggestions, please share them:

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Competence of ophthalmic healthcare professionals in self-administration of eye drops

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Abstract

Purpose: The purpose of this study was to evaluate the competence of ophthalmic healthcare professionals in the self-administration of eye drops.

Methods: Doctors and nurses from the ophthalmology department constituted the study group, while age-, gender-, and visual acuity-matched healthy individuals formed the control group. None of the participants were patients. All participants were given single-dose (monodose) sodium hyaluronate drops and were asked to self-administer the drops in both eyes. Eye drop instillation was assessed based on three criteria: (1) successful delivery of at least one drop onto the ocular surface or conjunctival fornix, (2) avoiding contact of the bottle tip with the ocular surface or surrounding tissues, and (3) instillation of one drop at a time. "Successful drop instillation" was defined as meeting all three criteria.

Results: Eighty-six cases were included (43 in each group). Successful instillation was observed in 26 participants (60.4%) in the study group, compared to 12 participants (27.9%) in the control group (p=0.002). Contact of the dropper tip with any surface occurred in 7 (16.2%) versus 23 cases (53.4%) in the study group and the control group (p<0.001).

Conclusion: Despite clinical experience, approximately 40% of the study group failed in proper self-instillation. The study group performed significantly better at steps requiring fine motor control, such as not allowing the bottle tip to touch any surface. These findings highlight the need for structured patient education to promote safer and more effective eye drop use.

Keywords: Eye drops, Patient compliance, Treatment compliance

Topical eye drops have a major role in the therapy of ophthalmological diseases due to their safety, direct delivery, non-invasiveness, and ease of application. Although topical eye drops undoubtedly deserve their popularity, the application of these drugs is not always as simple as it sounds. Previous studies have demonstrated that a significant proportion of glaucoma patients experience challenges in at least one aspect of the eye drop instillation process. These challenges may include failure to prevent bottle tip contamination, difficulty delivering a single drop, or inaccurate placement of the drop during administration.[1,2] Contributing factors to suboptimal instillation techniques have been identified as advanced age, impaired manual dexterity, reduced visual acuity, and lower levels of educational attainment.[3,4] In addition to user-related factors, the design of eye drop containers also influences the ease of self-administration. Previous studies have shown that multidose containers require

* This study was presented at the ECSLO (The European Contact Lens Society of Ophthalmologists) Congress 2024 in Istanbul on April 26, 2024.

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greater squeezing force and coordination compared with single-dose units, posing additional challenges for elderly or arthritic patients.[4]

The therapeutic effectiveness of eye drop therapy and the reduction of possible side effects depend heavily on effective instillation.[5,6] Visual impairments and musculoskeletal conditions – particularly those affecting the head and neck – can hinder the proper administration of eye drops. Moreover, insufficient patient education regarding correct usage techniques is a significant contributor to treatment failure.[7-9] An appropriate instillation technique involves gently retracting the lower eyelid to instill a single drop into the conjunctival fornix, ensuring the bottle tip does not contact the ocular surface or surrounding structures. Following instillation, the patient should close the eyelid and apply nasolacrimal occlusion to minimize systemic absorption.[5,6,10] Incorrect administration results in decreased therapeutic effect, increased periocular and systemic side effects, contaminated bottles, and corneal abrasions that may lead to corneal ulcers.[3,6,11,12]

This study aimed to evaluate the competence of ophthalmic healthcare professionals – who are expected to possess the necessary knowledge and experience regarding self-administration of eye drops – and to compare their performance with that of healthy individuals.

Materials and Methods

This cross-sectional clinical study was conducted in the ophthalmology department. The study protocol was approved by the Ethics Committee (March 21, 2024/24–3.1T/27). Written informed consent was obtained from all participants, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

This cross-sectional study included healthy doctors and nurses working at the ophthalmology clinic who had no musculoskeletal or ophthalmological problems as the study group and healthy, age-, gender-, and visual acuity-matched volunteers as the control group. Both groups consisted entirely of healthy volunteers with no ocular or systemic diseases, and none of the participants were patients. Participants with diseases that might have a negative impact on the administration of topical drops, such as hand or head tremors, movement disorders, movement limitations of the head and neck, and patients with any chronic or acute ophthalmological problems, were excluded from the study. None of the participants were on any kind of eye drop treatment at the time of the study. All participants underwent a comprehensive ophthalmologic assessment, including best-corrected visual acuity measured with a Snellen chart, intraocular pressure evaluation using Goldmann applanation tonometry, and slit-lamp biomicroscopic examination of both anterior and posterior segments. All participants were given a single-dose (monodose) unit (0.3 mL) of 0.15% sodium hyaluronate (Eyestil, SIFI, Italy) and were asked to instill one drop into each eye. The instillation process was observed by the researchers, and the following criteria were evaluated: instilling at least 1 drop into the ocular surface or conjunctival fornix, avoiding contact of the bottle tip with the ocular surface or surrounding tissues, and instilling one drop at a time. "Successful drop instillation" was defined as meeting all three criteria. Each instillation was assessed independently by two observers, who evaluated adherence to all predefined criteria for successful drop instillation. This approach allowed for objective assessment of instillation competence and minimized observer bias. Demographic data, examination findings, and the ability to apply eye drops were compared with the control group. Only monodose artificial tear preparations were used in this study; therefore, the results may differ from those obtained with multidose bottles.

Statistical analyses were conducted using IBM Statistical Package for the Social Sciences Statistics software (IBM Corp., Armonk, NY, USA). The Chi-square test was employed to assess associations between categorical variables. $P<0.05$ was considered statistically significant, and results were interpreted accordingly.

Results

A total of 43 healthcare professionals, 28 female (65.1%) and 15 male (34.9%), working in the ophthalmology clinic with an average age of 34.16±7.79 (24–51) years, were included in the study group. A total of 43 volunteers, 21 female (48.8%) and 22 male (51.2%), with an average age of 28.81±8.60, were included in the control group. The dominant hand was right in all study group participants and in 39 participants (90.7%) of the control group. Demographic characteristics of the study and control groups are presented in Table 1.

Successful instillation of both eyes was observed in 26 (60.4%) participants in the study group and 12 participants (27.9%) in the control group (p=0.002). For the right eye, successful instillation was observed in 30 (69.7%) participants in the study group versus 19 (44.1%) in the control group (p=0.017). Successful instillation in the left eye was observed in 29 (67.4%) participants in the study

Table 1. The demographic data and examination findings of the study group and control groups

	Study group	Control group
Age, mean±SD (min-max), years	34.16±7.79 (24–51)	28.81±8.60 (19–40)
Gender, *n* (%)		
Female	28 (65.1)	21 (48.8)
Male	15 (34.9)	22 (51.2)
Best-corrected visual acuity, mean±SD (min-max), (Snellen chart)	1.0 (100)	1.0 (100)
Dominant Hand *n* (%)		
Right	43 (100)	39 (90.7)
Left	-	4 (9.3)

SD: Standard deviation; Min: Minimum; Max: Maximum

group and in 15 (34.8%) participants in the control group (p=0.003). Success rates are displayed in Table 2, and the success rate of each criterion is displayed in Table 3.

In the right-handed participants of the study group, successful instillation drop in the right eye was achieved in 30 (69.7%) cases, and in the left eye in 29 (67.4%) cases (p=0.81). In the right-handed participants of the control group, successful instillation was achieved in the right eye of 18 (46.1%) participants and in the left eye of 14 (35.9%) participants (p=0.35). In the total sample of 82 right-handed participants, 48 (58.5%) exhibited successful instillation in

Table 4. Hand dominance and successful instillation

	Successful instillation in the right eye, *n* (%)	Successful instillation in the left eye, *n* (%)	*p*
Study Group (*n*=43)			
Right-hand dominant (*n*=43)	30 (69.7)	29 (67.4)	0.81
Left-hand dominant (*n*=0)	-	-	-
Control Group (*n*=43)			
Right-hand dominant (*n*=39)	18 (46.1)	14 (35.9)	0.35
Left-hand dominant (*n*=4)	1 (25)	1 (25)	
Total (*n*=86)			
Right-hand dominant (*n*=82)	48 (58.5)	43 (52.4)	0.43
Left-hand dominant (*n*=4)	1 (25)	1 (25)	

The sample size for left-handed participants (*n*=4) is too small for reliable subgroup analysis

Table 2. Complete success rates in the study and control groups

	Right eye			Left eye			Both eyes		
	Study group, *n* (%)	Control group, *n* (%)	*p*	Study group, *n* (%)	Control group, *n* (%)	*p*	Study group, *n* (%)	Control group, *n* (%)	*p*
Successful instillation	30 (69.7)	19 (44.1)	0.017	29 (67.4)	15 (34.8)	0.003	26 (60.4)	12 (27.9)	0.002

Table 3. Success rates for each criterion in the study and control groups

Success criterion	Right eye			Left eye			Both eyes		
	Study group, *n* (%)	Control group, *n* (%)	*p*	Study group, *n* (%)	Control group, *n* (%)	*p*	Study group, *n* (%)	Control group, *n* (%)	*p*
At least one drop on the ocular surface or lower fornix	32 (74.4)	28 (65.1)	0.3	31 (72.1)	27 (62.7)	0.3	28 (65.1)	22 (51.1)	0.2
No contact of the dropper tip with any surface	37 (86)	26 (60.4)	0.007	36 (83.7)	24 (55.8)	0.005	36 (83.7)	20 (46.5)	<0.001
One drop at a time	37 (86)	32 (74.4)	0.2	35 (81.3)	31 (72.1)	0.3	35 (81.3)	28 (65.1)	0.08

the right eye, whereas 43 (52.4%) demonstrated successful instillation in the left eye (p=0.43). In addition, among the four left-handed participants, 1 (25%) exhibited successful instillation in the right eye, and another 1 (25%) showed successful instillation in the left eye (Table 4). The sample size for left-handed participants (n=4) is too small for reliable subgroup analysis.

Discussion

When compared to the control group, ophthalmic healthcare professionals were found to be significantly better in successful eyedrop instillation: instilling at least one drop on the ocular surface or fornix, avoiding contact of the dropper tip with the ocular surface or surrounding tissues, and not dispensing multiple drops. Within the criteria, there was a significant difference in the contact of the dropper tip with the ocular surface or surrounding tissues between the two groups (16% in the study group vs. 53% in the control group, p<0.001). In the present study, awareness of proper instillation technique appears to play a key role in avoiding the contact of the dropper tip with the ocular surface or surrounding tissues, which is one of the criteria for successful drop instillation. Even with sufficient education and clinical experience, self-administration of eye drops remains a challenging task. Although education clearly improves drop instillation performance, a considerable proportion of failures still occurred despite clinical training and experience. In this study, 40% of ophthalmic healthcare professionals were unable to perform all steps correctly, indicating that even among trained individuals, perfect self-instillation cannot be guaranteed. This suggests that in elderly patients or those with systemic or musculoskeletal limitations, educational interventions alone may not be sufficient, and assistance by another person could be necessary.

A real-world study demonstrated that the success rate of eye drop instillation remains low even among patients who had been using topical drops for a minimum duration of 1 month. The most frequently observed error was inadvertent contact of the bottle tip with the ocular surface or eyelids, occurring in 40.7% of cases.[6] Contact of the bottle tip with periocular tissues can lead to contamination, while direct ocular contact may result in corneal abrasions and recurrent epithelial defects, potentially progressing to corneal ulceration.

Contamination of ophthalmic solutions has been associated with various adverse outcomes, including ocular surface irritation, conjunctival inflammation, interruption of necessary treatment, and ocular infections.[8] The most frequently isolated microorganisms from glaucoma eye drop bottles are components of the normal skin and conjunctival flora, predominantly Gram-positive bacteria such as *Staphylococcus aureus* and *Staphylococcus epidermidis*.[13] In some cases, microbial contamination may go undetected yet still lead to serious complications, including bacterial keratitis – especially in patients with underlying ocular surface disorders.[14]

Instilling more than one drop at a time could lead to accelerated depletion of the medication, potentially compromising treatment continuity in patients reliant on social health insurance coverage.[15] It is crucial for patients to have a sufficient amount of eye drops for a certain period of time, especially if their health insurance does not cover the costs when they run out of medicine sooner than expected. Previous studies have primarily focused on glaucoma patients, with multiple instillation rates reported across a wide range, from 3% to 40%.[2,4,16,17] Another potential consequence of administering multiple drops is an increased likelihood of systemic side effects, including bronchoalveolar and cardiovascular complications.[19] Furthermore, the incidence of local dermatological reactions – such as periocular dermatitis and skin hyperpigmentation – may also be heightened.[18-20]

A study was conducted to evaluate the relationship between hand dominance and the success of eye drop instillation.[21] The study found that hand dominance did not appear to have a significant impact on the outcome.[21] In the present study, most participants were right-handed. Among these individuals, the rate of successful eye drop instillation did not differ significantly between the right and left eyes (p=0.43). This suggests that right-handed participants were equally proficient in instilling drops into either eye. However, given the very small number of left-handed participants (n=4), any interpretation regarding the role of hand dominance should be made with caution. The limited sample size prevents reliable conclusions, particularly concerning the left eye, and the present results should not be viewed as evidence that hand dominance has no effect.

Following studies on ensuring successful drop instillation, devices that assist in instillation have been developed.[6] Eye drop dispensing aids allow a single drop to reach the ocular surface without contacting the eyelids, eyelashes, and surrounding tissues.[22,23] The need to clean the device after use and patient adaptation to the device present challenges in terms of use.

Study Limitations

This study evaluated only the use of monodose artificial tear applicators. The mechanical effort, bottle rigidity,

and squeezing strength required for multidose containers differ significantly from those for monodose units. Future studies comparing both types of applicators could provide more comprehensive insight into real-world drop instillation performance. A small number of left-handed participants (n=4) limits the statistical reliability of conclusions regarding the effect of hand dominance on eye drop instillation, particularly for the left eye. Therefore, the present findings should not be interpreted as evidence that hand dominance has no influence. The study did not assess ocular dominance, which could affect alignment and targeting accuracy during self-instillation. Future studies incorporating ocular dominance assessment and a larger, balanced sample of left- and right-handed participants would strengthen the findings.

Conclusion

Despite the development of new supportive methods, patient education remains one of the most critical components in achieving successful eye drop instillation. It is essential for healthcare professionals to spend time with their patients regarding successful instillation practice. Explaining the steps, precautions, and key considerations of eye drop instillation to patients can increase the effectiveness of the treatment and reduce potential side effects, thereby enhancing the efficacy of eye drop therapy. As this study suggests, even the most experienced and educated patients may encounter difficulties in adapting to their treatment and its administration. Therefore, patient-related factors in administration technique should always be considered potential contributors to treatment failure.

Ethics Committee Approval: This study was approved by The Ethics Committee of Ege University (March 21, 2024/24–3.1T/27).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Clinical features and frequency of microtropia identified in preschool screenings

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Abstract

Purpose: The purpose of this study was to determine the prevalence and clinical characteristics of microtropia (M) within a Turkish preschool screening cohort and to identify objective, data-driven diagnostic thresholds for the condition.

Methods: This retrospective study reviewed the comprehensive refraction and orthoptic examination records of 2106 children (median age 61 months) who underwent preschool eye screenings at a single tertiary hospital between January 2023 and September 2025. Key variables included cycloplegic spherical equivalent (SE), visual acuity (VA), amount of deviation, near stereopsis (Frisby test), and accommodative response (dynamic retinoscopy). Statistical analysis, including receiver operating characteristic (ROC) curves, was used to compare strabismic and non-strabismic groups and define diagnostic cutoffs for M.

Results: Strabismus was detected in 307 children (14.6% of the cohort). The prevalence of M was 1.6% (34 children) within the total sample, accounting for 11.0% of all strabismus cases. The strabismus group had significantly higher SE values ($p<0.001$), a greater prevalence of astigmatism (32.5% vs. 24.9%, $p=0.048$), and a significantly higher rate of weak accommodation (22.1% vs. 1.7%, $p<0.001$) compared to the non-strabismic group. The M group exhibited significantly lower VA and poorer stereopsis than the esophoria group ($p=0.046$ and $p=0.012$, respectively). ROC analysis identified an optimal deviation cutoff for diagnosing M at ≤8 prism diopters (PD) (100% sensitivity, 70.1% specificity) and a stereopsis cutoff of >75 seconds of arc (88.2% sensitivity).

Conclusion: In this tertiary clinic cohort, M was found in 1.6% of preschool children, suggesting it is a significant and potentially underestimated health burden. It is strongly associated with refractive errors (hyperopia and astigmatism), impaired accommodation, and reduced stereopsis. The ROC-defined threshold of ≤8 PD offers a robust, objective criterion for its diagnosis.

Keywords: Microtropia, Preschool, Screening, Stereopsis, Strabismus

Microtropia (M) is characterized by small-angle strabismus of <10 prism diopters (PD), often associated with monocular suppression and a significant impact on visual function, including anomalous retinal correspondence (ARC) and reduced stereopsis.[1] Children with M are less likely to attain equal visual acuity (VA) with amblyopia treatment compared to children with bifoveal fixation.[1,2] Although less frequently discussed than more prominent forms of strabismus, the prevalence and incidence of M are important for understanding its clinical implications and for developing effective screening protocols. Detecting strabismus early is crucial

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for preventing strabismic amblyopia and improving the likelihood of restoring binocularity, highlighting the need for early diagnosis and timely treatment.[3]

Research indicates that M is commonly linked to amblyopia, which can manifest particularly in cases of high hyperopia.[4] Previously, Tubing *et al*.[5] emphasized that variations exist across ethnic groups, indicating a need for targeted screening in different populations. Specifically, Kvarnström *et al*.[6] documented a prevalence of strabismus at 3.1% in Swedish children, emphasizing the necessity for consistent visual screenings to detect conditions like M early on. Even in large-scale studies such as the Nanjing Eye Study, the prevalence of M detected over 5 years has been reported to be 0.15%.[2]

Moreover, genetic predispositions have been suggested concerning M, with studies showing familial patterns indicating an underlying hereditary component.[7,8] Understanding genetics aids in anticipating the incidence and risk factors associated with M, allowing for better management strategies for those at higher risk.

In conclusion, M, despite being less prominent, is an important clinical condition that warrants attention due to its association with amblyopia and its prevalence in the pediatric population. Improved screening methods and understanding of genetic predispositions may facilitate better management and outcomes for affected individuals. Since there is no M data routinely monitored and reported in preschool screenings in our country, we aimed to report the clinical and demographic characteristics of these cases using data from the only tertiary hospital in (anonymized) province.

Materials and Methods

Between January 2023 and September 2025, we retrospectively reviewed the refraction and orthoptic examinations of 2481 children who underwent eye screenings as part of preschool assessments at our clinic.

The most common methods for diagnosing M are the 4-diopter prism test (4ΔPT) and ocular fixation assessment. M was diagnosed using the 4-diopter prism test and assessment of ocular fixation patterns. A diagnosis was established in children demonstrating small-angle manifest strabismus (≤10 PD), measurable VA, and an interocular difference in best-corrected VA. Children diagnosed with M underwent detailed anterior and posterior segment examinations, with their cycloplegic refraction recorded.

VA and photopic contrast sensitivity were evaluated using the FrACT10-Freiburg Vision Test via tablet (v.1.0.5-2023-11-30).[9,10] Refractive error for each eye was recorded as spherical equivalent (SE). The presence of age-related astigmatism requiring correction was documented as present or absent according to the AAO Guidelines for Refractive Correction in Infants and Young Children table.[11] Deviations were assessed separately for distance and near at nine diagnostic gaze positions using a Lang fixation cube. Manifest and latent deviations were measured both near and far with a prism bar (Luneau Technology Operations, Pont de l'Arche, France). The average of the near and distance deviation measures was included in the statistical analysis. Near stereopsis was tested with the Frisby Near stereotest using 6 mm, 3 mm, and 1.5 mm plates.

Accommodation was measured using dynamic retinoscopy with a near LEA-printed chart. An accommodative response was classified as normal when a myopic reflex was obtained in at least one quadrant during near fixation, indicating appropriate accommodative effort. Conversely, accommodation was classified as weak when a neutral or hyperopic reflex was consistently observed across all quadrants, indicating insufficient accommodative response for the near target.

In addition to the examinations mentioned above, the presence of accommodation insufficiency in either eye and a family history of strabismus or amblyopia in first-degree relatives was documented.

Exclusion criteria included a history of any intraocular or extraocular surgery, including prior strabismus surgery, congenital chromosomal abnormalities, and cases born before 34 weeks of gestation and/or weighing <1700 g, in accordance with the Turkey Premature Retinopathy 2021 Guidelines. Cases with developmental problems potentially linked to cerebral or cortical visual impairment were identified through the e-nabiz online database and health board report data, then excluded from the study. Since the primary objective of our study was to determine the prevalence of M, vertical deviations, accompanying inferior oblique overactions, and dissociated vertical deviations were also excluded.

All procedures involving human participants in this study adhered to the ethical standards of Usak University (Usak, TR) Non-Interventional Studies Ethical Committee (approval number: 822-822-11/September 11, 2025), the 1964 Helsinki Declaration and its later amendments, or equivalent ethical standards. Since all participants were pediatric, informed consent was obtained from parents or legal guardians.

Statistical Analysis

The Statistical Package for the Social Sciences 15.0 for Windows (IBM, Armonk, United States) software was used for statistical analysis. Descriptive statistics were presented as counts and percentages for categorical variables, and as mean, standard deviation, minimum, maximum, and median for numerical variables. Comparisons of numerical variables were conducted using the Mann–Whitney U Test for independent groups and the Kruskal-Wallis test for more than two independent groups when the normal distribution condition was not satisfied. Proportions between groups were compared with the Chi-square test. Relationships between numerical variables were assessed using Spearman Correlation Analysis since the parametric test assumptions were not met. Cutoff values were evaluated with receiver operating characteristic (ROC) curve analysis. The significance level was set at $P<0.05$.

Results

A total of 2106 cases were included in the study. Strabismus was present in 307 cases (14.6%), whereas it was not detected in 1799 cases (85.4%). There was no significant difference in age between the strabismus and non-strabismus groups (62 [43–78] and 61 [45–75] months, respectively; $p=0.454$). The gender distributions were similar; 48.1% of cases in the strabismus group were female, and 51.9% were male; in the control group, these rates were 49.3% and 50.7%, respectively ($p=0.779$). All variables of the cases are summarized in Table 1.

When examining the distribution of strabismus types, esophoria (EF) (39.6%) and exophoria (XF) (21.4%) were the most common, followed by esotropia (ET) (16.9%), M (11.0%), and exotropia (XT) (10.7%). The median deviation angle was 12 PD (range: 2–35 PD).

In terms of refraction values, SE-OD and SE-OS values were significantly higher in the strabismus group (median: +1.00 D [range: −4.50–+6.00] and +1.00 D [range: −4.50–+8.00], respectively) compared to the control group (+0.75 D [range: −2.00–+4.00] and +0.50 D [range: −2.75–+3.75], respectively) ($p<0.001$ and $p=0.008$). The prevalence of astigmatism was 32.5% in strabismus cases, which was significantly higher than in the control group (24.9%; $p=0.048$).

The accommodation response was impaired in the strabismus group; a weak accommodation response was detected in 22.1% of strabismus cases, whereas this rate was only 1.7% in the control group ($p<0.001$). The difference between the groups in terms of family history was borderline significant (11.0% in strabismus, 6.7% in control; $p=0.055$).

Table 1. The relationship between the presence of strabismus and variables

Variable	Strabismic *n*=307 (14.6%)	Non-strabismic *n*=1799 (85.4%)	*p*
Age (month)	62 (43–78)	61 (45–75)	0.454
Sex *n* (%)			
Female	148 (48.2)	886 (49.3)	0.779
Male	159 (51.8)	912 (50.7)	
SE-OD (D)	+1.00 (−4.50 to +6.00)	+0.75 (−2.00 to +4.00)	**<0.001**
SE-OS (D)	+1.00 (−4.50 to +8.00)	+0.50 (−2.75 to +3.75)	**0.008**
Astigmatism *n* (%)			
Present	100 (32.6)	448 (24.9)	**0.048**
Absent	207 (67.4)	1351 (75.1)	
Accommodation *n* (%)			
Normal	239 (77.9)	1768 (98.3)	**<0.001**
Weak	68 (22.1)	31 (1.7)	
Family history *n* (%)			
Positive	34 (11.1)	120 (6.7)	0.055
Negative	273 (88.9)	1679 (93.3)	
logMAR-OD	0.097 (0.00–0.523)	0.046 (0.00–0.301)	**<0.001**
logMAR-OS	0.097 (0.00–0.699)	0.046 (0.00–0.398)	**<0.001**
Binocular CS (logCS)	1.85 (1.55–2)	1.88 (1.62–2)	0.544

SE: Spherical equivalent; CS: Contrast sensitivity. Statistically significant results ($p<0.05$) are highlighted in bold

VA was significantly lower in strabismus cases; logMAR-OD median was 0.097 (range: 0.000–0.523), and logMAR-OS was 0.097 (range: 0.000–0.699), whereas in the control group, they were 0.046 (range: 0.000–0.301) and 0.046 (range: 0.000–0.398), respectively ($p<0.001$ for both). No significant difference in binocular contrast sensitivity logCS values was found between groups ($p=0.544$).

Based on our ROC curve analysis, an optimal cutoff of ≤8 PD was identified for defining M, demonstrating 100% sensitivity and 70.1% specificity (Youden index J=0.7007). This data-driven threshold was applied in the following subgroup analyses. The clinical characteristics of the 34 M cases are presented in Table 2.

Among strabismus patients, there was no significant correlation between age and the magnitude of deviation ($r=-0.032$, $p=0.694$). A weak positive and significant

Table 2. Clinical characteristics of the Microtropia (M) group

Variable	Microtropia group (*n*=34)
Age (months), median (range)	60 (44–76)
Sex, *n* (%) female/male	15 (44.1)/19 (55.9)
Deviation amount (PD), median (range)	6 (2–8)
SE-OD (D), median (range)	+1.25 (–1.50 to +4.50)
SE-OS (D), median (range)	+1.25 (–1.25 to +5.00)
Visual acuity logMAR-OD, median (range)	0.155 (0.046–0.398)
Visual acuity logMAR-OS, median (range)	0.125 (0.046–0.523)
Near stereopsis (sec/arc), median (range)	170 (55–340)
Astigmatism present, *n* (%)	12 (35.3)
Weak accommodation, *n* (%)	9 (26.5)
Positive family history, *n* (%)	0 (0)

SE: Spherical equivalent; PD: Prism diopters

correlation was identified between SE-OD refraction values and the extent of deviation (r=0.192, *P*=0.017). In addition, a positive but statistically insignificant relationship was noted between SE-OS and the amount of deviation (r=0.118, *p*=0.144).

For VA, no significant correlation was found between logMAR-OD (r=0.147, *p*=0.068) or logMAR-OS (r=0.125, *p*=0.122) values and the amount of deviation. The Spearman correlation analysis revealed a positive and significant relationship between the amount of deviation and stereo vision level (sec/arc) (r=0.359, *p*<0.001). This suggests that as the amount of deviation increases, near-stereo vision acuity decreases.

When examining the amounts of deviation, the median deviation angle was highest in the ET group at 20 PD and lowest in the M group at 6 PD. In terms of VA, logMAR values were significantly higher in the M group compared to the EF group (*P*=0.046), indicating that VA in M cases is significantly lower than in phoria cases. A similar trend was observed in the logMAR values of the left eye, but the difference did not reach statistical significance (*p*=0.151). When refraction values were analyzed, the SE of both eyes in the XF group was found to be significantly more myopic than all other types of deviation (*p*<0.001 for all).

Stereo vision values showed significant differences according to strabismus types (*p*=0.013). Subgroup analyses revealed that the difference was particularly due to the EF group having better stereovision. The stereo vision level in EF cases was significantly better than in the M and ET groups (*p*=0.012 and *p*=0.018, respectively). In contrast, stereo vision values in the XF group were weaker than in the M and ET groups (*p*=0.010 and *p*=0.016).

In the cross-tabulation analysis based on deviation types, a statistically significant difference was observed in family history (*p*=0.047). The presence of family history was notably higher in the EF (14.8%) and ET (19.2%) groups, whereas it was not detected in M and XF cases. In addition, no significant differences were identified between deviation types regarding gender (*p*=0.186), astigmatism (*p*=0.834), or accommodation response (*p*=0.119).

M represents a small-angle deviation that may be easily overlooked during routine clinical examination. To identify objective parameters that could aid in its detection, we analyzed VA and stereopsis thresholds using ROC curve analysis (Table 3 and Figure 1).

ROC curve analysis identified the optimal cutoff for deviation amount as ≤8 PD for M. At this threshold, sensitivity was 100%, and specificity was 70.1%. The Youden index (J) of 0.7007 indicates a strong discriminatory power of the variable.

The area under the curve (AUC) for the logMAR-OD variable was 0.684 (95% confidence interval [CI]: 0.604–0.756; *p*=0.0005), demonstrating moderate diagnostic accuracy for detecting visual impairment. The optimal cutoff was calculated as ≤0.0969 logMAR (equivalent to Snellen 0.8),

Table 3. Diagnostic performance and threshold values for predicting microtropia based on ROC curve analysis

Parameter	Degree of deviation	Visual acuity (either eye)	Near stereopsis
z statistics	12.724	3.458	3.170
p (Area=0.5)	<0.0001	0.0005	0.0015
Youden index J	0.7007	0.3641	0.3860
Threshold value	≤8 PD	≤0.0969 logMAR	>75 s/arc
Sensitivity (%)	100	88.2	88.2
Specificity (%)	70.1	48.2	50.4

ROC: Receiver operating characteristic

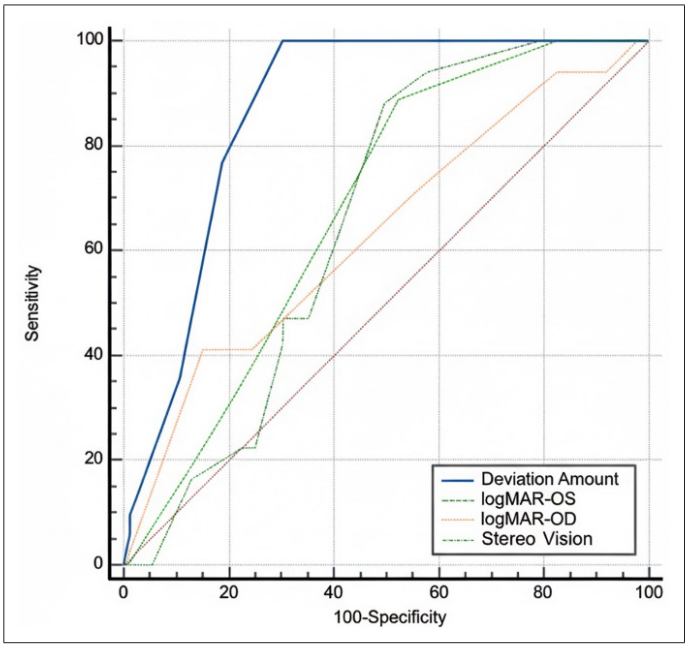

Fig. 1. Comparative receiver operating characteristic curves for deviation amount, visual acuity, and stereo Vision in discriminating microtropia.

with a sensitivity of 88.2% and specificity of 48.2%. For near stereo vision (sec/arc), the AUC was 0.660 (95% CI: 0.579–0.734; p=0.0015), indicating moderate diagnostic value. The optimal cutoff was >75 sec/arc, with sensitivity of 88.2% and specificity of 50.4%, and a Youden index of 0.386. These parameters may serve as useful screening indicators to identify children requiring further evaluation for M.

Discussion

Childhood studies have demonstrated that near-point phorias are particularly prominent in school-age children. Jang *et al*. found that the prevalence of EF increased with age, particularly among children aged 11–13 years, which they suggested could be influenced by the increased demands of near work as children advance in their schooling.[9] Similarly, Wajuihian reported a prevalence of near XF around 51.8%, which aligns with findings from various studies suggesting that asymptomatic phorias are common among students due to the demands of academic environments.[10] Age-related factors also significantly influence phoria measurements. Leat *et al*.[12] noted a divergence in phoria measurements with increasing age, wherein younger populations show variability while older populations exhibit more stability in their phoria prevalence.

This suggests that as individuals age, external psychosocial or environmental influences on binocular vision may diminish. The same situation may apply to the preschool age, where academic expectations and stressors are significantly lower. In a similar cohort study of infants conducted by Daldal *et al*.[13], strabismus was found in 1.4% of all infants and in 13.6% of all ophthalmological pathologies. However, in the current cohort, where we examined detailed examination data from preschool children, the prevalence of strabismus was calculated as 14.6% and the prevalence of M as 1.6%. However, Daldal *et al*.[13] only noted manifest deviations in their studies and examined all infants within the scope of the screening. In our study, since the cases were examined within the scope of preschool screening, cases with mental, auditory, or other severe systemic comorbidities that could not be included in formal education programs or whose inclusion would be delayed were excluded from the study.

Moreover, evidence suggests that external factors, such as prolonged screen time, can influence phoria symptoms. Gadget usage has been linked with increased visual strain, potentially leading to temporary changes in near point convergence and induced phorias, underscoring the contemporary relevance of visual ergonomics.[14,15]

The relationship between phorias and M is an area of interest in understanding binocular vision disorders. Both conditions are manifestations of strabismus, with phorias representing latent misalignments of the eyes that can often be compensated for, while M refers to a small-angle strabismus that may lead to significant visual disturbances, particularly amblyopia. Familial patterns of M have also been documented, with studies indicating an increased likelihood of related strabismic conditions among siblings or family members.[16,17]

The conventional 1–5% prevalence figure may largely represent the tip of the iceberg, capturing only the most cosmetically obvious or functionally debilitating deviations. The 14.6% figure found here, while not generalizable as a population-wide statistic, strongly suggests that a much larger proportion of children experience some form of binocular instability.[5,6,16]

A pivotal contribution of this research is the application of ROC curve analysis to establish objective, data-driven diagnostic thresholds for M. By analyzing the interplay between the degree of deviation, VA, and stereopsis, the study moves beyond traditional, often variable, definitions to propose a quantitative diagnostic framework. One of the most significant challenges in the study of M is the lack of a universally accepted definition for its angle of deviation. The literature presents a range of thresholds, with various authorities defining the condition as a deviation of <5 PD,

<6–8 PD, or ≤10 PD.[18] This inconsistency complicates the comparison of research findings, hinders the development of standardized clinical protocols, and creates ambiguity in diagnosis.

Our analysis identified an optimal cutoff for ocular deviation at ≤8 PD. This threshold demonstrated excellent discriminatory power, yielding 100% sensitivity and 70.1% specificity, with a Youden index (J) of 0.7007 indicating a strong ability to distinguish microtropic from other strabismic conditions. Similarly, for near stereopsis, a threshold of >75 s of arc, indicating poorer depth perception, also yielded a sensitivity of 88.2%. Our data also clearly show that the strabismic group possessed significantly higher SE values and a higher prevalence of astigmatism (32.5%) compared to the non-strabismic control group (24.9%). This finding is consistent with a large body of literature demonstrating a strong association between M and anisometropia.[19]

Similarly, multiple studies have identified astigmatism as a significant risk factor for strabismus, especially XT. Zhu *et al*.[20], for example, reported an odds ratio of 3.56 for concomitant XT in children with 0.50–1.00 D of astigmatism.

Moreover, the strong connection between strabismus and poor accommodation found in this study prompts a reconsideration of their relationship. Instead of seeing them as separate or just co-occurring conditions, it is reasonable to suggest a causal link. Someone with a weak or inefficient accommodative system must exert more effort to keep a clear focus on a near object. This extra effort can disturb the fragile balance between accommodative convergence and fusional vergence, causing binocular stress and fatigue. Over time, especially during the visually demanding tasks of childhood, this ongoing stress could cause the fusional vergence system to tire out and eventually fail, allowing a latent phoria to decompensate into a small-angle, manifest tropia.[21,22]

This perspective redefines accommodative insufficiency not just as a concurrent symptom but as a potential precursor and a crucial destabilizing factor in the binocular system. It indicates that a primary accommodative deficit might be an early, measurable risk factor for later development of strabismus. This marks a shift from treating an already established eye turn to proactively addressing underlying binocular instability.

Another defining characteristic of M is the disruption of high-grade stereopsis, which relies on precise bifoveal fusion. The study corroborates this, showing a strong, statistically significant positive correlation between the magnitude of the deviation and the degradation of near-stereo vision (Spearman's r=0.359, $p<0.001$). The M group exhibited significantly poorer stereoacuity compared to the EF group, underscoring the functional cost of even a small manifest misalignment. This is consistent with the established pathophysiology of the condition, in which the brain develops sensory adaptations, such as a central suppression scotoma and ARC, to avoid diplopia, thereby sacrificing fine stereoscopic vision.[18,20]

For photopic contrast vision, tested with the Freiburg VA/contrast test, values around 1.6 are considered normal contrast sensitivity. A contrast sensitivity score below 1.5 suggests visual impairment, and a score below 1.0 may indicate visual disability.[23] The absence of a significant CS difference between the two groups in our study and the fact that it is above the healthy threshold should be considered confirmation that neither group has an organic pathology caused by neuronal pathways or opacity in the ocular media.

Finally, we want to note that, as is well known, there is substantial evidence demonstrating the role of genetics in the cause of strabismus and that eye disorders run in families.[17] Regarding M, familial patterns have been documented, with one study indicating that siblings of children with accommodative ET experienced a significantly higher occurrence of M, implying a shared genetic predisposition.[17,22,7] However, contrary to this established understanding, the analysis in the current study found no cases with a positive family history among the M cases.

Several reasons might explain this difference. First, because the study was retrospective, data on family history were likely collected through parental reports, which can be affected by recall bias. Subtle conditions such as M or high phoria in a parent or sibling might have gone undiagnosed or been forgotten, leading to under-reporting. Second, the causes of strabismus are multifaceted, involving a complex interaction of genetic factors and environmental influences such as prematurity, low birth weight, and maternal smoking. It is possible that, in this specific clinical group, non-genetic factors were more influential. Third, the concepts of incomplete penetrance and variable expressivity are key principles in the genetics of strabismus; a genetic risk might not always result in a diagnosed condition or may present differently among family members.

This study provided valuable clinical data from a preschool screening cohort in Turkey. Unlike many large-scale screening studies, this investigation included detailed cycloplegic refraction and orthoptic assessments for all

participants, enabling the detection of subtle conditions like M and the analysis of multiple clinical variables, including the novel assessment of accommodative function. We found a high prevalence of strabismus (14.6%) and M (1.6%) within this tertiary center population. However, it is important to clarify that the 1.6% prevalence of M reported is specific to the 2106-child cohort that attended preschool screenings at this single tertiary hospital; this figure does not reflect the overall incidence or prevalence for all children in the region, as it is subject to selection bias and does not include healthy children who were not brought in for screening. The study's retrospective design prevents establishing definitive causal relationships and introduces the risk of information bias, especially in variables that depend on recall, such as family history. The cross-sectional nature of the data provides a valuable snapshot but cannot clarify the natural history of these conditions.

These limitations clearly define several priorities for future research. To establish more accurate prevalence rates and improve generalizability, future studies should use similarly thorough examination protocols within multi-center, truly population-based samples. Finally, to develop a more advanced understanding of the heritability of M and resolve the conflicting findings regarding family history, future research should combine systematic clinical examinations of first-degree relatives with modern genomic analysis.

Conclusion

This study offers strong evidence from a large clinical cohort that strabismus, especially in its more subtle forms such as M and high phorias, is a significant and potentially underestimated health burden in the preschool population. The ROC-derived threshold of ≤8 PD provides an objective, data-driven criterion for M diagnosis, whereas stereopsis (>75 sec/arc) and VA (≤0.1 logMAR) thresholds may serve as valuable screening parameters to identify children at risk for this often-overlooked condition.

Ethics Committee Approval: This study was approved by The Ethical Committee of Usak University (approval number: 822-822-11/September 11, 2025).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE

Investigation of macula and optic disc microvascular circulatory changes in patients undergoing pediatric cataract surgery

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Abstract

Purpose: This study reports changes in macular and optic disc microvascular parameters using optical coherence tomography angiography (OCTA) in pseudophakic patients undergoing pediatric cataract surgery.

Methods: This observational, controlled, cross-sectional study included patients who had previously undergone pediatric cataract surgery and age-matched healthy controls. Seventeen subjects aged 5–18 years were recruited to the treatment group (Group 1). Sixteen volunteers of similar age were recruited to the control group (Group 2). A total of 33 subjects underwent detailed ophthalmologic examinations and OCTA scans. The two groups were compared in terms of their foveal, parafoveal, and optic disc blood flow and vascular density (VD) parameters on OCTA images.

Results: The mean ages of the participants in Groups 1 and 2 were similar (11.88±3.60 years vs. 11.63±2.24 years, respectively). Foveal superficial and deep blood flow were lower in Group 1 than in Group 2 (1.33±0.12 vs. 1.47±0.13 and 1.23±0.34 vs. 1.56±0.23, respectively, $p<0.05$). A wider deep layer foveal avascular zone was observed in Group 1 than in Group 2 (0.41±0.19 vs. 0.31±0.12, respectively, $p=0.02$). Parafoveal superficial VD and optic disc head VD were lower in Group 1 than in Group 2 (51.46±4.00 vs. 55.35±4.69 and 56.46±3.01 vs. 59.37±3.06, respectively, $p<0.05$).

Conclusion: Macular and optic disc vascular parameters were lower in patients who had undergone pediatric cataract surgery than in healthy controls. This result may be insightful for investigating processes that may affect retinal microvascular circulation.

Keywords: Macula, Optic disc, Optical coherence tomography angiography, Pediatric cataract, Vascular density

Pediatric cataracts are the most common cause of treatable childhood blindness. Cataracts account for 5–20% of pediatric blindness worldwide, with a higher incidence in developing countries.[1] In 27% of congenital cataract cases, ocular abnormalities are associated with 22% of systemic abnormalities. The etiology of childhood cataracts is quite broad. It can be hereditary, usually autosomal dominant; metabolic, such as galactosemia; infectious, such as toxoplasmosis, syphilis, or cytomegalovirus-related; traumatic; or uveitic. Exclusion of these causes results in classifying a cataract as idiopathic. Associated ocular anomalies may include microphthalmia, buphthalmos, nystagmus, or persistent fetal vasculature.[2]

Amblyopia is defined as a dysfunction in the processing

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of visual information.[3] In amblyopia, a unilateral or bilateral decrease in visual acuity is detected during an eye examination. Causes of amblyopia include strabismus, anisometropia, and sensory deprivation, such as cataracts and ptosis. In these cases, there is abnormal functional development of the lateral geniculate nucleus and striate cortex.[4] Cataract formation in the pediatric age group leads to deprivation amblyopia by reducing retinal image quality and light transmission. The risk of amblyopia is higher in patients with unilateral cataracts. The reversibility of amblyopia depends on how early surgical intervention occurs (e.g., before visual maturation is complete) and how well visual rehabilitation is managed.

Optical coherence tomographic angiography (OCTA) is a high-resolution, rapid, and non-invasive method of producing images of blood flow in the retina and choriocapillaris. It detects motion contrast based on vascular blood flow and visualizes the vascular structure. While fluorescent angiography, which uses fluorescent material, only visualizes superficial vascular plexuses, OCTA allows for visualization of both superficial and deep capillary plexuses (DF) without the need for fluorescent material.[5] OCTA provides quantitative data, enabling a more objective evaluation. Previous studies have found that macular and optic disc head vascular blood flow is lower in amblyopic patients compared to healthy control groups.[6,7] We found only one study on macular blood flow and foveal avascular zone (FAZ) in pseudophakic children.[8]

This study compared the retinal and optic disc head blood flow in patients who had previously undergone pediatric cataract surgery with that of a healthy control group.

Materials and Methods

Study Population

This cross-sectional study was conducted after receiving Institutional Ethics Committee approval (ethics approval letter number: April 07, 2025–109). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Children aged 5–18 years who had undergone cataract surgery were included in this study. Children who underwent pediatric cataract surgery between January 2018 and December 2024 were retrospectively screened. A matched healthy control group (with a similar age and gender distribution) was also included. The exclusion criteria were the presence of any additional ocular pathology that would prevent reliable data interpretation (e.g., corneal opacity, posterior capsular opacification, or nystagmus), patients who developed glaucoma during postoperative follow-up, and systemic diseases that could affect vascular circulation (e.g., diabetes mellitus or cardiovascular disease). Participants with a signal strength index >60 in OCTA images were included in the evaluation.

Seventeen eyes of seventeen pediatric cataract patients met the study criteria (Group 1). Seven of the seventeen patients underwent bilateral cataract surgery. The right eyes of these patients were included in the study. Sixteen volunteers with a similar age and gender distribution were recruited to the control group (Group 2). Demographic data of the treatment group, age at cataract surgery, pre-operative and post-operative best-corrected visual acuity (BCVA, logMAR), post-operative refractive error, intraocular pressure, and post-operative follow-up duration were recorded. All surgeries were performed by a single surgeon (A.M.). Posterior capsulotomy was routinely performed during surgery for participants aged 5–8 years. Topical steroids, antibiotics, and mydriatic agents were prescribed for a 1-month post-operative period. OCTA imaging was performed after a follow-up period of at least 1 year following surgery. The healthy control group underwent detailed ophthalmologic examination, including biomicroscopic anterior and posterior segment examination, followed by OCTA imaging.

OCTA Imaging

All patients underwent pupil dilation, which was induced using a combination of 0.5% tropicamide and 2.5% phenylephrine HCL, and OCTA scans were performed. OCTA scans and measurements were performed by two experienced ophthalmologists (E.Z. and S.M.). Imaging was performed with a spectral-domain OCTA RTVue XR AngioVue (version 2015.1.0.90; Optovue, Inc., Fremont, CA, USA). This device uses the erythrocyte motion-dependent split-spectrum amplitude-decorrelation angiography algorithm. It provides 304 × 304 A volumetric exposures at a rate of 70,000 A scans per second with an 840 nm light source with an axial resolution of 5 mm. In addition, 5 repeat B scans were performed at 216 scanning positions during imaging, providing 3D scans per 3 × 3 mm region. In OCTA scans, the device automatically calculates and provides quantitative data on vascular density (VD) and flow area. VD represents the percentage of vessels and micro-vessels in a selected region. Flow area is obtained by calculating the total vascular area in mm^2 within the selected region for measurement. Analysis of the perifoveal region, foveal region, and FAZ was performed using a 3 × 3 mm frame from

the acquired images. The device automatically calculated the flow area of the superficial capillary plexuses (SF) and the DF in the foveal and parafoveal regions. Similarly, the device automatically calculated the superficial FAZ and deep FAZ measurements. Two independent raters evaluated the OCTA images (S.M. and E.Z.).

Statistical Analysis

The Statistical Package for the Social Sciences Statistics version 23.0 (IBM, Armonk, NY, USA) was used to analyze the data obtained in this study. Descriptive statistics for the continuous variables were expressed as means and standard deviations as well as medians (min–max), while categorical variables were expressed as numbers and percentages. Statistical analysis of the results that met the parametric measurement conditions was calculated using the independent Student's *t*-test. The linear relationship between the variables was examined using Pearson's correlation analysis. A $p<0.05$ was considered statistically significant. Inter-rater reliability was assessed using Cohen's kappa.

Results

Demographic and Clinical Features

The mean age was 11.88±3.60 years in Group 1 and 11.63±2.24 years in Group 2; no statistically significant difference was found ($p=0.80$). In Group 1, 47.1% of the patients were female and 52.9% were male, while in Group 2, 43.75% were female and 56.25% were male. No significant difference between the groups in terms of gender was found using the Chi-square test ($p=0.18$).

The mean age at diagnosis in Group 1 was 9.53±3.90 years. The mean follow-up period after surgery in Group 1 was 2.53±1.32 years. The mean axial length (AL) in Group 1 was 22.22±1.30 mm. In Group 1, the BCVA was 0.90±0.73 preoperatively and 0.12±0.17 logMAR postoperatively ($p<0.01$). The mean post-operative refractive deviation was calculated as a spherical equivalent, and its mean was −0.95±1.00.

OCTA Measurement Values

Inter-rater reliability was calculated as 0.76. The comparative results of retinal microvascular changes in pediatric cataract surgery patients and healthy controls are summarized in Table 1. The statistical analysis revealed lower foveal superficial and deep blood flow in Group 1 than in Group 2 (1.33±0.12 vs. 1.47±0.13 and 1.23±0.34 vs. 1.56±0.23, respectively, $p<0.05$). While sFAZ was similar across the groups ($p=0.87$), dFAZ enlargement was observed in Group 1 (0.41±0.19 vs. 0.31±0.12, respectively, $p=0.02$). Our analysis revealed similar VD parameters in the foveal region in both groups. However, superficial VD in the parafoveal region was found to be lower in Group 1 than in Group 2 (51.46±4.00 vs. 55.35±4.69, respectively, $p=0.01$). In addition, optic disc head VD was lower in Group 1 than in Group 2 (56.46±3.01 vs. 59.37±3.06, respectively, $p=0.01$).

Table 1. Comparative analysis of OCT-A data of pediatric cataract cases and healthy control group

???	Group 1 (mean±standard deviation) (*n*=17)	Group 2 (mean±standard deviation) (*n*=16)	*p*
Fovea SF (μm^2)	1.33±0.12	1.47±0.13	<0.01
Fovea DF (μm^2)	1.23±0.34	1.56±0.23	<0.01
Fovea sFAZ (μm^2)	0.29±0.08	0.29±0.13	0.87
Fovea dFAZ (μm^2)	0.41±0.19	0.31±0.12	0.02
Fovea sVD (%)	34.50±5.06	35.25±8.96	0.76
Fovea dVD (%)	36.57±5.42	37.15±10.88	0.84
Parafovea sVD (%)	51.46±4.00	55.35±4.69	0.01
Parafovea dVD (%)	60.57±4.15	62.76±7.11	0.28
OD head flow (μm^2)	1.68±0.14	1.69±0.14	0.96
OD head VD (%)	56.46±3.01	59.37±3.06	0.01

SF: Superficial flow; DF: Deep flow; sFAZ: Superficial foveal avascular zone; dFAZ: Deep foveal avascular zone; sVD: Superficial vascular density; dVD: Deep vascular density; OD: Optic disc; OCTA: Optical coherence tomography angiography

In Group 1, nine patients had mild amblyopia during the post-operative period; eight patients did not have amblyopia. To determine whether there was a difference between post-operative BCVA and OCTA parameters, eyes with and without amblyopia were compared using subgroup analysis. No significant difference was found between the two groups in terms of OCTA parameters. In addition, a Pearson correlation analysis was performed between the BCVA and OCTA parameters. Moderate negative correlations were found between BCVA (logMAR) and foveal superficial blood flow ($r=-0.38$, $p=0.03$) and foveal deep blood flow ($r=-0.44$, $p=0.01$).

Discussion

This study evaluated post-operative retinal microvascular circulation in pediatric cataract patients. Compared to the control group, decreased blood flow in the superficial and deep layers of the foveal region, widening of the deep

layer FAZ, and decreased VD in the superficial layer of the parafoveal region and the optic disc head were observed in the treatment group.

Previous studies have investigated OCTA parameters in healthy pediatric groups. Yang *et al*.[9] reported that gender may affect retinal blood flow, VD, and FAZ data. They found that SF, DF, FAZ, and VD values were higher in girls than in boys. İçel *et al*.[10] showed that VD in the deep capillary plexus decreased significantly with increasing age. In this study, we assume that the results are not affected because both groups are similar in terms of age and gender. Although some studies have proposed formulas that include AL to correct retinal VD and FAZ measurements for optical magnification resulting from refractive errors,[11] these formulas are not universally accepted because they may not account for all refractive components of the eye. The mean AL data of the cataract-surgical patients in our study were within normal limits, and to our knowledge, there were no developmental defects such as microphthalmia. Lonngi *et al*.[6] found reduced VD in the superficial and deep capillary plexus of children with amblyopia compared to healthy controls. They suggested that this finding may be related to stalled vascular development in amblyopic eyes due to a lack of visual stimulation.[6] Salerni *et al*.[12] compared OCTA findings in children who responded to amblyopia treatment with those of children who did not respond to it and those with normal eyes. In their study, macular VD and perfusion were higher in the group that responded to amblyopia treatment than in the other two groups.[12]

We offer several potential explanations for the decreased microvascular blood flow and VD in our treatment group. The first concerns developmental cataracts themselves. Foveal development is primarily supported by the force exerted by intraocular pressure on the foveal avascular space and by retinal tensile forces occurring during ocular growth.[13] The developmental defect causing cataract development may also lead to insufficient retinal microvascular development.

The second mechanism is cataract-induced deprivation amblyopia. Zhang *et al*.[8] reported increased superficial foveal VD, narrowing of the FAZ area, and decreased deep parafoveal VD in pediatric cataract surgery patients compared to healthy controls. They attributed the narrowing of the FAZ area to relative retinal immaturity compared with healthy eyes.[8] However, our results indicate that the FAZ area was wider in eyes that underwent pediatric cataract surgery. This result supports the reduction of vascular flow in other retinal layers. The widening of the FAZ area may be related to delayed retinal vascular development rather than to retinal development itself. Earlier cataract surgery in children is important to prevent the development of deprivation amblyopia. However, when examining the factors that affect visual acuity after cataract surgery, the age at which cataracts significantly impact vision and the time elapsed between cataract development and surgery stand out. Ledoux *et al*.[14] showed that surgery performed at an older age was associated with better visual acuity in both unilateral and bilateral cataracts. In our study, only mild amblyopia was present in half of the cases. This may have been due to the fact that the age of cataract onset was after 1–3 years, which is the most critical period for the development of amblyopia. Although our results apply to patients who underwent surgery at age 5 years or older, conclusions regarding OCTA parameters in patients operated on at a younger age cannot be drawn. Lempert *et al*.[15] observed narrowing of the optic disc margins in amblyopic eyes. This suggests that subclinical optic disc hypoplasia may be a component of vision loss in amblyopia.[15] Optic disc VD was reduced in amblyopic eyes compared to healthy eyes.[7,16] Li *et al*.[16] observed that optic disc and macular vascular blood flow were lower in amblyopic eyes than in contralateral eyes before treatment. After amblyopia treatment, VD improved significantly with an increase in VA and was even at levels similar to those of healthy eyes.[16] In our study, the decrease in optic disc head VD compared to the healthy group was consistent with the data in the literature.

Finally, the fact that visual stimulation is reduced due to cataracts may explain our results. This can slow vascular development in the retina and optic disc head, which can be explained by a decrease in vascular formation due to a decrease in oxygen demand resulting from inadequate visual stimulation. Some studies have reported changes in adult patients after cataract surgery, such as FAZ reduction and increased superficial and deep foveal/parafoveal vessel density compared to pre-surgical levels.[17] This could be explained by neurovascular remodeling. Neurovascular remodeling after cataract surgery is the process by which increased neuronal activity following the elimination of visual deprivation reorganizes the retinal microvascular structure according to metabolic needs. Even if postsurgical remodeling occurs, there may still be a permanent delay in patients' vascular development compared to a healthy control group. More detailed studies are needed to confirm these hypotheses.

The limitations of our study include its small sample size, its cross-sectional design, and its lack of repeated measurements. This study was not designed to compare vascular flow changes before and after surgery. Because

the presence of cataracts can affect the quality of OCTA scans, our study was designed to compare the treatment group (which consisted of patients who had undergone surgery) with a healthy control group. Furthermore, conditions such as inflammation-related cystoid macular edema and increased foveal thickness can develop after cataract surgery. Because these conditions could bias the data, only patients who were at least 1 year postoperatively were included. There was no significant ocular pathology other than congenital cataract in our treatment group, but we were unable to determine the presence of underlying systemic diseases. Finally, this study had a retrospective design, so our findings do not imply causality; they only suggest a possible association. Although it reflects a decrease in vascular parameters in pediatric cataract cases, a longitudinal study is needed to confirm causality.

Conclusion

This study found decreased macular and optic disc microvascular circulation and widening of the FAZ area in pediatric cataract surgery patients. Whether this result is directly related to pediatric cataract development or cataract-induced amblyopia can be clarified via further comprehensive studies.

Ethics Committee Approval: This study was approved by The Ethics Committe of Kahramanmaras Sutcu Imam University (April 07, 2025–109).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Authorship Contributions:

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Evaluation of keratoconus patients with or without surgery by both sub-scales of "Keratoconus End-Points Assessment Questionnaire"

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Abstract

Purpose: The purpose of the study was to evaluate the results of Keratoconus End-Points Assessment Questionnaire (KEPAQ) in patients who did or did not have any surgery for keratoconus.

Methods: This cross-sectional, single-center, observational study included 127 patients with keratoconus at the Cornea Service, Department of Ophthalmology, Dokuz Eylul University. Patients were classified as Group 1 (no ocular surgery) and Group 2 (any surgery for keratoconus). Best-corrected visual acuity (BCVA), spherical equivalent (SE), keratometry readings (Kmean), asphericity coefficient (Q value), and central corneal thickness values were recorded. Patients were asked to answer the questions of emotional (E) and functional (F) KEPAQ subscales.

Results: Group 1 consisted of 59 patients (46.5%), and Group 2 consisted of 68 patients (53.5%). In Group 2, 33 patients had cross-linking (CXL), 16 had intrastromal corneal ring segment (ICRS) implantation, 4 had both CXL and ICRS implantation, 5 had deep anterior lamellar keratoplasty (DALK), and 10 had penetrating keratoplasty (PK). KEPAQ-E scores were positively correlated with BCVA ($r=0.34$, $p<0.01$) and SE ($r=0.20$, $p=0.04$). KEPAQ-F scores were positively correlated only with BCVA ($r=0.25$, $p=0.01$). In Group 2, the worst E and F scores were found in patients who had ICRS implantation and PK, whereas the best E and F scores were obtained in patients who underwent DALK.

Conclusion: In this study, BCVA appeared to be the most important predictor of emotional and functional QoL, followed by SE. Other clinical parameters used to stage disease severity did not show any significant correlation with functional or emotional QoL measures.

Keywords: KEPAQ-E, KEPAQ-F, Keratoconus end-points assessment questionnaire, Keratoconus, Quality of life

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Keratoconus is the most common primary corneal ectasia worldwide. Since keratoconus causes a progressive decline in visual quality, affected individuals may have significant difficulty performing daily tasks.[1] Therefore, it is often necessary to rehabilitate patients with optical aids and/or surgery.

Recently, patient-reported outcome measurements (PROMs) have gained significant importance as an effective way to gather information about the burden of disease from patients' perspectives.[2] These instruments provide a reliable assessment of the subjective change in quality of life (QoL) patients experience due to the disease. This approach is fundamental because patient-directed visual disturbance is not necessarily related to factors the physician can directly measure. That visual change is highly subjective. Disease-specific PROMs are preferred as they provide much more information about the patient's current condition, suffering from a unique disease.[2] Balparda *et al.*[3] developed a keratoconus-specific "Keratoconus End-points Assessment Questionnaire" (KEPAQ), which has been tested and validated. KEPAQ measures both emotional well-being and functional compromise in keratoconus patients. Prior psychometric evaluation through Rasch analysis has demonstrated that KEPAQ is a robust and well-constructed instrument.[4] However, an easy E&F classification system was recently created, and KEPAQ scores were divided into 1–4 on a scale of 5.[5]

Herein, we aimed to evaluate the results of KEPAQ in patients who did or did not have any keratoconus surgery and assess whether the history of surgery makes any difference in the functional and emotional well-being of the patients.

Materials and Methods

This cross-sectional, single-center, observational study included 127 patients with keratoconus at the Cornea Service, Department of Ophthalmology, Dokuz Eylul University Hospital. The protocol of this study was approved by the Institutional Ethical Committee (2021/20–58) and was conducted in accordance with the tenets of the Declaration of Helsinki.

Keratoconus was diagnosed based on the requirements of the global consensus on ectatic diseases,[6] that is, the inclined appearance of posterior corneal elevations, an abnormal distribution of corneal thickness, corneal thinning, and an increase in corneal curvature. Patients at least 10 years of age were included in the study. The demographic data, including age, gender, underlying systemic diseases, and past medical history, were recorded. Complete ophthalmological examination was performed, including best-corrected visual acuity (BCVA) in Snellen lines with spectacles or contact lens correction, slit-lamp biomicroscopy, air-puff tonometry, and dilated fundoscopy. Refractive errors were tested under non-cycloplegic conditions via an auto-refractor (Nidek® ARK-510A autorefractor/keratometer, Japan), and spherical equivalent (SE) values were recorded. Average of steep and flat simulated keratometry readings (K_{mean}), asphericity coefficient (Q value), and central corneal thickness (CCT) measured with Scheimpflug corneal tomography (Pentacam®; Oculus Systems, Germany) were recorded. The BCVA, SE, Kmean, Q values, and CCT values of both eyes were averaged to yield one set of data per patient that would indicate the patient's overall status.

Patients were classified into Group 1 (patients who did not undergo any ocular surgery) and Group 2 (patients who underwent any keratoconus surgery). Group 2 was divided into subgroups based on the type of surgery performed: Collagen cross-linking (CXL), intrastromal corneal ring segment (ICRS) implantation, deep anterior lamellar keratoplasty (DALK), and penetrating keratoplasty (PK). All patients were reached by phone and asked to answer KEPAQ questions after receiving detailed information about the study.

The KEPAQ is a recently developed and validated self-administered keratoconus-specific scale questionnaire.[4] It consists of two subscales and 16 questions in total. The first part of the scale (i.e., KEPAQ-E) consists of seven questions. This subscale assesses patients' emotional adjustment secondary to the disease (Table 1). The second subscale (i.e., KEPAQ-F) consists of nine questions about functional status secondary to keratoconus (Table 2). All questions are written clearly and briefly to determine how much the disease hinders patients in various situations. All questions use a corresponding scoring system: "Not at all"=3; "A little"=2; "Quite a bit"=1; "A lot"=0. The "Not applicable" option is also offered to patients who believe the problem is unrelated to any aspect of daily life.

Statistical Analysis

Patients' questionnaire results were recorded in the Excel file provided by Harvard Dataverse, as suggested by Balparda *et al.*,[5] which is freely available from Harvard Dataverse at https://dataverse.harvard.edu/api/access/datafile/4289090. The Excel file used a linear transformation to convert the specified formulation to an associative scale between 0 and 100. Here, a higher score

Table 1. The subscale assesses patients' emotional adjustment secondary to the keratoconus

Question	Not at all	A little	Quite a bit	A lot	N/A
1. Do you feel your eye disease has affected your confidence to perform your daily tasks?	3	2	1	0	X
2. Do you feel your eye disease has affected your confidence to leave the house?	3	2	1	0	X
3. Do you feel your eye disease has affected your happiness in general?	3	2	1	0	X
4. Do you feel your eye disease has affected your confidence to go from one place to another?	3	2	1	0	X
5. Do you feel your eye disease has affected your self-esteem?	3	2	1	0	X
6. Do you feel your eye disease has affected your confidence about the future?	3	2	1	0	X
7. Do you feel your eye disease has caused you fear about the future?	3	2	1	0	X

Table 2. The subscale assesses patients' functional status secondary to the keratoconus (KEPAQ-F)

Question	Not at all	A little	Quite a bit	A lot	N/A
1. Do you feel your eye disease has affected your ability to play sports?	3	2	1	0	X
2. Do you feel your eye disease has affected your ability to see objects near you?	3	2	1	0	X
3. Do you feel your eye disease has affected your ability to perform your daily tasks?	3	2	1	0	X
4. Do you feel your eye disease has affected your ability to go to the movies?	3	2	1	0	X
5. Do you feel your eye disease has affected your ability to do your job?	3	2	1	0	X
6. Do you feel your eye disease has affected your ability to watch television?	3	2	1	0	X
7. Do you feel your eye disease has affected your ability to use the computer?	3	2	1	0	X
8. Do you feel your eye disease has affected your ability to read books?	3	2	1	0	X
9. Do you feel your eye disease has affected your ability to see objects that are faraway?	3	2	1	0	X

means having a better QoL. At the same time, the Excel file provides an easy E&F classification system by dividing KEPAQ scores on a 1–4 scale using Tukey's Hinges. E1 and F1 indicate better emotional and functional states, respectively; E4 and F4 indicate the worst emotional and functional states. This study used this approach to evaluate the E&F classification system with respect to the presence or absence of keratoconus surgery.

The Statistical Package for the Social Sciences (SPSS) software version 24 (IBM® SPSS® Statistics, USA) was used to analyze patient demographics and KEPAQ scores statistically. The Shapiro–Wilk test was used to assess the normality of the variables' distributions. Descriptive variables were addressed as means and standard deviations. The proportions of non-parametric variables between the groups were compared using the Chi-square test. Comparison of the parametric variables between groups was performed using an independent samples t-test when the data were normally distributed and a Mann–Whitney U test when the data were not normally distributed. Pearson correlation analysis was used for normally distributed data, and Spearman's rank correlation analysis was used for data without normal distribution. $P<0.05$ was defined as statistically significant.

Results

A total of 127 keratoconus patients were included in the study. Demographic data and baseline examinations of the groups were summarized in Table 3. Group 1 consisted of 59 patients (46.5%) who were followed up without surgery; Group 2 consisted of 68 patients (53.5%) who underwent surgery to rehabilitate keratoconus. Post-operative data of Group 2 patients are included in the demographic data. Groups were age and gender-matched. All demographic characteristics were statistically similar between the two groups ($p>0.05$ for all), except for the Q value, which was significantly more negative in Group 1 than in Group 2 ($p<0.05$). BCVA and Kmean values were distributed normally ($p>0.05$ for all). All other parametric variables did not follow a normal distribution ($p<0.05$ for all).

Table 3. Demographic data and examination results of Group 1 and Group 2

Characteristics	Group 1	Group 2	*p**
	n (%)		Chi-square test
Patient numbers	59 (46.5)	68 (53.5)	
Gender	F- 23 (39.0) M- 36 (61.0)	F- 25 (36.8) M- 43 (63.2)	0.80
Vernal keratoconjunctivitis	24 (40.7)	26 (38.2)	0.78
History of surgery	None (0)	CXL (33, 48.5) ICRS (16, 23.5) CXL+ICRS (4, 5.9) DALK (5, 7.4) PK (10, 14.7)	
	Mean ±SD (Range)		
Age (years)	29.42±11.47 (14–64)	30.13±10.9 (11–68)	0.72
Age at initial diagnosis (years)	22.82±7.86 (10–45)	21.66±7.84 (10–57)	0.41
Time from initial diagnosis (months)	19.09±38.53 (0–168)	23.35±42.65 (0–180)	0.60
BCVA	0.63±0.26 (0.13-1)	0.59±0.2 (0.1–1)	0.41
SE	−4.6±3.87 (−18–1.75)	−3.96±3.08 (−12.5–5.13)	0.30
CCT	473.24±54.35 (296.5–573.5)	468.99±53.66 (258–632.5)	0.67
K_{mean}	48.77±5.05 (40.88–63.37)	47.65±4.15 (40.6–69.25)	0.18
Q value	−0.9±0.46 (−2.09–0.06)	−0.66±0.5 (−2.3–0.51)	**<0.008***
KEPAQ-E scores	70.13±9.21 (36.15–76.78)	68.73±11.32 (29.12–76.78)	0.45
KEPAQ-F scores	58.68±15.3 (28.02–83.27)	57.94±17.23 (22.99–83.27)	0.80

BCVA: Best corrected visual acuity; CCT: Central corneal thickness; CXL: Collagen cross-linking; DALK: Deep anterior lamellar keratoplasty; F: Female; ICRS: Intrastromal corneal ring segment; K_{mean}: Mean keratometry; n: number of patients; M: Male; PK: Penetrating keratoplasty; SD: Standard deviation; SE: Spherical equivalent; Q value: Asphericity coefficient. *p<0.05 statistically significant.

In Group 2, 22/33 patients underwent bilateral CXL surgery, whereas 11/33 underwent unilateral CXL. Likewise, 6/16 had bilateral ICRS implantation surgery, whereas 10/16 had unilateral ICRS implantation. All four patients with both CXL and ICRS implantation were operated on in one eye only. Five eyes of 5 patients underwent DALK, 15 eyes of 10 patients underwent PK, and 1 PK patient was re-grafted in 1 eye. No surgical eyes had any intraoperative or post-operative complications. In the operated eyes, pre-operative BCVA was 0.32±0.21, which improved to 0.59±0.2 at the last follow-up (p<0.001).

Correlations between patient demographics and KEPAQ E/F scores were analyzed across all included patients. KEPAQ E scores were positively correlated with BCVA (r=0.34, P<0.01) and SE (r=0.20, p=0.04). KEPAQ F scores were positively correlated with BCVA (r=0.25, p=0.01) but not with SE (r=0.17, p=0.06). Both KEPAQ E and F scores were positively correlated with BCVA in better-seeing eyes (r=0.35, p<0.001; r=0.27, p<0.01, respectively) and BCVA in worse-seeing eyes (r=0.24, p<0.01; r=0.19, p=0.04, respectively).

The correlation analyses were also performed separately for both groups. In Groups 1 and 2, KEPAQ E and KEPAQ F scores were strongly positively correlated with each other (r=0.71, p<0.01 for both). On the other hand, in Group 2, KEPAQ E scores were negatively correlated with time from diagnosis (r=−0.27, p=0.04) and Kmean (r=−0.31, p=0.01); positively correlated with pre-operative and post-operative BCVA (r=0.43, p<0.01; r=0.38, p<0.01, respectively). KEPAQ F scores were negatively correlated with Kmean (r=−0.35, p=0.01); positively correlated with SE (r=0.35, p=0.01), pre-operative and post-operative BCVA (r=0.28, p=0.01; r=0.48, p<0.01, respectively).

The correlations between the KEPAQ E/F scores and the BCVA in the better-seeing and worse-seeing eyes were studied separately in Groups 1 and 2. In Group 1, only the positive correlation between KEPAQ E scores and BCVA in better-seeing eyes was significant (r=0.33, p=0.01). In Group 2, KEPAQ E scores were positively correlated with BCVA in better-seeing eyes (r=0.37, p<0.01) and BCVA in worse-seeing eyes (r=0.25, p=0.04). Similarly, KEPAQ F scores were positively correlated with BCVA in better-seeing eyes (r=0.46, p<0.001) and BCVA in worse-seeing eyes (r=0.33, p<0.01).

KEPAQ E and F classification data in both groups are summarized in Figure 1. The differences in the number of patients with E1, F1, E4, and F4 scores between the two groups were not statistically significant (p>0.05 for all). In the subgroup of patients with E4 and/or F4 scores in both groups (n=13), no significant differences were found between the age, age at diagnosis, time from diagnosis, BCVA, SE, CCT, Kmean, and Q values of the patients (p>0.05 for all).

In surgical subgroups of Group 2, KEPAQ E&F classification score results are summarized in Figure 2.

Fig. 1. Keratoconus end-points assessment questionnaire (KEPAQ) E and F classification data in both groups. This figure displays how the KEPAQ scores were distributed among patients who underwent and did not undergo any surgical procedure. (Group 1: Non-surgical keratoconus patients, Group 2: Surgically treated keratoconus patients). Emotional adjustment worsens progressively from score E1 to E4, and functional status from F1 to F4. (Materials and Methods for the calculation methodology)

The order of surgical procedures that yielded the poorest to better E scores was PK or ICRS surgery, CXL, DALK, or combined CXL and ICRS implantation. The order of surgical procedures that yielded the poorest to the best F scores was ICRS surgery, CXL, PK, combined CXL, and ICRS surgery or DALK.

Discussion

Clinicians and researchers have realized that the success of management in ophthalmologic conditions goes far beyond measurable variables such as BCVA, SE, keratometry readings, or Q values of asphericity.[7] As vision is inherently a subjective process, it is imperative for the ophthalmologist to examine the patient's perceptions. Kandel *et al.* [8] had previously stated that the impact of keratoconus on QoL may be disproportionate to clinical measures such as BCVA. Furthermore, some relationship has been demonstrated between corneal distortion and emotional distress.[9]

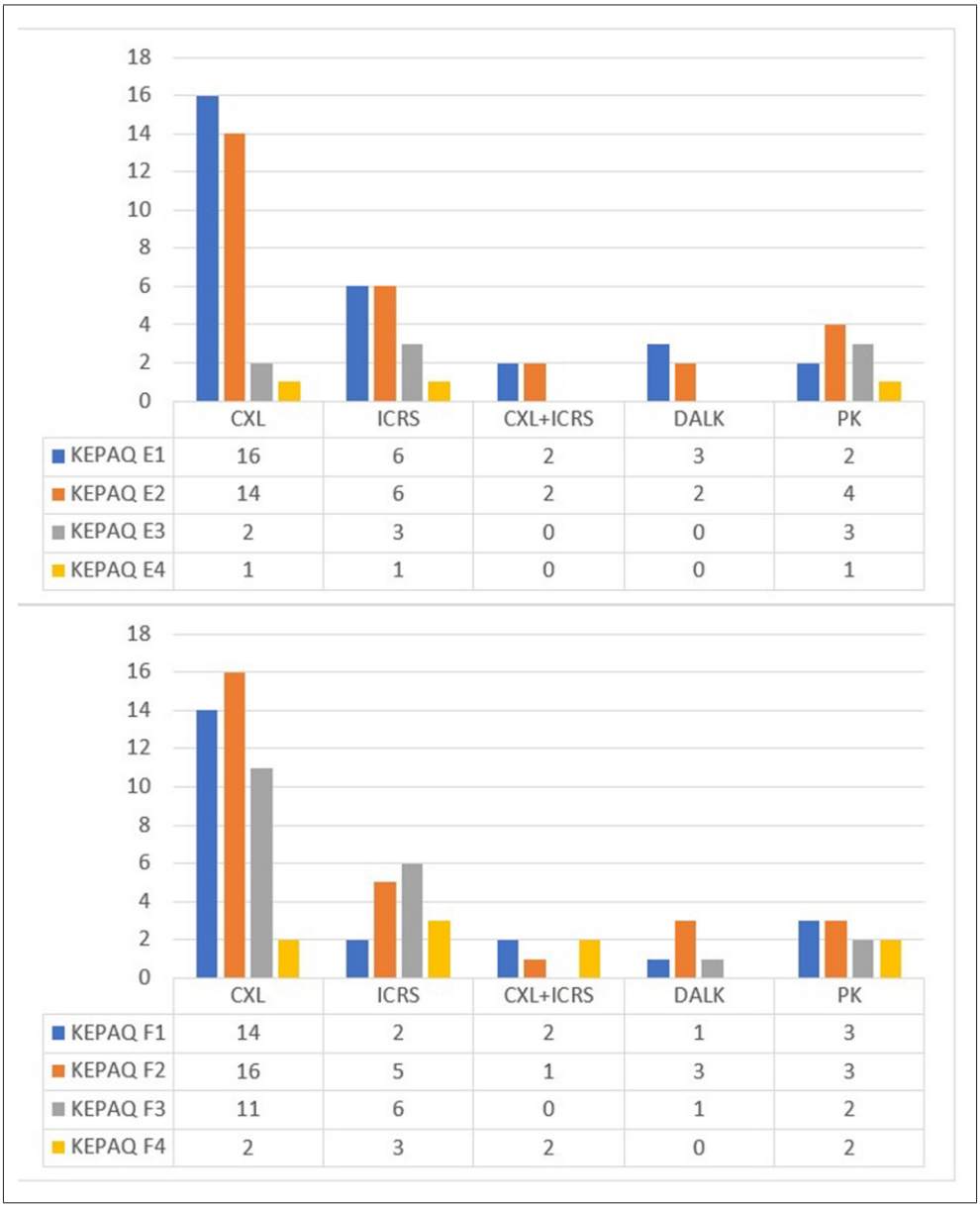

Fig. 2. In surgical subgroups of Group 2, keratoconus end-points assessment questionnaire (KEPAQ) E&F classification score results. This figure displays how the KEPAQ scores were distributed among patients who underwent different surgical procedures. (CXL: Collagen cross-linking, ICRS: İntrastromal corneal ring segment, DALK: Deep anterior lamellar keratoplasty, PK: Penetrating keratoplasty). Emotional adjustment worsens progressively from score E1 to E4, and functional status from F1 to F4. (Materials and Methods for the calculation methodology)

The World Health Organization defines the QoL as "the perception of an individual about their position in life in the context of culture and value systems in which they live, and in relation to his objectives, expectations, standards, and concerns." QoL is expected to be challenging to measure by the medical sciences, and ophthalmology is no exception.[10] To date, the best way of measuring QoL in patients has been through using PROMs,[11] i.e., validated and standardized tools that directly question the patient's subjective experiences in their daily lives. While general PROMs can be helpful under certain circumstances,[12] disease-specific PROMs will provide more insight into the burden on overall QoL from the patient's perspective.[11]

At present, only two keratoconus-specific scales have been validated. The first is the Keratoconus Outcomes Research Questionnaire (KORQ), designed by Khadka *et al.*[13] and recently studied by Kandel *et al.*[14] KORQ

exhibits many psychometric analyses. However, it completely ignores the emotional compromise caused by the illness. It has been emphasized that ectatic diseases affect emotionally, and keratoconus patients have a higher than normal prevalence of mental health-related diseases, especially clinical depression.[8,15,16]

Balparda *et al.*[3] previously developed, tested, and validated the "Keratoconus End-points Evaluation Questionnaire" to adequately measure both functional and emotional evaluation. KEPAQ is a recently developed, robust, unidimensional, well-designed disease-specific PROM designed to provide the clinician reliability of emotional and functional reconciliation from the patient's perspective (KEPAQ-E and KEPAQ-F, respectively).[3] KEPAQ is robust in its concept and the epidemiological and mathematical creation and validation process. In addition, the KEPAQ is shorter than the KORQ,[13] so its application in daily practice can be simpler and faster without compromising the test's psychometric properties. The main difference between KORQ and KEPAQ is that the KEPAQ also has a sub-scale to measure emotional affect and distress secondary to keratoconus,[4] as the progressive nature of the disease and the possible need for keratoplasty may cause anxiety.[8]

Our study used the latest proposed, easily understandable, and implemented KEPAQ E&F classification scores by Balparda *et al.*[5], which standardized the linear transformation to report KEPAQ results. This classification method has standardized the calculation, and the current status of patients with keratoconus can be better captured.[5]

Tan *et al.*[17] demonstrated that BCVA in the better eye was most strongly correlated with reading and mobility scores as measured by the Visual Impairment Questionnaire (IVI), a non-disease-specific PROM. In comparison, visual acuity in the worse eye was significantly associated with emotional scores.[17] Balparda *et al.*[9] reported that none of the better eye's topographical elevations, visual acuity, and corneal thickness correlated with KEPAQ scores on either subscale. However, in the worse eye, A (Anterior elevation), B (Posterior elevation), and D (Distance visual acuity) were significantly correlated with KEPAQ scores on both subscales. The only criterion that did not show correlation behavior was C (Corneal thickness).[9] These data showed that corneal distortion and visual function in the worse eye are associated with emotional distress and subjective functional handicap in keratoconus patients.

In this study, we evaluated KEPAQ scores with respect to BCVA, SE, CCT, Kmean, and Q values in surgery and no-surgery groups. While BCVA and SE values were correlated with emotional distress, only BCVA was correlated with functional compromise. This finding indicates that a low visual acuity yields functional and emotional compromise. However, the high refractive error also affects emotional well-being, possibly regarding self-esteem and confidence. The functional and emotional status of the patients was strongly correlated, as expected. Since most keratoconus patients are young, patients with low vision might have reduced functionality compared to peers and fear and anxiety with their progressive disease. Therefore, in our daily routines, it is far more critical to evaluate visual quality as a whole, that is, visual acuity, general visual, and mental comfort. Remarkably, neither functional nor emotional QoL was correlated with the current age, age at diagnosis, time from diagnosis, CCT, Q value, or Kmean values.

The correlation analyses in patients who did or did not undergo ocular surgery yielded that KEPAQ E and KEPAQ F scores were strongly correlated. In addition, in patients who had undergone any surgical intervention for keratoconus, both emotional and functional measures were poorer with increased disease duration and higher keratometry readings. They were increasingly better with higher pre-operative and post-operative visual acuities, but were not affected by the amount of change in visual acuity by the surgery. Unlike in the whole group of patients, SE of refractive error was correlated with functional compromise but not emotional distress.

In patients without surgery, emotional well-being was correlated with the BCVA in better-seeing eyes. BCVA in worse-seeing eyes was not correlated with emotional well-being, and BCVA in neither eye was correlated with functional well-being in this group of patients. On the other hand, both emotional and functional QoL data correlated with BCVA in better-seeing and worse-seeing eyes in patients who underwent any surgical intervention.

The distribution of E and F classification scores was similar in the surgery and no-surgery groups. In the severely reduced QoL patients (i.e., E4 and F4), there were no differences in BCVA, SE, CCT, Kmean, and Q values between the groups. One might conclude that patients experience similar emotional and functional QoL levels once the clinical parameters are similar. However,

correlations of those particular clinical parameters with KEPAQ E and F scores could not be identified. Only due to having had significant eye surgery, patients might also experience emotional and functional distress.

The surgical procedures that yielded the poorest E and F scores included ICRS implantation. In contrast, the best E and F scores were obtained in patients who underwent DALK, which can be another reason to prefer DALK over PK in keratoconus. PK patients reported moderate functional and poorest emotional well-being, possibly related to the invasiveness of PK. Surgical subgroups are relatively small, making subgroup comparisons less reliable.

This study is the first to use the E&F classification results in real life, in a cohort of various stages of keratoconus and treatment procedures. The main limitation of this study is having no pre-operative KEPAQ scores, as this study was not designed as a prospective study, but as a cross-sectional, observational study. Other limitations include a low number of patients in each surgical subgroup, as only patients whose phone calls could be reached were included, preventing interpretation of the effects of different types of surgeries. Age-specific evaluation of the results could also provide more insight into emotional and functional reconciliation from the patient's perspective. However, the sample size of this cross-sectional cohort was not high enough to make more groups and to evaluate patients with or without a history of surgery in age groups. Prospective studies with extensive and homogeneous series with respect to age and surgical intervention types could draw more accurate conclusions about factors affecting patients' QoL.

Conclusion

KEPAQ is a well-designed disease-specific questionnaire that measures the functional and emotional impact on QoL due to keratoconus. In this study, visual acuity was the most consistent indicator of functional and emotional well-being, particularly in patients who underwent surgery, followed by SE of refraction. Worst QoL patients had similar clinical characteristics in both surgery and no-surgery groups. However, clinical parameters commonly used to stage the disease severity did not correlate significantly with the functional or emotional QoL measures. The surgical procedures that yielded the poorest E and F scores included ICRS implantation and PK, whereas the best E and F scores were obtained in patients who underwent DALK. Further evaluations might improve the clinical evaluation and rehabilitation of patients with keratoconus.

Ethics Committee Approval: This study was approved by The Ethical Committee of Dokuz Eylul University (2021/20–58).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Evaluation of family physicians' knowledge, awareness, attitudes, behaviors and practice patterns regarding neonatal vision screening

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Abstract

Purpose: Eye examination and vision screening are an important part of screening programs, which are recommended for infants and children in family medicine practice. In the present study, it was aimed to assess the demographic features, working status, knowledge levels, awareness, attitudes, behaviors, and practice patterns of family physicians regarding neonatal vision screening.

Methods: The link to the questionnaire, consisted of 27 items pertaining to the demographic features, working status, knowledge levels, awareness, attitudes, behaviors and practice patterns of family physicians regarding neonatal vision screening was sent through WhatsApp to family medicine specialists and general practitioner family physicians working in Community Health and Family Health Centers across Turkey, family medicine specialists working in public/university hospitals, and family medicine medical residency students.

Results: Among 104 physicians, 55.8% performed neonatal vision screening while 44.2% did not. Ninety (86.5%) physicians reported that they evaluate infants through inspection, 66 (63.5%) obtain a medical history, 71 (68.3%) assess the blink reflex, fixation, and follow-up, and 57 (54.8%) perform the red reflex test. Forty-seven physicians (45.2%) who reported that they do not perform the red reflex test indicated that the most common reason was a lack of necessary equipment and experience, cited by 20 physicians (42.5%). All steps of the vision screening were performed by trained physicians at higher rates than untrained physicians, and this difference was statistically significant ($p<0.05$).

Conclusion: Although awareness of neonatal vision screening exists among family physicians in Turkey, actual practice varies significantly due to structural, educational, and logistical barriers. Targeted training, improved access to diagnostic tools, integration of structured referral pathways, and collaboration between primary and tertiary care is essential to ensure effective implementation of the vision screening.

Keywords: Congenital cataract, Family medicine, Newborn, Red reflex test, Retinoblastoma, Vision screening program

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In family medicine practice, routine health examinations and screening tests for infants and children are vital for early detection of conditions that may cause irreversible vision loss. In Turkey, eye and vision screening for the neonatal period is carried out within the framework of the "National Vision Screening Program" by family physicians. The guidelines for this program mandate that family physicians perform eye examinations for all newborns between 0 and 3 months of age and at every subsequent visit thereafter.[1-3] These mandatory screenings include external observation, assessment of risk factors, conducting a visual examination, and the red reflex test. The red reflex test is a non-invasive procedure used to identify media opacities and major refractive errors, and requires a direct ophthalmoscope, which is a mandatory equipment for all Family Health Centers. It is performed in a dimly lit room to allow the pupils to dilate naturally, and no eye drops are needed.[4,5]

Infants with identified risk factors – such as prematurity, congenital anomalies, or a positive family history of strabismus, amblyopia, high refractive errors (requiring more than five diopters of correction), childhood glaucoma/cataracts, and babies whose parents suspect that they have an eye pathology should be referred to an ophthalmologist for further evaluation.[6] The referral process is documented through the family medicine information system, and the ophthalmologist is required to provide a written report to ensure continuity of care.[6]

In the present study, it was aimed to evaluate the knowledge, awareness, and clinical practices of family medicine practitioners across Turkey regarding neonatal vision screening.

Materials and Methods

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of our hospital on December 25, 2024, with the decision number 2024/010.99/11/27. Participation in the study was voluntary, and informed consent was obtained from all participants.

The study questionnaire was developed by the authors after a comprehensive review of the existing literature and the National Vision Screening Program guidelines (Circular No. 2019/17) provided by the Ministry of Health. To ensure content validity, the survey items were designed to cover all clinical steps of neonatal eye assessment, and expert opinions from both family medicine and ophthalmology departments were obtained during the drafting phase. The questionnaire consisted of 27 items pertaining to the demographic features, working status, knowledge levels, awareness, attitudes, behaviors, and practice patterns of family physicians regarding neonatal vision screening. The full version of this questionnaire is available as Supplementary Material (Table 1).

Data were collected from 104 participants via WhatsApp between December 2024 and January 2025.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 27.0 (Armonk, NY). Descriptive statistics for each item in the questionnaire were shown as the number of individuals (n) and frequency (%).

To assess normality, the Kolmogorov-Smirnov test was applied. Parametric tests were used for normally distributed data, while non-parametric tests were used for non-normally distributed data. Different methods were employed for comparisons between groups and dependent group analyses. For comparing means, the t-test or Wilcoxon test was applied for the dependent groups, while the t-test or Mann–Whitney U test was applied for the independent groups, depending on normality. Chi-square or Fisher's exact test was used to compare proportions between groups. Friedman analysis was performed for dependent group comparisons. A $p<0.05$ was considered statistically significant for all analyses.

Results

Demographic and professional characteristics of the 104 participating physicians are summarized in Table 2. The study population predominantly consisted of family medicine residents and general practitioners working in family health centers. Notably, nearly half of the participants (42.3%) reported receiving no formal training on the national neonatal vision screening program, while others had received training at various stages of their medical education or through professional courses (Table 2).

The median number of infants examined per month was 6.6 (range: 1–70). When asked whether they performed vision screening during the neonatal period, 58 physicians (55.8%) stated that they did, while 46 (44.2%) stated not. Regarding the steps followed during screening, 90 physicians (86.5%) reported that they evaluate infants through inspection, 66 (63.5%) obtain a medical history, 71 (68.3%) assess the blink reflex, fixation, and follow-up, and 57 (54.8%) perform the red reflex test.

Table 1. Questionnaire including 27 survey questions and remote access link directed to the participants https://forms.gle/TZSURVZSA7P2GNKSA

1. What is your age

2. Gender
   Female
   Male
   I don't want to specify

3. What is your title
   General practitioner
   Medical residency student at family medicine
   Family medicine specialist
   Specialist lecturer/chief assistant/associate professor/professor

4. Where are you working at
   Family Health Center
   Community Health Center
   State Hospital
   City Hospital
   Training and Research Hospital
   Foundation University Hospital
   State University Hospital.

5. How many years have you been working as a family physician (Assistant physicians will write how many years they have been an assistant)

6. How many newborns do you examine in a month

7. Have you got any education about the newborn vision screening program
   Yes
   No

8. If your answer to the previous question is yes, please indicate where you received your education
   Medical school
   During residency training
   During the courses, congresses, or other meetings

9. Do you perform eye/vision screening in the newborn period
   Yes
   No

10. Do you have a direct ophthalmoscope in your working room
   Yes
   No

11. Do you perform red reflex test in your routine practice
   Yes
   No

12. If your answer to the previous question is no please mark the reason (you can mark multiple answers)
   Unaware of the test
   I don't have the required equipment (direct ophthalmoscope) and experience to perform the test
   I have got the required equipment, but I haven't got experience to perform the test
   I have got experience, but I haven't got the required equipment
   I have the required equipment and experience for the test, but I prefer referring

13. If you perform red reflex test, how often do you perform
   Only in suspicious cases
   All babies but only at the first visit
   All babies at each visit

14. Do you use mydriatic eyedrops while performing the test
   Yes
   No

15. If your answer to the previous question is yes which mydriatic eyedrop do you prefer

16. If you perform red reflex test, how often do you detect red reflex pathology
   Never
   Sometimes
   Frequently

17. Do you get a medical/familial history of the eye-related background from the patient's parents/ relatives?
   Yes
   No

18. Within the scope of newborn screening, do you examine patients with inspection Ministry of Health holds such as strabismus, facial/glob asymmetry?
   Yes
   No

19. Do you examine blink reflex to light /fixation/follow in infants?
   Yes
   No

20. Which of the reasons for referral to an ophthalmologist do you find closest to yourself
   I refer directly
   I refer if there is any pathology
   I refer if there is a history of preterm birth/ incubator
   I refer if there is family history
   I refer risky infants
   Other

21. If your answer to the previous question is "I refer risky patients", could you write down the risks

22. Do you fill out any forms when referring babies to the ophthalmologist?
   Yes
   No

23. What kind of feedback do you take from the patients of the infants whom you refer for the newborn eye screening program
   No feedback
   Verbal feedback
   Written feedback

24. Would you participate if the Ministry of Health hold a training program on the newborn eye screening?
   Yes
   No

25. If your answer to the previous question is no can you write your reason

26. Would you consider performing vision screening examination after such a program
   Yes
   No

27. If your answer to the previous question is no can you write your reason

Table 2. The distribution of the physicians according to their demographic characteristics, institution, working experience, and specialization degrees

	Female number (%)	Male number (%)	Total number (%)
Physicians	51 (49)	53 (51)	104 (100)
Mean age±SD (range)	34.0±10.5 (26–66)	39.0±11.7 (27–63)	38.0±11.2 (26–66)
Specialization degrees			
General practitioner	19 (37.1)	20 (37.7)	39 (37.5)
Family medicine resident	24 (47.1)	25 (47.2)	49 (47.1)
Family medicine specialist	8 (15.7)	7 (13.2)	15 (14.4)
Lecturer/assistant Professor/Associate Professor/Professor	0 (0.00)	1 (0.9)	1 (0.9.0)
Institution			
Family health center	35 (68.6)	45 (84.9)	80 (76.9)
State hospital	1 (2)		1 (0.9)
E City hospital	5 (9.8)	5 (9.4)	10 (9.6)
University hospital	10 (19.6)	3 (5.7)	13 (12.5)
Experience (years)			
<5 years	25 (49)	20 (37.8)	45 (43.2)
5–10 years	10 (19.6)	8 (15)	18 (17.3)
>10 years	16 (31.4)	25 (47.2)	41 (39.5)

Analysis of the responses from 47 physicians (45.2%) who reported that they do not perform the red reflex test revealed that the most common reason was a lack of necessary equipment and experience, cited by 20 physicians (42.5%). The remaining responses were as follows: having the necessary equipment but lacking experience (15 physicians, 31.9%), possessing both the necessary equipment and experience but still referring patients (6 physicians, 12.8%), having experience but lacking the necessary equipment (4 physicians, 8.5%), and being unaware of the test (2 physicians, 4.3%). Among the remaining 57 physicians (54.8%) who reported performing the red reflex test, 43 (75.4%) stated that they conducted the test on every infant only during their first examination. Thirteen physicians (22.8%) reported administering the test at every visit, while one physician (1.8%) performed the test only in cases with suspected pathology. When asked about the pathology rates, 42 (73.7%) physicians reported that they never detected any pathology while performing the red reflex test, while 15 (26.3 %) reported that they occasionally detected pathology. None of the physicians who performed the test indicated that they used mydriatic agents during the examination. Regarding the availability of the necessary equipment among 104 physicians, 38 (36.5%) reported having a direct ophthalmoscope at their workplace, whereas 66 (63.5%) stated they did not. Table 3 provides a summary of the reasons cited by physicians who did not perform the red reflex test, the frequency of the test performance, and the detected pathology rate among physicians who perform the red reflex test. Considering the steps of the screening examination and training, all steps were performed by trained physicians at higher rates than untrained physicians, and this difference was statistically significant ($p<0.05$). Notably, statistical analysis revealed no significant relationship between years of professional experience and the frequency of performing

Table 3. Summary of the reasons cited by physicians who did not perform the red reflex test, the frequency of the test performance, and the detected pathology rate among physicians who perform the red reflex test

Parameters (Answers)	Physicians not performing the red reflex test	
	Number	(%)
Reasons for not performing the red reflex test		
Unaware of the test	2	4.3
I don't have the necessary equipment (direct ophthalmoscope) and experience	20	42.5
I have the necessary equipment but I have no experience	15	31.9
I have experience, but I don't have the equipment	4	8.5
I have the necessary equipment and experience, but I prefer referring	6	12.8
Total	47	45.2
Frequency of test performance		
Only in suspicious cases	1	1.8
All babies only in first visit	43	75.4
All babies in every visit	13	22.8
Total	57	54.8
How often do you detect pathology		
Never	42	73.7
Occasionally	15	26.3
Total	57	54.8

comprehensive eye examinations, including ophthalmic examination, inspection, fixation/light reflex, and red reflex testing (p=0.447, p=0.105, p=0.970, and p=0.803, respectively), indicating that screening practices were consistent across all levels of experience.

Table 4 demonstrates a comparative overview of the extent to which physicians perform the steps of the neonatal screening examinations based on their institutional, academic characteristics, duration of professional experience, and training status. Notably, our analysis showed no statistically significant relationship between the duration of professional experience and the performance of screening steps (p>0.05 for all parameters), identifying prior training as the only significant determinant of clinical practice.

When asked about the reasons for referral to ophthalmologists, 28 physicians (26.9%) stated that they refer infants directly without detecting any pathology. 16 physicians (15.4%) implicate that they refer when they identify a pathology, nine (8.7%) refer infants with a history of preterm birth or incubator stay, 3 physicians (2.9%) refer infants with a family history of ocular problems. In addition, 42 physicians (40.4%) indicated that they refer infants if any of the aforementioned risk factors were present. Five physicians (4.8%) who reported that they refer high-risk patients did not specify the risk factors they considered. One physician (0.9%) did not answer the question.

A total of 79 (76%) participants stated that they do not fill out any form when referring infants to an ophthalmologist, while the remaining 24% (25 physicians) reported that they provided a referral form. Regarding feedback on the referrals, 71.2% (74 physicians) indicated that they received verbal feedback from the families of the referred infants, 22.1% (23 physicians) reported that they did not receive any feedback, and 6.7% (seven

Table 4. Physicians performing the steps of neonatal screening examinations based on their institutional, academic characteristics, duration of professional experience, and training status

		Ophthalmologic examination		p	Medical history		p	Inspection		p	Fixation/Light reflex		p	Red Reflex		p
		Yes	No		Yes	No		Yes	No		Yes	No		Yes	No	
Institution	Family Health Center	47	33		54	26		70	10		56	24		43	37	
	State hospital	1	0		1	0		1	0		1	0		1	0	
	City Hospital	4	6	p=0.462	5	5	p=0.308	8	2	p=0.890	6	4	p=0.762	6	4	p=0.807
	University Hospital	6	7		6	7		11	2		8	5		7	6	
Academic characteristics	General practitioner															
	Family medicine resident	24	15		25	14		36	3		31	8		23	16	
	Family medicine specialist/ academic staff	26	23	p=0.579	30	19	p=0.903	42	7	p=0.315	32	17	p=0.104	26	23	p=0.669
		8	8		11	5		12	4		9	7		8	8	
Professional experience	<5 years	23	22		24	21		37	8		27	18		24	21	
	5–10 years	9	9	p=0.447	10	8	**p=0.044**	14	4	p=0.105	11	7	p=0.097	9	9	p=0.803
	>10 years	26	15		32	9		39	2		33	8		24	17	
Training status	Yes	39	19		43	15	**p=0.008**	55	3	**p=0.005**	43	15	p=0.127	42	16	**p<0.001**
	No	19	27	**p=0.011**	23	23		35	11		28	18		15	31	

physicians) stated that they received written feedback. The physicians were asked whether they would participate if the Ministry of Health organized a training program about the newborn eye screening. About 98 (94.2%) of the physicians responded yes, while six (5.8%) answered no. Among the six physicians who declined participation, the reasons cited were as follows: three (50%) stated that they were not ophthalmologists, one (16.7%) indicated that this training was not included in their job description, one (16.7%) expressed concerns about the high risk of malpractice associated with the examination, and one (16.7%) stated that it is late for such a training. When 46 physicians who did not perform routine examinations were asked whether they would perform screening examinations after such a training program, six of them (13%) answered no. When asked about the reasons, the answers of these six physicians were as follows: their workload was high, and they were not experts in this field (*n*=3, 50%), they did not have the equipment (*n*=2, 33%), and they thought that this examination had a high risk of malpractice (*n*=1, 17%).

Discussion

The present study highlights significant gaps between the established national guidelines and the actual clinical practices of family physicians in Turkey regarding neonatal vision screening. Although the national program provides a clear framework for early intervention, our findings reveal a notable variability in how these screenings are implemented in primary care settings.

Our findings indicate that nearly half of the participating physicians do not routinely perform neonatal vision screenings, with only 54.8% implementing the red reflex test. These rates align with previous literature suggesting insufficient implementation of vision screening in primary care settings, especially the red reflex test.[7,8] For instance, our results are comparable to the study by Erdoğan and Erol, [8] which reported slightly higher (65.4%), but still suboptimal screening rates and similar red reflex screening (58.2%) rates among family physicians in Ankara. This consistent gap across different studies underscores a persistent challenge in integrating essential ocular assessments, such as the red reflex test, into routine clinical practice. The slightly lower rates observed in our study may be attributed to the broader geographic distribution of our participants, representing various cities with diverse working conditions, whereas previous studies were limited to a single province.

The primary barrier to performing the red reflex test was the lack of necessary equipment and clinical experience, reported by 42.5% of the 47 physicians who did not conduct the test. Interestingly, while an ophthalmoscope has been a mandatory piece of equipment for Family Health Centers in Turkey since 2013, only 38 (36.5%) of our participants reported having access to one.[9] This finding is notably lower than the rates reported by Gürsel Özkurt et al. [7] (95%) and Erdoğan and Erol (98.1%).[8] This discrepancy may stem from our study's broader geographical scope, which reflects more diverse and potentially more challenging working conditions compared to previous studies centered in single metropolitan areas like Ankara or Diyarbakır. Furthermore, the fact that some physicians reported performing the test despite lacking a direct ophthalmoscope suggests inconsistencies in examination techniques or the use of non-standard tools, which warrants further investigation into the quality of these screenings. Beyond equipment shortages, a lack of clinical confidence remains a significant barrier. In the present study, 31.9% of the physicians reported feeling inadequately prepared or lacking the necessary knowledge to use a direct ophthalmoscope effectively. This finding aligns with Biten et al.,[10] who observed that a vast majority of family medicine residents (84%) felt incompetent in managing eye diseases; among those, 77% attributed their lack of competence specifically to feeling inadequate in the use of an ophthalmoscope. These consistent results across different stages of medical careers – from residents to practicing specialists – highlight a critical need for targeted, hands-on training programs. Addressing this knowledge gap is essential to ensure that the national screening guidelines are not only known but also competently applied in clinical practice.

Among the 57 physicians who reported performing the test, most (73.7%) stated they had never detected any pathology, while only 26.3% reported occasional abnormalities. These results suggest that the clinical effectiveness of the red reflex test remains limited in practice. While this low detection rate may partly reflect the rarity of certain ocular pathologies in the screened population, it also suggests potential gaps in examination technique, diagnostic sensitivity, or interpretation skills. Given that early detection is crucial for preventing irreversible vision loss, these findings underscore the necessity of enhancing the quality of screenings. Therefore, beyond simply increasing screening frequency, professional development should focus on refining diagnostic proficiency to ensure that subtle but critical pathologies are not overlooked.

The inconsistencies in clinical interpretation are further supported by Zorlutuna Kaymak et al.,[11] who investigated the referral reasons to ophthalmologists and the outcomes

of the examinations in term infants aged one year or younger. Their study highlighted a concerning mismatch: infants with confirmed red reflex abnormalities were often referred for other reasons, while those referred specifically for suspected red reflex pathology were frequently found to be healthy on specialist examination. These findings, coupled with our own results, reinforce the conclusion that there are significant inconsistencies in both the recognition and interpretation of red reflex abnormalities among physicians in primary care settings. This diagnostic variability underscores the urgent need for standardized training to improve the reliability of neonatal vision screenings.

Recent international literature highlights that even when current screening standards are followed, significant "gaps in care" remain due to the diagnostic limitations of traditional methods like red reflex testing and direct ophthalmoscopy. While global discussions are shifting towards the integration of advanced technologies – such as ultra-widefield imaging – to detect complex retinal pathologies that standard exams might miss, our findings reveal a more fundamental challenge. In the primary care landscape of Turkey, the primary "gap" is not yet the lack of advanced imaging, but rather the inconsistent application of existing basic screening protocols due to equipment shortages and insufficient training. This suggests that while global standards move toward high-tech diagnostics, ensuring the proficiency and accessibility of current bedside tools remains the most critical priority for national health policies.[12]

A key finding of our study is the statistically significant association between prior training and the consistent performance of neonatal vision screenings ($p<0.05$). Interestingly, professional experience (years in practice) was not a statistically significant determinant (p-values ranging from 0.105 to 0.970), suggesting that specific, targeted education is more vital for clinical proficiency than seniority. This indicates that while years of practice increase general medical knowledge, specialized neonatal screening requires focused professional development. Consequently, the standardization and dissemination of in-service training programs are essential to improve screening quality. Enhancing physician awareness through these programs will directly facilitate the timely detection of vision- and life-threatening conditions such as congenital cataracts and retinoblastoma.

Another concern is the frequency of screening; while the red reflex test is recommended at every visit, only 22.8% of our participants adhered to this practice. The majority (75.4%) performed the test only during the initial newborn examination, which increases the risk of overlooking ocular pathologies that may manifest later in infancy. Regarding the technique, the complete absence of mydriatic use among our participants aligns with current national guidelines, which discourage pharmacological dilation in primary care. However, this lack of dilation, while guideline-compliant, further emphasizes the need for high diagnostic proficiency to ensure adequate visualization of the red reflex in undilated pupils.

Regarding referrals, our findings demonstrate a lack of standardization in clinical decision-making and documentation. While nearly one-third of physicians referred infants without detecting specific pathology, a significant majority (76%) failed to complete formal referral forms. Furthermore, most physicians relied on verbal feedback from families rather than structured written reports from ophthalmologists. This breakdown in professional communication hinders the continuity of care and prevents family physicians from effectively monitoring patient outcomes. Establishing standardized referral protocols and feedback loops is essential to ensure a seamless transition between primary care and specialist services.

An encouraging finding was the high willingness (94.2%) of physicians to participate in Ministry of Health-organized training programs. Notably, even those with prior training expressed interest in updated guidance, suggesting a strong recognition of the need for continuous professional development. However, a small minority cited significant barriers to participation, such as high workloads, equipment shortages, and concerns regarding malpractice or professional scope. Addressing these systemic issues within training curricula and health policies is essential to foster broader engagement and ensure the long-term success of national vision screening programs.

Study Limitations

The limitations of this study include its survey-based design and the relatively small number of participants, which may affect the generalizability of the results. In addition, the questionnaire was developed specifically for this research and did not undergo formal statistical validation or reliability testing before administration. Furthermore, the data are based on self-reports from physicians, which may be subject to recall or social desirability bias, potentially leading to an overestimation of actual clinical practices.

Conclusion

This study demonstrates that while family physicians in Turkey possess an awareness of neonatal vision screening, actual practice varies significantly due to structural, educational, and logistical barriers. To bridge this gap, national health policies must prioritize standardized training and improved access to essential equipment, such as direct ophthalmoscopes. Strengthening these pillars, alongside structured referral pathways, is essential to ensure the successful implementation of screening programs and the early detection of preventable childhood blindness.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Influence of Lamellar Keratoplasty on donor trends and eye banking: A longitudinal review from a Turkish tertiary eye bank

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Abstract

Purpose: This study aimed to evaluate trends in the procurement, preservation, and utilization of corneal tissues at a tertiary eye bank in Turkey over a 7-year period.

Methods: A retrospective review of eye bank records was conducted from January 2017 to December 2023. Variables analyzed included donor demographics (age, gender), cause of death, death-to-preservation interval (DPI), voluntary organ donor status, serological test results, preservation-to-utilization interval (PUI), endothelial cell density, donor tissue source, reasons for corneal discards, contamination status, indications for keratoplasty, usage rate of full-thickness vs. split grafts, keratoplasty types, and annual keratoplasty trends.

Results: A total of 775 donors (69% male) and 1342 corneal grafts were analyzed. The mean donor age was 51.35±13.80 years, with the majority aged between 50 and 69 years. Only 5.4% of donors had voluntarily pledged organ donation. Serological screening was negative in 99.2% of cases. The mean DPI was 4.74±2.67 h, and the mean PUI was 4.64 days. The overall corneal utilization rate was 95.5%. Over the study period, the proportion of lamellar keratoplasty increased significantly, while penetrating keratoplasty declined. Logistic regression analysis demonstrated that calendar year was significantly associated with increased use of lamellar keratoplasty (odds ratio: 1.18, 95% confidence interval: 1.11–1.25; p<0.001). Approximately 30% of donor corneas were used in a split manner. The most common indications for transplantation were graft failure, corneal scarring, keratoconus, and bullous keratopathy.

Conclusion: The low rate of voluntary cornea donation and the limited utilization of split graft techniques highlight important areas for improvement and underscore the need for strategies to enhance donor awareness and optimize tissue utilization.

Keywords: Corneal donation, Corneal transplantation, Eye bank, Keratoplasty

Bilateral corneal blindness affects approximately 10 million individuals worldwide, ranking as the third leading cause of blindness following glaucoma and cataracts.[1] Corneal transplantation is the most frequently performed type of transplantation globally, due to the relative ease with which corneal tissue can be harvested postmortem and preserved for extended periods. Nevertheless, there remains a significant disparity between supply and demand, with only one cornea available for every seventy needed.[2]

Eye banks play a critical role in addressing this gap by coordinating the donation, procurement, testing, processing, storage, and distribution of corneal tissue for transplantation. These institutions must not only ensure an adequate supply of donor corneas to meet urgent surgical

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needs but also maintain tissue quality to optimize surgical outcomes and graft survival rates.

In recent years, there has been a paradigm shift from full-thickness (penetrating) keratoplasty to lamellar surgical techniques, such as Descemet Membrane Endothelial Keratoplasty (DMEK) and Deep Anterior Lamellar Keratoplasty (DALK). These advances have enabled the selective use of specific corneal layers, allowing for the transplantation of tissues previously deemed unsuitable due to low endothelial cell counts or stromal scarring. As a result, utilization rates of donated corneas have improved, and in some cases, a single donor cornea can be used to treat multiple recipients.

Several studies have reported statistical data on eye bank operations and donor demographics.[3-7] Such data are invaluable for understanding global trends, evaluating temporal changes in corneal tissue utilization, and informing strategies to address the persistent shortage of transplantable corneas.

The primary aim of this study is to evaluate the impact of the increasing adoption of lamellar keratoplasty techniques on corneal tissue utilization, donor trends, and eye banking practices over a 7-year period at a tertiary eye bank in Turkey.

Materials and Methods

Study Design, Setting, and Data Acquisition

This retrospective, cross-sectional study was conducted at a single tertiary hospital in Turkey and was approved by the institutional Research Ethics Committee. All procedures adhered to the principles outlined in the Declaration of Helsinki (1964) and its subsequent revisions. Eye bank records spanning a 7-year period, from January 2017 to December 2023, were analyzed.

The following variables were extracted and evaluated:

Donor Demographics

Age, sex, year of death, unilateral or bilateral corneal harvesting, cause of death, death-to-preservation interval (DPI), prior voluntary organ donation status, and serology test results.

Donor Cornea Data

Preservation-to-utilization interval (PUI), endothelial cell density (ECD), source of donor tissue, reasons for tissue exclusion, and contamination status.

Graft Utilization

Type and distribution of keratoplasty, surgical indications, full-thickness versus split (lamellar) use, and annual transplantation trends.

Keratoplasty types – including Penetrating Keratoplasty (PKP), DMEK, DALK, and patch grafting – were compared annually. Trends in split graft utilization were also assessed, including whether single donor corneas were used for one or multiple recipients.

Tissue Procurement and Preservation

Donor tissues were obtained from three sources: our hospital, affiliated hospitals, and external eye banks. Corneas registered in our eye bank were either used locally or distributed to other centers based on demand. Donors included both voluntary organ donors and individuals who died in hospital settings; the proportion of voluntary donors was calculated.

All donors were screened in accordance with the Eye Bank Association of America Donor Screening Guidelines. Exclusion criteria included infectious or transmissible diseases, neurodegenerative conditions, ocular infections, corneal pathologies, and risk factors for human immunodeficiency virus (HIV) and hepatitis. Postmortem blood samples were collected and tested for HIV, hepatitis B, and hepatitis C.

Corneal tissue was procured under sterile conditions by trained eye bank technicians. A corneal button with a surrounding scleral rim was excised and placed in a sterile storage container filled with a short-term preservation medium (Eusol-C, Corneal Chamber, Alchimia, Ponte San Nicolò, Italy) and stored at 4°C. Tissue was initially examined under a biomicroscope for transplant eligibility, followed by endothelial cell evaluation using specular microscopy. During transplantation, the preservation medium was routinely cultured to assess for bacterial and fungal contamination.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables were expressed as mean±standard deviation, while categorical variables were presented as frequencies and percentages.

Differences in categorical variables across years were assessed using the Pearson Chi-square test. Temporal trends in keratoplasty techniques, particularly the proportion of lamellar versus penetrating keratoplasty, were further evaluated using a Chi-square test for trend. To evaluate temporal changes in surgical techniques, logistic regression analysis was performed with lamellar keratoplasty utilization (DMEK or DALK vs. PKP) as the

dependent variable and calendar year as the independent variable. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Selected donor characteristics and temporal changes in transplantation techniques were illustrated using graphical representations. A two-tailed $p<0.05$ was considered statistically significant.

Results

A total of 775 corneal donors (69% male) and 1342 grafts harvested from them were included in the analysis. The mean donor age was 51.35±13.80 years, with the majority (62.44%) falling within the 50–69-year age group (Table 1 and Fig. 1). Bilateral (double) corneal retrieval was performed in 74.1% of cases. Throughout the study period, only 5.4% of donors were registered voluntary cornea donors, while the remainder were either hospital-based deaths or postmortem donations obtained through forensic autopsies. Serological testing for HIV, hepatitis B, and hepatitis C was negative in 99.2% of donor blood samples.

The DPI – defined as the time from donor death to placement of the cornea in preservation medium – averaged 4.74 ± 2.67 h (Table 1). Of the corneal tissues retrieved, 57.08% were preserved within 2–5 h postmortem, 30.25% within 6–10 h, and 3.68% within 11–15 h following death. The leading cause of donor death was acute cardiac arrest (55.5%), followed by other causes summarized in Table 2.

Table 1. Demographic and clinical characteristics of the donors, *n*=775

Variable	Value
Age (years)	51.35±13.80 (range: 6-84)
Gender, *n* (%)	
Female	240 (31.0)
Male	535 (69.0)
Death-to-preservation interval, h	4.74±2.67 (range: 1–15)
PUI (days) mean±SD	4.64±2.93 (range: 1–20)
Number of eyes used, *n* (%)	
Single graft	201 (25.9)
Double graft	574 (74.1)
Volunteer organ donor, *n* (%)	42 (5.4)
Serology results, *n* (%)	
Negative	769 (99.2)
HBsAg+	4 (0.5)
HCV+	1 (0.1)
Other	1 (0.1)
ECD (mean±SD)	3055.33±401.59
Graft contamination, *n* (%)	5 (0.4)
Graft destruction, *n* (%)	61 (4.5)

Values are presented as mean±SD or number (%). ECD: endothelial cell density; SD: standard deviation; PUI: preservation-to-utilization interval; HBsAg: Hepatitis B surface antigen

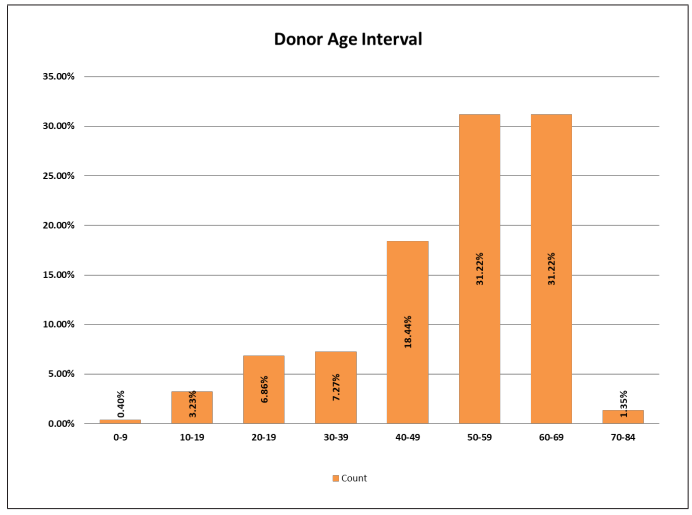

Fig. 1. Percentage distribution of age ranges of donors.

Annual analysis of donor cornea retrieval showed a marked decrease in 2020, attributed to the COVID-19 pandemic. In other years, procurement numbers remained relatively stable (Fig. 2). While 34.28% of corneal tissues were sourced from external hospitals, the majority originated from our institution and affiliated centers. Donor grafts were discarded due to graft damage (1%), hepatitis B surface antigen positivity (0.8%), corneal scarring or haze (0.7%), and the presence of infection (0.4%). Of the usable grafts, 64.7% were utilized within our clinic, and 30.8% were distributed to other healthcare institutions. The mean PUI was 4.64 days (range, 1–20). A total of 53.46% of the grafts were utilized within the first 4 days of storage, 39.76% between 5 and 9 days, and 6.40% between 10 and 14 days. Additional corneal tissue parameters are also detailed in Table 1.

Trends in keratoplasty techniques revealed a decline in the use of PKP over the years, with a notable rise in DMEK, particularly in 2022 and 2023. DALK procedures were performed at relatively lower rates between 2020 and 2022 but remained stable in other years (Fig. 3).

While 70.16% of donor corneal grafts were used as full-thickness grafts for penetrating keratoplasty, 29.84% were utilized in a split manner for lamellar keratoplasty. Of the split grafts, 24.61% were utilized in a single recipient for either DMEK or DALK, while 5.23% were allocated to two different recipients, enabling split graft utilization of a single donor cornea. Transplantation indications are summarized in Table 3. The most common indications included

Table 2. Causes of donor death

Cause of donor death	*n (%)*
Acute cardiac arrest	417 (55.5)
Heart failure	55 (7.3)
Cancers	36 (4.8)
Gunshot wound	24 (3.2)
Cerebral hemorrhage	59 (7.8)
Accidents/falls	52 (6.9)
Mechanical asphyxia (suicide)	16 (2.1)
Acute respiratory failure	22 (2.9)
Aortic aneurysm rupture	12 (1.6)
Pulmonary embolism	6 (0.8)
Death by stabbing	4 (0.5)
Intoxication	5 (0.7)
Pneumonia	7 (0.9)
Ileus	5 (0.7)
Acute renal failure	10 (1.3)
Gastrointestinal bleeding	9 (1.2)
Chronic renal failure	5 (0.7)
Drowning in water	2 (0.3)
Portal vein thrombosis	1 (0.1)
Liver failure	1 (0.1)
Death from unknown cause	4 (0.5)

graft failure, corneal scarring, keratoconus, and bullous keratopathy. Yearly trends of the top five indications are presented in Table 4. Notably, keratoconus was a leading indication in 2017 and 2018 but declined in subsequent years, whereas graft failure emerged as the most frequent indication from 2019 onward.

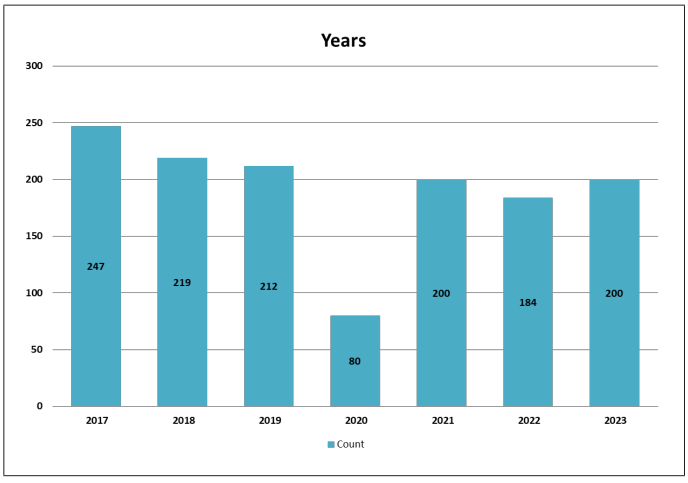

Fig. 2. Numbers of corneas received from donors by year.

Table 3. Indications for corneal transplantation of donor corneas

Indication	*n (%)*
Graft failure	274 (22.8)
Corneal scar	242 (20.1)
Keratoconus	212 (17.6)
Bullous keratopathy	202 (16.8)
Corneal stromal dystrophy	87 (7.2)
Perforation/melting	66 (5.5)
Fuchs dystrophy	22 (1.8)
Infection	16 (1.3)
CHED	6 (0.5)
Post-operative ectasia	5 (0.4)
Other	8 (0.7)
Unknown	63 (5.2)

Analysis of temporal trends demonstrated a progressive increase in the use of lamellar keratoplasty techniques over the study period. The proportion of lamellar procedures (DMEK and DALK) increased from 17.4% in 2017 to 41.5% in 2023, indicating a significant upward trend (p for trend <0.001).

Logistic regression analysis further confirmed that calendar year was significantly associated with lamellar keratoplasty utilization. Each additional year was associated with an approximately 18% increase in the likelihood of performing lamellar keratoplasty (OR: 1.18, 95% CI: 1.11–1.25; p<0.001). These findings indicate a significant temporal shift in surgical practice toward lamellar keratoplasty techniques during the study period.

Discussion

In Turkey, all eye bank records are registered within the Transplantation, Dialysis, and Monitoring System, operated

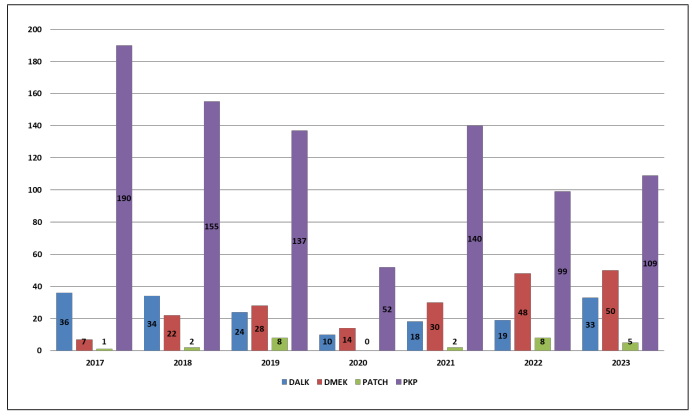

Fig. 3. Keratoplasty rates by year.

Table 4. Change in indication rates over the years

Indication	2017	2018	2019	2020	2021	2022	2023
Keratoconus *n* (%)	49 (24.3)	46 (22.5)	35 (17.2)	16 (21.3)	33 (17.1)	19 (10.3)	32 (16.1)
Dystrophy *n* (%)	19 (9.4)	16 (7.8)	9 (4.4)	3 (4)	12 (6.2)	9 (4.9)	23 (11.6)
Corneal scar *n* (%)	48 (23.8)	50 (24.5)	42 (20.6)	12 (16)	27 (14)	39 (21.2)	33 (16.6)
Graft failure *n* (%)	36 (17.8)	46 (22.5)	46 (22.5)	19 (25.3)	46 (23.8)	43 (23.4)	49 (24.6)
Bullous keratopathy *n* (%)	29 (14.4)	23 (11.3)	35 (17.2)	13 (17.3)	39 (20.2)	38 (20.7)	38 (19.1)

CHED: Congenital hereditary endothelial dystrophy

by the Ministry of Health.[8] According to the most recent data, there are 49 authorized eye banks and 657 corneal transplant centers nationwide.[9] Between 2017 and 2023, a total of 23,130 corneal transplantations were performed in the country, averaging approximately 3,300/year. As of 2021 (the latest available national data), 1,204 patients remained on the corneal transplant waiting list.[9,10] During the same 7-year period, our eye bank performed 1,281 corneal transplantations using 1,342 registered grafts, accounting for 5.5% of all procedures performed nationally. Although annual cornea procurement rates in this study are consistent with findings from other centers in Turkey and globally. [7,11,12], higher procurement volumes have been reported elsewhere.[6] In our series, an average of 210 transplantations were conducted annually, with a notable decline in 2020 due to the COVID-19 pandemic. This trend parallels national data, which also showed a decrease in corneal procurement and transplantation during that year.[8]

The mean age of donors in our study was 51.35±13.80 years, with the majority aged between 50 and 69 years, and predominantly male. These findings are consistent with global reports indicating a mean donor age over 50 years in most countries.[13,14] In contrast, studies reporting younger donor demographics often attribute this to trauma-related deaths, including traffic accidents or violence.[5,15,16] In our cohort, the most common cause of death was acute cardiac arrest. While most studies indicate a male donor predominance,[4,5,12,13] one study noted a higher proportion of preregistered female donors with a younger mean age.[17]

In modern corneal transplantation, donor corneas are preserved using various techniques, and with the increasing adoption of lamellar keratoplasty, a single donor cornea may be divided into two partial grafts for transplantation in separate recipients. In split graft utilization, the anterior stromal portion is used for DALK, while the posterior Descemet membrane–endothelium complex is allocated for DMEK. In the present study, 70% of donor corneas were used as full-thickness grafts. Among split grafts, 24.61% were utilized for a single recipient, whereas only 5.23% were successfully allocated to two different recipients. While no significant temporal trend was observed for DALK, DMEK procedures increased markedly after 2020, with each successive year associated with a 34% increase in the likelihood of DMEK use.

Importantly, the relatively low rate of dual-recipient split graft utilization should be interpreted in the context of the absence of pre-cut and pre-loaded DMEK tissue infrastructure in Turkey. Unlike eye banking systems in Europe and North America, where lamellar grafts are routinely prepared and distributed by eye banks, endothelial graft preparation in our setting must be performed intraoperatively by the surgeon through manual separation of the endothelium from the stroma. This approach increases surgical complexity and carries an inherent risk of graft loss, particularly during the early learning curve. Consequently, posterior lamellar tissues may be discarded when intraoperative separation fails, limiting effective split graft utilization despite adequate donor availability and tissue quality.

Previous studies have demonstrated that the use of eye bank–prepared tissues reduces intraoperative complexity, shortens surgical time, and minimizes graft preparation–related failures.[18] Moreover, centralized preparation of split grafts within the eye bank has been shown to improve tissue utilization, surgical efficiency, and safety.[19] The potential impact of such infrastructure is illustrated by Oganesyan *et al.*[20] who reported successful transplantation of five recipients from a single donor cornea using anterior lamellar keratoplasty and quarter-DMEK techniques.

The interval between death and corneoscleral button retrieval, the timing of postmortem blood sample collection, and the duration of tissue storage are considered critical factors influencing graft quality and safety.[21] Previous studies have indicated that a DPI exceeding 6 h is associated with an increased risk of donor epithelial

sloughing, potentially compromising tissue integrity.[22] Moreover, delayed blood sampling – beyond 12 h postmortem – has been correlated with a higher incidence of serology-positive results, increasing the likelihood of tissue discard.[21] In the present study, the mean DPI was 4.74±2.67 h, with 57.08% of corneas retrieved between 2 and 5 h postmortem. Notably, 77.3% of donor eyes were harvested within 6 h of death, aligning with recommended timeframes for optimal preservation. While DPI durations reported in some studies from India range from 3.5 to 3.9 h on average, [5,15] significantly longer intervals have been observed in studies from other countries, with reported DPIs ranging from 10.2 to 72 h.[16,23]

According to the regulations of the United States Food and Drug Administration, corneal tissues can be preserved in storage media for up to 14 days.[24] The Cornea Preservation Time Study, a multicenter clinical trial conducted by Rosenwasser *et al.*[25] in 2017, demonstrated that donor corneas remain suitable for transplantation for up to 11 days, ensuring favorable outcomes in terms of graft survival and visual restoration. In the present study, the mean PUI was 4.64 days. A total of 53.46% of the grafts were used within the first 4 days post-preservation, and 93.22% within the first 9 days. Only five corneas were utilized between 15 and 20 days of preservation. The rare use of corneas beyond 14 days may be attributed to logistical challenges, such as intercity transfer of corneal tissue, or delays related to the transportation and surgical preparation of patients scheduled for transplantation.

In the current study, only 5.4% of donors were registered voluntary cornea donors. The remaining tissues were obtained from individuals who had died in hospitals or had undergone autopsy at the forensic medicine institution. Practices related to organ and tissue donation differ substantially across countries due to varying legal, cultural, and ethical frameworks. For example, in China, regulations allow family members to veto organ and tissue donations from deceased relatives, regardless of prior consent.[17] In Germany, organ and tissue retrieval is permitted only if the deceased had provided explicit consent during their lifetime or if family members authorize donation based on the presumed wishes of the deceased.[6] According to the Regulation on Organ and Tissue Transplantation Services published in Turkey in 2000, corneal tissue – being a non-disfiguring tissue – may be procured without explicit consent, unless the deceased had previously refused donation. In a study by Sharma *et al.*,[14] it was reported that 59.6% of corneal tissues were obtained through voluntary eye donation (VED), while 40.4% came from the hospital cornea retrieval program. Compared to such findings, the voluntary donation rate in our eye bank appears to be considerably low, underscoring the need for increased public awareness and donor registration efforts.

In the present study, the overall corneal tissue utilization rate was 95.5%. The most common reasons for graft discard were mechanical damage to the tissue (1%) and positive serological test results (0.8%). This high utilization rate can be attributed to the rigorous pre-screening process conducted by experienced eye bank technicians, who exclude contraindicated donors before tissue retrieval. In addition, strict adherence to aseptic techniques during tissue procurement and minimizing the duration of storage before transplantation likely contributed to the increased utilization rate. Corneal utilization rates reported in previous studies vary significantly across countries. For instance, a study involving 12 eye banks in India reported a utilization rate of 50.5%.[14], while studies from China and New Zealand documented rates of 65%.[17] and 88%.[16] respectively. In a global analysis covering 82 countries, Gain *et al.*[2] reported an average utilization rate of 65.1%. Lower utilization rates in developing countries have been primarily attributed to two factors: (1) The prevalent use of McCarey–Kaufman medium for corneal storage instead of organ culture systems, and (2) the predominance of therapeutic and emergency keratoplasties in these regions, for which shorter-term storage solutions are sufficient. In contrast, elective corneal transplantation procedures are more commonly performed in Europe and the United States, where long-term storage methods are more widely available and routinely used.[14]

In the present study, 0.8% of donor tissues were found to be seropositive based on routine serological testing. Reported seropositivity rates vary widely, ranging from 1.44% to 10.5% in studies conducted in Turkey,[7,11] and from 1.82% to as high as 27.4% in international studies.[16,18,26,27]

Regarding indications for corneal transplantation, the most common clinical indications in our cohort were graft failure (22.8%), corneal scarring (20.1%), keratoconus (17.6%), and bullous keratopathy (16.8%). In comparison, a study from New Zealand identified keratoconus as the leading indication (41.1%), followed by regrafts (17.0%), aphakic/pseudophakic bullous keratopathy (13.9%), and corneal dystrophies (10.7%).[4] Regional variation in transplantation indications is evident across the literature. While keratoplasty is most frequently performed for infectious keratitis in studies from China and India,[17,14] keratoconus remains the predominant indication in Western countries.

[4,28] In a global survey by Gain *et al.*,[2] the most common indications were Fuchs endothelial dystrophy (39%), followed by keratoconus (27%) and sequelae of infectious keratitis (20%).

As the indications for keratoplasty evolve, the rate of endothelial keratoplasty (EK) and consequently, the use of split graft has increased significantly in developed countries.[28,29] However, PKP remains the predominant technique in many Asian countries.[14,30] In the present study, although PKP remained the most frequently performed surgical procedure, a declining trend was observed over the years, while DMEK procedures increased progressively. This temporal shift toward lamellar techniques was also supported by regression analysis, which demonstrated a significant year-to-year increase in the likelihood of lamellar keratoplasty. Despite this trend, the overall rate of split graft utilization remains low.

Taken together, these findings suggest that corneal transplantation practices in Turkey share characteristics reported in both developing and high-income eye banking systems, rather than fitting strictly within either category. Similar to trends reported in Europe and North America, our data demonstrate a gradual shift from penetrating keratoplasty toward EK, particularly DMEK. However, in contrast to countries with well-established eye bank infrastructures where split graft utilization and pre-cut or pre-loaded lamellar tissues are routinely available, the overall rate of split graft use in our cohort remains relatively low. This difference appears to be driven not primarily by donor availability or tissue quality, but rather by structural and technical factors such as limited access to eye bank–prepared lamellar grafts and the intraoperative preparation burden placed on surgeons. These observations suggest that, while surgical practice patterns in Turkey are evolving in parallel with global trends, further optimization of eye banking infrastructure is required to fully translate these advances into improved tissue utilization.

This study has several limitations that should be considered when interpreting the findings. First, the retrospective design may introduce potential sources of bias, including information bias and residual confounding. Second, the study was conducted at a single tertiary referral center, and donor selection as well as tissue procurement practices may have been influenced by local eye bank protocols, which could introduce selection bias and limit the generalizability of the results. Although eye bank records were systematically reviewed, the possibility of incomplete documentation inherent to retrospective data collection cannot be entirely excluded; cases with incomplete records were therefore excluded from the relevant analyses as described in the methods section. In addition, unmeasured factors such as surgeon experience, institutional case mix, and referral patterns may have influenced the observed temporal trends. Split graft utilization in our cohort may also have been affected by the learning curve associated with manual intraoperative preparation of lamellar grafts, as graft splitting was performed by surgeons rather than prepared centrally by the eye bank. Despite these limitations, the relatively large donor cohort and the extended observation period provide valuable insight into temporal trends in corneal transplantation and eye bank utilization. Nevertheless, the observed increase in lamellar keratoplasty techniques likely reflects evolving surgical preferences and advances in EK rather than changes in donor characteristics.

Conclusion

This study provides a 7-year analysis of donor demographics, tissue utilization patterns, surgical indications, and keratoplasty trends in a tertiary eye bank in Turkey. Although the high corneal utilization rate reflects efficient tissue use, the persistently low rate of VED and the limited use of split graft techniques highlight important areas for improvement. Efforts should therefore focus on increasing public awareness of organ and tissue donation and strengthening the infrastructure required for the preparation and distribution of precut and preloaded lamellar grafts. Such measures may improve tissue availability, enhance graft utilization, and ultimately reduce waiting times for corneal transplantation.

Ethics Committee Approval: This study was approved by The University of Health Sciences Ankara Training and Research Hospital (project number: E-24-128)

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Peripapillary microvasculature and retinal nerve fiber layer thickness in active and quiescent phases of intermediate uveitis

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Abstract

Purpose: Optic nerve head changes can be observed due to direct involvement or as a result of complications of intermediate uveitis (IU) and can lead to visual impairment. The purpose of this study was to investigate retinal nerve fiber layer thickness (RNFLT) and microvasculatory changes in the peripapillary region, and to determine their relationship with disease activity.

Methods: This study was a cross-sectional analysis. The peripapillary RNFLT and radial peripapillary capillary (RPC) vessel densities (VDs) of IU patients, presented to our clinic between December 2017 and March 2023, were retrospectively analyzed using optical coherence tomography angiography (Avanti RTVue-XR; Optovue, Fremont, CA) and compared with healthy subjects.

Results: Twenty-eight eyes with IU (12 in active, 16 in quiescent phase) and 23 healthy control eyes were included. Decreased RPC VDs were observed in the quiescent phase of IU compared with the healthy control group in the whole image, superior hemisphere, and inferior hemisphere areas (p=0.002, p=0.003, and p=0.007, respectively). Peripapillary VD values were reduced in the quiescent phase compared with the active phase and control eyes (p=0.013 and p=0.002, respectively). No significant differences were observed between the active and control groups (p>0.05 for all). Increased RNFLT was observed in the active phase compared with quiescent and control groups (p<0.001).

Conclusion: RNFLT increases during the active phase of IU due to possible inflammation in the peripapillary area, whereas vascular parameters do not change quantitatively. In the quiescent phase, the resolution of inflammation and possible permanent vascular changes may affect the vascular structure.

Keywords: Glaucoma, Intermediate uveitis, Optical coherence tomography, Vascular density

The persistent inflammation of the ciliary body, anterior vitreous, and peripheral retina is referred to as intermediate uveitis (IU).[1] Although the disease is generally considered to have a favorable course, ocular complications are reported in the majority of patients.[1] Optic nerve head changes can be observed due to direct involvement or as a result of complications of the disease. In general, the incidence of glaucoma in acute uveitis is 7.6%, and in chronic uveitis, it is 11.1% at 5 years.[2] In patients with IU, glaucoma is reported as a frequent complication and is most substantially associated with worse visual acuity compared with other complications of the disease.[3-5] Apart from glaucomatous damage, IU can also cause direct optic nerve involvement, resulting in peripapillary changes depending on the underlying disease.[3] Although rarely reported, peripapillary choroidal neovascularization (CNV) can also be observed in these patients.[6]

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Optical coherence tomography angiography (OCTA) has gained popularity and become a widely used non-invasive imaging modality to assess retinal vessel density (VD). Peripapillary microvascular changes have been reported in a wide range of neuro-ophthalmologic pathologies, including papilledema, optic neuropathy, multiple sclerosis, papillitis, and glaucoma.[7] OCTA is also a rapid and non-invasive method for detecting peripapillary CNV formations.[8] Based on this, peripapillary OCTA findings may be useful in the follow-up of patients with IU. However, there is limited data in the literature regarding OCTA findings in IU. Previously decreased macular VD was shown.[9-11] Microvascular changes in the peripapillary region, however, have not yet been investigated.

IU can directly or indirectly affect the optic nerve head and may predispose to elevated intraocular pressure and glaucoma; therefore, the evaluation of peripapillary microvasculature is of particular clinical relevance.[12,13] Retinal nerve fiber layer thickness (RNFLT) measurements alone may be confounded by inflammatory changes, and OCTA provides complementary information by visualizing microvascular alterations. Therefore, investigating peripapillary OCTA findings in IU could enhance our understanding of disease-related optic nerve involvement and support more accurate monitoring of patients at risk of glaucomatous damage.[14,15]

In this study, our purpose was to evaluate RNFLT and optic nerve head microvasculature using OCTA, and to determine the relationship of any observed changes with disease activity.

Materials and Methods

This was a cross-sectional study conducted at a tertiary hospital in adherence to the Declaration of Helsinki. The study was ethically approved by the local ethics committee of our institution (Project number: KA23/171-Date: May 09, 2023). Patients who were examined at the uvea department and diagnosed with IU between December 2017 and March 2023 were enrolled in the study. Age-matched healthy controls were also included. Written informed consent was obtained from all patients. Only one eye of each subject was included in the analysis. When both eyes were eligible, one eye was randomly selected for analysis.

The diagnosis of IU was based on the criteria established by the Standardization of Uveitis Nomenclature (SUN) Working Group.[16] Disease activity was assessed clinically using the National Eye Institute "Vitreous Haze Score" system published in 1985 and fundus fluorescein angiography findings.[17] All patients diagnosed with IU were screened for sarcoidosis, Lyme disease, syphilis, multiple sclerosis, and tuberculosis. As part of the baseline examination, the following tests were performed: Complete blood count, venereal disease research laboratory test, erythrocyte sedimentation rate, purified protein derivative test for tuberculosis, chest radiography, serum lysozyme and angiotensin-converting enzyme levels, Borrelia serology, and brain magnetic resonance imaging. Additional tests, including Bartonella henselae serology, toxocara serology, pulmonary computed tomography, and human leukocyte antigen typing, were performed when necessary.

Exclusion criteria included the presence of systemic vascular diseases (hypertension, diabetes, cardiovascular disease), spherical equivalents ≥6 diopters, any history of ocular trauma, intraocular surgery within the 12 months before study enrollment, congenital or acquired ocular disorders unrelated to IU, prior anti-vascular endothelial growth factor injections, glaucomatous peripapillary changes on clinical examination, and intraocular pressure readings >20 mmHg by applanation tonometry.

Three groups were formed according to the SUN Working Group criteria.[16] The active group included eyes with active IU; the quiescent group included eyes with inactive IU; and the control group included healthy eyes of subjects with similar demographic characteristics. Data on demographic characteristics, related systemic diseases, systemic and ocular medical history, follow-up time, best-corrected visual acuity, Goldmann applanation tonometry values, and detailed biomicroscopic and fundoscopic findings were retrieved from the patients' medical records. Available multimodal imaging results – including fundus photography, spectral domain optical coherence tomography (OCT), fundus fluorescein angiography, and OCTA – were also evaluated. The same uveitis specialist examined all patients, and the same ophthalmology technician captured all OCTA images. The OCTA scans were assessed by a blinded, experienced clinician for image quality, motion artifacts, and segmentation errors.

OCTA scans were captured using the RTVue XR Avanti device, version 2017.1.0.151 (Avanti RTVue-XR; Optovue, Fremont, CA), following the standardized protocol based on the split-spectrum amplitude-decorrelation algorithm. The peripapillary region was scanned in a 4.5 × 4.5 mm square area. VD in the peripapillary region and its sectors was automatically analyzed by software using two concentric rings centered on the optic nerve head, with diameters of 2 mm and 4 mm. The intrapapillary region was defined as

the area within the inner circle, whereas the area between the inner and outer rings was defined as the peripapillary region.[18]

Radial peripapillary capillary (RPC) VD was automatically segmented between the inner limiting membrane and the retinal nerve fiber layer using the AngioVue disc mode of the device. The parameters evaluated included whole-image VD, inside disc VD, and peripapillary VD. Sectoral analysis of the peripapillary region also included superior and inferior hemisphere VDs, as well as nasal superior, nasal inferior, inferior nasal, inferior temporal, temporal inferior, temporal superior, superior temporal, and superior nasal VDs. Peripapillary RNFLT in the same sectors was simultaneously measured using the inner optic nerve head analysis mode of the Angio DiscVue software. A signal strength ≥6/10 in OCTA scans was considered eligible for analysis. The OCTA images with poor quality or artifacts were excluded from the study. All quantifications were automated.

Statistical Analysis

IBM's Statistical Package for the Social Sciences, version 25.0; Chicago, IL, USA was used for the statistical analyses. The Shapiro–Wilk test was used to assess the normality of the data. As the group data were not normally distributed, non-parametric tests were employed in the analysis. For descriptive statistics of quantitative variables, mean values with standard deviation and median values with interquartile range were reported. For categorical variables, the number of cases with percentages was provided. The Kruskal–Wallis variance analysis test was used to analyze differences between groups. The Mann–Whitney U test with Bonferroni-adjusted alpha values was used to identify specific group differences. In all analyses, a significance threshold of $p<0.05$ was applied.

Results

The medical records of 43 patients with IU were reviewed retrospectively. Fifteen patients were excluded at initial evaluation due to inadequate OCTA image quality caused by vitreous inflammation. A total of 28 eyes from 28 patients with IU who fulfilled the inclusion criteria and 23 eyes from 23 healthy control subjects were enrolled. Among the IU group, 12 eyes were evaluated as having active disease and 16 as quiescent. The demographic characteristics of the subjects are presented in Table 1. The groups were similar in terms of age, gender distribution, and spherical equivalent values (p=0.257, p=0.899, and p=0.099, respectively). The mean intraocular pressures were also comparable among the groups: 16.00±3.24 mmHg in the active group, 15.28±2.52 mmHg in the quiescent group, and 15.74±2.45 mmHg in the control group (p=0.685).

The etiologies of IU in our study included 10 patients with sarcoidosis (8 definite ocular sarcoidosis and 2 presumed ocular sarcoidosis), 6 with multiple sclerosis, 2 with presumed tuberculosis, and 2 with pars planitis. The remaining 8 patients had idiopathic IU. Treatments at the time of data collection were as follows: 6 patients were receiving only azathioprine, 2 were receiving both

Table 1. The demographic characteristics of the subjects

Variable	Active IU group (*n*=12)	Quiescent IU group (*n*=16)	Control group (*n*=23)	*p*
Age (years) (Mean±SD)	27.67±19.46	39.75±22.09	35.65±16.89	0.257*
Sex				0.899**
Female (*n*/%)	8 (66.7)	10 (62.5)	16 (69.6)	
Male (*n*/%)	4 (33.3)	6 (37.5)	7 (30.4)	
Spherical equivalent (Diopter) (Mean±SD)	−0.27±1.02	−0.78±0.74	−0.85±1.09	0.099*
Intraocular pressure (mmHg) (Mean±SD)	16.00±3.24	15.28±2.52	15.74±2.45	0.685
Disease duration (months) Median (IQR)	39.00 (3.00–89.00)	117.50 (22.25–124.75)		0.027***
Etiology				
Idiopathic (*n*/%)	6 (75)	2 (25)	N/A	N/A
Sarcoidosis (*n*/%)	4 (40)	6 (60)	N/A	N/A
Multiple sclerosis (*n*/%)	2 (33.3)	4 (66.6)	N/A	N/A
Pars planitis (*n*/%)	0	2 (100)	N/A	N/A
Tuberculosis (*n*/%)	0	2 (100)	N/A	N/A

*Kruskal–Wallis test; **Chi-square test; ***Mann–Whitney U test. IU: Intermediate uveitis; IQR: İnterquartile range; SD: Standard deviation; N/A: Not applicable

azathioprine and prednisolone, 2 were receiving infliximab, prednisolone, and cyclosporine, 2 were receiving only prednisolone, 2 were receiving infliximab, 2 were receiving azathioprine and cyclosporine, and 2 patients were under glatiramer acetate treatment. Ten patients were not receiving any medication.

At the time of data collection, 16 eyes were in the quiescent phase, with no evidence of vitreous haze, cells, or vascular leakage, whereas 12 eyes were in the active phase. Of the active cases, 4 eyes had 2+ vitritis and segmental vascular leakage; 2 had 3+ vitritis with peripheral vascular leakage and optic disc hyperfluorescence; 2 had 1+ vitreous haze and peripheral vascular leakage; and 4 had 1+ vitritis with peripheral vascular leakage and optic disc hyperfluorescence.

The peripapillary OCTA VD values and comparisons are presented in Table 2. Statistically significant differences were observed among the three groups in whole image, peripapillary, superior, and inferior hemisphere VD values (p=0.007, p=0.004, p=0.008, and p=0.020, respectively). In sectoral peripapillary VD analysis, significant differences were noted in inferior temporal, temporal inferior, and temporal superior VD values (p=0.012, p=0.010, and p=0.001, respectively). Further pairwise comparisons revealed decreased RPC VD values in the quiescent group compared with the control group in the whole image, superior, and inferior hemispheres (p=0.002, p=0.003, and p=0.007, respectively). Peripapillary VD values were also decreased in the quiescent group compared with the active

Table 2. The radial peripapillary capillary vessel densities of the subjects measured by optical coherence tomography angiography

Vessel density (%)	Active IU group (n=12) Median (IQR) Minimum-maximum	Quiescent IU group (n=16) Median (IQR) Minimum-maximum	Control group (n=23) Median (IQR) Minimum-maximum	p
Whole image	50.40 (3.00) 46.60–53.60	49.00 (3.33) 39.60–51.70	51.05 (2.92) 44.70–53.50	**0.007**[a], 0.045[b], 0.504[c], **0.002**[d]
Inside disc	45.50 (12.65) 28.30–52.90	47.55 (5.95) 36.90–52.90	50.30 (7.30) 38.10–59.30	0.077[a]
Peripapillary	54.10 (3.05) 47.10–55.80	50.95 (2.98) 38.40–53.70	53.10 (3.52) 47.60–56.20	**0.004**[a], **0.013**[b], 0.849[c], **0.002**[d]
Superior hemi	52.70 (3.75) 45.90–55.80	50.45 (2.67) 41.40–54.10	53.25 (2.65) 47.00–56.30	**0.008**[a], 0.038[b], 0.593[c], **0.003**[d]
Inferior hemi	54.90 (5.15) 48.40–57.40	51.30 (4.05) 35.10–53.20	53.40 (4.70) 48.30–57.00	**0.020**[a], 0.051[b], 0.804[c], **0.007**[d]
Nasal superior	51.30 (3.70) 48.40–53.90	49.05 (4.05) 41.40–53.90	50.65 (4.88) 44.80–57.70	0.061[a]
Nasal inferior	52.40 (3.75) 45.80–56.80	48.90 (5.80) 36.90–53.10	49.50 (5.35) 43.80–55.80	0.089[a]
Inferior nasal	51.00 (5.35) 43.10–56.40	50.90 (6.20) 33.90–56.00	50.90 (7.65) 45.20–59.00	0.406[a]
Inferior temporal	59.00 (6.60) 37.70–64.50	56.50 (4.25) 39.40–61.80	59.90 (6.65) 52.30–65.70	**0.012**[a], 0.126[b], 0.260[c], **0.003**[d]
Temporal inferior	56.80 (4.95) 50.70–60.00	51.75 (9.17) 28.20–57.00	53.00 (4.90) 48.10–59.80	**0.010**[a], **0.006**[b], 0.208[c], 0.027[d]
Temporal superior	57.40 (4.60) 54.90–63.20	54.30 (5.77) 40.50–57.60	55.80 (4.30) 51.50–63.10	**0.001**[a], **<0.001**[b], 0.056[c], **0.011**[d]
Superior temporal	54.20 (5.45) 41.90–60.40	53.40 (5.92) 44.10–59.10	57.00 (3.38) 43.30–60.50	0.050[a]
Superior nasal	49.10 (7.70) 31.20–56.80	48.70 (4.35) 39.70–52.20	49.75 (5.35) 40.20–56.70	0.346[a]

IQR: interquartile range; IU: Intermediate uveitis. All reported pairwise P-values are Bonferroni-adjusted. [a]Statistical significance in Kruskal–Wallis test (comparison among three groups) (P<0.05 is significant). [b]Statistical significance of pairwise comparison between active and quiescent groups (Mann–Whitney U test) (p<0.017 is significant). [c]Statistical significance of pairwise comparison between active and control groups (Mann–Whitney U test) (p<0.017 is significant). [d]Statistical significance of pairwise comparison between quiescent and control groups (Mann–Whitney U test) (p<0.017 is significant)

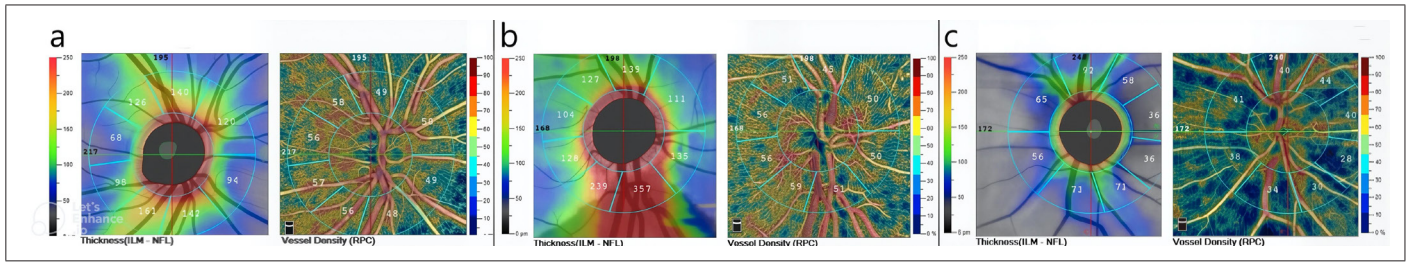

Fig. 1. The peripapillary optical coherence tomography angiography images of **(a)** a healthy control subject, **(b)** a patient with active intermediate uveitis (IU), **(c)** a patient with quiescent IU. The increase in retinal nerve fiber layer thickness of the patient with active IU and the decrease in vascular density of the patient with quiescent IU are observed.

and control groups (p=0.013 and p=0.002, respectively). No significant differences were observed between the active and control groups (p>0.05 for all).

When sectoral peripapillary VDs were evaluated, temporal inferior and temporal superior VDs were significantly decreased in the quiescent group compared with the active group (p=0.006 and p<0.001, respectively). In addition, inferior temporal and temporal superior VDs were significantly reduced in the quiescent group compared with the control group (p=0.003 and p=0.011, respectively). Peripapillary OCTA image comparisons of eyes in the active phase, quiescent phase, and a healthy control eye are shown in Figure 1. Overall, our results indicate that peripapillary VD reduction was observed in the quiescent phase of IU, whereas VD values in the active phase were comparable to those of healthy controls.

Table 3. The retinal nerve fiber layer thickness of the subjects measured by optical coherence tomography angiography device

Retinal nerve fiber layer thickness (µ)	Active IU group (n=12) Median (IQR) Minimum-maximum	Quiescent IU group (n=16) Median (IQR) Minimum-maximum	Control group (n=23) Median (IQR) Minimum-maximum	p
Peripapillary	174.00 (87.00) 106.00–297.00	106.00 (18.00) 90.00–145.00	107.00 (14.00) 93.00–132.00	**<0.001**[a], <**0.001**[b], **<0.001**[c], 0.616[d]
Superior hemi	149.00 (94.00) 101.00–325.00	99.00 (18.00) 92.00–143.00	107.00 (13.00) 93.00–134.00	**0.001**[a], **0.001**[b], **0.002**[c], 0.174[d]
Inferior hemi	196.00 (69.00) 111.00–267.00	111.00 (21.00) 83.00–149.00	108.00 (18.00) 93.00–139.00	**<0.001**[a], **<0.001**[b], **<0.001**[c], 0.742[d]
Nasal superior	173.00 (92.00) 110.00-321.00	99.00 (20.00) 85.00–128.00	108.00 (19.00) 77.00–134.00	**<0.001**[a], **<0.001**[b], **<0.001**[c], 0.058[d]
Nasal inferior	154.00 (68.00) 93.00–254.00	91.00 (45.00) 60.00–133.00	88.00 (20.00) 54.00–149.00	**<0.001**[a], **<0.001**[b], **<0.001**[c], 0.952[d]
Inferior nasal	294.00 (112.00) 98.00–342.00	139.00 (39.00) 99.00–202.00	139.00 (36.00) 89.00–210.00	**0.001**[a], **0.001**[b], **<0.001**[c], 0.622[d]
Inferior temporal	228.00 (82.00) 94.00–346.00	156.00 (37.00) 108.00–185.00	143.00 (23.00) 111.00–182.00	**0.003**[a], **0.004**[b], **0.001**[c], 0.455[d]
Temporal inferior	114.00 (24.00) 83.00–166.00	69.00 (6.00) 52.00–85.00	68.00 (19.00) 53.00–101.00	**<0.001**[a], <**0.001**[b], **<0.001**[c], 0.976[d]
Temporal superior	121.00 (25.00) 67.00–182.00	73.00 (18.00) 57.00–112.00	75.00 (12.00) 60.00–91.00	**<0.001**[a], **<0.001**[b], **<0.001**[c], 0.788[d]
Superior temporal	173.00 (114.00) 64.00–363.00	119.00 (25.00) 89.00–174.00	132.00 (19.00) 100.00–175.00	**0.035**[a], 0.031[b], 0.036[c], 0.199[d]
Superior nasal	172.00 (154.00) 93.00–440.00	121.00 (18.00) 105.00–207.00	123.00 (26.00) 98.00–165.00	0.053[a]

IQR: interquartile range; IU: Intermediate uveitis. All reported pairwise p-values are Bonferroni-adjusted. [a]Statistical significance in Kruskal–Wallis test (comparison among three groups) (p<0.05 is significant). [b]Statistical significance of pairwise comparison between active and quiescent groups (Mann–Whitney U test) (p<0.017 is significant). [c]Statistical significance of pairwise comparison between active and control groups (Mann–Whitney U test) (p<0.017 is significant). [d]Statistical significance of pairwise comparison between quiescent and control groups (Mann–Whitney U test) (p<0.017 is significant)

The peripapillary RNFLT evaluations revealed significantly increased RNFLT in the active group compared with the quiescent and control groups ($p<0.001$). Based on fluorescein angiography findings, patients with optic disc staining appeared to have slightly higher RNFLT values compared with those without staining; however, the subgroup size was too small to allow a reliable statistical analysis. The RNFLT values were similar between the quiescent and control groups ($p=0.616$). Comparable patterns were observed in subregional analyses of the peripapillary area. A detailed evaluation of RNFLT is presented in Table 3.

Discussion

IU is a chronic, relapsing inflammatory condition, which may lead to ocular complications despite its generally favorable visual prognosis.[3] However, IU-associated complications can be observed in up to 70% of patients and may lead to serious visual morbidity.[1] A recent study investigating the prevalence of ocular complications of IU showed that glaucoma is one of the most sight-threatening complications, often diagnosed at the initial presentation.[3] Therefore, it is important to determine if and how RNFLT and the vascular features of the peripapillary area are affected by ocular inflammation caused by IU.

Previous studies have shown substantially decreased RPC VD values in glaucomatous eyes.[19,20] It has been hypothesized that capillary insufficiency in the optic nerve head can induce ischemic damage leading to glaucoma.[21] Secondary glaucoma is reported in 10% of uveitic patients.[2] However, the detection and monitoring of uveitic glaucoma using only OCT is challenging due to the possible influence of uveitis on RNFLT measurements.[22] Therefore, alternative methods for early detection and follow-up of uveitic glaucoma are being investigated. Lommatzsch *et al*.[23] showed that peripapillary VD values in uveitic glaucoma patients were substantially decreased compared with both healthy eyes and uveitic eyes without glaucoma. However, the authors concluded that uveitis itself can cause OCTA changes, and they could not attribute the changes directly to uveitic glaucoma without further studies exploring those possible associations.[23]

The RPC network, which is the vascular layer we evaluated in peripapillary OCTA images, runs parallel to the retinal nerve fiber layer and represents the most superficial part of the retinal vasculature.[24] The RPC is considered vulnerable to both ischemic and inflammatory damage, and decreased RPC VD may offer insight into optic nerve head circulatory disorders.[25] In our study, we observed decreased VD values in the whole image, peripapillary region, superior and inferior hemispheres, and temporal sectoral regions during the quiescent phase of IU compared with healthy eyes. VD values were similar between eyes in the active phase and those in the healthy control group across all regions. These findings suggest that IU affects the microvascular structures of the optic nerve head.

Based on our findings, we noted that no substantial quantitative changes are observed in peripapillary VDs during the active phase of IU compared with healthy subjects, possibly due to the masking effect of ongoing inflammation. However, in the quiescent phase, with the regression of inflammation, possibly permanent vascular changes – such as reduced VD and network complexity – become more apparent. A recent study has shown that OCTA can help differentiate ischemic from inflammatory optic nerve head changes. As blood flow increases during inflammation, OCTA may detect an increase in VD in the optic nerve head during the active inflammatory phase of IU.[24,25] Inflammation in the vitreous is the main feature of IU and is often accompanied by inflammatory changes in the retinal microvasculature.[25]

There is limited literature exploring the relationship between any type of uveitis and peripapillary OCTA, and none of the existing studies have assessed the correlation between microvascular changes and disease activity.[26,27] Studies examining macular OCTA findings in IU have shown reduced macular VD values in these patients and suggested that macular OCTA imaging is not useful for determining disease activity.[9-11] Our findings highlight an important difference compared to previous OCTA studies, which have largely focused on the macula. In our cohort, peripapillary VD was preserved during the active phase, while a reduction became evident in the quiescent phase. This suggests that peripapillary OCTA may not be a reliable marker of present inflammatory activity alone, but rather reflects cumulative vascular damage that becomes apparent once inflammation subsides. From a clinical perspective, this distinction is important: Normal VD does not rule out active disease, whereas reduced VD in quiescence may indicate lasting microvascular loss. The preserved VD in IU may possibly reflect acute vasodilation or transient flow changes, and the reduction in the quiescent phase may most likely indicate permanent capillary loss that becomes more apparent with the subsiding inflammation. This concept is further supported by structural markers, such as RNFLT, which have been shown to thicken during active uveitis due to inflammatory swelling and return to normal or reduced levels in quiescent disease.[14]

We have also evaluated the peripapillary RNFLT changes between the groups in our study. We observed that RNFLT substantially increased during active disease, whereas no difference was observed between the quiescent phase of IU and healthy control subjects. Since we excluded eyes with glaucomatous changes and intraocular pressure above 20 mmHg, we think it is important that no substantial difference in RNFLT was found between the healthy and quiescent IU groups. This finding may be important in the follow-up of secondary glaucoma as a complication of IU, as it shows that RNFLT thinning is not seen in the quiescent phase of IU without glaucoma. However, although no RNFLT thinning was observed in the quiescent group without glaucoma in our cohort, this finding should be interpreted with caution due to the limited sample size.

Our finding that RNFLT is increased in active IU is in accordance with previous literature on uveitis and RNFLT changes. Yılmaz *et al*.[15] recently reported their study investigating the effect of different types of uveitis on peripapillary RNFLT. They included 12 patients with IU and found that RNFLT was increased in the patient group compared with healthy subjects. Although their IU subgroup was relatively small, the authors showed that this effect was associated with disease activity, similar to our finding.[15] Furthermore, we observed a trend toward higher RNFLT in eyes with optic disc staining on FFA compared to those without staining. Given the very small number of patients in each subgroup, no meaningful statistical analysis could be performed. Nevertheless, this exploratory finding may suggest an association between angiographic disc leakage and transient RNFL thickening in IU, in line with previous reports *showing increased RNFLT in cases of papillitis*.[14]

Glaucoma is a common sight-threatening complication of IU.[4,5,28] Based on our results, active IU can be a confounding factor in RNFLT analysis and may cause "green disease" in OCT images, masking possible retinal nerve fiber layer defects. Therefore, this effect should be considered, especially in glaucoma patients. RNFLT increase can be evaluated as an indicator of disease activity in the follow-up of patients with IU. These points should be kept in mind when monitoring patients for uveitis, secondary glaucoma, and other optic nerve manifestations of IU.

This is, as far as we are aware, the first study to use OCTA to examine the peripapillary microvasculature in patients with IU. Our study will contribute to the literature showing that IU alters the microvascular structure of the optic nerve head, but this effect becomes evident in the inactive phase, when the inflammatory changes seen in the active phase have subsided. However, it should be emphasized that establishing a relationship between OCTA findings and glaucoma requires demonstration of a progressive course. Both structural changes, such as RNFLT thinning, and vascular alterations need to be shown to progress over time. Since our study has a cross-sectional design, it does not allow evaluation of longitudinal changes or progression. Therefore, our findings should be interpreted with caution in terms of direct association with glaucomatous damage, and future studies are required to clarify this relationship.

Macular OCTA was not included in our analysis because cystoid macular edema, which is highly prevalent in IU, can markedly distort macular VD measurements and confound interpretation.[11,29] Instead, we focused on peripapillary OCTA, which is less affected by macular edema and more directly relevant to optic nerve involvement and glaucoma risk in IU. Future studies, including both macular and peripapillary OCTA analyses, may provide more comprehensive insights.

Study Limitations

The primary limitations of this study include the small patient cohort and its retrospective design. Due to our study's retrospective, cross-sectional design, we cannot assess or draw conclusions about causality in relation to longitudinal changes in VD. Furthermore, the potential influence of systemic therapy on OCTA findings should also be acknowledged. A comprehensive review notes that anti-inflammatory therapies can alter ocular blood flow signals. Anti-inflammatory treatments, such as systemic corticosteroids or immunosuppressive agents, can alter ocular blood flow and microvascular signals, which in turn may affect VD measurements.[30] Therefore, it should be kept in mind that ongoing systemic therapy in our cohort and the treatment status variation among our patients may represent a potential confounder that should be considered when interpreting our results. Different systemic diseases underlying IU, such as sarcoidosis and multiple sclerosis, may also influence vascular and RNFLT findings, and this represents a limitation of our study. To better define vascular dynamics in IU, future prospective research evaluating OCTA metrics before and after disease activity or treatment initiation with subgroup analysis according to different underlying etiology and treatment modalities will be crucial.

Conclusion

RNFLT analysis can be affected by IU disease activity and may be misleading when monitoring glaucomatous retinal nerve fiber layer defects and other optic nerve

manifestations of IU, especially in patients with active disease. The peripapillary vasculature can also be influenced by the course of IU, and possible alterations in the optic nerve head microvasculature should be considered when monitoring these patients. The decreased RPC VD we have identified may contribute to the development of future glaucoma as a complication of IU by leading to capillary insufficiency and impaired blood flow to the optic nerve head. In addition, earlier glaucoma treatment and closer follow-up may be warranted in these patients when intraocular pressure levels are slightly elevated during follow-up visits, as the RPC may already be affected by IU. Further research is needed to better understand this relationship and the clinical significance of our findings.

Ethics Committee Approval: This study was approved by the Başkent University Medical and Health Sciences Research Board (Project number: KA23/171-Date: May 09, 2023).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The author declare that there is no conflict of interest.

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ORIGINAL ARTICLE

Evaluation of systemic inflammatory markers in retinal venous occlusions

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Abstract

Purpose: The objective of the study was to evaluate the potential role of systemic inflammatory indices in distinguishing patients with retinal vein occlusion (RVO) from healthy individuals.

Methods: This retrospective study included 75 patients diagnosed with RVO and 80 age- and sex-matched healthy controls. Complete blood counts were analyzed to calculate systemic inflammation indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), systemic inflammation modulation index (SIMI), and aggregate index of systemic inflammation (AISI). Group comparisons were performed, and receiver operating characteristic (ROC) analysis was used to assess the diagnostic value of each marker.

Results: Significant differences were observed between RVO patients and controls across all inflammatory indices. Notably, NLR (2.22 vs. 1.86), PLR (130.9 vs. 113.3), SII (485.3 vs. 440.3), SIRI (1.13 vs. 0.91), SIMI (65.48 vs. 56.00), and AISI (282.33 vs. 215.94) were all elevated in the RVO group ($p<0.05$). However, ROC analysis revealed only limited discriminative power, with AUC values ranging from 0.602 to 0.640 and sensitivities/specificities around 55–61%.

Conclusion: Systemic inflammation-based indices were significantly elevated in patients with RVO compared with healthy controls. Although these markers demonstrated limited discriminative performance, their consistent elevation may reflect the presence of systemic inflammatory activity associated with RVO. To the best of our knowledge, this study is among the first to evaluate SIMI and AISI in this context. Further prospective studies are needed to better clarify their clinical relevance and potential role in the inflammatory background of RVO.

Keywords: Diagnostics, Inflammatory markers, Retinal venous occlusion

Retinal venous occlusion (RVO) represents a major contributor to vision-impairing retinal conditions. It typically leads to visual deterioration due to complications such as macular edema and retinal ischemia, and is frequently observed in individuals with underlying systemic disorders like hypertension and arteriosclerosis.[1] Early detection and management of modifiable risk factors play a critical role in reducing both the incidence and the long-term visual sequelae of RVO.[2] The disease mechanism is complex and multifaceted, encompassing endothelial dysfunction, altered blood flow dynamics, genetic predispositions, and inflammatory pathways.[1]

Both local and systemic inflammatory processes are believed to play a significant role in the pathogenesis

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of RVO by facilitating atherosclerotic changes and enhancing blood coagulability. Moreover, recent studies have reported elevated intraocular concentrations of inflammatory cytokines, growth factors, chemokines, adhesion molecules, and other proinflammatory mediators in individuals diagnosed with RVO.[1]

In recent years, hematological inflammation-based markers have attracted increasing attention due to their association with various systemic and ocular pathologies. These parameters are gaining recognition as useful tools for identifying subclinical inflammatory activity. Exploring the relationship between systemic inflammation and eye diseases – such as pseudoexfoliation syndrome, diabetic macular edema, and central retinal artery occlusion – may offer meaningful insights into the etiopathogenesis of RVO. In these diseases, systemic and local inflammatory responses may promote vascular instability, increased vascular permeability, and prothrombotic alterations within the retinal circulation. Therefore, investigating systemic inflammatory activity across these conditions may provide broader insight into shared pathophysiological mechanisms and help clarify the potential contribution of inflammation to the development of retinal vein occlusion (RVO). Accordingly, the primary objective of the present study was to assess inflammation-related indices derived from routine blood tests in individuals diagnosed with RVO.[3-10]

Materials and Methods

Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine at Zonguldak Bulent Ecevit University on April 17, 2024, and the study protocol complied with the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for written informed consent was waived.

This study retrospectively included patients diagnosed with RVO who were followed at Zonguldak Bülent Ecevit University Hospital between June 2011 and March 2024. Patients were selected consecutively from hospital records to minimize selection bias. RVO diagnosis was confirmed by both fundus examination and fluorescein angiography (Canon CX-1, Tokyo, Japan). Both central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) RVOs were included in the analysis; however, subgroup comparisons were not conducted due to limitations in sample size.

Peripheral blood samples were obtained within 24 h of diagnosis and before the initiation of any ophthalmological treatment. Patients were excluded if they had active systemic infections, inflammatory diseases, or concurrent ocular conditions such as age-related macular degeneration, uveitis, diabetic retinopathy, or glaucoma. The control group consisted of 80 age- and sex-matched individuals who had normal ophthalmologic findings and met the same exclusion criteria as the RVO group. While systemic comorbidities were recorded, data regarding systemic medications (e.g., antihypertensives, antiplatelets, statins) were not available for all participants and were therefore not included in the analysis.

Complete blood counts obtained at the time of diagnosis were used to calculate several systemic inflammatory indices, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), systemic inflammation modulation index (SIMI), and aggregate index of systemic inflammation (AISI). These indices were derived using the following formulas: SII=(neutrophils × platelets)/lymphocytes, SIRI=(neutrophils × monocytes)/lymphocytes, SIMI=(monocytes × platelets)/lymphocytes, and AISI=(neutrophils × monocytes × platelets)/lymphocytes. All laboratory analyses were performed using standard hematology analyzers available in the hospital's clinical laboratory.

Statistical Analysis

Statistical analyses were carried out using IBM Statistical Package for the Social Sciences (SPSS) Statistics software (version 22.0; SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was assessed via the Shapiro–Wilk test. Depending on data characteristics, comparisons between the RVO and control groups were conducted using the Mann–Whitney U test, independent samples t-test, or Chi-square test. To evaluate differences in inflammatory indices among the control, BRVO, and CRVO groups, the Kruskal–Wallis test was applied. When significant differences were detected, pairwise comparisons were performed using the Mann–Whitney U test with Bonferroni correction. Receiver operating characteristic (ROC) curve analysis was employed to determine the area under the curve (AUC), optimal cutoff values, and the corresponding sensitivity and specificity for significant predictors identified through logistic regression. A $p<0.05$ was considered indicative of statistical significance.

Results

The study cohort comprised 75 patients diagnosed with RVO and 80 age- and sex-matched control subjects. There were no significant differences between the groups in terms of age (65±13 vs. 67.9±7.66 years, $p=0.205$) or sex

Table 1. Demographic and clinical characteristics of the study population

Variable	RVO group (*n*=75) (%)	Control group (*n*=80) (%)	*p*
Age, years (mean±SD)	65±13	67.9±7.66	0.205*
Sex			0.137**
Female	36 (48.0)	36 (45.0)	
Male	39 (52.0)	44 (55.0)	
Comorbidities			
Hypertension	53 (70.7)	55 (68.7)	0.933**
Diabetes mellitus	22 (29.3)	25 (31.2)	0.933**
Coronary artery disease	7 (9.3)	8 (10.0)	1.000**
RVO subtype			
CRVO	34 (45.3)	–	–
BRVO	41 (54.7)	–	–

Values are presented as mean±standard deviation or number (%). RVO: Retinal vein occlusion; CRVO: Central retinal vein occlusion; BRVO: Branch retinal vein occlusion. *Independent samples t-test; **Chi-square test

distribution (p=0.137). Similarly, the prevalence of systemic comorbidities, including hypertension, diabetes mellitus, and coronary artery disease, did not differ significantly between the groups (all p>0.05). Among the RVO patients, 34 (45.3%) had CRVO and 41 (54.7%) had BRVO. In the RVO group, subretinal fluid was detected in 29 (38.7%) patients at the time of diagnosis. Of the 75 patients with RVO, 24 (32%) were classified as ischemic and 51 (68%) as non-ischemic. The detailed demographic and clinical characteristics of the study population are presented in Table 1.

Statistically significant differences were observed between the RVO and control groups regarding the median values of several systemic inflammatory indices: NLR (2.22 vs. 1.86, p=0.004), PLR (130.9 vs. 113.3, p=0.010), SII (485.3 vs. 440.3, P=0.007), SIRI (1.13 vs. 0.91, P=0.003), SIMI (65.48 vs. 56.00, p=0.027), and AISI (282.33 vs. 215.94, p=0.006) (Table 2).

Table 2. Comparison of blood-count-derived inflammatory markers

Parameter	RVO group (*n*=75)	Control group (*n*=80)	*p**
NLR median	2.22	1.86	0.004
PLR median	130.9	113.3	0.01
SII median	485.3	440.4	0.007
SIRI median	1.13	0.91	0.003
SIMI median	65.48	56.00	0.027
AISI median	282.33	215.94	0.006

NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammatory response index; SIMI: Systemic inflammation modulation index; AISI: Aggregate index of systemic inflammation; *: Mann–Whitney U test

However, ROC curve analysis indicated that these markers had limited discriminatory power in distinguishing RVO patients from healthy controls. The AUC values were as follows: 0.634 for NLR, 0.619 for PLR, 0.625 for SII, 0.640 for SIRI, 0.602 for SIMI, and 0.628 for AISI.

Subgroup analyses were performed to further explore the relationship between inflammatory indices and different clinical phenotypes of RVO. First, patients were stratified according to RVO subtype. Inflammatory indices were compared among control, BRVO, and CRVO groups using the Kruskal–Wallis test, which demonstrated significant differences for NLR, PLR, SII, SIRI, SIMI, and AISI. *Post hoc* pairwise comparisons revealed significantly higher SIRI, SII, SIMI, and AISI levels in CRVO patients compared with controls, whereas no significant differences were observed

Table 3. Comparison of inflammatory indices among control, BRVO, and CRVO groups

Parameter	Control (*n*=80)	BRVO (*n*=41)	CRVO (*n*=34)	*P**	Control versus BRVO**	Control versus CRVO**	BRVO versus CRVO**
NLR	1.86 (0.95)	2.24 (1.56)	2.11 (1.71)	0.020	0.027	0.021	0.835
PLR	113.33 (55.84)	124.44 (53.04)	138.98 (63.89)	0.043	0.066	0.031	0.539
SII	440.33 (332.96)	462.81 (363.04)	501.40 (492.78)	0.026	0.076	0.014	0.477
SIRI	0.91 (0.76)	1.35 (1.39)	1.09 (1.39)	0.005	0.034	0.003	0.706
SIMI	56.00 (47.49)	61.82 (47.86)	70.94 (46.43)	0.040	0.148	0.016	0.398
AISI	215.94 (216.59)	295.21 (289.19)	284.42 (289.31)	0.010	0.064	0.004	0.513

Values are presented as median (interquartile range). *Kruskal–Wallis test was used to compare the three groups. **_Post hoc_ pairwise comparisons were performed using the Mann–Whitney U test with Bonferroni correction. Brvo: Branch retinal vein occlusion; CRVO: Central retinal vein occlusion; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammatory response index; SIMI: Systemic inflammation modulation index; AISI: Aggregate index of systemic inflammation

Table 4. ROC analysis of systemic inflammatory indices

Marker	AUC	Cut-off	Sensitivity (%)	Specificity (%)
NLR	0.634	1.95	58.6	55.0
PLR	0.619	119.04	61.3	61.2
SII	0.625	477.37	53.3	55.0
SIRI	0.640	0.97	61.3	61.2
SIMI	0.602	61.09	58.7	55.0
AISI	0.628	238.68	61.3	60.0

Summary of area under the curve (AUC), cut-off values, sensitivity, and specificity for each inflammatory marker used in distinguishing patients with RVO from healthy controls. NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammatory response index; SIMI: systemic inflammation modulation index; AISI: Aggregate index of systemic inflammation

between BRVO and CRVO patients (Table 3).

In addition, subgroup analysis based on the presence of subretinal fluid was performed among RVO patients. Patients with subretinal fluid showed significantly higher NLR (p=0.039) and SIMI (p=0.027) levels compared with those without subretinal fluid, while other inflammatory indices did not differ significantly.

Finally, inflammatory indices were compared between ischemic and non-ischemic RVO patients. No statistically significant differences were observed between the groups for NLR (p=0.986), SII (p=0.833), PLR (p=0.511), SIRI (p=0.336), SIMI (p=0.213), or AISI (p=0.354).

The optimal cutoff values and their corresponding diagnostic performance metrics were also determined for each marker. For NLR, a threshold of 1.95 yielded a sensitivity of 58.6% and a specificity of 55.0%. In the case of PLR, the best cutoff point was identified as 119.04, with 61.3% sensitivity and 61.2% specificity. The SII marker demonstrated a cutoff of 477.37, resulting in 53.3% sensitivity and 55.0% specificity, while SIRI had a threshold of 0.97 with sensitivity and specificity values of 61.3% and 61.2%, respectively. SIMI showed the most appropriate cutoff at 61.09, achieving 58.7% sensitivity and 55.0% specificity. Finally, for AISI, the optimal threshold was calculated as 238.68, with corresponding sensitivity and specificity values of 61.3% and 60.0% (Fig. 1 and Table 4). These findings indicate that, although statistically significant differences were observed between groups, the ability of these indices to serve as reliable discriminative markers was limited, as reflected by the AUC values, all of which remained below 0.65.

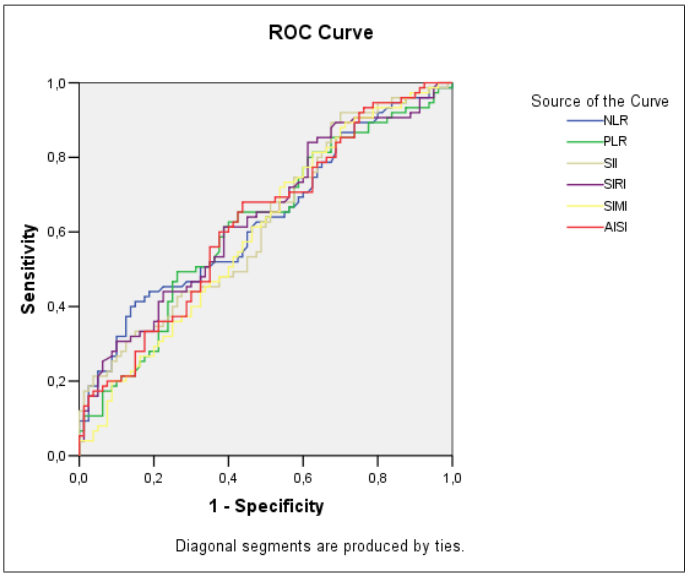

Fig. 1. Receiver operating characteristic curve for inflammatory markers. Best cut-off systemic inflammatory response index value, and sensitivity and specificity results.

Discussion

RVO is recognized as a prevalent retinal disorder contributing to vision loss. In the present study, we aimed to explore the association between systemic inflammatory indices and the presence of RVO. Although the levels of NLR, PLR, SIRI, SII, SIMI, and AISI differed significantly between patients with RVO and the control group, the ability of these markers to discriminate between the two groups remained limited.

Although the underlying pathophysiological mechanisms of RVO have not yet been fully elucidated, accumulating evidence suggests that inflammation plays a critical role in promoting hypercoagulable states. Vascular occlusion is thought to arise from aberrant thrombosis, potentially driven by the abnormal activation of platelets, circulating immune components, and vascular endothelial cells.[11] In addition, increased concentrations of various inflammatory mediators – such as interleukin-6 (IL-6), IL-8, monocyte chemoattractant protein-1, placental growth factor, platelet-derived growth factor, and intercellular adhesion molecule-1 – have been identified in patients diagnosed with RVO.[12-17] Furthermore, elevated intraocular levels of FLT-3L, IL-8, macrophage inflammatory protein-3 beta, growth-regulated oncogene-beta, and vascular endothelial growth factor (VEGF) have also been observed in the aqueous humor of individuals with RVO.[18]

In recent years, growing evidence has highlighted the utility of systemic inflammatory markers as cost-effective and readily available tools for evaluating both systemic

and ocular inflammatory conditions.[19-22] Among these, the AISI stands out, as it integrates hematological data from four key immune-related cell types: Neutrophils, monocytes, lymphocytes, and platelets. Initially proposed in 2018 to predict post-operative outcomes in surgical populations,[23] AISI has since gained attention as a potentially valuable indicator of systemic inflammatory activity in a wide range of clinical settings. Its incorporation of multiple cell lineages offers a broader perspective on the inflammatory status than conventional indices that rely on single-parameter measurements.[19]

The SIMI, calculated as the product of monocyte and platelet counts divided by lymphocyte count, is thought to reflect the potential role of platelets in regulating monocyte function. Given that platelets can modulate both the differentiation and activation of monocytes, this composite index may offer meaningful insights into inflammatory mechanisms that contribute to a hypercoagulable state. Thus, SIMI has been proposed as a potential biomarker indicative of platelet-monocyte interactions underlying systemic inflammation.[17]

Several prior studies have explored the association between RVO and systemic inflammation-based indices, particularly focusing on markers such as NLR, PLR, SIRI, and SII.[24,26] Notably, research conducted by Ucer *et al.*[24] and Zuo *et al.*[26] suggested that variations in NLR levels may offer greater diagnostic relevance under certain clinical contexts. This similarity may be attributed to comparable patient selection criteria and similar exclusion of confounding systemic conditions. Another investigation reported that patients with serous retinal detachment secondary to RVO exhibited higher NLR and SIRI values compared to those without detachment. This finding highlights that inflammatory markers may vary depending on the presence of specific complications in RVO. In our study, we did not stratify patients based on the presence or absence of retinal detachment. Therefore, the overall inflammatory profile we observed may represent a broader spectrum of RVO severity and may partially explain the more modest diagnostic performance of these markers.

In line with previous research, the present study observed elevated levels of NLR, PLR, SII, SIRI, as well as SIMI and AISI in patients with RVO, and these differences were statistically significant. However, despite these significant differences, the discriminative performance of these markers remained modest in ROC analysis. One possible explanation for the discrepancy with earlier findings may be the larger sample size in our cohort, as increasing the number of participants can influence sensitivity and specificity estimates – potentially lowering their discriminative power.

The current study observed elevated NLR, PLR, SII, and SIRI levels in patients with RVO, similar to findings reported by Niu *et al.*[28] However, their reported diagnostic performance (AUCs ranging from 0.675 to 0.702) was slightly higher than ours (AUCs 0.602–0.640), possibly due to differences in patient population and inclusion criteria. While Niu *et al.*[28] focused on younger patients receiving anti-VEGF therapy, our cohort included a broader age range and treatment-naïve patients, which may have influenced the inflammatory profile and diagnostic accuracy.

In subgroup analyses, inflammatory indices were compared between patients with BRVO and CRVO. Although inflammatory markers tended to be higher in CRVO patients, no statistically significant differences were observed between the two subtypes after correction for multiple comparisons. This finding may suggest that systemic inflammatory activity contributes to the pathogenesis of both forms of RVO through similar underlying mechanisms. However, the relatively small sample size within each subgroup may have limited the statistical power to detect subtle differences between BRVO and CRVO patients. Future studies with larger cohorts and more detailed clinical stratification are needed to further clarify whether inflammatory indices differ between RVO subtypes and whether they are associated with disease severity or ischemic status.

In additional subgroup analyses, patients with subretinal fluid demonstrated significantly higher NLR and SIMI levels compared with those without subretinal fluid. The presence of subretinal fluid in RVO has been suggested to reflect increased vascular permeability and inflammatory activity within the retinal microenvironment. Previous studies have also reported higher systemic inflammatory marker levels in RVO patients with serous retinal detachment. For instance, Timur *et al.*[25] demonstrated that NLR and SII were significantly elevated in patients with serous retinal detachment secondary to RVO, suggesting a potential link between systemic inflammation and this clinical phenotype. Similarly, Doğan *et al.*[8] reported increased levels of inflammatory markers in RVO patients presenting with serous macular detachment. Consistent with these findings, the elevated NLR observed in our study further supports the association between systemic inflammation and the development of subretinal fluid in RVO. In addition, the higher SIMI levels observed in our cohort may indicate that platelet–monocyte–related inflammatory pathways could also contribute to the inflammatory milieu associated

with subretinal fluid formation.[8] However, these findings should be interpreted cautiously, given the relatively small sample size of the subgroup analysis.

In the present study, inflammatory indices were also evaluated according to ischemic status; however, no significant differences were observed between ischemic and non-ischemic RVO patients. This finding may suggest that systemic inflammatory activity is associated with the presence of RVO rather than with the ischemic severity of the disease. Previous studies have reported heterogeneous results regarding the relationship between inflammatory markers and ischemic status in RVO. For example, Wang *et al.*[27] reported that inflammatory indices such as NLR, SII, and SIRI were significantly higher in patients with ischemic RVO compared with non-ischemic cases, suggesting that increased systemic inflammation may be associated with more severe retinal ischemia. Similarly, Üçer *et al.*[24] demonstrated elevated inflammatory markers in RVO patients and suggested that these indices may reflect disease activity related to vascular occlusion and retinal ischemia. In contrast, the absence of a significant difference in our cohort may be related to the relatively limited sample size of the ischemic subgroup or differences in patient characteristics and inclusion criteria. Therefore, larger prospective studies are required to clarify whether systemic inflammatory indices are associated with the ischemic severity of RVO.

Our findings suggest that subclinical systemic inflammation may be associated with the development of RVO. Notably, this study is, to the best of our knowledge, the first to evaluate the SIMI and the AISI in patients with RVO. Although these indices are derived from similar hematologic parameters, they integrate interactions among neutrophils, monocytes, lymphocytes, and platelets, potentially providing a broader representation of systemic inflammatory activity. Therefore, the evaluation of these composite indices may contribute to a more comprehensive understanding of the inflammatory milieu underlying retinal vascular disorders. However, given their limited discriminative performance in our analysis, these markers should not be considered standalone diagnostic tools. Further prospective studies are needed to clarify their clinical relevance and potential role in the pathophysiology of RVO.

Despite the promising results, this study has several notable limitations. First, its retrospective design may have introduced selection bias and unmeasured confounding variables. Subgroup analyses according to RVO subtype (CRVO vs. BRVO) or disease severity were not performed, which may have limited the ability to explore potential associations between inflammatory indices and specific clinical phenotypes. Second, although statistically significant differences were observed, the relatively small sample size may have influenced the power of ROC analyses and the generalizability of results. Third, inflammatory markers were limited to indices derived from complete blood count; cytokine profiles and other systemic biomarkers were not assessed. In addition, systemic medication use (e.g., antihypertensives or antiplatelets) was not consistently available and therefore could not be analyzed, potentially affecting inflammatory marker levels. Although hypertension is associated with low-grade systemic inflammation, its prevalence was similar in both study groups, which may have minimized its potential confounding effect. Future prospective studies with broader biomarker panels and subgroup analyses (e.g., based on RVO subtype or presence of complications) are needed to validate and expand upon these findings. Due to the retrospective nature of the study, the exact time between symptom onset and diagnosis could not be determined for all patients, which may have influenced the inflammatory marker profiles.

Taken together, the findings of the present study support the concept that low-grade systemic inflammation may play a role in the complex pathophysiology of RVO. Hematological inflammation-based indices derived from routine blood tests may therefore provide accessible indicators reflecting the inflammatory milieu associated with retinal vascular disorders.

Conclusion

Systemic inflammatory indices, including NLR, PLR, SII, SIRI, SIMI, and AISI, were significantly elevated in patients with RVO compared with healthy controls. Although these markers demonstrated limited diagnostic performance in ROC analysis, their consistent elevation supports the potential contribution of systemic inflammation to the pathophysiology of RVO. To the best of our knowledge, this is the first study to evaluate SIMI and AISI in this context. However, these indices did not demonstrate a clear role in distinguishing RVO subtypes (CRVO vs. BRVO) or ischemic status in our cohort. Further large-scale prospective studies are required to clarify their clinical significance and potential role in understanding the inflammatory background of RVO.

Ethics Committee Approval: This study was approved by The Ethics committee of Zonguldak Bulent Ecevit University (April 17, 2024 – 2024/07).

Informed Consent: Due to the retrospective nature of the study, the requirement for written informed consent was waived.

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ORIGINAL ARTICLE

Choroidal morphological and microvascular differences in patients with hypertensive retinopathy

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Abstract

Purpose: To investigate alterations in choroidal structure, including changes in choroidal microvasculature and thickness, in patients with hypertensive retinopathy (HR) of Grades I–III.

Methods: This retrospective study included 110 eyes from 63 patients with HR and 56 eyes from 30 healthy controls. The mean choroidal vascularity index (CVI), choroidal stromal index (CSI), and subfoveal choroidal thickness (SFCT) were assessed using enhanced depth imaging optical coherence tomography.

Results: Lower CVI and SFCT values were associated with higher HR grades ($p<0.001$ and $p=0.001$, respectively). The mean luminal area was significantly lower in both the Grade II and Grade III HR groups than in the controls ($p<0.008$ and $p<0.001$, respectively). Although the CSI was significantly higher in the Grade II and Grade III HR groups than in the controls ($p<0.009$ and $p<0.002$, respectively), the stromal area (SA) did not differ between groups. After adjusting for relevant confounders, age, axial length, and diastolic blood pressure (DBP) were determined to be negatively associated with the CVI in individuals with HR (all, $p<0.05$).

Conclusion: A lower CVI and choroidal thickness were associated with higher-grade HR; however, the SA was similar between groups. Greater HR severity can lead to more profound disruptions in choroidal structure due to the enhanced severity of choroidal microvascular damage, and elevated DBP can exacerbate damage to the choroidal microvasculature.

Keywords: Choroid, Hypertensive retinopathy, Microvasculature, Optical coherence tomography

Hypertension is a risk factor for several chronic diseases with high morbidity and mortality rates, and chronic blood pressure elevation may lead to renal, cardiac, cerebral, and retinal end-organ damage.[1] Hypertensive retinopathy (HR) is a prevalent complication of hypertension, the incidence of which has been shown to increase in accordance with the severity of the condition.[2] Furthermore, the risk of cardiovascular and cerebrovascular events increases as HR progresses.[3] Fortunately, the transparent media of the eyeball facilitates the detection of HR through direct observation,[4] providing potential insights into vascular disease in different parts of the body.[5,6]

The potential connection between hypertension and the formation of choroidal lesions has led to various studies investigating choroidal vascular anomalies induced by blood pressure elevation. Elevated blood pressure damages the vascular beds of the choroid, and the resulting autoregulatory dysfunction compromises the integrity of choroidal blood flow, thereby increasing the sensitivity to high perfusion pressures.[7] The resulting

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choroidal ischemia and hyperperfusion could be major contributors to hypertensive chorioretinopathy.[8] Therefore, prior studies investigating choroidal alterations in patients with HR have focused on systolic blood pressure (SBP) and diastolic blood pressure (DBP), along with the other parameters that may contribute to such changes, including the age of the patient, intraocular pressure, and axial length.[9-11]

In most cases, HR is asymptomatic and is diagnosed through fundoscopic examination. Numerous categorization methods have been developed to evaluate HR severity; still, the Keith–Wagener–Barker (KWB) grading system is the most frequently employed.[12] Enhanced depth imaging optical coherence tomography (EDI-OCT) facilitates rapid, non-invasive, quantitative analysis of the choroid *in vivo*. Although the choroidal thickness in HR tends to decrease from Grade 1 to Grade 3 based on the KWB grading system, one study showed that the change was not statistically significant.[9] Another study that investigated superficial and deep retinal microvascular alterations reported that both the vessel and perfusion densities tended to diminish as HR progressed,[13] and several groups have suggested that the deep retinal capillary plexus is especially susceptible to ischemia and oxidative injury.[13-15] The choroidal vascularity index (CVI) has been proposed as an independent surrogate measure of choroidal health based on the assessment of the luminal and vascular components of the choroid[16]; however, no studies conducted to date have evaluated how the luminal and vascular components of the choroid change according to HR severity.

In the present study, to advance the understanding of the pathophysiological processes underlying the choroidal alterations observed in HR by comparing the choroidal thickness, CVI, and choroidal stromal index (CSI) between healthy controls and patients with HR of Grades I to III. The relationships between choroidal parameters and several factors, including age, intraocular pressure, axial length, SBP, and DBP, were also investigated.

Materials and Methods

This retrospective study was conducted in adherence with the Declaration of Helsinki and received approval from a local ethics committee (January 08, 2024, No: E-22686390-050.99-36935). The charts of all participants were examined retrospectively.

Patients were eligible for inclusion if they were diagnosed with hypertension and HR and underwent EDI-OCT for both eyes during the 2-year period from November 2021 to November 2023. This study included 110 eyes of 63 patients with HR and 56 eyes of 30 healthy controls. Essential hypertension was diagnosed based on a seated SBP of >140 mmHg and/or a DBP of >90 mmHg across a minimum of three measures.[17]

All patients with hypertension and healthy controls underwent regular ocular examinations and EDI-OCT (software version 6.3.3.0, Heidelberg Engineering Inc., Heidelberg, Germany) by an experienced clinician. Before the acquisition of the OCT scans, the HR stage was assessed through fundus examinations conducted by the same clinician based on the KWB grading system, which categorizes the degree of retinal damage into the following four grades: Grade I (arterial narrowing); Grade II (arteriovenous crossings); Grade III (hemorrhages and exudates); and Grade IV (papilledema).[18]

Participants exhibiting the following characteristics were excluded: Axial length <22.0 or >25.0 mm; myopia or hyperopia exceeding 5 diopters; a history of chronic ocular diseases, such as glaucoma and uveitis; a history of diabetes, chronic kidney disease, cardiovascular events, and other known systemic diseases; prior ocular surgery; macular edema; chorioretinal or corneal disorders; and the presence of cataracts that compromised the image quality. The sex- and age-matched control group comprised patients visiting the ophthalmology clinic for regular examinations. All subjects underwent thorough eye examinations, and their medical histories were extensively reviewed. Several patients involved in the study received antihypertensive medications, including monotherapy with angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, calcium channel blockers, or combination therapy. Goldmann applanation tonometry was conducted to assess intraocular pressure. Central corneal thickness and axial length were assessed by optical biometry (AL-Scan, Nidek Co. Ltd., Gamagori, Japan).

Assessment of Choroidal Parameters

All measurements were performed using OCT following the administration of 0.5% tropicamide for mydriasis. To guarantee data quality, only measures with a signal level of 6 or above were utilized. The device utilized its EDI mode together with high-definition single-line and seven-line raster techniques to evaluate choroidal thickness. The subfoveal choroidal thickness (SFCT) was calculated by measuring the vertical distance from the inner surface of the choroidal-scleral junction to the hyper-reflective line of Bruch's membrane.

The CVI was computed using image binarization, employing the methods established previously, with

modifications outlined.[19,20] The study was performed using ImageJ software (version 1.47; National Institutes of Health, Bethesda, MD, USA), which is publicly accessible and extensively utilized for image processing. The preliminary stage was transforming the OCT B-scan into an 8-bit image with the default parameters. Niblack's autolocal thresholding technique was utilized to differentiate between the luminal area (LA) and stromal areas (SA). The total choroidal area (TCA) was manually defined through the polygon selection tool, with the upper margin established by Bruch's membrane and the lower margin matching to the choroid-scleral interface (Fig. 1). This investigation utilized the whole length of the OCT B-scan. Consequently, the CVI was determined as the LA/TCA ratio. The ratio of the SA to the TCA was designated as the CSI. To avoid diurnal variations, all OCT assessments were conducted between 9:00 and 11:00 a.m. in a temperature-regulated room (maintained between 24°C and 27°C).

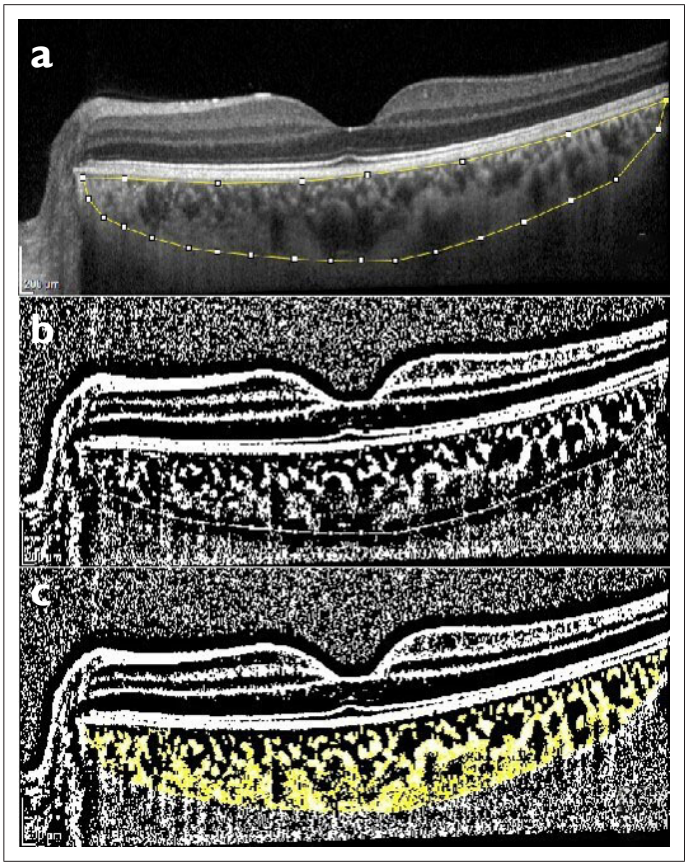

Fig. 1. Binarization and identification of the luminal and stromal areas of the choroid. **(a)** The EDI-OCT scans were binarized to determine the total choroidal area with the superior boundary set at the Bruch's membrane and the inferior boundary set at the choroid–scleral junction; **(b)** The image was downgraded to 8-bit, and Niblack auto local threshold was applied; **(c)** Color threshold was used to select the luminal area. EDI-OCT: Enhanced depth imaging optical coherence tomography.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) (version 26.0; SPSS Inc., Chicago, IL, USA). Descriptive data are presented as either means ± standard deviations or as ratios, if appropriate. The Kolmogorov–Smirnov test was used to analyze the data distribution for each variable. Student's *t*-tests were used for comparisons between two groups, whereas analysis of variance or Chi-square tests were conducted for intergroup comparisons of the four groups. Subsequent to the univariate linear regression analysis, multivariate linear regression was performed with CVI and SFCT as dependent variables and intraocular pressure, age, axial length, spherical equivalent, central corneal thickness, and systolic and DBPs as independent variables to adjust for potential confounders. $P<0.05$ was considered statistically significant.

Results

A comparison of the clinical and demographic characteristics between the patients with HR, categorized according to the grade, and the healthy controls is demonstrated in Table 1. No statistically significant variance was observed in the distribution of antihypertensive treatment among the three groups.

Table 2 presents a comparison of the variables between the eyes of patients with different HR stages and these of the controls. The average CVI was significantly lower in both the Grade I and Grade II HR groups than in the controls ($p<0.003$ and $p<0.001$, respectively); however, no significant difference in the mean CVI was found between the Grade I and Grade II HR groups. The CVI was lower in the Grade III HR group compared to that in all other groups (all $p<0.05$). Moreover, the average LA was significantly lower in both the Grade II and Grade III HR groups than in the controls ($p<0.008$ and $p<0.001$, respectively). The CSI was significantly higher in the Grade II and Grade III HR groups than it was in the controls ($p<0.009$ and $p<0.002$, respectively); however, the SA did not differ significantly between groups (all $p>0.05$). The SFCT was significantly lower in the Grade II and Grade III HR groups than in the controls ($p<0.005$ and $p<0.001$, respectively).

As shown in Figure 2, lower CVI and SFCT values were associated with a higher HR grade ($p<0.001$ and $p=0.001$, respectively). Multivariate linear regression analysis was conducted to identify potential variables influencing the CVI. After adjusting for relevant confounders, age, axial length, and DBP were negatively associated with the CVI in patients

Table 1. Demographics and clinical characteristics of participants

Number of participants	**Grade 1 HR 16**	**Grade 2 HR 29**	**Grade 3 HR 18**	**Controls 30**	***p***
Age (years)	44.3±6.6	49.3±5.4	45.5±7.3	46.8±6.1	0.06*
Gender (m/f)	10/6	16/13	11/7	18/12	0.960¥
Body mass index (kg/m^2)	23.4±1.7	23.6±1.9	23.3±2.0	22.6±1.4	0.197*
Present or previous smoker, *n* (%)	5 (31)	11 (37)	10 (55)	8 (26)	0.232¥
Anti-hypertensive treatment (%)	12 (75)	20 (69)	11 (61)	-	0.682¥
Systolic pressure (mmHG)	128.3±5.3	139.5±8.0	147.8±9.0	121.4±5.1	<0.001*
Diastolic pressure (mmHG)	78.6±5.5	82.5±7.0	94.7±10.4	76.3±2.4	<0.001*
Duration (years)	1.71±1.07	4.35±2.77	4.47±2.59	-	0.001*

HR: Hypertensive retinopathy. Data are given as mean±standard deviation. Values indicated in bold are statistically significant with $P<0.05$. *Analysis of variance test, ¥Chi-square test

Table 2. Comparisons of ocular parameters of the study participants

Number of eyes	**Controls 56**	**Grade 1 HR 30**	**Grade 2 HR 44**	**Grade 3 HR 36**
IOP (mm HG)	16.3±4.3	17.4±4.0	16.5±4.2	17.2±3.9
AL (mm)	23.3±2.2	22.7±2.6	23.5±2.2	22.8±2.5
SE (diopters)	−0.97±0.60	−1.26±0.69	−1.01±0.59	−1.17±0.64
CCT (µm)	544.8±38.6	541.8±46.7	539.5±43.7	538.7±47.3
SFCT (µm)	310.1±33.8	296.8±38.7	289.7±36.0[a]	279.6±41.3[a]
CVI (%)	0.60±0.03	0.58±0.04[a]	0.57±0.03[a]	0.55±0.04[abc]
CSI (%)	0.40±0.04	0.42±0.05	0.43±0.04[a]	0.45±0.06[a]
TCA (mm^2)	0.67±0.10	0.65±0.16	0.63±0.13	0.61±0.15
LA (mm^2)	0.40±0.03	0.37±0.08	0.36±0.07[a]	0.33±0.08[a]
SA (mm^2)	0.27±0.03	0.28±0.04	0.27±0.03	0.28±0.04

HR: Hypertensive retinopathy; IOP: Intraocular pressure; SE: Spherical equivalent; AL: Ocular axial length; CCT: Central corneal thickness; SFCT: Subfoveal choroidal thickness; CVI: Choroidal vascularity index; CSI: Choroidal stromal index; TCA: Total choroidal area; LA: Luminal area; SA: Stromal area. Data are given as mean±standard deviation. The Student *t*-test was used to compare two groups. [a]Statistically significant in comparison to controls ($p<0.05$). [b]Statistically significant in comparison to grade 1 HR ($p<0.05$). [c]Statistically significant in comparison to grade 2 HR ($p<0.05$)

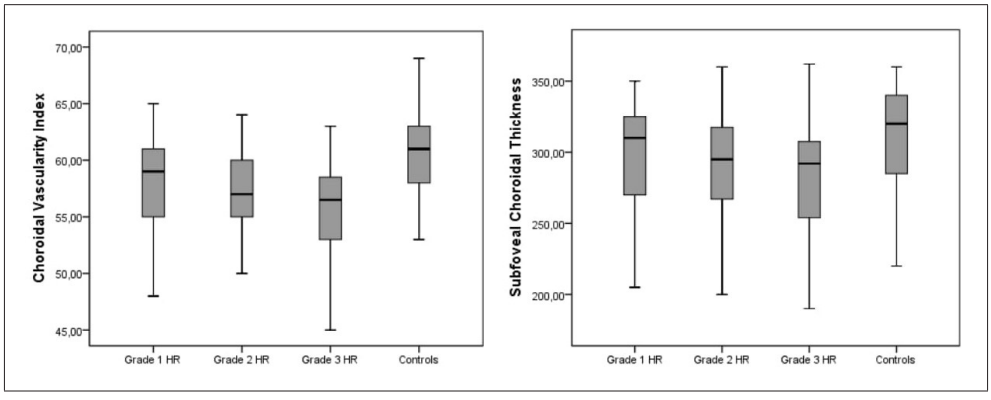

Fig. 2. Decreased choroidal vascularity index and subfoveal choroidal thickness were associated with a higher grade of hypertensive retinopathy (P<0.001, P=0.001, respectively). Choroidal metrics were plotted against the grade of hypertensive retinopathy

Table 3. Univariate and multivariate analysis for CVI in eyes with HR

Independent variables	Univariate analysis			Multivariate analysis		
	β	95% CI	*p*	β	95% CI	*p*
Age	−0.308	−0.310, −0.036	**0.014**	−0.272	−0.286, −0.020	**0.025**
BMI	0.144	−0.219, 0.794	0.261	0.068	−0.339, 0.612	0.567
SE (diopters)	0.165	−0.515, 2.438	0.198	0.021	−1.291, 1.537	0.862
AL	−0.350	−0.929, −0.174	**0.005**	−0.297	−0.853, −0.084	**0.018**
IOP	−0.014	−0.244, 0.218	0.910	−0.034	−0.252, 0.191	0.784
CCT	0.017	−0.020, 0.023	0.893	0.036	−0.017, 0.024	0.761
SBP	−0.170	−0.149, 0.029	0.184	−0.057	−0.113, 0.073	0.666
DBP	−0.292	−0.200, −0.018	**0.020**	−0.281	−0.201, −0.009	**0.033**

HR: Hypertensive retinopathy; BMI: Body mass index; IOP: Intraocular pressure; SE: Spherical equivalent; AL: Ocular axial length; CCT: Central corneal thickness; CVI: Choroidal vascularity index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CI: Confidence interval. Values indicated in bold are statistically significant with $p<0.05$

Table 4. Univariate and multivariate analysis for SFCT in eyes with HR

Independent variables	Univariate analysis			Multivariate analysis		
	β	95% CI	*p*	B	95% CI	*p*
Age	−0.385	−3.641, −0.871	**0.002**	−0.341	−3.360, −0.638	**0.005**
BMI	0.147	−2.204, 8.340	0.249	0.055	−3.717, 5.996	0.640
SE (diopters)	0.188	−3.831, 26.773	0.139	0.042	−11.898, 16.990	0.725
AL	−0.382	−10.141, −2.380	**0.002**	−0.309	−8.991, −1.135	**0.013**
IOP	−0.005	−2.454, 2.358	0.968	−0.029	−2.541, 1.991	0.809
CCT	−0.039	−0.263, 0.193	0.759	−0.009	−0.216, 0.200	0.939
SBP	−0.099	−1.304, 0.574	0.440	0.010	−0.913, 0.987	0.938
DBP	−0.224	−1.840, 0.099	0.078	−0.250	−1.956, 0.011	0.052

HR: Hypertensive retinopathy; BMI: Body mass index; IOP: Intraocular pressure; SE: Spherical equivalent; AL: Ocular axial length; CCT: Central corneal thickness; SFCT: Subfoveal choroidal thickness; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CI: Confidence interval. Values indicated in bold are statistically significant with $p<0.05$

with HR (p=0.025, p=0.018, and p=0.033, respectively; Table 3). In addition, the SFCT was negatively associated with both age and axial length (p=0.005 and p=0.013, respectively; Table 4).

Discussion

The present study revealed that a lower CVI and choroidal thickness were associated with HR of a higher grade. The LA significantly diminished as the severity of HR increased; however, TCA and SA were similar between the groups. Collectively, these findings suggest that as the severity of HR increases, progressive choroidal microvascular damage can disrupt the choroidal structure through morphological alterations. Furthermore, DBP, age, and axial length were negatively associated with choroidal vascularity.

Systemic hypertension is associated with several ocular disorders, and increased arterial blood pressure reduces choroidal blood flow, thereby elevating intraocular pressure; such changes have been shown to be linked with retinal microvascular abnormalities.[21-23] Choroidal arteriolar narrowing and the subsequent fibrinoid necrosis that occurs in the choroidal arterioles can lead to segmental infarction of the choriocapillaris, and this pathology may result in a decrease in choroidal thickness.[24] However, variable outcomes have been observed in cases involving severe hypertension with concomitant HR. It was reported that an initial choroidal thickening in patients with HR and malignant hypertension; however, subsequent thinning was observed as the blood pressure stabilized as a result of treatment.[25] Shao *et al*.[9] showed that the choroidal thickness was 187.04±78.80 µm in patients with hypertension without HR, while the thickness was much higher in those with Grade 1 HR at 289.11±100.87 µm. They also reported that as the severity of HR increased,

the thickness tended to decrease, although it did not reach statistical significance, at 286.10±111.07 μm and 280.28±92.39 μm in those with Grade II and Grade III HR, respectively. In the present study, a lower SFCT was associated with HR of a higher degree, with the Grade II and Grade III HR groups exhibiting significantly lower SFCT values compared to that in the controls. In addition, we also evaluated the associations between choroidal structural parameters, including CVI, CSI, and LA, and HR severity in this study.

A common conception is that choroidal ischemic alterations and hypoperfusion are the primary constituents driving the pathology of hypertensive chorioretinopathy.[7] Angiographic findings have indicated that Elschnig spots signify areas of localized infarction and ischemia of the choriocapillaris and choroidal arterioles.[26] While the retinal vascular damage induced by HR is comparatively well understood, there are limited findings regarding the impact of HR on choroidal microvessels.[2] While a study reported a lower choroidal vascularity in the HR group than the control group,[2] no studies have reported on alterations associated with HR severity. In the present study, the mean CVI value diminished significantly as the HR grade increased. Patients with Grade II and Grade III HR exhibited a lower mean LA compared to that in the controls. Furthermore, although the CSI was significantly higher in those with Grade II and Grade III HR than in the controls, the SA did not differ significantly between the groups. Collectively, these findings are indicative of a thinner choroid in patients with HR due to damage to choroidal microvascular vessels.

Liu *et al*.[13] identified initial pathological alterations occurring in the eyes of patients with HR, which were characterized by deep focal retinal capillary sparseness and retinal arch abnormalities. Moreover, they demonstrated that the deep vascular densities tended to decrease as the severity of HR increased. Furthermore, Saito *et al*.[27] reported that choroidal thickness and blood flow velocity increased during the acute phase of hypertensive chorioretinopathy. It was suggested that choroidal hyperperfusion may contribute to the pathology of hypertensive chorioretinopathy. Furthermore, these results indicate changes in microvascular blood flow in both the retina and choroid in HR patients.

There are many reports of CVI and choroidal structural changes related to hypertension, and these changes have also been associated with vascular diseases in other parts of the body, including the heart, brain, and kidneys, linked to hypertension-related end-organ damage.[28-30] To minimize confounding, we excluded participants with chronic kidney disease, heart failure, and other systemic conditions known to influence choroidal parameters. DBP, age, and axial length were found to be negatively associated with the CVI after adjusting for potential confounders in the present study. Another group reported a link between SBP and DBP with retinal arteriolar narrowing,[31] and elevated SBP was shown to be an independent variable that correlated with a reduction in the artery-to-vein ratio.[11] Moreover, higher visual acuity was reported following treatment-induced blood pressure stabilization in patients with HR and concomitant malignant hypertension.[25] In addition, previous studies had reported that choroidal thickness and CVI are affected by age and axial length.[9,10,32] In the present study, an association was revealed between age and the CVI and SFCT, consistent with a previous histological study that revealed that choroidal thinning correlated with ageing and was related to the loss of small- and medium-sized blood vessels.[33]

Present study has some limitations. Due to the retrospective nature of the study, it was not possible to examine longitudinal changes in choroidal vasculature during follow-up and with respect to alterations in blood pressure. Moreover, although the distribution of antihypertensive medications did not differ significantly between hypertensive subgroups, we did not record dose, duration, or the exact time interval between the last antihypertensive dose and OCT imaging. This is relevant because antihypertensive therapy and drug administration timing may affect choroidal vascular parameters.[34,35] Furthermore, the binarization of a single horizontal OCT slice across the fovea could only provide CVI information particular to that section of the choroid; further insights could be gained by examining the wider macular region. Finally, the relationship between the OCT parameters and clinical indicators, including cotton-wool spots, retinal hemorrhages, and exudates, was not evaluated, and further studies are required to assess those relationships.

Conclusion

Ultimately, the findings of this study demonstrate that a lower CVI and choroidal thickness were associated with greater HR severity. The mean LA was significantly lower in the Grade 2 and Grade 3 HR groups compared to that in the controls; however, there was no significant difference in the SA. As HR progresses and becomes more severe, choroidal structural impairments may accumulate due to the exacerbation of damage to the choroidal microvasculature.

Moreover, DBP, age, and axial length were confirmed to be negatively associated with choroidal vascularity. Additional longitudinal studies will be necessary to investigate alterations in these choroidal indicators during disease progression.

Ethics Committee Approval: This study was approved by The Ethic committee of Istanbul Atlas University (January 08, 2024, No: E-22686390-050.99-36935).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

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Authorship Contributions: Concept: G.D.A., A.S.; Design: G.D.A., H.K.; Supervision: A.S., H.K.; Resource: G.D.A., A.S.; Materials: G.D.A., A.S., H.K.; Data Collection and/or Processing: G.D.A.; Analysis and/or Interpretation: G.D.A., H.K.; Literature Search: G.D.A., A.S.; Writing: G.D.A., A.S.; Critical Reviews: G.D.A., A.S., H.K.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Effect of the timing of corneal suture removal after phacoemulsification on post-operative astigmatism

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Abstract

Purpose: To evaluate the effect of corneal suture removal timing after phacoemulsification on refractive and corneal astigmatism and best-corrected visual acuity (BCVA).

Methods: This prospective, single-center comparative study included 34 patients (34 eyes, aged 40–60 years). All eyes underwent uncomplicated phacoemulsification through a 2.75-mm superior corneal incision closed with a single 10-0 nylon suture. Patients were randomized into two groups: Suture removal at 1 week (Group 1) or at 1 month (Group 2). Refractive astigmatism, keratometric astigmatism, and BCVA were evaluated immediately before suture removal and at 1 h, 1 week, and 1 month afterward.

Results: Baseline characteristics were similar between groups ($p>0.05$), and no wound-related complications occurred. In Group 1, refractive astigmatism decreased significantly from 2.18±0.87 D to 0.88±0.42 D at 1 month after suture removal ($p<0.001$), with most of the reduction occurring within the first post-operative week. In Group 2, refractive astigmatism showed only a minimal change and did not reach statistical significance (1.61±0.68 D to 1.31±0.53 D; $p=0.057$). Corneal astigmatism reduction was also more pronounced in Group 1. At 1 month, Group 1 demonstrated significantly lower refractive astigmatism than Group 2. ($p=0.037$) Vector analysis further supported these findings. The early removal group demonstrated significantly greater surgically induced astigmatism correction (SIA 1.68±0.51 D vs. 1.43±0.54 D; $p=0.041$) and a lower difference vector (0.49±0.28 D vs. 0.77±0.31 D; $p=0.012$), indicating more effective reduction of suture-induced astigmatism.

Conclusion: Early corneal suture removal after cataract surgery provides a faster and greater reduction in post-operative astigmatism and accelerates visual rehabilitation. When wound stability is adequate, suture removal at approximately 1 week post-operatively may be recommended to optimize early refractive outcomes.

Keywords: Astigmatism, Corneal suture removal timing, Corneal suture, Phacoemulsification

Post-operative astigmatism following cataract surgery is a common refractive problem that can significantly impair visual quality and patient satisfaction.[1,2] With advances in modern phacoemulsification techniques, self-sealing clear corneal incisions are widely used, thereby reducing the need for sutures in routine cases. Nevertheless, in certain situations – such as enlargement of the incision, inadequate wound stability, or the occurrence of intraoperative complications – suturing of the corneal incision may be required to ensure wound integrity.

The placement of a corneal suture introduces additional biomechanical tension to the corneal tissue, which may alter

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corneal curvature and induce astigmatism. This surgically induced astigmatism (SIA) can adversely affect refractive outcomes and delay post-operative visual rehabilitation. [3] Therefore, effective management of suture-related SIA remains a critical consideration in cataract surgery, particularly when the goal is to achieve optimal visual outcomes in the early post-operative period.

The timing of corneal suture removal plays a critical role in determining both the magnitude and the duration of suture-induced astigmatism. Early suture removal – typically performed within several days to 1–2 weeks after cataract surgery – may facilitate more rapid normalization of corneal shape and minimize permanent astigmatism; however, it may carry a potential risk of reduced wound stability if performed too early in the post-operative period. In contrast, late suture removal – undertaken weeks or even months after surgery – allows additional time for wound healing, but the corneal deformation caused by the suture may persist until removal, thereby prolonging its astigmatic effect.[4,5]

Recent studies have emphasized the influence of factors, such as suture tension, incision location, and corneal biomechanics on post-operative astigmatic outcomes. [6-8] Despite this growing body of evidence, controlled studies directly comparing early versus late suture removal in the context of contemporary small-incision phacoemulsification surgery remain limited. Many of the classical studies addressing suture timing were conducted during the era of larger corneal incisions or extracapsular cataract extraction, under surgical conditions that differ substantially from present techniques.[9-11]

Previous reports have yielded conflicting results: some have suggested that early suture removal accelerates astigmatic correction without significantly affecting long-term astigmatism, whereas others have proposed that delayed removal may reduce astigmatism by allowing greater wound maturation.[4,11] This lack of consensus indicates that surgeons still lack clear guidance on how to balance rapid visual rehabilitation against refractive stability when determining the optimal timing of corneal suture removal.

This study prospectively evaluates the effect of corneal suture removal timing after phacoemulsification surgery on refractive and corneal astigmatism as well as visual outcomes. Early (post-operative week 1) and late (post-operative month 1) suture removal strategies were compared under standardized surgical conditions. Changes in astigmatism were quantitatively assessed using vector analysis based on the Alpins method. We hypothesized that earlier suture removal would result in a more rapid reduction of astigmatism and faster visual recovery. The findings of this study aim to provide clinical guidance on determining the optimal timing of corneal suture removal after cataract surgery, thereby improving post-operative refractive outcomes and overall visual rehabilitation.

Materials and Methods

Study Design and Patients

This prospective, comparative clinical study was conducted at a tertiary eye care center. The study protocol was approved by the Istanbul Cam and Sakura City Hospital Clinical Research Ethics Committee (approval number: KAEK/2023.05.176, May 2023) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment. A total of 34 patients (34 eyes) aged 40–60 years who were scheduled for cataract surgery due to senile cataract was included. All eyes underwent uncomplicated phacoemulsification, and a single 10-0 nylon suture was placed to ensure corneal incision stability. Only one eye per patient (the first operated eye meeting the inclusion criteria) was included in the analysis. Patients with traumatic or complicated cataracts, a history of previous ocular surgery, ocular pathologies that could influence post-operative astigmatism (such as significant corneal degeneration or keratopathy), high corneal astigmatism or ectatic disorders (e.g., keratoconus), uncontrolled diabetes mellitus (due to its potential effect on wound healing), or systemic conditions likely to interfere with scheduled follow-up visits were excluded.

Surgical Technique

All surgeries were performed by a single experienced surgeon to eliminate inter-surgeon variability. Following topical anesthesia (supplemented with peribulbar anesthesia when necessary), standard phacoemulsification was carried out. A 2.75-mm superior clear corneal incision was created at the 12 o'clock position, through which phacoemulsification and cortical aspiration were performed. In all cases, a foldable intraocular lens was implanted in the capsular bag. At the end of surgery, the main incision was closed with a single interrupted 10-0 nylon suture (Ethilon®), tied with standardized tension sufficient to maintain wound apposition and prevent leakage without inducing excessive corneal deformation; the knot was buried within the corneal stroma. Paracentesis incisions were left unsutured. All patients received the same post-operative medication regimen, consisting of

topical antibiotic and steroid eye drops in tapering doses for 4 weeks, and were instructed to use a protective eye shield at night and to follow standard post-operative care instructions.

Randomization, Suture Removal Procedure, and Outcome Assessment

Patients were randomly assigned to two groups using a computer-generated randomization sequence. Randomization was performed using a computer-generated sequence implemented with sealed opaque envelopes opened on the first post-operative day. Group 1 (17 eyes) underwent early suture removal at post-operative week 1, whereas Group 2 (17 eyes) underwent late suture removal at post-operative month 1. Patients and outcome assessors were not informed of the study hypothesis; however, complete masking was not feasible because the presence of a corneal suture could be observed during follow-up examinations. To minimize measurement bias, all post-operative examinations and measurements were performed by an ophthalmologist who did not perform the surgery and was not involved in group allocation. Complete masking was not feasible because the presence of a corneal suture could be directly observed during slit-lamp examination. However, the examiner was unaware of the study hypothesis. In addition, all measurements were obtained using the same devices, under standardized lighting conditions, and by a single experienced examiner throughout the study.

Suture removal was performed in the outpatient clinic under topical anesthesia with 0.5% proparacaine eye drops. In Group 1, sutures were removed at the 1-week post-operative visit (7±1 days after surgery). In Group 2, sutures were removed at the 1-month post-operative visit (30±3 days), while being inspected and left in place at the 1-week visit. In all cases, the procedure was standardized: The buried suture knot was gently exposed using fine sterile forceps, cut with Vannas scissors, and carefully removed. Wound integrity was assessed immediately after removal, and a Seidel test was performed to confirm the absence of leakage. A prophylactic topical antibiotic drop was instilled after the procedure, and patients were advised to continue topical antibiotic therapy for 3–5 days.

Patients were followed according to a standardized protocol to assess refractive astigmatism, corneal astigmatism, and visual acuity at pre-defined time points: İmmediately before suture removal and at approximately 1 h, 1 week, and 1 month after suture removal. These follow-up intervals were defined relative to the time of suture removal. Consequently, the corresponding absolute post-operative time points differed between groups: approximately post-operative weeks 1–6 in Group 1 and weeks 4–8 in Group 2.

At each visit, the following measurements were obtained: refractive astigmatism was assessed by objective autorefraction, with cylindrical power and axis recorded and refined by subjective refraction when necessary; Corneal astigmatism was evaluated using standard optical keratometry and corneal topography with the Tomey TMS-5 corneal topography system (Tomey Corporation, Nagoya, Japan). Refractive astigmatism was measured using automated refraction followed by subjective refinement when necessary; and best-corrected visual acuity (BCVA) was measured using a LogMAR chart (also reported in Snellen equivalents). All measurements were performed using the same devices under similar lighting conditions by a single experienced examiner.

Vector Analysis of Astigmatism

To quantitatively compare the effect of suture removal on astigmatism between the two groups, vector analysis based on the Alpins method was performed. The following key parameters were calculated: Target-induced astigmatism (TIA), defined as the astigmatic change required to neutralize the suture-induced astigmatism measured immediately before suture removal (the magnitude and axis of pre-suture removal astigmatism were used as the intended correction for each eye); SIA, defined as the vectorial change in astigmatism following suture removal, calculated as the vector difference between pre-suture removal astigmatism and astigmatism measured at 1 month after removal (analyzed separately for refractive and corneal astigmatism); the difference vector (DV), representing the residual astigmatism remaining 1 month after suture removal; the correction index (CI), calculated as the ratio of SIA to TIA (a value of 1.0 indicating complete correction, values >1 indicating overcorrection, and values <1 indicating undercorrection); and the index of success (IOS), defined as the ratio of DV to TIA, with lower values indicating less residual astigmatism relative to the intended correction. Double-angle plots and centroid analysis were not performed in this study. Although these methods may provide additional insight into vector distribution, the primary aim of the present analysis was to compare overall vector parameters between groups using the Alpins method.

All vector parameters were calculated using keratometric data for corneal astigmatism and refractive data for refractive astigmatism obtained before and after suture

removal. Mean values were used for group comparisons. This vector-based approach allowed a more comprehensive evaluation of astigmatic correction by accounting for both magnitude and axis changes rather than relying solely on scalar differences.

Statistical Analysis

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Data distribution was assessed using the Shapiro–Wilk test. Given the small sample size and non-normal distribution of some variables, non-parametric tests were primarily applied. Continuous variables were expressed as mean±standard deviation or median (interquartile range), as appropriate. Baseline characteristics between groups were compared using the independent-samples *t*-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables, while categorical variables were analyzed using the chi-square test. Within-group changes over time were evaluated using the Wilcoxon signed-rank test. Changes at intermediate time points (1 h and 1 week after suture removal) were analyzed relative to baseline within each group. A $P<0.05$ was considered statistically significant. Given the focused clinical endpoints and limited sample size, formal adjustment for multiple comparisons was not applied; instead, emphasis was placed on clinically meaningful outcomes, particularly the final reduction in astigmatism. Results were presented using tables and figures to facilitate interpretation. Due to the relatively low frequency of cases requiring corneal suturing after modern small-incision phacoemulsification, an a priori sample size calculation was not performed. The study was therefore designed as an exploratory prospective comparative study, including all eligible cases during the study period.

Within-group comparisons relative to baseline (pre–suture removal) were not systematically performed for all time points; therefore, only between-group comparisons are presented.

Results

Study Population

All 34 patients completed follow-up through 1 month after suture removal. Baseline demographic and clinical characteristics of Group 1 (early suture removal at post-operative week 1) and Group 2 (late suture removal at post-operative month 1) are summarized in Table 1. Refractive and corneal astigmatism values presented in Table 1 represent measurements obtained immediately before suture removal and therefore reflect the level of suture-induced astigmatism rather than true pre-operative astigmatism. The groups were comparable in terms of age (Group 1: 53.2±5.6 years; Group 2: 54.0±6.1 years; $p=0.68$) and sex distribution (Group 1: 9 females/8 males; Group 2: 8 females/9 males; $p=0.73$). Pre-operative corneal astigmatism was similar between groups (Group 1: 1.45±0.70 D; Group 2: 1.38±0.65 D; $p=0.81$), as were other baseline parameters, including pre-operative refractive astigmatism and axial length. Astigmatism values measured immediately before suture removal – representing the baseline for suture-induced astigmatism – were generally comparable between groups. Corneal astigmatism was similar (1.69±0.72 D vs. 1.70±0.71 D), whereas refractive astigmatism was numerically higher in Group 1 than in Group 2 (2.18±0.87 D vs. 1.61±0.68 D), with a borderline *p*-value ($p=0.058$). No intraoperative or post-operative complications occurred. Seidel tests were negative at all visits, including immediately after suture removal, and no wound leakage, infection, or unexpected inflammation was observed. All sutures were removed as planned without difficulty.

Table 1. Demographic and pre-suture removal refractive astigmatism/Baseline demographic and clinical characteristics of the two groups (Group 1: Early suture removal at 1 week; Group 2: Late suture removal at 1 month). Values are given as mean±standard deviation or *n* (%) as appropriate. There were no significant differences between the groups in age, sex distribution, pre-operative corneal astigmatism, refractive astigmatism, or axial length ($p>0.05$ for all comparisons)/

Variable	Group 1 (*n*=17)	Group 2 (*n*=17)	*p*
Age (years), mean±SD	53.4±5.1	54.1±4.9	0.642
Sex (m/f)	9/8	8/9	0.745
Preoperative Refractive Astigmatism (D), mean±SD	2.18±0.87	1.61±0.68	0.058
Preoperative corneal astigmatism (D), mean±SD	1.69±0.72	1.70±0.71	0.974
Systemic conditions (e.g., DM, HT)	None included	None included	N/A

D: Diopters; SD: Standard deviation; M: Male; F: Female; DM: Diabetes mellitus; HT: Hypertension; N/A: Not applicable

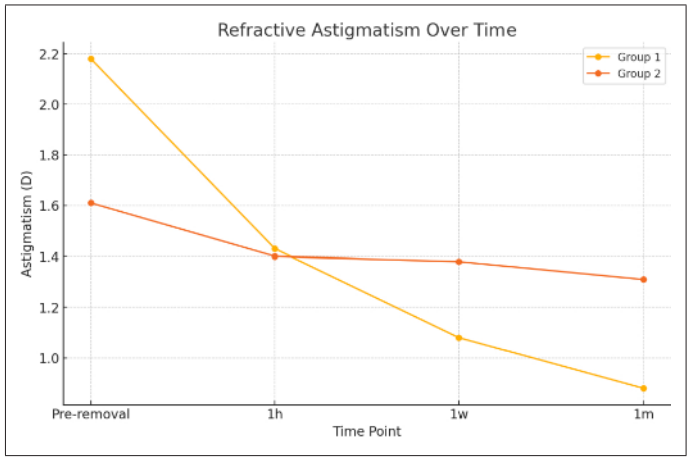

Fig. 1. Change in refractive astigmatism over time in the two groups. The graph illustrates the rapid decline in refractive astigmatism in Group 1 after early suture removal, with most of the reduction occurring by 1 week post-removal, compared to the more gradual and limited change in Group 2.

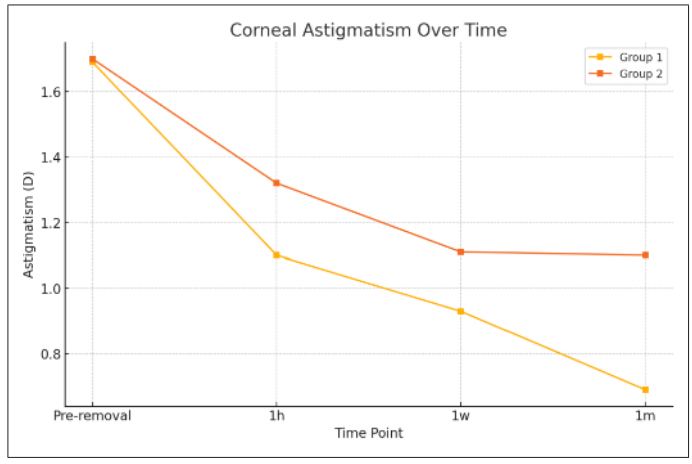

Fig. 2. Change in corneal (keratometric) astigmatism over time in the two groups. Group 1 demonstrates a marked decrease in corneal astigmatism soon after suture removal, whereas Group 2 shows a smaller reduction. Error bars indicate standard deviations at each time point.

Astigmatism Outcomes – Refractive Astigmatism

Refractive astigmatism measured immediately before suture removal was numerically higher in Group 1 than in Group 2 (2.18±0.87 D vs. 1.61±0.68 D), with a borderline *p*-value (p=0.058). In Group 1, refractive astigmatism decreased markedly following suture removal, with most of the reduction occurring within the 1st post-operative week (Fig. 1). In contrast, Group 2 showed only a modest decrease from 1.61±0.68 D to 1.31±0.53 D at 1 month, which did not reach statistical significance (p=0.057). By the end of the early post-operative period (~6–8 weeks after surgery), mean refractive astigmatism was significantly lower in Group 1 than in Group 2 (0.88 D vs. 1.31 D; p=0.037).

Astigmatism Outcomes – Corneal (Keratometric) Astigmatism

A similar pattern was observed for corneal astigmatism. In Group 1, keratometric astigmatism decreased markedly from 1.69±0.72 D to 0.69±0.35 D at 1 month after suture removal (p<0.001). In Group 2, the reduction was smaller and not statistically significant (from 1.70±0.71 D to 1.10±0.45 D; p=0.127). At 1 month after suture removal, mean corneal astigmatism was lower in Group 1 than in Group 2, although this difference was of borderline significance (0.69 D vs. 1.10 D; p=0.057) (Table 2 and Fig.2).

BCVA

BCVA improved in both groups over time; however, visual recovery occurred earlier in the early suture removal group. At 1 week after suture removal, mean BCVA was 0.08±0.06 LogMAR in Group 1 and 0.21±0.09 LogMAR in Group 2 (p<0.05). By 1 month after suture removal, BCVA improved further in both groups and became comparable between groups (Figure 3).

Vector Analysis of Astigmatism

Vector analysis results (Table 3) further supported the greater effectiveness of early suture removal. SIA was significantly higher and the DV significantly lower in Group

Table 2. Changes in refractive and corneal astigmatism over time/Refractive and corneal astigmatism in Group 1 and Group 2 at predefined time points after suture removal. Between-group p values represent comparisons at each time point. Baseline values correspond to measurements obtained immediately before suture removal

Time point	Group 1 refractive astigmatism (D)	Group 2 refractive astigmatism (D)	Between-group *p*	Group 1 corneal astigmatism (D)	Group 2 corneal astigmatism (D)	Between-group *p*
Pre-suture removal	2.18±0.87	1.61±0.68	0.058	1.69±0.72	1.70±0.71	0.94
1 h post-removal	1.43±0.75	1.40±0.64	0.87	1.10±0.55	1.32±0.60	0.18
1 week post-removal	1.08±0.54	1.38±0.59	0.04	0.93±0.41	1.11±0.50	0.12
1 month post-removal	0.88±0.42	1.31±0.53	0.01	0.69±0.35	1.10±0.45	0.003

D: Diopters; SD: Standard deviation

Table 3. Vector analysis parameters (alpins method)/Vector analysis of astigmatic changes following suture removal. Key Alpins parameters (target-induced astigmatism, surgically induced astigmatism, difference vector, correction index, and index of success) are presented for refractive astigmatism and corneal astigmatism in each group. Group 1 had a higher correction index and lower index of success, indicating more effective astigmatic correction with early suture removal.

Parameter	Group 1 (mean±SD)	Group 2 (mean±SD)	*p*	Interpretation	Unit
TIA	1.95±0.56	1.85±0.61	0.624	Planned correction	D
SIA	1.68±0.51	1.43±0.54	0.041	Actual correction	D
DV	0.49±0.28	0.77±0.31	0.012	Residual astigmatism	D
CI	0.86±0.24	0.77±0.27	0.298	Ratio SIA/TIA	-
IOS	0.25±0.14	0.42±0.18	0.007	DV/TIA	-

TIA: Target induced astigmatism; SIA: Surgically induced astigmatism; DV: Difference vector; CI: Correction index; IOS: Index of success; D: Diopters

1 compared with Group 2, indicating a more effective reduction of suture-induced astigmatism. In addition, the IOS was lower in the early removal group, reflecting smaller residual astigmatic error after suture removal. Although the CI did not differ significantly between groups, the overall vector profile suggests that earlier suture removal resulted in a more favorable astigmatic correction pattern.

Discussion

In this study, we demonstrated the effects of corneal suture removal timing on post-operative astigmatism and visual rehabilitation following cataract surgery. Early suture removal at post-operative week 1 resulted in a faster and greater reduction in astigmatism and more rapid visual recovery. Although eyes undergoing late suture removal at post-operative month 1 ultimately achieved satisfactory visual outcomes, astigmatic blur persisted for a longer

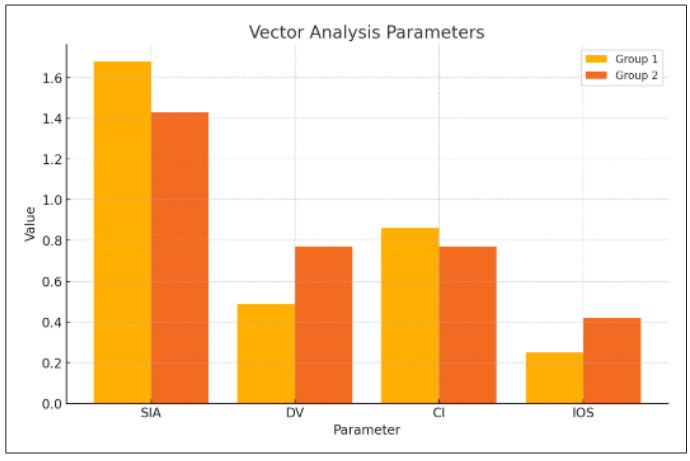

Fig. 3. Post-operative best-corrected visual acuity (BCVA) recovery in the two groups (in LogMAR units). Group 1 achieved significantly better visual acuity in the early post-operative period, reaching approximately 20/20 vision by 4–6 weeks after surgery. Group 2 experienced slower visual recovery, achieving similar final acuity only after suture removal at 1 month.

period during the early post-operative period. Notably, refractive astigmatism at 1 month after suture removal was significantly lower in the early removal group, and these patients reached optimal visual acuity in a shorter time. A borderline difference in baseline refractive astigmatism between groups was observed (2.18 D in Group 1 vs. 1.61 D in Group 2, p=0.058). Although this difference did not reach statistical significance, the numerically higher baseline astigmatism in the early removal group could theoretically influence the magnitude of change observed after suture removal. In particular, a regression-to-the-mean effect cannot be completely excluded. However, vector analysis using the Alpins method was applied to evaluate astigmatic changes, which incorporates both magnitude and axis of astigmatism and therefore partially accounts for baseline differences between groups. It should also be noted that although follow-up intervals were standardized relative to the time of suture removal (1 h, 1 week, and 1 month after removal), the absolute post-operative time differed between groups. Specifically, suture removal occurred at post-operative week 1 in Group 1 and at post-operative month 1 in Group 2. Consequently, eyes in the late removal group were at a more advanced stage of wound healing at the time of suture removal, which may have influenced the magnitude of astigmatic change and should be considered when interpreting between-group comparisons.

Our findings are generally consistent with previously published literature. Loriaut *et al.*[4] reported a marked immediate reduction in astigmatism following early suture removal, whereas late removal was associated with minimal astigmatic change. In their classical study, Stanford *et al.*[11] observed that the difference did not reach statistical significance in astigmatism at 6 months when sutures were removed at 2 versus 12 weeks post-operatively; however, they noted that astigmatism resolved more rapidly in the

early removal group. Within the context of modern small-incision cataract surgery, our results further support the notion that early suture removal facilitates faster refractive recovery and early stabilization of refraction. In our early removal group, the transient refractive fluctuations described in the literature were minimal. Consistent with this observation, Loriaut *et al*.[9] also emphasized that refraction can be safely and reliably measured shortly after early suture removal.

The observation that most of the improvement in astigmatism occurs immediately after suture removal is consistent with previous reports. Potamitis *et al*.[10] and Churchill and Hillman[12] demonstrated that astigmatism improves markedly within minutes following suture removal. Our findings in Group 1 similarly indicate that the majority of astigmatic reduction occurred within the 1st h to days after suture removal.

The theoretical advantage of late suture removal is allowing additional time for wound healing. Indeed, no wound-related complications were observed in Group 2, and previous studies have suggested that very late suture removal (8–12 weeks post-operatively) may provide greater security in terms of incision integrity.[13] However, in the present study, no adverse events were observed in eyes that underwent suture removal at post-operative week 1. It has been reported that corneal incisions generally achieve sufficient tensile strength within 1–2 weeks after surgery.[14] Consistent with this evidence, all wounds in our early suture removal group remained stable, supporting the safety of early suture removal in appropriately selected cases.

Beyond its refractive benefits, early suture removal may also have a positive impact on patient satisfaction. Patients in the early removal group experienced clearer vision during the initial post-operative weeks, whereas those in the late removal group were exposed to longer-lasting visual fluctuations related to persistent astigmatism. In a study involving absorbable sutures, astigmatism was shown to remain relatively high as long as the suture was present and to decrease only after suture absorption, typically occurring 6–8 weeks post-operatively.[15] This observation supports the concept that suture-related astigmatism largely persists while the suture remains in place and diminishes once it is eliminated, allowing the cornea to gradually return toward its natural curvature.

The magnitude of SIA is also influenced by factors, such as incision location and suture technique.[3,5] In the present study, these variables were minimized by standardizing the surgical technique and incision parameters. O'Driscoll *et al*.[16] investigated the use of different suture materials, such as flexible polypropylene sutures, to modulate astigmatism and demonstrated that appropriate suture selection may significantly influence refractive outcomes.

Recent studies on modern small-incision cataract surgery have highlighted that incision architecture and wound biomechanics play an important role in SIA and post-operative refractive outcomes.[17,18]

Vector analysis allows a more comprehensive evaluation of astigmatic changes by incorporating both the magnitude and axis of astigmatism, which cannot be fully captured by scalar measurements alone. Vector analysis provided additional insight into the mechanism of astigmatic correction following suture removal. SIA was significantly higher in the early removal group, indicating a greater magnitude of astigmatic change after suture removal. In addition, the DV and IOS were significantly lower in this group, reflecting smaller residual astigmatic error relative to the intended correction. Although the CI did not differ significantly between groups, CI represents the proportional relationship between achieved and intended astigmatic correction and may be influenced by interindividual variability. Overall, these vector parameters support the clinical observation that earlier suture removal results in a more effective reduction of suture-induced astigmatism.

The lack of a significant difference in CI may reflect variability in the magnitude of SIA relative to the target astigmatism. However, IOS is generally considered a more direct indicator of residual astigmatic error, and the significantly lower IOS observed in the early removal group supports the clinical effectiveness of early suture removal in reducing post-operative astigmatism. It should also be noted that the main corneal incision in this study was created at the superior 12 o'clock position in all cases. Incision location is known to influence the direction and magnitude of SIA, and superior incisions are often associated with a tendency toward against-the-rule astigmatic changes. However, because the incision location and surgical technique were standardized across all cases, this factor is unlikely to have influenced the comparison between groups.

This study has several limitations. First, the follow-up period was limited to 1 month after suture removal, which restricts the evaluation of long-term corneal stability and refractive predictability. Because corneal remodeling and wound healing may continue for several months after cataract surgery, longer follow-up periods (e.g., 3–6 months) would

provide better insight into long-term refractive stability. Second, the tension of the sutures (tight vs. loose) was not quantitatively controlled or standardized, which may have influenced post-operative astigmatism. Third, the relatively small sample size (17 eyes per group) represents a methodological limitation that may limit the statistical power and generalizability of the study. In addition, the absence of a formal a priori sample size calculation represents a methodological limitation, and the possibility of type II error cannot be excluded.

A borderline difference in baseline refractive astigmatism between groups was also observed before suture removal (2.18 D in Group 1 vs. 1.61 D in Group 2, p=0.058). Although this difference did not reach statistical significance, the numerically higher baseline astigmatism in the early removal group could have influenced the magnitude of change after suture removal, and a regression-to-the-mean effect cannot be excluded. However, astigmatic changes were evaluated using vector analysis based on the Alpins method, which incorporates both the magnitude and axis of astigmatism and partially compensates for baseline differences. Nevertheless, this baseline imbalance should be considered when interpreting the results.

Conclusion

The timing of corneal suture removal should be individualized with careful consideration of wound stability. In uncomplicated cataract surgery, early suture removal (approximately 1 week post-operatively) may facilitate faster reduction of post-operative astigmatism and earlier refractive stabilization. However, longer follow-up is required to determine whether similar refractive outcomes are maintained over time. In this cohort, no wound-related complications were observed following early suture removal.

Ethics Committee Approval: This study was approved by the Istanbul Cam and Sakura City Hospital Clinical Research Ethics Committee (approval number: KAEK/2023.05.176, May 2023)

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Clinical characteristics, device prescription patterns, visual function, and quality of life in patients referred to a low-vision unit: A single-center retrospective study

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Abstract

Purpose: To describe the clinical characteristics, visual outcomes, prescribed low-vision aids, and vision-related quality of life of patients referred to a tertiary low-vision unit.

Methods: This single-center retrospective study included 94 patients referred between January 2023 and November 2024. Clinical, demographic, diagnostic, and visual function data were extracted from medical records. Baseline best-corrected visual acuity (BCVA) and distance- and near-visual acuity after correction with low-vision aids were collected. Vision-related quality of life was evaluated using the low vision quality of life questionnaire (LVQOL).

Results: The mean age was 43.6±28.0 years (median, 34), and 55.3% of patients were male. The most common diagnoses were age-related macular degeneration (27.6%), retinitis pigmentosa (17.0%), Stargardt disease (14.9%), and albinism (12.8%). The mean baseline BCVA of the better eye was 0.96±0.47 LogMAR. With low-vision aids, BCVA was 0.28±0.21 LogMAR (P<0.001), and near visual acuity improved from 0.58±0.30 to 0.18±0.13 LogMAR (p<0.001). Telescopic devices for distance vision were prescribed to 68 patients (72.3%), including Galilean (n=56) and Keplerian (n=12) telescopes. Near-vision aids were prescribed to 34 patients (36.2%), mainly high-diopter near spectacles (n=28). Magnifiers were prescribed to 26 patients (27.7%), and filtered lenses to 22 patients (23.4%). LVQOL subscales for reading/fine work, activities of daily living, and distance/mobility/illumination correlated significantly with age and best-eye visual acuity (p<0.05).

Conclusion: Task-specific optical aids provide meaningful improvements in distance and near visual functions in low-vision rehabilitation. Quality-of-life outcomes were associated with age and visual acuity, underscoring the importance of timely referral to low-vision units and a multidimensional approach to low-vision care.

Keywords: Low vision, Low vision aids, Low-vision rehabilitation, Quality of life

Low vision represents a significant public health issue worldwide, affecting millions of individuals and substantially impacting their quality of life, independence, and safety.[1] Low vision is defined according to the World Health Organization (WHO) as best-corrected visual acuity (BCVA) of <6/18 but equal to or better than 3/60 in the better-seeing eye, or a visual field of 20° or less from the point of fixation. Unlike individuals with blindness, those diagnosed

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with low vision retain residual visual functions that can be utilized in daily activities with appropriate rehabilitation and assistive devices. A 2017 systematic review estimated that approximately 216.6 million people had moderate-to-severe visual impairment (<6/18), while 36 million were blind.[1] Globally, the most common causes of visual impairment are treatable conditions such as uncorrected refractive errors and cataracts. In developed countries, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy (DR) remain the leading causes of low vision.[2] Low vision, particularly in older adults, hinders basic activities such as reading, walking, mobility, and driving. Furthermore, it limits participation in community, social, and civic life, and may adversely affect interpersonal relationships.[3] In children and adolescents, low vision interferes with sensory, physical, psychological, and social development, as participation is influenced by external factors such as education and parental support.[4] Despite its substantial impact, low-vision service provision remains inadequate in many countries owing to barriers related to funding, awareness, and access, particularly for women, rural, and disabled populations. Low vision is associated with an increased risk of falls, disability, and reduced quality of life.[5] Low vision rehabilitation is based on the principles of optical magnification, appropriate lighting, glare reduction, and contrast enhancement. Rehabilitation strategies include optical aids (e.g., telescopes, magnifiers, and high-diopter near spectacles), non-optical aids (e.g., lighting, large-print materials, and filtered lenses), electro-optical and electronic systems (e.g., closed-circuit television, tablets, and digital applications), and individualized education and rehabilitation programs.[6,7] The low vision quality of life questionnaire (LVQOL) is a widely used, vision-specific instrument designed to assess the impact of low vision on daily functioning and well-being.[8] The items in this scale relate to difficulties experienced by individuals with low vision in performing daily activities. It is frequently employed in clinical and research settings to evaluate the effectiveness of low-vision rehabilitation and quantify the quality of life in visually impaired populations.[8] The questionnaire consists of 25 items across four domains: distance vision/mobility/illumination, adaptation, reading/precision work, and activities of daily living. The Turkish version of the LVQOL was validated by Sahli and Idil *et al*.[9] This study aimed to describe the diagnostic distribution and clinical characteristics of patients referred to a low vision unit, and to report their visual outcomes, prescribed low-vision aids, and vision-related quality of life as assessed using the LVQOL.

Materials and Methods

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (approval no. 09.25.25-0296). This single-center retrospective study included 117 visually impaired patients referred to a tertiary care low vision unit between January 2023 and November 2024. Clinical and demographic data were retrospectively obtained from the medical records. Of the 117 referred patients, 23 were excluded for not meeting the diagnostic criteria for low vision, leaving 94 patients for analysis. LVQOL data were available for 48 patients.

Inclusion criteria were based on the WHO definition of low vision, defined as BCVA <6/18 and ≥3/60 in the better-seeing eye, or a visual field of ≤20° from the point of fixation. Patients with extremely limited residual visual function (BCVA worse than 3/60 or only light perception/hand motion) were excluded due to the expected lack of benefit from low-vision rehabilitation.

Among the excluded patients, two had decreased visual acuity secondary to blepharoptosis rather than intrinsic ocular pathology. Four patients did not meet the low-vision criteria. In five patients, visual impairment was due to uncorrected refractive error and resolved following appropriate refraction and spectacle prescription. The remaining patients were excluded due to insufficient residual visual function (Fig. 1).

Distance vision was assessed using telescopic spectacles at different magnification levels, whereas near vision was

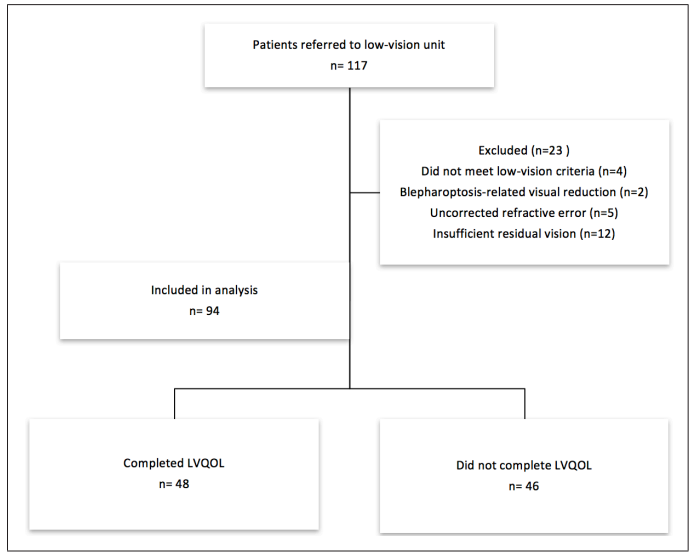

Fig. 1. Flow diagram illustrating patient selection, exclusion criteria, and availability of low vision quality of life questionnaire data in the study cohort.

evaluated using high-diopter near spectacles, telescope-mounted near attachments (referred to as "reading caps"), and magnifiers of varying strengths to determine the most appropriate device. Near visual acuity was measured using a standardized Turkish near reading chart at the patient's optimal working distance, defined as the distance at which the patient achieved the best visual performance.[10] Reading caps provide additional positive dioptric power and enable near tasks through telescopic systems. The need for filtered lenses, particularly in patients with photophobia, was also assessed, and the spectral characteristics of the prescribed filters were recorded. Filtered lenses refer to wavelength-specific absorptive filters (e.g., band-pass filters such as 527 nm), prescribed based on individual symptom profiles to reduce glare and enhance contrast sensitivity. Distance and near visual acuity achieved with low-vision aids were documented. Some patients were prescribed more than one type of low-vision aid based on their individual needs.

In addition to functional vision testing, vision-related quality of life was assessed using the LVQOL, a 25-item vision-focused instrument that assesses the impact of low vision on daily functioning and well-being. Responses were scored on a total scale of 120 points, and four domain-specific subscale scores were calculated. The LVQOL questionnaire could not be administered to all patients due to practical limitations, including low literacy levels, absence of caregiver assistance, and reduced cooperation, particularly among older individuals.

Statistical Analysis

For statistical analysis, continuous variables are presented as mean±standard deviation or median, depending on data distribution, and categorical variables as number (percentage). Normality of continuous variables (including age, BCVA, and LVQOL scores) was assessed using the Shapiro–Wilk test. Comparisons of distance and near visual acuity before and after low-vision aid prescription were performed using paired analyses on the same patients. Paired t-tests were used when assumptions of normality were met, and the Wilcoxon signed-rank test was used otherwise. Associations between age, best-eye BCVA, and LVQOL outcomes were quantified using Spearman rank correlation coefficients (ρ), as LVQOL scores did not meet normality assumptions and represent ordinal-like data, with results reported as ρ and two-sided *P*-values. LVQOL analyses were cross-sectional and restricted to questionnaire completers (*n*=48). Effect sizes and confidence intervals were not calculated due to the exploratory nature of the study. No imputation or adjustment for multiple comparisons was performed, and α=0.05 defined statistical significance.

Results

The 94 patients included in the study had a mean age of 43.63±28.03 (median, 34; range, 8–80), and 52 patients (55.31%) were male (Table 1). The most common diagnosis was AMD (*n*=26, 27.6%), followed by retinitis pigmentosa (RP; *n*=16, 17.02%), Stargardt disease (*n*=14, 14.89%), and albinism (*n*=12, 12.76%). Less common diagnoses included cone dystrophy (*n*=6, 6.4%), retinal detachment (*n*=4, 4.3%), glaucoma (*n*=3, 3.2%), retinal artery occlusion (*n*=2, 2.1%), coloboma (*n*=2, 2.1%), epiretinal membrane (*n*=2, 2.1%), optic neuritis (*n*=2, 2.1%), hydroxychloroquine toxicity (*n*=2, 2.1%), amblyopia (*n*=2, 2.1%), and Bardet–Biedl syndrome (*n*=1, 1.1%) (Table 2). Mean baseline BCVA

Table 1. Demographic and baseline clinical characteristics (*n*=94)

Variable	Baseline
Age, years, mean±SD (median, range)	43.6±28.0 (34, 8–80)
Sex, male, *n* (%)	52 (55.3)
Better-eye BCVA (LogMAR) mean±SD	0.96±0.47
Worse-eye BCVA (LogMAR), mean±SD	1.40±0.75
Near visual acuity (LogMAR) mean±SD	0.58±0.30

BCVA: Best-corrected visual acuity; SD: Standard deviation

Table 2. Distribution of primary diagnoses in the study population (*n*=94)

Diagnosis	*n* (%)
Age-related macular degeneration	26 (27.6)
Retinitis pigmentosa	16 (17.0)
Stargardt disease	14 (14.9)
Albinism	12 (12.8)
Cone dystrophy	6 (6.4)
Retinal detachment	4 (4.3)
Glaucoma	3 (3.2)
Retinal artery occlusion	2 (2.1)
Coloboma	2 (2.1)
Epiretinal membrane	2 (2.1)
Optic neuritis	2 (2.1)
Hydroxychloroquine toxicity	2 (2.1)
Amblyopia	2 (2.1)
Bardet–Biedl syndrome	1 (1.1)

was 0.96±0.47 LogMAR in the better eye and 1.40±0.75 LogMAR in the worse eye. BCVA with telescopic low-vision devices under standardized testing conditions was 0.28±0.21 LogMAR (p<0.001) [Table 3]. Best-achieved near visual acuity with high-diopter near spectacles and magnification devices under testing conditions was 0.18±0.13 LogMAR, compared with a baseline value of 0.58±0.30 LogMAR (p<0.001; [Table 3]). A total of 68 patients were prescribed telescopic devices to improve their distance vision. Of these, 56 patients (82.3%) were provided with Galilean telescopic spectacles at 2.2× magnification (n=10, 17.8%), 2.5× magnification (n=14, 25.0%), and 3× magnification (n=32, 57.0%). Keplerian telescopes were prescribed to 12 patients (17.7%), with 4× magnification (n=6, 50.0%) and 6× magnification (n=6, 50.0%). Low-vision aids for near tasks were prescribed to 34 patients (36.2%). Among them, 28 patients (82.4%) received high-diopter near spectacles: 14 (41.2%) with +10 D lenses, 8 (23.5%) with +8 D lenses, and 6 (17.6%) with +6 D lenses. Reading caps were prescribed to 6 patients (17.6%), including four (11.8%) with +6 D and two (5.9%) with +5 D. In addition to high-diopter near spectacles and reading caps, magnifiers were prescribed to 26 patients (27.7%), including 7 × 28 illuminated handheld magnifiers (n=4, 15.4%), 3× illuminated stand magnifiers (n=6, 23.1%), 1.8× spherical (dome) magnifiers (n=12, 46.2%), and 2.5× clip-on spectacle magnifiers (n=4, 15.4%). Filtered lenses were prescribed to 22 patients (23.4%) with photophobia. Etiologies in this subgroup included RP (n=10, 45.5%), albinism (n=8, 36.4%), Stargardt disease (n=2, 9.1%), and AMD (n=2, 9.1%). Filter selection was individualized based on the symptom profile and task demands, and the most frequently prescribed filter was the 527-nm band-pass filter (n=12, 54.5%). The distribution of prescribed low-vision aids is summarized in Table 4.

Forty-eight patients completed LVQOL assessment. The mean total score was 49.83±17.13 (range, 0–120). The mean subscales were 21.29±9.54 for distance/mobility/illumination, 7.95±3.73 for adaptation, 10.62±4.32 for reading/fine work, and 9.95±4.84 for activities of daily living. Increasing age was inversely correlated with reading/fine work (ρ=−0.576, p=0.003), activities of daily living (ρ=−0.509, p=0.011), and the LVQOL total score (ρ=−0.478, p=0.018). Worse best-eye LogMAR was inversely correlated with distance/mobility/illumination (ρ=−0.749, p<0.001) and the LVQOL total score (ρ=−0.556, p=0.005).

Table 3. Visual outcomes before and after low-vision aid prescription

Variable	Baseline	With low-vision aids	p
Better-eye BCVA (LogMAR)	0.96±0.47	0.28±0.21	<0.001
Near visual acuity (LogMAR)	0.58±0.30	0.18±0.13	<0.001

Values are presented as mean±standard deviation. BCVA: Best-corrected visual acuity

Table 4. Prescribed low vision aids for distance vision, near tasks, and photophobia (n=94)

Vision category	Device type/specification	n (%)
Distance vision aids	Any telescopic device	68 (72.3)
	Galilean telescopes	56/68 (82.3)
	2.2× magnification	10/56 (17.8)
	2.5× magnification	14/56 (25.0)
	3× magnification	32/56 (57.0)
	Keplerian telescopes	12/68 (17.7)
	4× magnification	6/12 (50.0)
	6× magnification	6/12 (50.0)
Near vision aids	Any near vision aid	34 (36.2)
	High-diopter near spectacles	28/34 (82.4)
	+10 D	14/28 (41.2)
	+8 D	8/28 (23.5)
	+6 D	6/28 (17.6)
	Reading caps	6/34 (17.6)
	+6 D	4/6 (66.7)
	+5 D	2/6 (33.3)
	Magnifiers	26/94 (27.7)
	7×28 illuminated handheld	4/26 (15.4)
	3× illuminated stand	6/26 (23.1)
	1.8× spherical (dome)	12/26 (46.2)
	2.5× clip-on spectacle	4/26 (15.4)
Filtered lenses	Any filtered lens	22/94 (23.4)
	527-nm band-pass filter	12/22 (54.5)
	Other filters	10/22 (45.5)

Percentages are reported according to the relevant denominators. Overall values are calculated from the total cohort (n=94), whereas subgroup percentages are calculated within each device category

Discussion

Low-vision rehabilitation is a fundamental approach aimed at optimizing remaining vision and enabling individuals with severe vision loss to continue their daily activities. The present cohort represents a valuable sample, given the limited number of low-vision units in Turkey.

The present study represents one of the limited reports from Turkey describing a predominantly young/adult referral profile (median age, 34 years). This age distribution differs from that reported in most European series, which are typically dominated by older age groups, but it aligns more closely with data from Jordan.[11-13] In a study by Ozen Tunay *et al*.,[14] hereditary fundus dystrophies (36%) were the most common cause of low vision in children with a median age of 10 years. The present study shows a similar etiologic distribution in younger patient populations. This difference may reflect variations in referral pathways, access to low-vision services, and regional demographic characteristics.

In our cohort, acquired macular diseases and hereditary or early-onset conditions (e.g., RP, Stargardt, albinism) accounted for a substantial portion of low-vision etiologies. Similarly, a study conducted in Jordan reported that RP was predominant among younger individuals, whereas DR and AMD were more prominent in those aged >60 years.[13] In contrast, studies from China have identified degenerative myopia and congenital cataracts as leading causes among younger patients.[6] In Europe, the burden of AMD and DR is higher.[11] A study by Ozen Tunay *et al*.[14] in Turkey reported that the most common cause of low vision in children with a median age of 10 was hereditary fundus dystrophy (36%), followed by cortical visual impairment (18%). The high proportion of hereditary conditions in our cohort may be related to regional patterns of consanguineous marriage; however, this factor was not assessed in the present study.

Management strategies for distance vision in our cohort are comparable to those reported in Jordan and China, where telescopic glasses are the most frequently utilized.[6,13] In contrast, some European centers report a higher use of electronic distance systems.[12] To address issues of near vision, high-diopter near spectacles and reading caps that can be mounted on telescopic glasses were provided, along with complementary magnifiers. A pediatric cohort in Turkey that utilized telescopic lenses for distance vision and magnifiers or telemicroscopes for near vision corroborated a regional predilection for uncomplicated, task-specific optical aids in both adults and children. The limited use of electronic devices among Turkish cohorts may be associated with factors such as cost, accessibility, and unmet training requirements.

Perrault *et al*.[12] reported improvements of 0.2 LogMAR in distance visual acuity and 0.3 LogMAR in near visual acuity in a study involving 501 patients using visual aids. In the present study, distance and near visual acuity values measured with low-vision aids differed significantly from baseline measurements, consistent with findings from previous studies.[15,16] The improvements in visual acuity observed in this study should be interpreted in the context of device-assisted performance. The reported values represent best-achieved visual acuity under standardized testing conditions using telescopic devices for distance vision and high-diopter near spectacles and magnifiers for near tasks, and do not indicate restoration of underlying visual function. Furthermore, these measurements may not fully reflect real-world visual performance, which depends on factors such as patient adaptation, training, environmental conditions, and long-term device use.

In the present study, filtered lenses were prescribed for photophobia associated with RP, albinism, Stargardt disease, and AMD. Existing evidence indicates that optical filters can reduce glare, improve contrast sensitivity, and enhance visual acuity.[7,14,17] For instance, in a prospective study of patients with RP, filtered lenses were superior to telescopic glasses in terms of contrast sensitivity, maximum reading speed, and LVQOL total scores, while no difference was observed in distance visual acuity.[17] In a pediatric Turkish cohort, filters were used in 14% of children with albinism.[14] Our findings suggest that filtered lenses may be beneficial not only for patients with albinism but also for those with other diagnoses who experience photophobia.

Low vision is associated with reduced health-related and vision-related quality of life, affecting physical, psychological, and social domains. Patients report difficulties with daily activities, increased risk of depression, loss of independence, and greater need for assistance, particularly as visual acuity declines below critical thresholds.[3,18] The mean LVQOL total score in our study (49.83±17.13) is comparable to values reported in previous studies conducted in Turkish low-vision populations. Sahli and Idil reported a mean LVQOL score of 42.31±16.19 in a similar cohort, indicating a similar level of vision-related quality-of-life impairment across cohorts.[19] This similarity supports the external validity of our findings. Patient-reported functioning displayed domain-specific associations: age was more strongly related to reading ability and activities of daily living, whereas best-eye acuity was most closely associated with distance/mobility/illumination and total LVQOL scores. This pattern underscores that visual acuity alone is an incomplete surrogate for everyday visual ability and supports task-matched prescriptions (e.g., telescopes for distance and high-diopter near spectacles or magnifiers for reading) combined with appropriate training and follow-up in low-vision rehabilitation. These findings support a multidimensional assessment beyond visual acuity alone.

Our findings demonstrate that clinically meaningful gains can be achieved using simple and accessible low-vision aid solutions. The number of low-vision outpatient clinics in Turkey is limited, which is reflected in the paucity of national studies conducted in the field of low-vision rehabilitation. International literature primarily includes data from Western countries, and differences in patient profiles, socioeconomic factors, and device preferences are evident.[12] The predominance of telescopic and high-diopter near spectacles in our cohort may be related to economic considerations and patient compliance. Therefore, this study fills a significant gap in the national literature by revealing the diagnostic distribution, clinical characteristics, and device requirements of patients presenting to low-vision units in Turkey. The inclusion of patients across a wide age range with diverse etiologies contributes to a more comprehensive understanding of the low vision spectrum in our country. Future multicenter prospective studies incorporating long-term use and adaptation outcomes will further clarify diagnosis-specific rehabilitation strategies.

Study Limitations

The retrospective design limits causal inference, and the sample size was relatively small and heterogeneous. The cross-sectional assessment of the LVQOL precluded evaluation of longitudinal changes in quality-of-life and long-term device use. In addition, unmeasured sociodemographic or genetic factors may have influenced the outcomes, and referral bias inherent to a tertiary care center setting may limit generalizability. LVQOL data were available for only a subset of patients, which may have introduced selection bias. Patients with low literacy, absence of caregiver assistance, or reduced cooperation, particularly among older individuals, were less likely to complete the questionnaire, potentially resulting in overrepresentation of individuals with better functional and cognitive status. Therefore, the LVQOL findings should be interpreted with caution.

Conclusion

Low-vision rehabilitation with task-specific optical aids provides meaningful improvements in distance and near visual function. Among patients who completed the LVQOL, quality-of-life outcomes were associated with age and visual acuity, underscoring the importance of timely referral to low-vision units and a multidimensional approach to low-vision care.

Ethics Committee Approval: This study was approved by The Ethics committee of Marmara University Faculty of Medicine (18.04.2025 – Approval no. 09.2025.25-0296).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Clinical and morphological predictors of visual outcomes following inverted internal limiting membrane flap surgery for large macular holes

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Abstract

Purpose: The purpose of the study was to evaluate the anatomical and functional outcomes of the inverted internal limiting membrane (ILM) flap technique in patients with large macular holes (MHs) and identify independent prognostic factors that predict post-operative visual acuity.

Methods: This retrospective study included 48 eyes of 48 patients who underwent pars plana vitrectomy and inverted ILM flap technique for idiopathic MHs ≥400 µm. Pre-operative and post-operative best-corrected visual acuity (BCVA), swept-source optical coherence tomography (SS-OCT) parameters, and various clinical factors were evaluated. Multivariate regression analysis was performed to identify independent prognostic factors for the post-operative BCVA.

Results: The mean BCVA improved significantly from 1.27±0.41 logMAR preoperatively to 0.62±0.37 logMAR at 6 months postoperatively ($p<0.001$). U-shaped closure was associated with better BCVA than V- and W-shaped closures ($p=0.001$). Patients with symptom duration ≤6 months and complete post-operative restoration of the external limiting membrane (ELM) and ellipsoid zone demonstrated significantly better BCVA ($p<0.01$). Pre-operative BCVA ($\beta=0.637$, $p<0.001$) and MH index (MHI) ($\beta=-0.261$, $p=0.029$) were significant independent determinants of post-operative BCVA.

Conclusion: The inverted ILM flap technique provides high anatomical closure rates and significant visual improvement in large MH surgery. Pre-operative BCVA and MHI were significant independent prognostic factors for post-operative visual outcomes. Structural SS-OCT parameters can be clinically useful in predicting post-operative functional outcomes.

Keywords: Inverted internal limiting membrane flap, Macular hole, Optical coherence tomography, Pars plana vitrectomy, Prognostic factors, Visual acuity

Idiopathic full-thickness macular hole (MH) is a foveal disorder characterized by a complete discontinuity of the neurosensory retina, extending from the internal limiting membrane (ILM) to the retinal pigment epithelium.[1] Advanced age and female sex have been consistently reported as the main risk factors for idiopathic full-thickness MH, with an estimated prevalence of approximately 0.2–0.8% in the general population.[1] Both anteroposterior

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and tangential vitreoretinal traction are considered key mechanisms contributing to the development of this condition.[2]

Surgical intervention remains the cornerstone of MH treatment.[3] The introduction of pars plana vitrectomy (PPV) combined with ILM peeling and gas tamponade, first described by Kelly and Wendel, marked a significant advancement in MH surgery.[4] This technique has substantially enhanced anatomical closure rates and has been established as the standard treatment approach.

In recent years, the inverted ILM flap technique has emerged as an alternative surgical strategy, particularly for large and chronic MHs, due to its association with higher closure rates and better visual outcomes compared with conventional ILM peeling.[5,6] In addition to enhancing anatomical success, this technique has been shown to support restoration of the foveal architecture and preservation of photoreceptor layer integrity.[7,8]

Previous research has reported multiple prognostic factors associated with functional outcomes after MH surgery. These factors mainly include pre-operative clinical characteristics such as patient age, baseline visual acuity, and symptom duration, in addition to optical coherence tomography (OCT)–derived measurements and indices, as well as post-operative foveal microstructural recovery.[9-12] Nevertheless, the relative contribution of each prognostic parameter to surgical outcomes remains controversial. Although a substantial number of studies have evaluated the prognostic significance of OCT parameters in conventional ILM peeling surgery, data regarding their relevance in patients treated with the inverted ILM flap technique are limited.[13] Considering the unique biological and structural characteristics of the inverted ILM flap technique – particularly its ability to provide a scaffold for retinal tissue and facilitate glial cell proliferation – it has been hypothesized that the prognostic impact of OCT parameters may differ in this surgical setting.[14] A clearer understanding of these prognostic indicators is essential for optimizing patient selection, refining surgical strategies, and ultimately improving visual outcomes in patients undergoing this procedure.

In this study, anatomical and functional results after inverted ILM flap surgery for large MHs were analyzed, and variables independently associated with post-operative visual acuity were examined.

Materials and Methods

Study Design

This retrospective study was performed at the Department of Ophthalmology, Kartal Lütfi Kırdar City Hospital. Ethical approval was obtained from the Ethics Committee of Kartal Lütfi Kırdar City Hospital (approval no: 2024/010.99/3/3), and all procedures adhered to the tenets of the Declaration of Helsinki. A total of 48 eyes from 48 consecutive patients who underwent PPV with the ILM flap technique for idiopathic MH between January 2020 and November 2024 were included in the analysis. Patients were eligible if the minimum MH diameter was ≥400 μm and the post-operative follow-up period was at least 6 months. Patients were excluded if they had a history of vitreoretinal surgery other than for MH, coexisting retinal vascular or degenerative disorders (including diabetic or hypertensive retinopathy, retinal vascular occlusion, high myopia, age-related macular degeneration, or uveitis), glaucoma, or a history of ocular trauma. Clinical data were retrieved from medical records and included the duration of visual symptoms, baseline and final best-corrected visual acuity (BCVA), findings from anterior and posterior segment examinations, concomitant cataract surgery performed during PPV, and the type of endotamponade used. BCVA measurements obtained using the Snellen-based optotypes were converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis.

OCT Image Measurements

All participants underwent swept-source OCT (SS-OCT) imaging (Topcon, Tokyo, Japan) both preoperatively and postoperatively. For consistency, identical scan locations were analyzed in both examinations. SS-OCT assessments included the minimum diameter (MD) of MH, defined as the shortest distance between the opposing hole margins; the base diameter (BD), representing the widest dimension at the base; hole height (H); cone height (CH); and the presence of discontinuities in the external limiting membrane (ELM) and ellipsoid zone (EZ) (Fig. 1). All measurements were obtained manually using the built-in caliper tool. In addition, the presence of an epiretinal membrane (ERM) was documented.

Using these parameters, MH–related indices and MH volume (MHV) were calculated according to the truncated cone model, as previously described.[12] The MH–related indices were defined as follows:

MH Index (MHI): H/BD

Tractional hole index (THI): H/MD

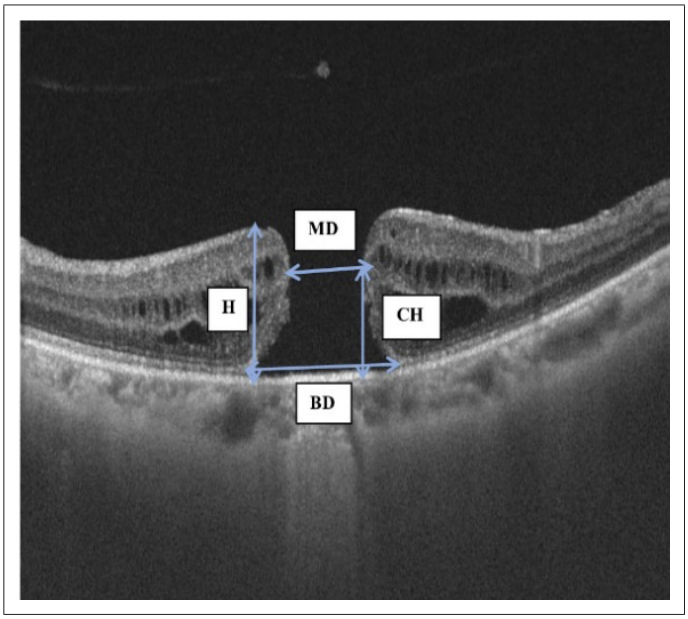

Fig. 1. Optical coherence tomography image showing various measurements.

Diameter hole index (DHI): MD/BD

MHV: (1/3) * π *CH*((BD/2) ^{2}+BD/2*MD/2+(MD/2)^2)

Based on cross-sectional SS-OCT images, post-operative foveal closure configurations were classified into three patterns: U-shaped, V-shaped, and irregular closed (W-shaped). Image assessments were conducted independently by two investigators (D.C.Y. and U.K.).

Surgical Technique

All surgical procedures were performed using PPV systems (DORC, Holland) under retrobulbar anesthesia by an experienced vitreoretinal surgeon (G.A.). In patients with coexisting cataract, PPV was combined with phacoemulsification and intraocular lens implantation. Following core vitrectomy, the ILM was visualized using 0.025% Brilliant Blue G dye (Brilliant Peel, Fluoron, Germany). When an ERM was present, it was carefully removed before ILM manipulation. The ILM was then peeled using 23-gauge forceps in a semicircular configuration spanning approximately 180° from the temporal aspect of the MH, extending 2–2.5 disc diameters from the optic disc. The peeled ILM flap was intentionally left attached to the temporal margin of the MH to serve as a hinge. Any irregular ILM edges were trimmed using a vitrector. Subsequently, approximately 3 mL of perfluorocarbon (PFC) liquid was slowly injected from the temporal side of the MH, allowing controlled inversion and stable positioning of the ILM flap over the macular defect. While the PFC fluid provided mechanical stabilization of the ILM flap over the MH, peripheral vitrectomy was completed. Liquid–air exchange was then performed, and the PFC was aspirated from the nasal side using a backflush cannula. Adequate stabilization of the ILM flap was achieved in all patients. Finally, either 12% perfluoropropane (C3F8) or 25% sulfur hexafluoride (SF6) gas was injected. Postoperatively, patients were instructed to maintain a face-down position for 3 days.

Statistical Analysis

All statistical analyses were conducted with the Statistical Package for the Social Sciences software (version 25.0; IBM Corp., New York, USA). Continuous variables are reported as mean±standard deviation (SD). The distribution of the data was examined using the Shapiro–Wilk test. Depending on data distribution, parametric or non-parametric statistical methods were applied. Changes between pre-operative and 6-month post-operative measurements were assessed using either the paired samples t-test or the Wilcoxon signed-rank test. Comparisons between independent groups were performed using the Mann–Whitney U test or the Kruskal–Wallis test, as appropriate. Associations between continuous variables were evaluated using Pearson correlation analysis. Multivariate regression analysis was applied to identify factors independently associated with post-operative outcomes. A $p<0.05$ was considered indicative of statistical significance.

Results

A total of 48 patients were included in the analysis. Of these, 21 patients (43.8%) were male, and 27 (56.2%) were female. The mean age of the study population was 66.7±8.45 years (range, 45–85 years). At the time of surgery, 37 eyes were phakic, whereas 11 eyes were pseudophakic. Detailed demographic and baseline characteristics of the participants are summarized in Table 1.

Based on SS-OCT measurements, the mean MD of the MH was 563.87±116.13 µm, while the mean BD measured 1097.95±336.98 µm. The average hole H was calculated as 431.46±81.73 µm. The calculated values for the THI, DHI, and MHI were 0.79±0.20, 0.53±0.11, and 0.41±0.11, respectively. In addition, the mean MHV was determined to

Table 1. Demographic characteristics of patients

Characteristic	Values
Age, years (median, min–max)	67.50/45–85
Eye, right/left *n* (%)	22 (45.8)/26 (54.2)
Gender, male/female *n* (%)	21 (43.8)/27 (56.2)
Lens status: Phakic/Pseudophakic *n* (%)	37 (77.0)/11 (23.0)

Table 2. Evaluation of post-operative BCVA (LogMAR) according to MH closure shapes

Closure shape	Number (*n*)	Post-operative BCVA	*p*
U-shape	28/48 (58.4)	0.36±0.20	0.001*
V-shape	16/48 (33.3)	0.88±0.15	
W-shape	4/48 (8.3)	1.35±0.10	

BCVA: Best corrected visual acuity; MH: Macular hole. *Kruskal–Wallis Test

be 0.18±0.13 mm^3.

The mean BCVA (LogMAR) improved from 1.27±0.41 before surgery to 0.62±0.37 at the 6th month following the procedure. This visual improvement was found to be statistically significant (p<0.001), and none of the patients experienced post-operative visual deterioration during follow-up. Eyes demonstrating a U-shaped foveal closure achieved superior visual outcomes compared with those showing V-shaped or irregular (W-shaped) closure patterns (Table 2). Structural analysis revealed a marked reduction in both ELM and EZ defect dimensions by the 6th post-operative month (p<0.001). Complete restoration of the ELM was observed in 30 eyes, while full recovery of the EZ occurred in 27 eyes (Fig. 2). Among these, total EZ restoration was documented in 21 eyes with U-shaped closure and in six eyes with V-shaped closure. In contrast, persistent EZ disruption was noted in all eyes exhibiting a W-shaped closure configuration.

Post-operative visual acuity was further analyzed in relation to several clinical parameters. Significantly better post-operative BCVA outcomes were observed in patients with a symptom duration of <6 months and in those showing complete post-operative restoration of the ELM and EZ on SS-OCT imaging (p<0.01). Conversely, the presence of an ERM did not show a statistically significant relationship with post-operative BCVA (p=0.092). Moreover, post-operative visual outcomes did not differ significantly according to the type of endotamponade applied or the surgical approach used (Table 3).

Significant correlations were identified between post-operative BCVA and multiple pre-operative variables. Positive correlations were observed with pre-operative BCVA, MD, BD, MDH, and EZ and ELM defect lengths, whereas MDI and TDI were negatively correlated with post-operative BCVA. The most pronounced associations were noted for EZ defect length (r=0.626, p=0.001) and MDI (r=−0.594, p=0.001) (Table 4).

Variables demonstrating significant associations with post-operative BCVA in correlation analyses were entered

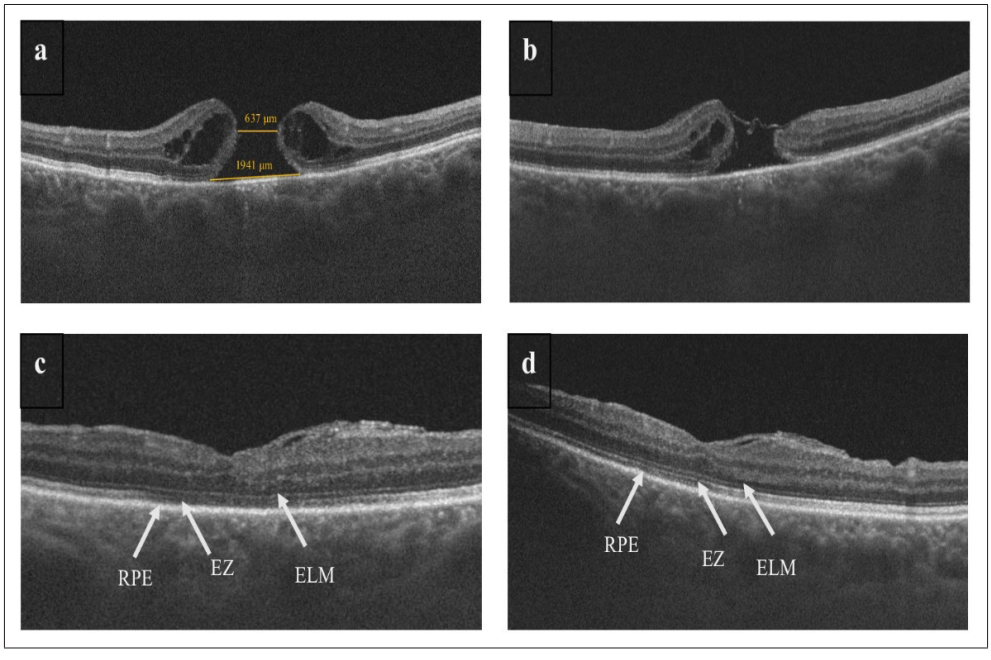

Fig. 2. **(a)** Pre-operative cross-sectional B-scan swept-source optical coherence tomography image of a 68-year-old man with Macular hole (MH). **(b)** Fifteen days after surgery, the internal limiting membrane flap was placed, but the opening of the hole continued to be observed. **(c)** One month after surgery, the MH was closed; however, incomplete restoration was observed in the outer retinal layers. **(d)** Six months after surgery, complete restoration of the ellipsoid zone and external limiting membrane was observed.

Table 3. Comparison of post-operative BCVA (LogMAR) with parameters

Parameter	Group	N	Mean	SD	*p*
Symptom duration	≤6	25	0.34	0.21	<0.01
	>6	23	0.92	0.25	
Post-operative ELM	Intact	30	0.37	0.22	<0.01
	Lost	18	0.93	0.26	
Post-operative EZ	Intact	27	0.37	0.22	<0.01
	Lost	21	0.93	0.26	
ERM	Present	23	0.72	0.41	0.092
	Absent	25	0.53	0.3	
Tamponade	SF6	26	0.57	0.32	0.367
	C3F8	22	0.68	0.42	
Surgical Type	Combined PPV	37	0.6	0.4	0.258
	PPV	11	0.7	0.23	

* Mann–Whitney U-test, M; BCVA: Best corrected visual acuity; ELM: External limiting membrane; EZ: Elipsoid zone; ERM: Epiretinal membrane; PPV: Pars plana vitrectomy

Table 4. Pearson correlation analysis between post-operative BCVA (LogMAR) and parameters

Parameter	R	*p*
Pre-operative BCVA	0.549	0.001
Minimum Diameter	0.542	0.001
Base Diameter	0.543	0.001
Height	−0.005	0.975
MHI	−0.594	0.001
THI	−0.415	0.007
DHI	−0.256	0.107
MHV	0.419	0.006
Pre-operative EZ defect length	0.626	0.001
Pre-operative ELM defect length	0.618	0.001
Post-operative CMT	−0.235	0.108

BCVA: Best corrected visual acuity; MHI: Macular hole index; THI: Tractional hole index; DHI: Diameter hole index; MHV: Macular hole volume; EZ: Ellipsoid zone; ELM: External limiting membrane; CMT: Central macular thickness

into a multiple linear regression model. During model construction, MD, BD, MHV, and the pre-operative lengths of EZ and ELM defects were identified as sources of multicollinearity, reflected by elevated variance inflation factor values, and did not provide a statistically meaningful contribution ($p>0.05$); therefore, these variables were removed from the model. In the final forward stepwise regression analysis, pre-operative BCVA (β=0.637, $p<0.001$) and MHI (β=−0.261, $p=0.029$) emerged as independent predictors of post-operative visual acuity, while all remaining variables were excluded due to lack of statistical significance (Fig. 3 and 4).

During the follow-up, none of the patients experienced major post-operative adverse events, including endophthalmitis, retinal detachment, vitreous hemorrhage, or secondary glaucoma.

Discussion

Advances in surgical approaches for MH repair have led to substantial improvements in anatomical closure rates. Nevertheless, successful anatomical closure does not invariably translate into satisfactory visual recovery. Previous studies have explored multiple clinical and morphological factors that may influence both functional and structural outcomes following MH surgery.[8,12,14] Despite this, evidence regarding the prognostic relevance of these parameters in cases treated specifically with the inverted ILM flap technique remains limited. In the present study, we systematically analyzed the prognostic

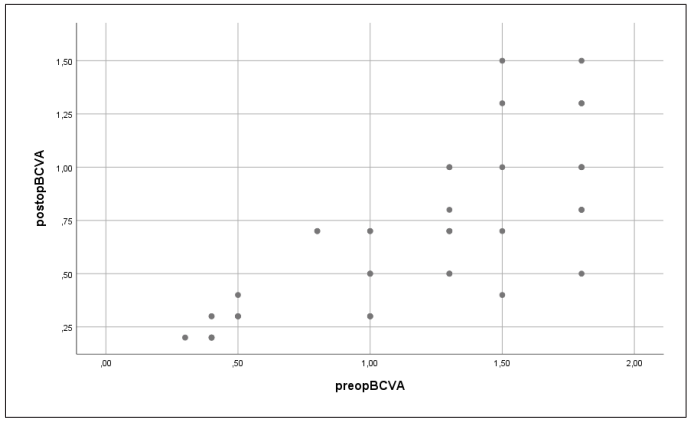

Fig. 3. Regression analysis between pre-operative best-corrected visual acuity (BCVA) and post-operative BCVA.

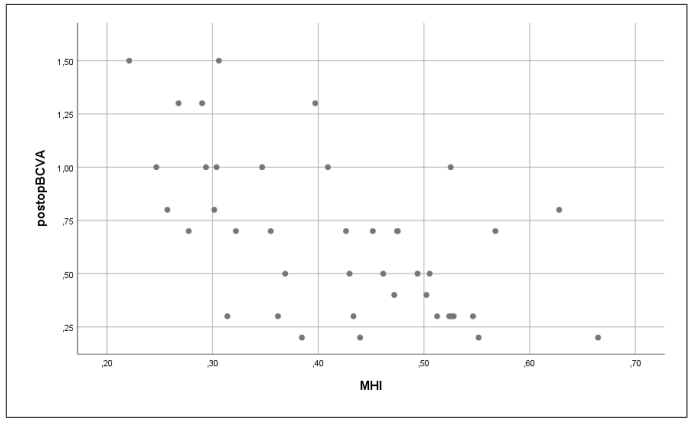

Fig. 4. Regression analysis between Macular hole index and post-operative best-corrected visual acuity.

significance of SS-OCT–derived structural measurements alongside a range of pre-operative and post-operative clinical variables in predicting post-operative BCVA in patients with large MH treated using the inverted ILM flap technique. Anatomical hole closure was achieved in all cases, and post-operative visual acuity improved in every patient included in the analysis. Multivariate evaluation revealed that baseline BCVA and the MHI were the only independent predictors of post-operative visual outcomes.

Earlier reports by Michalewska *et al*. [15] drew attention to the potential instability of the inverted ILM flap during the air–fluid exchange phase, identifying this step as a notable technical limitation of the procedure. In response to this issue, Andrew *et al*. [16] proposed the adjunctive use of viscoelastic materials to enhance flap stability, while Shin *et al*. [17] introduced PFC liquid (PFCL) before air–fluid exchange and reported complete anatomical closure in all treated cases. In the present cohort, no instances of ILM flap dislocation were observed. We consider that the application of PFCL, combined with gentle manipulation of the ILM flap, played a key role in maintaining its adherence to the macular surface, thereby supporting optimal anatomical and structural restoration.

Michalewska *et al*. [18] reported that post-operative visual outcomes were most favorable in eyes exhibiting a U-shaped foveal configuration after surgery. In the same study, the temporal inverted ILM flap approach was shown to promote U-shaped closure, thereby contributing to superior visual acuity results. The outcomes of the present study align with these observations. In our cohort, U-shaped closure occurred more frequently than V- or W-shaped patterns and was accompanied by significantly better post-operative BCVA.

Research on the influence of ERM on surgical outcomes is limited. Iwasaki *et al*.[19] found that the presence of ERM hinders morphological improvement; however, its impact on visual outcomes is not consistently significant. In our investigation, although patients with ERM exhibited a slightly reduced final BCVA, this reduction was not statistically significant.

Residual Müller cell fragments within the inverted ILM flap are believed to promote glial proliferation, thereby facilitating photoreceptor realignment and structural reorganization. The gradual restoration of the ELM and EZ has been shown to be closely associated with visual recovery, and these reparative processes may continue for several months following successful full-thickness MH closure. Bleidißel *et al*.[20] reported that both the reduction in ELM and EZ defect size and complete layer restoration continued up to 12 months after surgery in patients treated with the inverted ILM flap technique. In contrast, Kocak *et al*.[21] observed complete ELM and EZ recovery rates of 57.1% and 53.6%, respectively, at post-operative month 6 in eyes managed with the temporal inverted ILM flap approach. In the present study, complete restoration of the ELM and EZ was achieved in 62.5% and 56.2% of cases, respectively, yielding results comparable to those previously reported. Previous investigations have consistently demonstrated a strong association between post-operative ELM and EZ integrity and final visual acuity outcomes.[18,22,23] Wakabayashi *et al*. [22] and Ramtohul *et al*. [23], emphasized that preservation of these outer retinal layers is a key determinant of post-operative BCVA. While Michalewska *et al*. [18] noted significantly poorer visual outcomes in eyes with persistent ELM and EZ disruption. Similarly, in our cohort, defect sizes of the ELM and EZ showed a significant post-operative reduction, and patients with complete restoration exhibited superior BCVA outcomes.

Advances in SS-OCT technology have made it possible to evaluate retinal microstructure in greater detail, thereby improving insight into how anatomical characteristics influence post-operative visual function. Bleidißel *et al*.[20] demonstrated that larger MH dimensions, including increased MD and BD, were associated with less favorable post-operative BCVA, whereas eyes with higher MHI values achieved better visual outcomes. Consistent with these findings, other researchers have also reported a positive association between MHI and post-operative BCVA.[9] Ruiz-Moreno *et al*.[10] similarly showed that MD, BD, THI, and MHI correlated significantly with post-operative visual outcomes; however, hole H and DHI were not associated with post-operative BCVA.

In the present study, greater MD and BD values, as well as longer pre-operative EZ and ELM defect lengths, were significantly related to poorer post-operative BCVA. Conversely, higher MHI and THI values were associated with superior visual outcomes. Taken together, these results are in agreement with previously published data and further emphasize the prognostic importance of morphological parameters – particularly MHI and MD – in predicting visual recovery after MH surgery.

The association between post-operative BCVA and MHV has been investigated in a limited number of studies, with inconsistent findings reported across the literature. Xu *et al*. [24] demonstrated a significant relationship between

MHV and BCVA at the 6th post-operative month, whereas Pilli *et al*. [25] emphasized the role of inner macular volume in predicting visual outcomes. In another study, Unsal *et al*.[12], identified BD and MHV as the parameters most strongly correlated with post-operative BCVA. In the present study, MHV showed a significant positive correlation with post-operative BCVA in univariate analysis. However, when MHV, pre-operative EZ defect length, and other statistically significant variables were entered into the multivariate regression model, none of these parameters retained independent predictive significance. These findings suggest that MHV, MD, BD, pre-operative EZ/ELM defect length, and THI should not be considered independent prognostic indicators, but rather interpreted in conjunction with other structural characteristics of the MH. Notably, multivariate regression analysis in our cohort identified pre-operative BCVA and MHI as the only independent predictors of post-operative visual acuity, indicating that these two parameters may serve as more robust and reliable prognostic markers for visual outcomes following surgery.

Symptom duration has also been shown to influence post-operative visual outcomes. Kazmerczak *et al*.[26] reported better post-operative BCVA in patients with a shorter duration of symptoms. Similarly, Bleidebel *et al*.[20] demonstrated that shorter symptom duration was associated with a smaller MD of MH. Consistent with these findings, our study showed that patients with symptom duration of <6 months achieved more favorable post-operative BCVA. These results emphasize the importance of early surgical intervention to optimize functional recovery.

The impact of different intraocular tamponade agents on post-operative visual outcomes has been previously investigated. Unsal *et al*.[12] demonstrated that patients receiving C3F8 exhibited greater visual improvement compared with those treated with SF6, a finding they attributed to the higher proportion of combined phacoemulsification and PPV procedures in the C3F8 group. Conversely, Modi *et al*.[27] reported no significant differences between SF6 and C3F8 with respect to either visual recovery or anatomical closure rates. Consistent with these observations, our study did not reveal a statistically significant difference in post-operative BCVA improvement between patients treated with SF6 and those treated with C3F8.

Study Limitations

Several limitations should be acknowledged when interpreting the results of this study. First, the retrospective nature of the design may have introduced selection bias and limited control over confounding variables. Second, the relatively small sample size may have reduced the statistical power, particularly in subgroup and regression analyses. In addition, the follow-up duration was restricted to 6 months, which may not be sufficient to capture the full extent of long-term anatomical remodeling and functional recovery following MH surgery. Structural restoration of retinal layers such as the ELM and EZ is known to be a gradual process that may continue beyond the early post-operative period. Therefore, evaluating ELM and EZ defect lengths only up to the 6th post-operative month may underestimate their true impact on long-term visual outcomes. Furthermore, the absence of serial long-term SS-OCT assessments precluded a detailed analysis of dynamic changes in retinal microstructure over time. Finally, this study did not include a control group treated with alternative surgical techniques, which limits direct comparison of prognostic factors across different surgical approaches. Future prospective studies with larger cohorts, extended follow-up periods, and standardized imaging protocols are warranted to validate and expand upon our findings.

Conclusion

The inverted ILM flap technique achieved favorable anatomical and visual outcomes in large MH surgery. Pre-operative BCVA and MHI emerged as key predictors of post-operative visual acuity, highlighting the potential role of SS-OCT–based structural parameters in outcome prediction. Nevertheless, further prospective studies with extended follow-up and larger cohorts are required to validate these findings and clarify their clinical applicability.

Ethics Committee Approval: This study was approved by The Ethics Committee of Kartal Lütfi Kırdar City Hospital (approval no: 2024/010.99/3/3).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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EUROPEAN EYE RESEARCH

CASE REPORT

Bilateral acute angle-closure glaucoma occurring after the initiation of hydrochlorothiazide

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Abstract

Acute angle-closure glaucoma (ACG) is an ocular emergency that can result in vision loss. In the literature, there are a limited number of studies reporting that sulfonamide-derived drugs could cause ACG. The case was a 68-year-old male who was started to be followed up with a diagnosis of bilateral primary open-angle glaucoma 3 years ago, and whose intraocular pressures were within normal limits with topical treatments. He presented with bilateral ocular pain, redness, blurred vision, headache, and nausea that started the day before. On examination, a sudden onset of bilateral myopic shift, choroidal effusion, and ACG was detected. Medical history revealed hydrochlorothiazide initiation 3 days ago for hypertension. Hydrochlorothiazide was suspected to be the cause of this clinical picture. After discontinuation of hydrochlorothiazide, along with administration of antiglaucomatous, anti-inflammatory, and cycloplegic agents, these changes were resolved within 2 weeks. It would be better for physicians to inform patients about these potential risks when prescribing hydrochlorothiazide-containing medications.

Keywords: Acute angle-closure glaucoma; choroidal effusion; hydrochlorothiazide; myopia.

Acute angle-closure glaucoma (ACG) is an ocular emergency that can result in vision loss. In the literature, there are a limited number of studies reporting that sulfonamide-derived drugs such as topiramate, sulfasalazine, indapamide, and acetazolamide could cause ACG.[1-3] Hydrochlorothiazide is also a sulfonamide-derived drug used in hypertension treatment. The purpose of the study is to present findings related to bilateral acute myopic shift, choroidal effusion, and ACG occurring after hydrochlorothiazide initiation in a patient previously followed up with a diagnosis of bilateral primary open-angle glaucoma (POAG).

Case Report

The case was a 68-year-old male who was started to be followed up with a diagnosis of bilateral POAG 3 years ago, and whose intraocular pressures (IOP) were within normal limits with topical treatments. He was using fixed-combination bimatoprost 0.03%/timolol 0.5% medication (Ganfort-Allergan) once daily and brimonidine tartrate 0.15% (Alphagan P-Allergan) twice daily. This case presented to our clinic with bilateral ocular pain, redness, blurred vision, headache, and nausea that had started the day before. Medical history showed that systemic hypertension

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had been diagnosed 3 days ago, and a combination of 5 mg ramipril and 25 mg hydrochlorothiazide (Delix 5 mg plus tablet, Sanofi-Aventis) had been started. Systemic inquiry revealed that he had no other accompanying systemic disease or medication use, but he had undergone cataract surgery on his left eye 2 months ago. Laboratory tests on admission showed normal serum sodium (141 mmol/L), potassium (4.8 mmol/L), and calcium (9.5 mmol/L) levels. At presentation, uncorrected visual acuity (VA) was counting fingers from 2 m in oculus dexter (OD), and 1/10 in oculus sinister (OS). Automatic-refraction examination showed myopia and astigmatism of −4.00 (−1.75 × 90°) diopters in OD and −2.00 (−1.00 × 115°) in OS. Best-corrected VA was 1/10 in OD and 3/10 in OS. IOP was measured as 38 mmHg in OD and 36 mmHg in OS by Goldmann applanation tonometry. Anterior-segment examination revealed bilateral conjunctival hyperemia, microcystic corneal edema, anterior-chamber shallowness without pupillary block, right nuclear cataract, and left pseudophakia. On gonioscopy, according to Schaffer classification, the anterior-chamber angle (ACA) of the right eye was found to be appositionally grade 0 without peripheral anterior synechiae in the superior and nasal regions, whereas Grade 1 in the inferior and temporal regions. In addition, ACA of the left eye was detected to be Grade 1 in the superior and nasal regions, whereas Grade 2 in the inferior and temporal regions. Anterior-chamber depth (ACD) was 1.80 mm in OD and 2.35 mm in OS on biometry. The cup-to-disc ratio was 0.6 in OD and 0.5 in OS using a slit lamp and a 90-diopter lens. Bilateral 360° choroidal effusions were observed during indirect ophthalmoscopy. Anterior segment-optical coherence tomography (AS-OCT) showed narrowing of the iridocorneal angle in both eyes. Magnetic resonance imaging (MRI) was also ordered to rule out other possible cranial and orbital pathologies. In our case, who was previously followed up for bilateral POAG, the presence of a history of hydrochlorothiazide initiation, bilateral involvement, absence of iris bombe, myopic status, and gonioscopic and ophthalmoscopic findings suggested secondary ACG related to sulfonamide-derived drugs. Therefore, the hydrochlorothiazide-containing antihypertensive drug was discontinued. In addition, since the topical antiglaucomatous medications he had been using previously contained a prostaglandin analog, the bimatoprost part was also stopped. Fixed-combination brimonidine tartrate 0.2%/timolol maleate 0.5% drops (Combigan-Allergan) twice daily were given as a new antiglaucomatous medication. IOP was also controlled by administering 20% mannitol intravenously at 1 g/kg/day for 3 days. Cycloplegia was induced in both eyes using cyclopentolate hydrochloride 1% (Sikloplejin-Abdi Ibrahim) 3 times daily. Prednisolone acetate 1% drops (Pred Forte-Allergan) 4 times daily were started to reduce the inflammatory response. Following these treatments, myopic shift decreased, and choroidal effusion resolved within 2 weeks. At the 2nd-week examination after the initial presentation, automatic-refraction values were −2.25 (−1.25 × 90°) in OD and −0.75 (−0.75 × 115°) in OS. Best-corrected VA improved to 5/10 in OD and 10/10 in OS. IOP was measured as 14 mmHg in OD and 12 mmHg in OS. ACD increased to 3.41 mm in OD and 3.82 mm in OS. During 1-year follow-up, there were no significant changes in the patient's findings, and no recurrence was observed. MRI and AS-OCT images at admission and after treatment are given in Figures 1-4.

Discussion

Our patient, who was previously followed up for bilateral POAG, had a sudden onset of bilateral myopic shift, choroidal effusion, and ACG. Medical history revealed hydrochlorothiazide initiation 3 days ago due to systemic hypertension. Previous studies have reported that some systemic drugs containing the sulfonamide group might cause uveal effusion, ciliary body edema, reduced zonular tension, and anterior displacement of the lens-iris diaphragm through an idiosyncratic reaction.[1,3,4] As a result of these

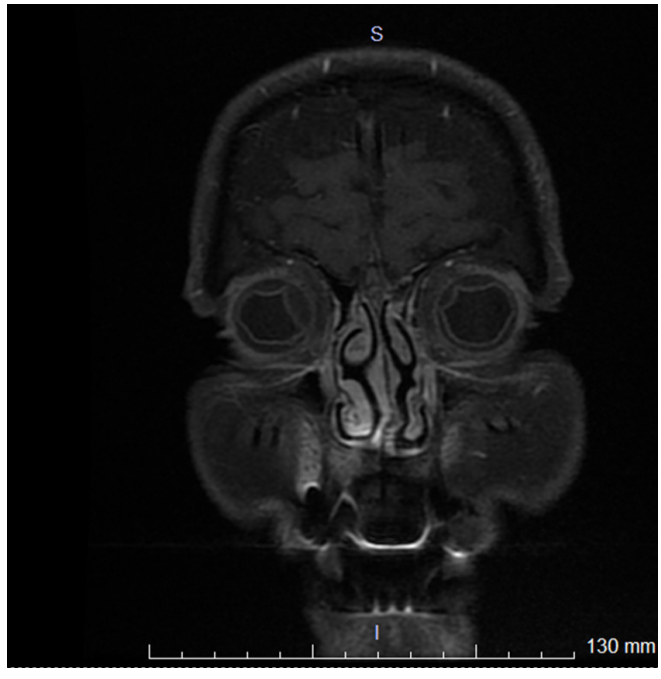

Fig. 1. Bilateral 360° choroidal effusions were detected on magnetic resonance imaging at the time of admission.

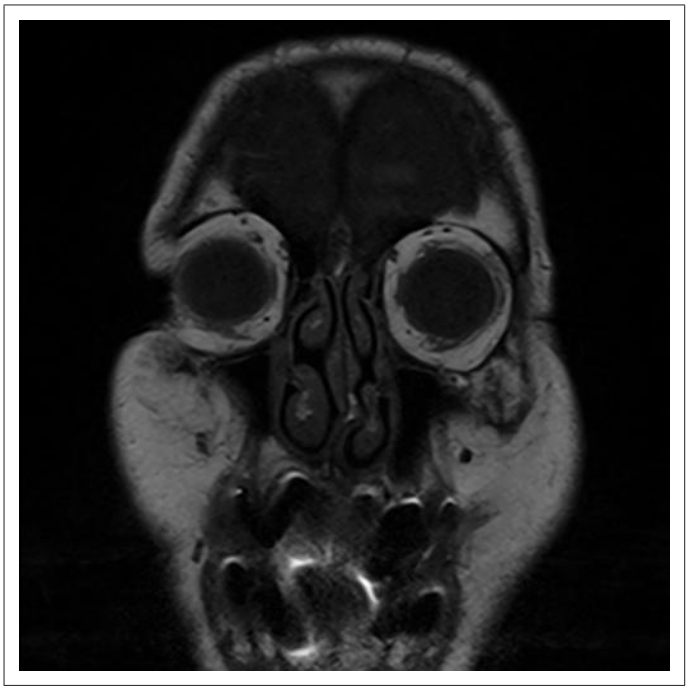

Fig. 2. Bilateral choroidal effusions were no longer visible on magnetic resonance imaging after treatment.

ocular changes, transient myopia and secondary ACG may develop.[1,3-6] To distinguish pupillary block from angle closure in such a case, it is important to assess whether the closure mechanism is due to pupillary block or anterior rotation of the lens-iris diaphragm. In sulfonamide-derived drug-induced ACG, the mechanism is not due to pupillary block but due to ciliochoroidal effusion and anterior rotation of the lens-iris diaphragm.[1,3,4] The presence of a history of sulfonamide-derived drug initiation, bilateral involvement, absence of iris bombe, myopic status, and gonioscopic and ophthalmoscopic findings helps differentiate it.[1,4,5] In addition, acute primary angle closure with pupillary block is often unilateral and is mostly observed in elderly and hyperopic individuals.[1] Based on the clinical findings and medical history, we considered that this clinical picture was due to hydrochlorothiazide initiation. Therefore, hydrochlorothiazide was discontinued. Although the primary mechanism causing choroidal effusion is not fully understood, it may be related to hyponatremia, prostaglandin-mediated effects, or carbonic anhydrase enzyme inhibition.[2,3,7,8] The previous case report associated hydrochlorothiazide-induced bilateral acute ACG with hyponatremia as a potential contributing factor.[7] However, in our patient, serum sodium and other electrolytes were within normal limits, suggesting that the mechanism of angle closure was not electrolyte-mediated. Prostaglandin analogs used in glaucoma treatment were also reported to be associated with ciliary body edema and secondary ACG.[1,9] Hence, the fixed-combination drug containing a prostaglandin analog, which our patient had been using previously, was changed. In addition, it was stated that ACG induced by sulfonamide-derived drugs might have an underlying inflammatory

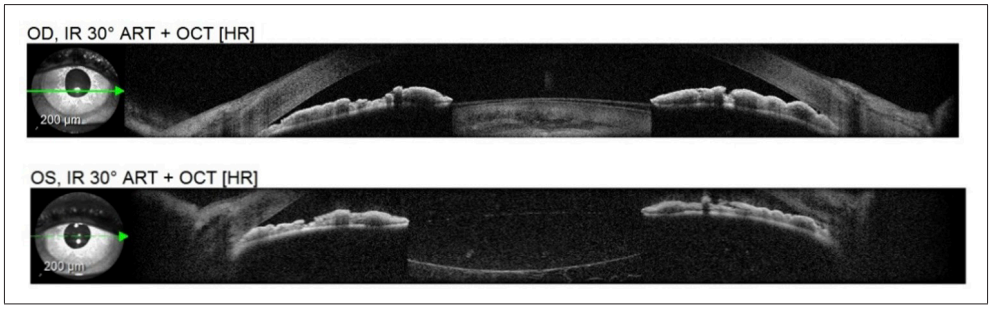

Fig. 3. Anterior segment optical coherence tomography images of the right and left eyes at the time of admission are shown, respectively.

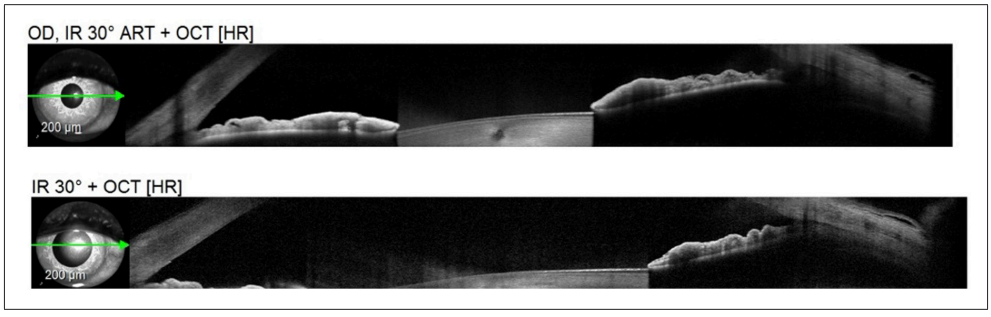

Fig. 4. Anterior segment optical coherence tomography images of the right and left eyes after treatment were given, respectively.

component.[1] For this reason, he was started on steroid medication to reduce the inflammatory response. Although cross-sensitivity between sulfonamide derivatives is rare, it is advisable to avoid using carbonic anhydrase inhibitors in the treatment of secondary ACG that may occur in these patients.[4,10] Therefore, acetazolamide, which contains a sulfonamide group, was not preferred for reducing IOP. In a patient with a cloudy cornea and high IOP, cycloplegic measurement may not be the initial choice. However, it becomes important in cases of forward rotation of the lens-iris diaphragm caused by ciliochoroidal effusion, which is a common mechanism in non-pupillary block angle-closure induced by sulfonamide derivatives.[1,3] In our case, based on bilateral involvement, absence of iris bombe, myopic status, and gonioscopic and ophthalmoscopic findings, the topical cyclopentolate was used. In ACG induced by sulfonamide-derived drugs, cycloplegic agents can be given to relax ciliary muscles, causing the lens-iris diaphragm to shift posteriorly. This increases ACD and opens the narrow angle.[1,6] In our patient, using pilocarpine (a miotic agent) instead of cycloplegics would worsen the clinical picture. Pilocarpine causes anterior rotation of the lens-iris diaphragm and may exacerbate the angle closure. Therefore, cycloplegics are the preferred agents.[1,6] Similarly, since the angle-closure mechanism in these cases is not associated with pupillary block, peripheral iridotomy or iridectomy is ineffective.[1,4,5] YAG laser iridotomy would not have relieved the ciliochoroidal effusion or anterior rotation of the lens-iris diaphragm. Although primary ACG is often considered in the differential diagnosis of secondary ACG induced by sulfonamide-derived drugs, primary ACG is rarely bilateral.[1]

Conclusion

In cases with bilateral acute myopic shift, choroidal effusion, and ACG, hydrochlorothiazide use should be questioned. Discontinuation of hydrochlorothiazide, along with administration of antiglaucomatous, anti-inflammatory, and cycloplegic agents, can lead to resolution of sudden ocular changes. It would be better for physicians to inform patients about these potential risks when prescribing hydrochlorothiazide-containing medications.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consents were obtained from patient and his family.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: B.O., H.O.; Design: B.O., H.O.; Supervision: B.O., H.O.; Resource: B.O.; Materials: B.O., H.O.; Data Collection and/or Processing: B.O.; Analysis and/or Interpretation: B.O., H.O.; Literature Search: H.O.; Writing: B.O., H.O.; Critical Reviews: B.O., H.O.

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EUROPEAN EYE RESEARCH

CASE REPORT[

Orbital and craniofacial involvement of aneurysmal bone cyst: A rare case report

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Abstract

Aneurysmal bone cyst (ABC) is a rare, benign but expansile osteolytic lesion that most commonly involves the long bones, vertebrae, and cranial bones. Orbital and craniofacial involvement is exceptionally rare and may present with rapidly progressive symptoms due to mass effect. We report the case of a 15-year-old patient who presented with a progressive swelling extending from the nasal cavity to the right orbit and frontal region over a period of 3 months. Ophthalmic examination revealed proptosis, restricted ocular motility, and decreased visual acuity in the right eye. Imaging studies, including computed tomography and magnetic resonance imaging, demonstrated a multiloculated, cystic, and solid lesion with fluid–fluid levels, destroying the frontal, ethmoidal, maxillary, and orbital bones, and displacing the right globe laterally. Multidisciplinary surgical excision via fronto-orbital craniotomy was performed, and histopathological evaluation confirmed the diagnosis of ABC. Postoperatively, significant regression of proptosis and improvement in visual acuity were observed. Orbital involvement of ABC is extremely rare but should be considered in the differential diagnosis of destructive craniofacial masses in children and adolescents. Radiological identification of characteristic fluid–fluid levels combined with histopathological confirmation is essential for accurate diagnosis. Early surgical intervention can prevent further visual deterioration and provide favorable functional and cosmetic outcomes.

Keywords: Aneurysmal bone cyst; craniofacial involvement; orbit; proptosis.

Aneurysmal bone cyst (ABC) is a benign, expansile osteolytic lesion characterized by blood-filled spaces separated by connective tissue septa containing osteoid and giant cells.[1-3] Although its exact etiology remains unclear, ABCs may arise *de novo* (primary) or develop secondary to pre-existing bone lesions such as angiomas, fibromas, osteoblastomas, chondroblastomas, or fibrous dysplasia.[1-3] The reported incidence of ABC is approximately 0.14 per million population, with a marked predilection for patients under the age of 20 years.[1-3] The metaphyses of long bones, vertebrae, and cranial bones are the most common sites of involvement.[4-6] Within the skull, frontal, occipital, and temporal bones are most frequently affected, whereas orbital involvement is exceedingly rare, accounting for <0.25% of cases.[7-9] Both sexes are equally affected.[1-3]

Clinically, orbital ABCs may present with rapidly progressive proptosis, downward displacement of the globe, painful swelling, and focal neurological deficits depending on the extent of bone destruction and intracranial involvement.[9-11] Despite their benign nature, these lesions may behave

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aggressively, causing significant functional and cosmetic morbidity.[8-11]

Herein, we report a rare case of ABC with concomitant orbital and craniofacial involvement in a 15-year-old patient, highlighting the clinical presentation, radiological findings, surgical management, and post-operative outcomes.

Case Report

A 15-year-old patient with no known systemic disease or history of surgery presented with a 3-month history of progressive swelling originating in the nasal cavity, which had further enlarged over the past month to involve the right orbit and frontal region. The patient was initially evaluated at another medical center, where a biopsy was reported as suspicious for nasal polyp or angiofibroma, and was subsequently referred to our institution for further management.

On ophthalmic examination, a large expansile mass was observed, extending from the medial aspect of the left brow to the lateral canthus and frontal region, involving the right hemiface and elevating the globe (Fig. 1). Direct and consensual light reflexes were intact bilaterally. The right eye demonstrated marked proptosis, restricted extraocular motility in all directions, and lateral displacement of the globe, whereas ocular motility of the left eye was normal. Best-corrected visual acuity was 4/10 in the right eye and 10/10 in the left eye. Intraocular pressures were within normal limits in both eyes. Slit-lamp examination revealed punctate epithelial erosions in the inferior cornea of the right eye, whereas the iris and lens were normal. The left anterior segment was unremarkable. Fundus examination of the right eye showed a mildly blurred nasal margin of the optic disc, normal macula, and increased vascular tortuosity, whereas the left fundus was normal (Fig. 2). Optical coherence tomography through the macula was within normal limits bilaterally.

Computed tomography (CT) demonstrated a 67 × 56 × 90 mm multiloculated lesion consistent with an ABC. The lesion destructively involved the frontal bone, medial orbital walls, orbital roof, ethmoid bone, anterior wall of the sphenoid sinus, bilateral nasal bones, maxilla, and hard palate. It also extended intracranially into the frontal region, displacing the right orbit laterally, and contained multiple fluid–fluid levels (Fig. 3). Magnetic resonance imaging (MRI) of the brain and orbit revealed a multiloculated cystic lesion of osseous origin occupying the frontal, ethmoidal, maxillary, and nasal cavities, with fluid–fluid levels and significant mass effect on the frontal lobe (Fig. 4).

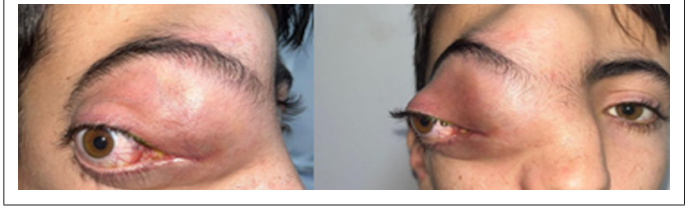

Fig. 1. Expansile mass extending from the medial aspect of the left eyebrow toward the lateral canthus and frontal region, involving the right half of the face and displacing the globe inferolaterally.

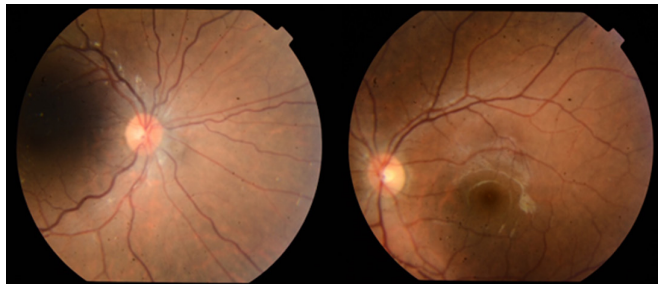

Fig. 2. Fundus examination revealed a slightly blurred nasal margin of the optic disc, normal macula, and increased vascular tortuosity in the right eye, whereas the left eye appeared normal.

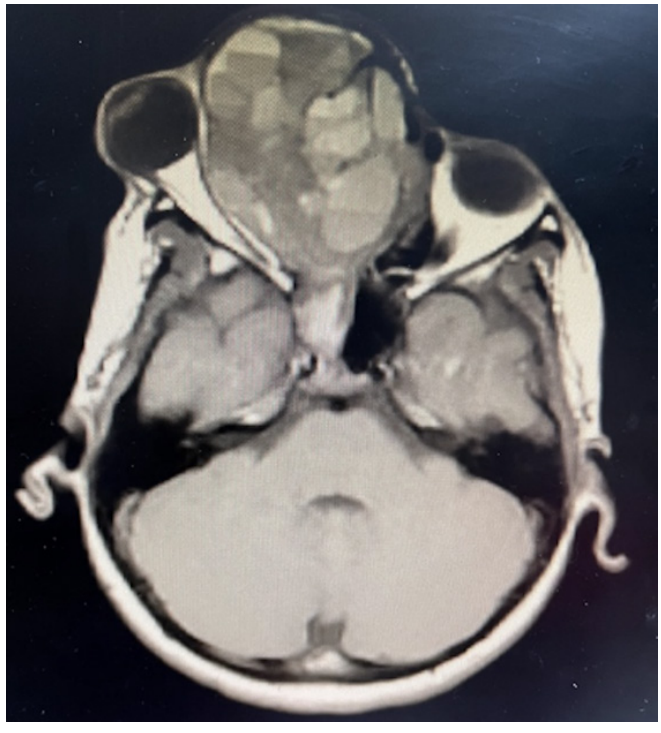

Fig. 3. Axial computed tomography scan showing a lesion consistent with an aneurysmal bone cyst filling the left nasal cavity, causing destruction of the frontal bone, medial walls and roofs of both orbits, ethmoid bone, anterior wall of the right sphenoid sinus, bilateral nasal bones, maxilla, and hard palate. The lesion extends intracranially into the frontal region, contains both cystic and solid components with fluid–fluid levels, and displaces the right orbit laterally and out of the cavity.

The patient underwent multidisciplinary surgical excision with the participation of neurosurgery, ophthalmology, and plastic surgery teams. A fronto-orbital craniotomy was performed, and the mass was completely excised. Histopathological examination confirmed the diagnosis of ABC. In the post-operative period, a marked regression of proptosis was achieved, accompanied by a notable improvement in vision, as the best-corrected visual acuity improved to 7/10 (Fig. 5). The patient was scheduled for regular ophthalmologic follow-up, and no recurrence was observed during the 3-month follow-up period. Written informed consent was obtained from the patient and his family for publication.

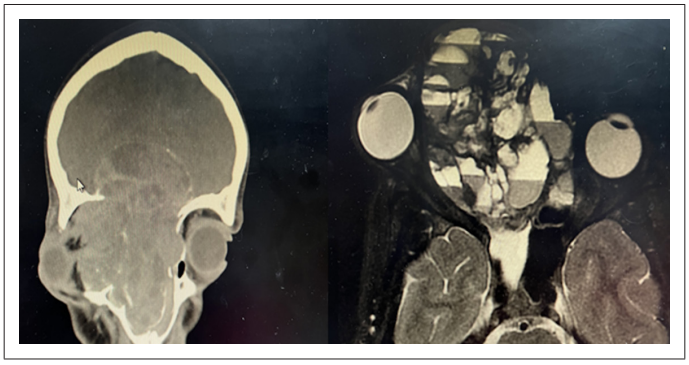

Fig. 4. Coronal and axial magnetic resonance images of the brain and orbits demonstrate a multiloculated cystic lesion of osseous origin, filling the frontal, ethmoidal, right maxillary sinus, and right nasal cavity. The lesion contains fluid–fluid levels, and extends into the intracranial extradural space, compressing the adjacent brain parenchyma.

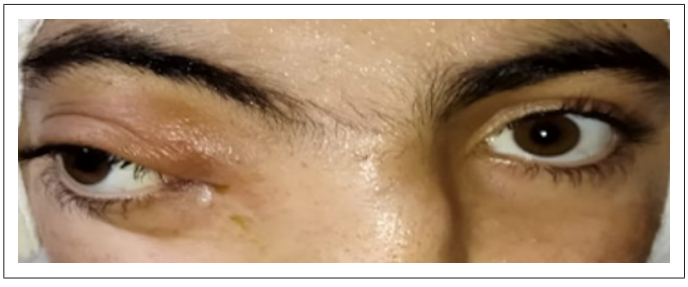

Fig. 5. Clinical appearance of the patient in the early post-operative period.

Discussion

ABC is an uncommon benign lesion that most frequently arises in the metaphysis of long bones, but it can also occur in any bone of the body. Orbital involvement, as observed in our case, is exceedingly rare.[2-5] The clinical manifestations of ABC depend on the location, size, and degree of compression on adjacent structures. Neurological deficits are more likely in cases involving the skull base.[4-7] In our patient, the lesion involved the frontal, ethmoidal, and maxillary bones with intracranial extension, producing a large expansile orbital mass with proptosis, but without neurological deficits.

Histopathological evaluation is essential to establish the diagnosis and to differentiate ABC from vascular tumors such as hemangiomas.[8-11] Microscopically, ABCs are characterized by blood-filled spaces, fibroblastic septa without endothelial lining, and scattered bone trabeculae.[8-11] These classical features were present in our patient. Despite their benign nature, ABCs are locally destructive and can demonstrate rapid growth.

Radiological imaging plays a pivotal role in diagnosis. CT typically shows a heterogeneous expansile mass with both cystic and solid components. Previous studies have reported that approximately 87% of ABCs appear radiolucent and about 2% radiopaque.[5-8] Additional findings may include ground-glass appearance, cortical expansion, narrowing of foramina, and variable contrast enhancement. Fluid–fluid levels are observed in up to 35% of cases on CT. On MRI, ABCs commonly demonstrate fluid–fluid levels, multiple internal septations, and lobulated contours.[5-8] These imaging features, although not pathognomonic, strongly suggest an ABC when combined with clinical findings. In our case, fluid–fluid levels were the most prominent radiological feature.[5-8]

The differential diagnosis of orbital and craniofacial ABC includes fibrous dysplasia, hemorrhagic bone cyst, giant cell tumor, metastasis, and plasmacytoma.[2-4] Surgical excision remains the treatment of choice and is generally curative.[8] Recurrence rates after surgical excision of ABCs are reported between 10% and 28%, typically occurring within the first 1–2 years postoperatively.[8-11] Close radiological follow-up is therefore recommended to ensure early detection of recurrence.[8-11] In our patient, fronto-orbital craniotomy with excision of the cystic cavity and removal of hyperostotic bone was performed. Following surgery, significant regression of proptosis and improvement in ocular motility and visual function.

Orbital involvement of ABCs is extremely rare. These lesions are most often identified based on their characteristic radiological features, with CT and MRI playing a key role in defining bone destruction and intracranial extension. Histopathological confirmation remains essential for an accurate diagnosis. Early recognition and timely surgical intervention are critical to prevent progressive visual loss and to achieve favorable functional and cosmetic outcomes.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consents were obtained from patient and his family.

Authorship Contributions: Concept – A.A.O., B.U.; Design – M.B., N.T., R.D.O.; Supervision – A.A.O., B.U.; Resource: M.B., N.T., R.D.O.; Materials – N.T., R.D.O.; Data Collection and/or Processing – .A.O., M.B, R.D.O. Analysis and/or Interpretation– B.U., M.B., N.T.; Writing – A.A.O., B.U., M.B., N.T., R.D.O.; Critical review – A.A.O, B.U.

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EUROPEAN EYE RESEARCH

CASE REPORT[

Spontaneous idiopathic full-thickness macular hole closing and re-opening

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Abstract

The purpose of this study was to evaluate the spontaneous closure and recurrence of idiopathic macular holes. This was a single-patient case report with optical coherence tomography imaging analysis. Written informed consent was obtained from the patient for participation and publication of this report. A 40-year-old healthy female experienced spontaneous closure of an idiopathic macular hole, followed by re-opening after several years. Surgical intervention successfully resolved the recurrent macular hole, with visual acuity improving significantly postoperatively. Spontaneous closure and recurrence of idiopathic macular holes are rare phenomena with complex underlying mechanisms. Observation may be an option in certain cases, but surgical treatment remains effective for recurrences.

Keywords: Internal limiting membrane peeling, Macular hole, Recurrent macular hole, Re-opening, Spontaneous closure.

A macular hole is a defect in the retinal layers, typically involving the fovea. Macular holes are classified into several types, including full-thickness, recurrent, lamellar, myopic, and traumatic holes.[1] Although the formation of macular holes in young individuals is more likely to be due to traumatic causes, idiopathic macular holes have been reported at a rate of approximately 3% under the age of 50.[2] Spontaneous closure of idiopathic macular holes has been documented, with reported closure rates ranging from 0% to 15.8%.[3]

This report describes a rare case of a young patient who experienced spontaneous closure of a full-thickness macular hole, followed by recurrence, and eventually underwent surgical intervention.

Case Report

A 39-year-old female patient presented to our clinic with complaints of decreased vision in the left eye. She was emmetropic with no significant systemic disease history. She reported experiencing increased stress due to personal circumstances and had a 5-pack-year smoking history.

In initial examination, visual acuity (VA) was 20/20 in the right eye, 20/33.3 in the left eye. The anterior segment was normal, with no cells or reactions. In the posterior segment, no vitritis was observed. However, hyperpigmentation in the macular region of the left eye was noted. Optical coherence tomography (OCT) revealed a pseudohole and epiretinal membrane (ERM) in the left eye (Fig. 1a).

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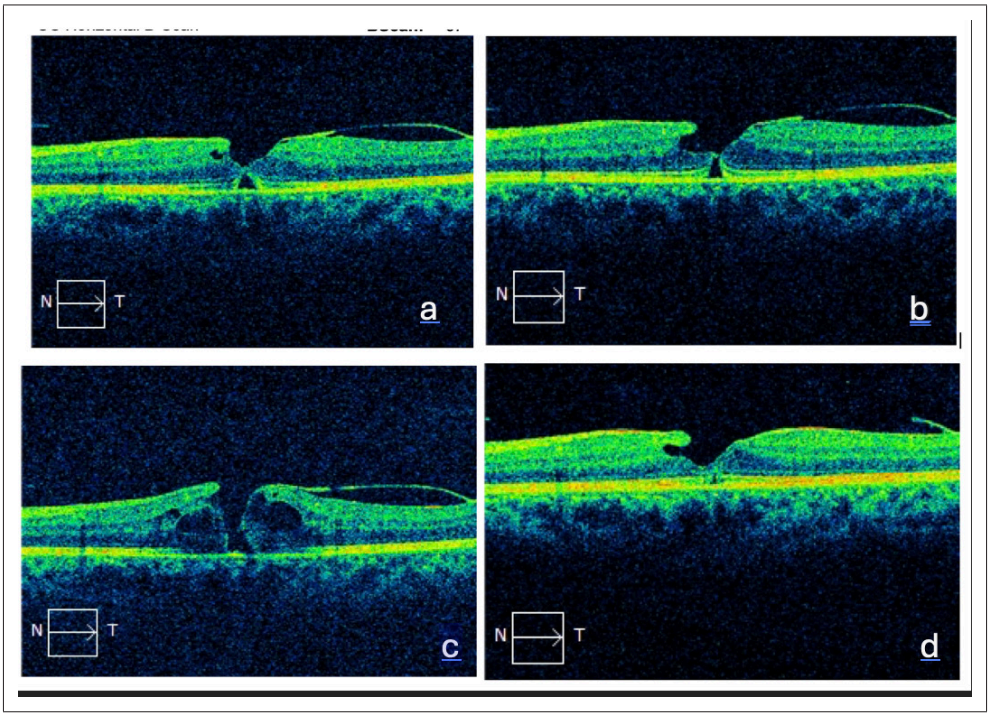

Fig. 1. Optical coherence tomography imaging of 40 year-old patient. **(a)** Pseudohole **(b)** Lamellar hole **(c)** Full-thickness hole **(d)** Lamellar hole.

A follow-up examination was scheduled for 3 months. At the 3-month visit, VA was the same, but a lamellar hole with ERM appearance was present in OCT (Fig. 1b), and another follow-up was planned.

By the 6th month, the patient's VA was stable. However, OCT revealed the development of a full-thickness macular hole with ERM (Fig. 1c). A surgical intervention was planned. Despite this, pre-operative assessment revealed a VA of 20/100, corresponding to a 25-letter decline on the ETDRS chart. Interestingly, subsequent OCT imaging demonstrated spontaneous closure of the macular hole, which was now characterized as a lamellar hole, with the ERM no longer detectable (Fig. 1d).

The COVID-19 pandemic disrupted further follow-up, and the patient could not come to the clinic for 5 years. Upon re-evaluation, the patient reported a gradual worsening of vision in recent months. Her VA had declined to 20/640 (40 letters decreased in ETDRS), and OCT confirmed a recurrent full-thickness macular hole. At this stage, the surgical intervention was scheduled to manage the recurrent full-thickness macular hole.

Despite the recurrence of the full-thickness macular hole, no significant progression was observed before surgery, and the macular hole remained stable until the operation (Fig. 2).

Macular hole surgery was performed. The inner limiting membrane was peeled and inserted into the hole, followed by the administration of SF6 gas. Two weeks postoperatively, VA improved to 20/25 (70 letter increase in ETDRS). Follow-up OCT confirmed closure of the macular hole (Fig. 3).

The patient remains under regular follow-up in our clinic. Written informed consent was obtained from the patient for participation in this report and for the publication of clinical data and images. The study adhered to the tenets of the Declaration of Helsinki.

Discussion

This report describes a rare case of a macular hole that initially closed spontaneously, subsequently reopened, and was successfully treated with surgical intervention. Although cases of spontaneous macular hole closure have been documented in the literature, the exact mechanisms remain unclear. Proposed mechanisms include bridging by retinal cell proliferation, posterior hyaloid membrane detachment, and circumferential ERM formation, all of which may contribute to the closure process.[3]

In this case, idiopathic macular hole formation at a young age, combined with risk factors such as female sex, a stressful lifestyle, and smoking history, is noteworthy. However, it is known that a sudden decline in estrogen levels can cause cone cell degeneration in the fovea, contributing to macular hole formation.[4] This makes the case particularly interesting,

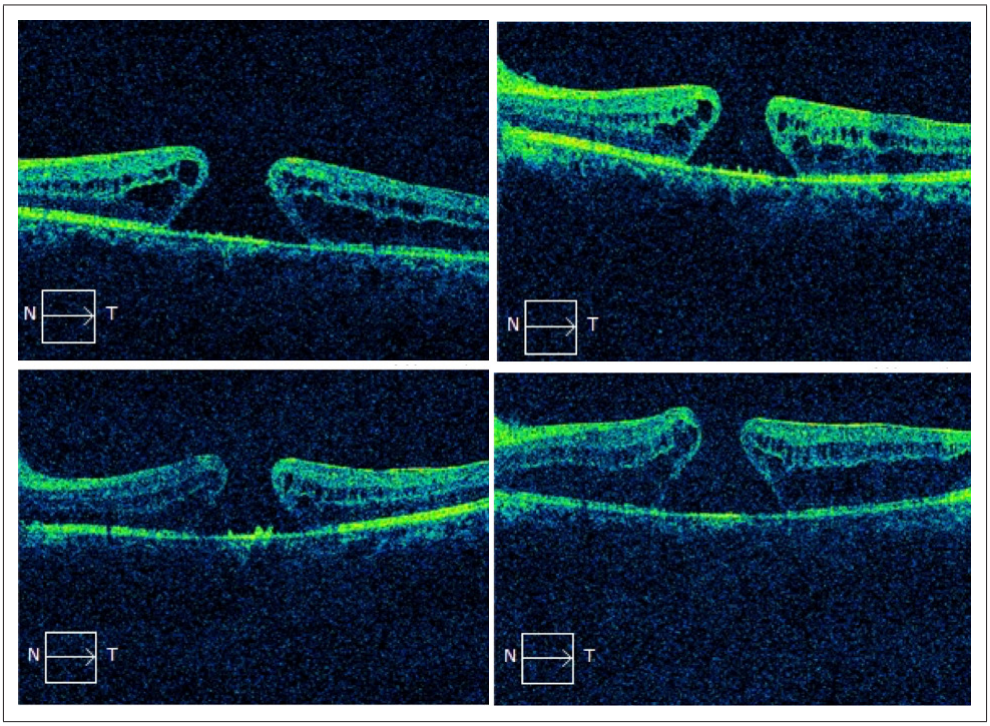

Fig. 2. The optical coherence tomography image of the patient's macular hole demonstrates no progression over the course of several visits leading up to the surgical intervention.

as the patient remains in the premenopausal period. While stress and corticosteroids have not been conclusively linked to macular hole formation, topical steroid drops have been reported in the literature to promote macular hole closure in some cases.[5] This paradoxical effect suggests that stress-related hormonal or inflammatory changes may not fully explain the pathogenesis of idiopathic macular holes. Furthermore, studies have suggested that smoking is not directly associated with idiopathic macular hole formation.[6] In our case, any predisposing systemic or ocular factor could not be identified.

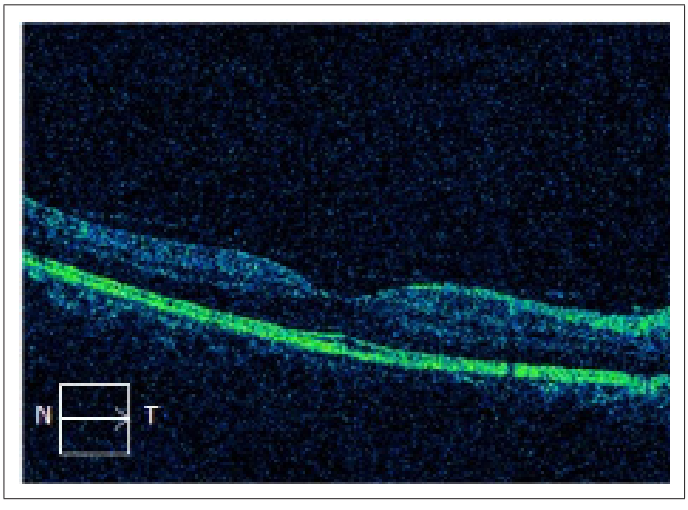

Fig. 3. Optical coherence tomography image of the patient's final visit.

The timing and mechanism of macular hole re-opening remain poorly understood, with prior studies reporting variable recurrence intervals ranging from 4 to 24 months.[7,8] In this patient, the absence of vision loss during the pandemic period suggests a recurrence-free interval of at least 5 years. Possible mechanisms for hole re-opening include progressive glial proliferation, recurrent vitreofoveal traction, or the limited elasticity of the inner retina counteracting the forces responsible for hole closure.[9]

Conclusion

This case represents the youngest reported instance of macular hole re-opening in the literature, with a notably long duration between spontaneous closure and recurrence. This highlights the limited understanding of macular hole pathophysiology, despite its recognition in ophthalmology for over 150 years.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

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

Authorship Contributions: Concept: D.G., H.Ç.; Design: D.G., S.O., H.Ç.; Supervision: H.Ç.; Resource: D.G., H.Ç.; Materials: D.G., S.O., H.Ç.; Data Collection and/or Processing: S.O.; Analysis and/or Interpretation: D.G., S.O., H.Ç.; Literature Search: S.Ö.; Writing: D.G., S.O.; Critical Reviews: H.Ç.

Peer-review: Externally peer-reviewed.

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EUROPEAN EYE RESEARCH

CASE REPORT

Spontaneous bleeding of a hidden deep orbital hemangioma following routine retinopathy of prematurity screening examination

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Abstract

To report a rare case of spontaneous bleeding in a hidden orbital deep infantile hemangioma (IH) presenting with acute swelling and ptosis following retinopathy of prematurity (ROP) screening. A 2-month-old baby presented with progressive swelling in the left medial canthus and glabella immediately following a ROP screening. Ophthalmological evaluation revealed swelling in the superior nasal region of the left eye, causing ptosis, with an underlying superficial lesion on the forehead. Spontaneous hemorrhage was considered, prompting Pediatric Cardiology consultation. Ultrasound demonstrated a highly vascularized, hypoechoic lesion (3 × 1 cm) extending from the supraorbital region. The patient was diagnosed with orbital mixed IH, and oral propranolol therapy (1 mg/kg, twice daily) was initiated. ROP screening tools (speculums/indenters) may induce spontaneous bleeding in underlying orbital IH. Early identification of vision-threatening orbital hemangiomas and prompt pediatric cardiology consultation for systemic propranolol are critical for preventing amblyopia and optimal functional outcomes.

Keywords: Infantile hemangioma, Orbital hemangioma, Retinopathy of prematurity screening, Retinopathy of prematurity, Spontaneous bleeding

Infantile hemangiomas (IHs), affecting approximately 4.5% of infants, are the most common benign tumors of infancy.[1] IHs have a characteristic growth and spontaneous resolution pattern, appearing in early infancy, growing rapidly during the first few months, and then gradually regressing spontaneously. 80% of IHs achieve final size by 3 months of age.[2] Although spontaneous regression occurs in most IHs, 10–15% require treatment due to complications including obstruction, ulceration, functional impairment, anatomic distortion, or cosmetic disfigurement.[1-3] IHs are categorized as superficial, deep, or mixed hemangiomas. Superficial IHs manifest as telangiectatic red macules, papules, nodules, or plaques in the upper dermis. Deep IHs extend to the adipose tissue, presenting as bluish tumors with indistinct borders. Due to their fragile neovascular architecture, orbital hemangiomas are susceptible to spontaneous rupture or minor trauma-induced bleeding. This case report presents spontaneous bleeding of a hidden deep orbital IH following an uneventful retinopathy of prematurity (ROP) screening examination.

Case Report

A 2-month-old infant was presented to our Pediatric Ophthalmology department with complaints of progressive

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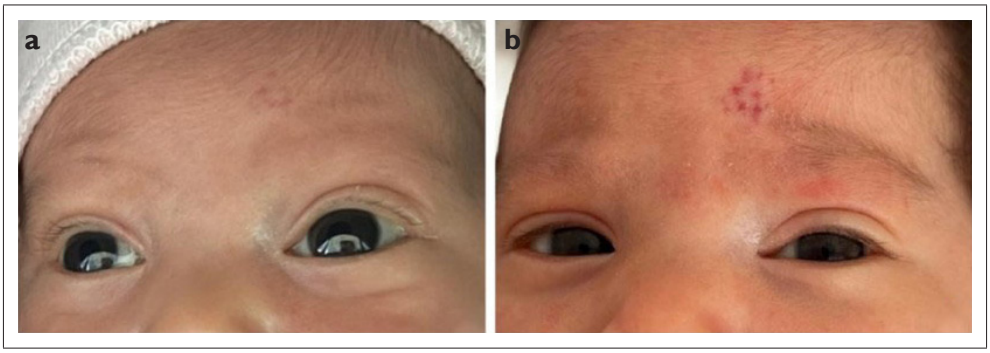

Fig. 1. Superficial hemangioma, located in the middle forehead, superomedial to the left eyebrow, (**a:** 2-weeks-old, **b:** 6-weeks-old). *Courtesy of the mother of the baby.

swelling around the left eyelid after a routine ROP screening examination. The baby was born spontaneously at 33 weeks' gestation, weighing 2,150 g; otherwise healthy, presenting only with a superficial capillary hemangioma on her forehead, superomedial to the left eyebrow, which required no treatment (Fig. 1a and b). First ROP screening at postmenstrual 38 weeks revealed peripheral avascular retina in zone 3 without ROP. The follow-up visit which was performed 3 weeks later, was uneventful and demonstrated a fully vascularized peripheral retina in both eyes without any sign of ROP. Later that day, the baby returned with progressive swelling extending from the left medial canthus and adjacent nasal area up to the superior orbital rim and glabella. The mother noted the swelling following the ROP screening and observed that the swelling was expanding toward the middle forehead. The parents denied any traumas such as scratching, rubbing, lying face down, or falling. Ophthalmological evaluation revealed a soft, irregular-shaped swelling in the superior nasal region of the left eye, extending superiorly to the left eyebrow and glabella. Superotemporal to the main lesion, a superficial hemangioma, 1 × 1 cm in diameter, was noted in the middle forehead on the upper nasal aspect of the left eyebrow. The nasal part of the left eyelid was ptotic; however, the pupillary axis was not obstructed (Fig. 2). Anterior and posterior segment examinations were normal in both eyes. Complete blood count and coagulation parameters were within normal limits. The swelling was presumed to be spontaneous hemorrhage from a possible orbital hemangioma considering the use of a pediatric eyelid speculum and scleral indentation during ROP screening. The patient was consulted with the pediatric cardiology department. Ultrasound imaging demonstrated a hypoechoic solid lesion, 3 × 1 cm in size, with indistinct borders, extending from the left frontal region to the left medial supraorbital region (Fig.3a). Color Doppler ultrasonography showed increased vascularity and a high-flow pattern of the lesion (Fig. 3b). The patient was diagnosed with orbital mixed IH, and oral propranolol therapy was administered twice daily, at a total dose of 2 mg/kg/day. No cardiac or metabolic abnormalities were detected before, during, or after the treatment. The patient is continuing follow-up visits in our pediatric ophthalmology and pediatric cardiology departments. The patient's examination at 6 months old revealed that the forehead IH persisted without mass appearance; notably, the pupillary axis remained unaffected (Fig. 4). Written informed consent was obtained from the patient's parent for the publication of this case report and any accompanying images.

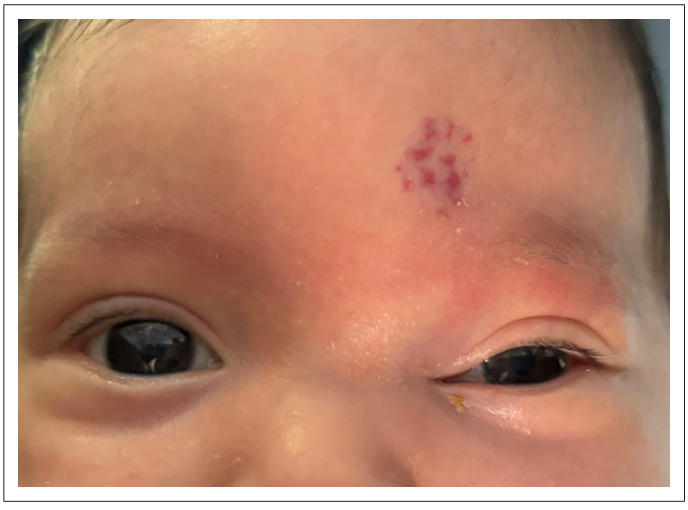

Fig. 2. Swelling in the superior nasal region of the left eye, extending superiorly to the left eyebrow, superior orbital rim, and glabella. A superficial hemangioma in the middle forehead on the upper medial aspect of left eyebrow. Mechanical ptosis in the nasal part of left eyelid that did not obstruct the pupillary axis.

Discussion

This case report presents a 2-month-old female infant with a hidden deep orbital IH diagnosed by acute enlargement due to spontaneous intralesional hemorrhage following a routine

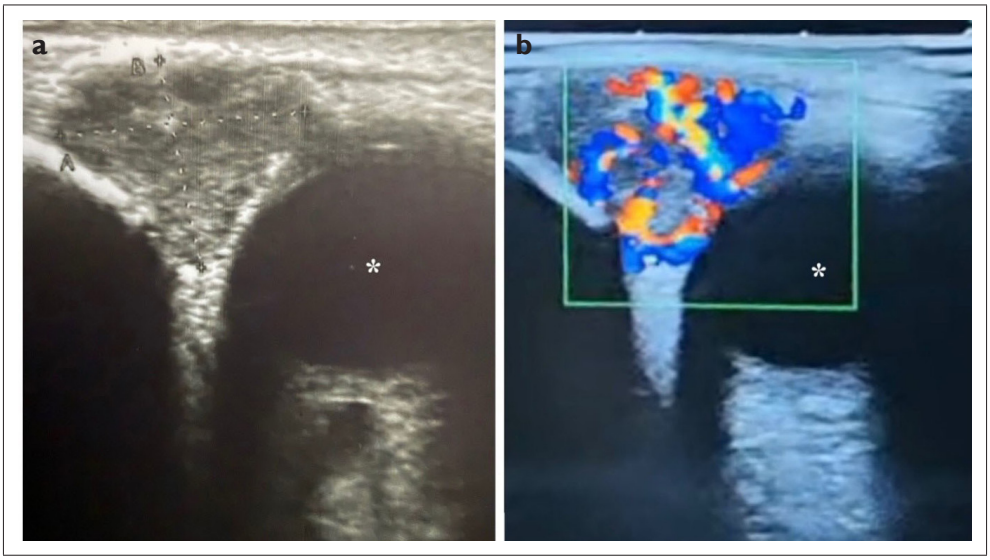

Fig. 3. Ultrasonography revealed hypoechoic solid lesion, 3 × 1 cm in size, with indistinct borders **(a)**. Doppler ultrasonography showed an increased vascularity and high-flow pattern **(b)**. *Left eye

uneventful ROP screening using a pediatric eyelid speculum and scleral indentation instrument. Prematurity (<37 weeks), low BW (<2500 g), female gender, advanced maternal age, positive family history of IH, history of multiple gestations, *in vitro* fertilization, and gestational complications such as preeclampsia and placental anomalies were reported as risk factors for IHs.[4] Accordingly, this patient was a female premature infant with a GA of 33 weeks and BW of 2150 g. Superficial IHs typically appear weeks after birth, whereas deep IHs emerge later and may persist for up to 2 years.[5] A superficial IH was noted in our patient as a red macule in the early weeks of life, and no treatment was required. However, acute, progressive swelling in the glabella and left periorbital region was noted immediately after the second ROP screening at 2 months. Although IHs usually involute spontaneously, our case required early intervention due to acute intralesional hemorrhage causing eyelid ptosis and visual axis obstruction. Systemic propranolol was started to prevent deprivation amblyopia and cosmetic disfigurement. IHs are fragile; minimal intervention may cause blood extravasation mimicking trauma. In our case, routine ROP screening using an eyelid speculum and scleral indentation_probably induced spontaneous hemorrhage within the deep orbital IH. The Doppler-confirmed high-flow pattern of the mass, besides the absence of trauma or coagulation disorder, distinguished it from traumatic or coagulation disorder-related bleeding. Orbital IHs rapidly cause functional deficits, including ptosis, astigmatism, and deprivation amblyopia; moreover, IHs >1 or those involving the medial orbit, ptosis, or eyelid margin alteration present a high risk for amblyopia.[6] Therefore, systemic therapy should not be delayed for vision-threatening hemangiomas.[7] Oral propranolol (2–3 mg/kg/day) is the established first-line treatment, which rapidly arrests proliferation and initiates involution via vasoconstriction, anti-angiogenesis, and apoptosis.[7,8] Ophthalmologists performing fundoscopic exams must closely monitor periorbital IHs, requiring careful manipulation of the speculum and scleral indentation. Any sudden swelling or enlargement in a pre-existing orbital IH, even after non-traumatic procedures, necessitates urgent treatment.

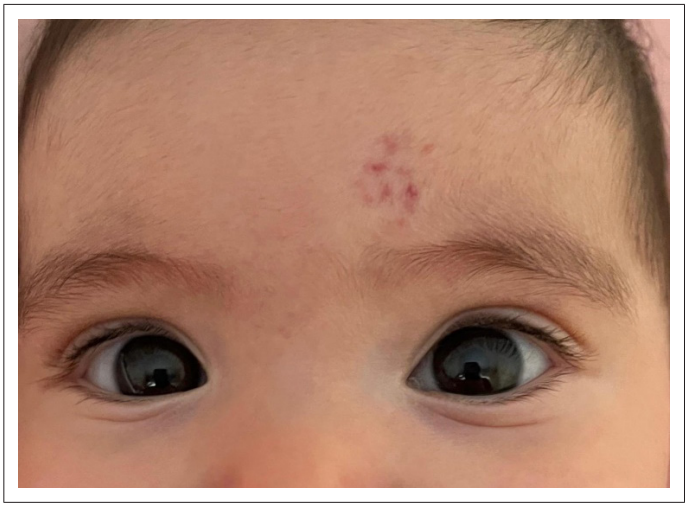

Fig. 4. Superficial hemangioma, located middle forehead, superomedial to the left eyebrow, 6-months-old

Conclusion

This case highlights rare but significant acute orbital IH expansion caused by spontaneous hemorrhage following

routine ROP screening. Ophthalmologists should be aware that ophthalmological examinations using an eyelid speculum (even the pediatric speculums) and scleral indentation instruments can induce bleeding in IHs, resulting in severe acute morbidity. Accurate diagnosis and timely systemic propranolol are critical for successfully managing periorbital IHs and reducing permanent complications.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consents were obtained from patient and his family.

Peer-review: Externally peer-reviewed.

Authorship Contributions:

Concept: A.U., T.K.; Design: E.N.I., A.U.; Supervision: A.U.; Resource: A.U., T.K.; Materials: E.N.I., A.U., T.K.; Data Collection and/or Processing: E.N.I., A.U., T.K.; Analysis and/or Interpretation: E.N.I., A.U., T.K.; Literature Search: E.N.I.; Writing: E.N.I., A.U.; Critical Reviews: E.N.I., A.U., T.K.

Conflict of Interest: None declared.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

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