HONG KONG JOURNAL of OPHTHALMOLOGY

December 2025 Vol. 29 No. 1 ISSN 1027-8230 Online ISSN 2957-7098

The Official Publication of
The College of Ophthalmologists of Hong Kong

香港眼科醫學院

香港眼科學刊

香港醫學專科學院出版社
HONG KONG ACADEMY OF MEDICINE PRESS

CONTENTS

香港眼科學刊

香港眼科醫學院

HONG KONG
JOURNAL OF
OPHTHALMOLOGY

The Official Publication of
the College of Ophthalmologists
of Hong Kong

December 2025

Volume 29 Number 1

ISSN 1027-8230

Editor-in-Chief
Jason CS Yam

Correspondence
The College of Ophthalmologists of Hong Kong
Room 802, 8/F, Hong Kong Academy of
Medicine Jockey Club Building
99 Wong Chuk Hang Road
Aberdeen, Hong Kong SAR, China.
Tel (852) 2761 9128
Fax (852) 2715 0089
E-mail: info@cohk.org.hk

Published by
HONG KONG ACADEMY OF MEDICINE PRESS

EDITORIAL BOARD

Information for Authors

Aims and Scope

- The *Hong Kong Journal of Ophthalmology* (HKJO) is the official publication of the College of Ophthalmologists of Hong Kong. The Journal aims to promote academic developments in ophthalmology, and to maintain continuing ophthalmological education of doctors of this specialty and other related disciplines. It is hoped that through achieving these aims, the quality of eyecare we offer to our patients can be lifted to new heights. The Journal will consider any submissions that fulfill these aims for publication.
- The Journal accepts high-quality submissions in the following categories: Original Article, Review, Perspective, Case Report, Photo Essay, Clinical Quiz, or Letter to the Editor. Editorials are by invitation only.
- The Journal is circulated to all members of the College of Ophthalmologists of Hong Kong and other professional societies and academic institutions in Hong Kong and internationally.

Journal Policies

- The HKJO adheres to the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org) and the Core Practices of the Committee on Publication Ethics (COPE; https://publicationethics.org).
- Submitted manuscripts must be original works that have not been published elsewhere (in whole, in part, or as a preprint) and are not under consideration by another publication.
- To improve the quality and clarity of published articles, the Journal recommends the use of reporting guidelines in the preparation of manuscripts, such as those advocated by the EQUATOR Network (http://www.equator-network.org/), for example, CONSORT for randomized trials, or CARE for case reports.
- Any sponsor(s) of the research involved, along with grant number(s) should be provided.
- All authors must provide a statement reporting any conflicts of interest. Where none exist, please state 'The authors have no conflicts of interest to declare.' Authors may use the ICMJE Conflict of Interest form.
- For all research involving living humans (including studies involving human tissue, retrospective studies, and database studies), an appropriate research ethics committee must be consulted. A statement must be included in the manuscript that provides the name of the research ethics committee and approval number (or waiver).
- A statement on consent must also be included, indicating how patient(s)/guardian(s) provided informed consent (eg, written or verbal), or that the requirement for patient consent was waived by the review board.
- The authors shall make available the complete data on which the manuscript is based. A statement describing how the data can be accessed must be included in the manuscript. For clinical trials and other large datasets, the Journal recommends that data are deposited in a public repository and shared using a permanent identifier (such as a DOI).
- For details of the Journal policies on publication ethics, including authorship, plagiarism, and processes for handling appeals or complaints, please see the Journal website.

Submissions

- Manuscripts should be submitted through the HKJO online submission system at https://hkjo.hk/index.php/hkjo/about/submissions. Please register for an account with the system and upload files according to the instructions. All files must be submitted through the system.
- Please provide a blinded manuscript as a single file. Any identifying information (eg, references to past publications, name of an author's institution) should be masked or removed from the blinded manuscript.
- Manuscripts should be submitted in Word format (.doc or .docx).
- Manuscripts must be written in English (US spellings as per the Merriam-Webster Dictionary).
- In general, manuscripts should be prepared following the 'IMRaD' structure as recommended by the ICMJE (http://icmje.org/recommendations/browse/manuscript-preparation/preparing-for-submission.html).
- For each author, please provide the full name, professional qualifications, and affiliation (where the study was conducted).
- The full name, postal address, telephone and fax numbers, and email address of the corresponding author must be provided. The corresponding author, on behalf of the authors, is responsible for all contact with the Journal.
- A structured abstract of ≤250 words is required for Review Articles and Original Articles. The abstract should provide a complete summary of the article, including the aims/purpose, main methods, key results, and conclusions. Abbreviations and clinical or technical jargon should be avoided.
- Tables should be typed using the 'Insert Table' feature of MS Word, with one item of data per cell and minimal formatting. Large tables may be provided in MS Excel format. Tables should be numbered and concisely titled. Abbreviations should be defined in footnotes.
- The number of figures should be restricted to the minimum necessary to support the textual material. Figures should be .JPG format with a resolution of ≥350 dpi and should be included in the manuscript file; large image files may be submitted separately. Legends should be provided for each figure to indicate the anatomical area and pathological condition shown. All symbols and abbreviations should be defined in the legend.
- The references should be numbered in the order in which they are first cited in the text. Each reference citation should be in superscript Arabic numerals after full-stops and commas. At the end of the article, the full list of references should be presented in Vancouver style. Include the names of all authors, title of the article, abbreviated name of journal, year of publication, volume number, and inclusive pages, in that order.
- Please refer to the latest ICMJE recommendations on Manuscript Preparation for further information on references and for general guidance on style: http://icmje.org/recommendations/browse/manuscript-preparation/

Peer Review

- HKJO operates a double-blind peer-review process. Details of the peer review process can be found on the Journal website.

Copyright

- On acceptance of an article for publication in HKJO, copyright of the article is transferred to the Journal.
- The Journal has a fully Open Access policy and publishes all articles under a Creative Commons license (CC BY-NC-ND 4.0). For any use other than that permitted by this license, written permission must be obtained from the Journal.

Correspondence

- All correspondence on editorial issues should be addressed to the Editorial Office (editorial@hkjo.hk).

香 港 眼 科 醫 學 院

THE HONG KONG JOURNAL OF OPHTHALMOLOGY
BEST ORIGINAL ARTICLE AWARD

Purpose

To encourage submissions to the *Hong Kong Journal of Ophthalmology* (HKJO) by trainees and fellows of the College of Ophthalmologists of Hong Kong (COHK).

Awards and Prizes

Two awards will be given out every year. Each awardee will be given a $2000 cash prize (HK dollars), which is supported generously by the Timothy KC Liu Fund.

Eligibility

- One award is open to all fellows and members of the College; another one is limited to trainees only.
- Applicants must be a paid-up member or fellow of COHK at the time of submission.
- Trainees refer to those who have not been conferred the title 'FCOphthHK' at the time of submission.
- Only the first author of the article will be eligible for the prize. If the first author is not eligible for the award, i.e. not a member or fellow of COHK, then the order of consideration of awardee will be from the second author onwards to the last author.
- Original articles (including, but not limited to, prospective or retrospective clinical studies, observational studies, epidemiological studies, basic science studies, meta-analysis, etc) published in the HKJO during the year will automatically enter the selection process.
- Case reports (with case number <3), review articles and letters to the editor will not be eligible for this award.
- Submissions pending acceptance will not be eligible for the award.
- Entries will be based on the article as a unit, but not the author. Because of this, it is possible that one single author wins both awards, given that he/she is the first author of the two best original articles published that year (but he/she has to be a trainee in this case as one award is open for trainees only).

Selection Panel

- Editor-in-Chief
- 1 representative from The University of Hong Kong
- 1 representative from The Chinese University of Hong Kong and
- President of the College

Selection Criteria

- Originality
- Scientific merit
- Methodology
- Presentation style

Award Presentation Ceremony

The awards will be given out at the following year's conferment ceremony.

ORIGINAL ARTICLE

Generative artificial intelligence for diabetic retinopathy screening in Hong Kong

Tsz Ho Shum[1], *MB BS (HK), FHKAM (Medicine)*, *Sunny Chi Lik Au*[2,3], *FCOphthHK, FHKAM (Ophthalmology)*, *Steffi Shing Yee Chong*[3], *MB BS (HK)*, *Yuen Fun Emmy Lau*[1], *MB ChB (CUHK), FHKAM (Medicine)*

[1] *Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*

[2] *Department of Ophthalmology, Tung Wah Eastern Hospital, Hong Kong SAR, China*

[3] *Department of Ophthalmology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*

Correspondence and reprint requests:
Dr Tsz Ho Shum, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China.
Email: drgthshum@gmail.com

Abstract

Objectives: To compare the performances of EyeArt and endocrinologists in diagnosing more-than-mild diabetic retinopathy (mtmDR) among patients with diabetes in a Hong Kong hospital.

Methods: Medical records of consecutive patients with diabetes mellitus aged ≥18 years who were screened for diabetic retinopathy (DR) at Pamela Youde Nethersole Eastern Hospital in February 2021 were retrospectively reviewed. Two fundus photographs (one macula-centered and one optic nerve head-centered) were taken from each eye and saved electronically. The photographs were independently graded by endocrinologists, and then by the EyeArt system and by two ophthalmologists specializing in vitreoretinal diseases (the gold standard). mtmDR is defined as moderate nonproliferative DR, severe nonproliferative DR, or proliferative DR, with or without the presence of clinically significant macular edema. Performances of EyeArt and the endocrinologists in diagnosing mtmDR were determined, as were factors associated with EyeArt's diagnostic accuracy and the variability between EyeArt and the endocrinologists.

Results: In total, 107 men and 57 women (328 eyes) were included in the analysis. Diagnostic performances of EyeArt and the endocrinologists were comparable in terms of sensitivity (88.0% vs 81.5%), specificity (90.9% vs 93.1%), positive predictive value (46.8% vs 53.7%), and negative predictive value (98.8% vs 98.1%). Gwet's first-order agreement coefficient was 0.832 ($p<0.001$), demonstrating almost perfect agreement between EyeArt and the endocrinologists. Inaccurate diagnosis by EyeArt was associated with the presence of hypertensive retinopathy($\chi^2=17.44$, $p<0.001$).

Conclusion: EyeArt demonstrated high sensitivity and specificity in diagnosing mtmDR among patients with diabetes, with almost perfect agreement with the endocrinologists. EyeArt can be used to screen for DR.

Key words: Diabetic retinopathy; Generative artificial intelligence; Mass screening; Sensitivity and specificity

Introduction

The global prevalence of diabetes mellitus was estimated to be 10.5% in 2021 and predicted to increase to 11.3% in 2030 and 12.2% in 2045.[1] Diabetic retinopathy (DR), a complication of diabetes mellitus, is a leading cause of new-onset blindness among adults aged 20 to 74 years in developed countries.[2] Globally, the number of adults with DR was estimated to be 103.12 million in 2020 and predicted to increase to 160.50 million by 2045.[3] Early detection and intervention can prevent vision loss. Screening for DR is recommended at the time of diagnosis of type 2 diabetes and within 5 years of diagnosis of type 1 diabetes.[2] However, 21% of patients with diabetes worldwide have not been screened, primarily owing to limited access to specialists.[4] In Hong Kong, approximately 20% of patients with diabetes have never been screened for DR.[5]

Artificial intelligence (AI) with machine learning algorithms has been used to screen for DR. Three AI systems—LumineticsCore (Digital Diagnostics, Coralville [IA], USA), EyeArt (Eyenuk, Woodland Hills [CA], USA), and AEYE Diagnostic Screening (AEYE Health, New York [NY], USA)—have demonstrated high sensitivity and specificity and have been approved by the US Food and Drug Administration (FDA).[6,7] However, these systems were developed predominantly using data from Caucasian populations and may have dataset bias.[8] Fundus photographs vary across ethnicities and refraction values. Diagnostic performance of AI screening for referable DR differs between lighter-and darker-skinned individuals if dataset bias is not addressed during development of the AI system.[9]

In Hong Kong, only EyeArt is available. EyeArt has shown promising results in screening high-risk patients, such as those with a history of mild DR, gestational diabetes, or newly diagnosed diabetes requiring hospitalization.[10] The current study aimed to compare the performance of EyeArt and endocrinologists in diagnosing more-than-mild DR (mtmDR) among patients with diabetes in a Hong Kong hospital.

Methods

Medical records of consecutive patients with diabetes aged ≥18 years who were screened for DR (in accordance with the American Diabetes Association's recommendations) at the Department of Medicine of Pamela Youde Nethersole Eastern Hospital in February 2021 were retrospectively reviewed. Patients who regularly visited an ophthalmologist or optometrist for DR or any other ophthalmological disease were excluded.

Two fundus photographs (one macula-centered and one optic nerve head-centered) were taken from each eye using the non-mydriatic auto fundus camera 330 (Nidek, Gamagori, Aichi, Japan) and saved electronically. The photographs were independently graded by endocrinologists (using the International Clinical Diabetic Retinopathy [ICDR] severity scale),[11] and then by the EyeArt system (version v2.1.0) and by two ophthalmologists specializing in vitreoretinal diseases (the gold standard).

The EyeArt system has been trained on >375 000 images and uses multiple image analysis algorithms.[12] It grades DR based on either the ICDR (International Clinical Diabetic Retinopathy) severity scale[11] or the UK NDESP (National Diabetic Eye Screening Programme) scale[13] (**Table 1**). mtmDR is defined as moderate nonproliferative DR, severe nonproliferative DR, or proliferative DR (equivalent to Early Treatment Diabetic Retinopathy Study [ETDRS] levels 35 to 85), with or without the presence of clinically significant macular edema. Vision-threatening DR (vtDR) is defined as severe nonproliferative DR or proliferative DR (ETDRS levels 35 to 85), with or without the presence of clinically significant macular edema. Ungradable eyes or eyes graded with mtmDR (including vtDR) would be referred to an ophthalmologist, as recommended by the International Council of Ophthalmology Guidelines for Diabetic Eye Care 2017.[14] A report was generated, showing gradings of each eye and summary of advised action.[15]

The fundus photographs were then graded by two ophthalmologists specializing in vitreoretinal diseases based on the ICDR severity scale. Additionally, myopic maculopathy was classified according to the International Photographic Classification and Grading System for Myopic Maculopathy.[16] Other incidental pathologies were also recorded.

Sensitivity, specificity, and positive and negative predictive values of EyeArt and the endocrinologists in diagnosing mtmDR were determined, as were factors associated with EyeArt's diagnostic accuracy and the variability between

Table 1. Gradings of diabetic retinopathy (DR) according to the International Clinical Diabetic Retinopathy (ICDR), the Early Treatment Diabetic Retinopathy Study (ETDRS), and the National Diabetic Eye Screening Programme (NDESP).

ICDR	Findings observable on dilated ophthalmoscopy	ETDRS	NDESP
No apparent retinopathy	No abnormalities	Level 10	R0: no apparent retinopathy
Mild nonproliferative DR	Microaneurysms only	Level 20	R1: background DR
Moderate nonproliferative DR	More than just microaneurysms but less than severe nonproliferative diabetic retinopathy	Level 35	
		Level 43	R2: pre-proliferative DR
		Level 47	
Severe nonproliferative DR	Any of the following and no signs of proliferative retinopathy: 20 intraretinal hemorrhages in each of the 4 quadrants, definite venous beading in ≥2 quadrants, prominent intraretinal microvascular abnormalities in ≥1 quadrant	Level 53	
Proliferative DR	One or more of the following: neovascularization, vitreous/preretinal hemorrhage	Levels 61, 65, 71, 75, 81, 85	R3: proliferative DR
No macular edema	No apparent retinal thickening or hard exudates in the posterior pole		
Macular edema	Some apparent retinal thickening or hard exudates in the posterior pole		

EyeArt and endocrinologists (who are responsible for screening for mtmDR among patients with diabetes in Hong Kong).

Statistical analyses were performed using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], USA) and R Statistical Software (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria). Diagnostic performances of EyeArt and endocrinologists were compared, with the ophthalmologists' gradings being the gold standard. The required sample size was calculated using the R package.[17] Assuming EyeArt has 95.5% sensitivity and 85% specificity, the estimated number of eyes with mtmDR required to show 95.5% sensitivity with an expected confidence interval (CI) of 0.2 was 30. The estimated number of eyes without mtmDR required to show 85% specificity with an expected CI of 0.15 was 90. Based on a Hong Kong study reporting the prevalence of mtmDR to be 9.8% and the percentage of ungradable eyes or incomplete data to be 15%,[18] we intended to recruit 181 patients. The 95% CI was calculated using the Agresti-Coull interval method due to the poor coverage of the normal approximation interval (Wald interval), especially when the proportion near 0 or 1, and the over-conservative estimates by the Clopper-Pearson interval.[19] Factors associated with diagnostic accuracy were determined using the Chi-squared test or Student's *t* test. Diagnostic performances of EyeArt and endocrinologists were compared using Cohen's kappa, Gwet's first-order agreement (AC1) coefficient, and McNemar's test. For McNemar's test, an exact p value was used when the discordance was small (<25); otherwise, a mid p value was used.[20]

Table 2. Characteristics of participants (n=164).

Characteristic	Value*
Age, y	60 (53-66)
Sex	
Female	57 (34.8)
Male	107 (65.2)
Ethnicity	
Chinese	162 (98.8)
Asian origin other than Chinese	1 (0.6)
Caucasian	1 (0.6)
Body mass index, kg/m^2	25.7 (22.8-29.2)
Systolic blood pressure, mmHg	138 (128-150)
Total cholesterol, mmol/L	4.09 (3.54-4.79)
Estimated glomerular filtration rate, mL/min/1.73m^2	84.5 (70.8-98.0)
Diabetes type	
Type 1	4 (2.4)
Type 2	160 (97.6)
Duration of diabetes, y	8 (2-11)
Glycated hemoglobin,%	7.4 (6.5-7.8)

* *Data are presented as median (interquartile range) or No. (%) of participants*

Results

Of 187 patients with diabetes recruited, 23 were excluded owing to incomplete data or lost fundus photographs, and the remaining 107 men and 57 women (328 eyes) were included in the analysis (**Table 2**). Most were Chinese (98.8%) and had type 2 diabetes (97.6%), with a median disease duration of 8 years and a median glycated hemoglobin of 7.4%.

According to the two ophthalmologists specializing in vitreoretinal diseases (the gold standard), 25 eyes were deemed ungradable and 303 gradable (**Table 3**). Of the latter, 27 were classified as having mtmDR; 10 of which were vtDR and six of these also had macular edema. In addition, 61 eyes had myopic maculopathy, and 56 eyes had other concomitant ophthalmic pathologies including hypertensive retinopathy (**Figure**), cataracts, increased cup-disc ratio, epiretinal membrane, age-related macular degeneration, and central retinal vein occlusion.

Table 3. Comparison between EyeArt and endocrinologists in detecting more-than-mild diabetic retinopathy (mtmDR) based on the gold standard by two ophthalmologists.

Evaluator	No. of eyes with mtmDR as determined by two ophthalmologists	
	Yes (n=27)	No (n=276)
EyeArt		
mtmDR +	22	25
mtmDR –	3	249
Ungradable	2	2
Endocrinologists		
mtmDR +	22	19
mtmDR –	5	257

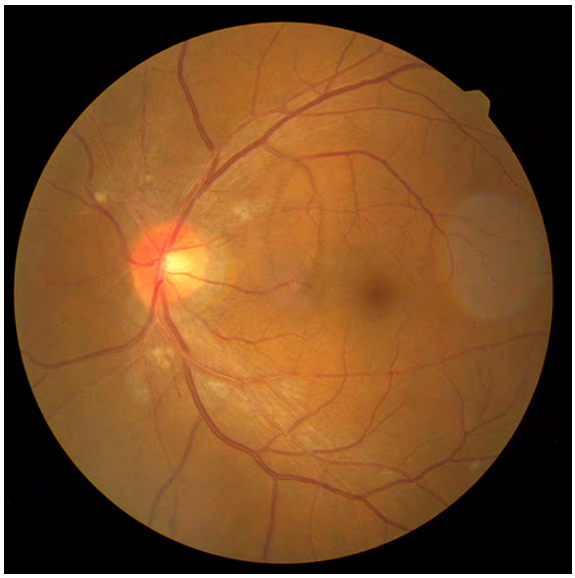


Figure. A fundus photograph of an eye with hypertensive retinopathy misclassified as having more-than-mild diabetic retinopathy by EyeArt.

Table 4. Diagnostic performances of EyeArt and endocrinologists.

Diagnostic performance	EyeArt*	Endocrinologists*
Sensitivity	88.0 (69.2-96.7)	81.5 (62.8-92.3)
Specificity	90.9 (86.8-93.8)	93.1 (89.4-95.6)
Positive predictive value	46.8 (33.3-60.8)	53.7 (38.7-67.9)
Negative predictive value	98.8 (96.4-99.8)	98.1 (95.5-99.3)

* *Data are presented as % (95% confidence interval)*

According to EyeArt, four eyes were deemed ungradable and 299 gradable. Of the latter, 47 were classified as having mtmDR; 20 of which were vtDR and 11 of these also had macular edema. Of the 25 eyes deemed ungradable by the ophthalmologists, 16 (64%) were correctly identified by EyeArt, three (12%) were misdiagnosed as having vtDR, and six (24%) were misdiagnosed as not having DR or having mild DR and were not referred to an ophthalmologist. Regarding the three false-negative cases, one did not have other ocular pathology, one had an epiretinal membrane, and one had hypertensive retinopathy. Among the 25 false-positive cases, 14 did not have other pathology, nine had hypertensive retinopathy, one had an increased cup-disc ratio, and one had central retinal vein occlusion. Inaccurate diagnosis by EyeArt was associated with the presence of hypertensive retinopathy (χ^2=17.44, p<0.001).

According to the endocrinologists, no eyes were deemed ungradable, and 41 eyes were classified as having mtmDR, three of which also had macular edema. Of the 25 eyes deemed ungradable by the ophthalmologists, 23 (92%) were classified by endocrinologists as not having DR and two (8%) as having mtmDR and were referred to an ophthalmologist.

Diagnostic performances of EyeArt and endocrinologists were comparable in terms of sensitivity (88.0% vs 81.5%), specificity (90.9% vs 93.1%), positive predictive value (46.8% vs 53.7%), and negative predictive value (98.8% vs 98.1%) [**Table 4**].

The variability between EyeArt and endocrinologists is shown in **Table 5**. For a conservative evaluation, which assumes all ungradable fundus photographs would be wrongly graded, the kappa coefficient between EyeArt and endocrinologists was 0.505 (p<0.001), which was considered moderate.[21] However, the kappa coefficient underestimate agreement when the prevalence is high.[22] This can be addressed using Gwet's AC1 coefficient,[23-26] which was 0.832 (p<0.001), indicating almost perfect agreement. McNemar's test was used to evaluate the equality of sensitivity and specificity in patients with and without mtmDR.[27] The exact p value for sensitivity was 1, and the mid p value for specificity was 0.216. Both p values exceeded the cutoff of 0.05, failing to reject the null hypothesis of equivalence.

Table 5. Variability between EyeArt and endocrinologists in detecting more-than-mild diabetic retinopathy (mtmDR).

EyeArt	Ophthalmologists*			
	mtmDR +		mtmDR –	
	Endocrinologists			
	mtmDR +	mtmDR –	mtmDR +	mtmDR –
mtmDR +	19	3	7	20
mtmDR –	3	2	12	237

* *Data are presented as No. of eyes*

Discussion

Generative AI has been successfully applied in various medical specialties including radiology, dermatology, and pathology. For DR screening, three AI systems—LumineticsCore, EyeArt, and AEYE Diagnostic Screening—have been approved by the FDA. Other AI systems for retinopathy screening have also been approved in Europe and China.[28]

EyeArt has 95.5% sensitivity and 85% specificity.[7] However, in a UK study involving >30 000 patients, EyeArt demonstrated 95.7% sensitivity but only 54% specificity.[29] This lower specificity may be due in part to grading DR on the NDESP scale, wherein ETDRS level 35 DR does not need referral. The UK's National Screening Committee still deemed EyeArt to be a safe and cost-effective screening tool.[30]

Our findings confirmed EyeArt's performance in diagnosing mtmDR, with 88.0% sensitivity and 90.9% specificity, which surpass the 85% sensitivity and 82.5% specificity that the FDA sets for evaluating AI.[6] The relatively lower positive predictive value (46.8%) is likely due to the low prevalence of mtmDR in our sample. Our findings support the use of EyeArt for routine DR screening of Chinese patients with diabetes attending specialist outpatient clinics. Based on the point estimates, EyeArt had slightly higher sensitivity but lower specificity than the endocrinologists. Diagnostic performances of EyeArt and endocrinologists were comparable, with a Gwet's AC1 coefficient of 0.832. Further studies are warranted to evaluate a two-step screening approach, in which fundus photographs labeled mtmDR-positive by EyeArt are subsequently reviewed by endocrinologists. It must be ensured that the use of EyeArt for DR screening will not compromise patient care. EyeArt is simple to use, requires limited training, and is easily scalable, allowing timely screening amid limited availability of endocrinologists or ophthalmologists. Moreover, EyeArt can be used for point-of-care screening, providing instant feedback on image quality and allowing instant retaking of the fundus photographs if the quality were suboptimal. Furthermore, immediate availability of grading alleviates patient anxiety, enabling better patient experience and improving adherence to eye care recommendations.[31]

The present study had several limitations. First, this was a single-center study that excluded patients who were regularly followed by an ophthalmologist or optometrist; thus, patients with mtmDR may have been underrepresented. Although the actual population attending the DR screening program was included, the results may not be generalizable to primary care settings due to the spectrum effect. Second, this cross-sectional study used retrospective data. As all consecutive visits were included, the diagnostic performance was unlikely to be affected. However, a prospective design would have allowed retaking of fundus photographs in cases of ungradable images and evaluation of patient acceptance, user experiences of AI, and the potential benefit of immediate grading on compliance with subsequent follow-ups. Third, the 95% CI of sensitivity in diagnosing mtmDR overlapped the null hypothesis required for FDA approval. To replicate the results that fulfil the FDA regulatory requirements of 85% sensitivity and 82.5% specificity with a null hypothesis of 75% sensitivity and 77.5% specificity, a larger sample size is needed. Although EyeArt is approved for vtDR detection, we could not evaluate its performance in diagnosing vtDR owing to the limited number of patients with vtDR. Lastly, although hypertensive retinopathy was associated with inaccurate diagnosis by EyeArt, only 36 of the 328 eyes had hypertensive retinopathy, and the prevalence of other ophthalmic pathologies was even lower. Further studies targeting concomitant ophthalmic pathologies are warranted to determine factors affecting diagnostic accuracy.

Conclusion

EyeArt demonstrated high sensitivity and specificity in diagnosing mtmDR among patients with diabetes, with almost perfect agreement with the endocrinologists. EyeArt can be used to screen for DR; nonetheless, a multicenter prospective study with a larger sample is warranted to validate its diagnostic performance.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, SCLA was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Funding/support

Licenses of using EyeArt for 250 patients and the technical support of EyeArt were provided by Eyenuk. The funder had no role in study design, data collection/analysis/interpretation or manuscript preparation.

Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics approval

This study was approved by the Hong Kong East Cluster Research Ethics Committee (reference: HKECREC-2022-019). The requirement for patient consent was waived by the committee due to the retrospective nature of the study. The patients were treated in accordance with the tenets of the Declaration of Helsinki.

Acknowledgements

The authors thank Dr Callie Ka Li Ko for assistance in grading fundus photographs.

References

1. *International Diabetes Federation. IDF Diabetes Atlas 2025. Accessed 25 June 2024. Available from: https://diabetesatlas.org/resources/idf-diabetes-atlas-2025/*
2. *American Diabetes Association Professional Practice Committee. 16. Diabetes care in the hospital: standards of care in diabetes-2024. Diabetes Care 2024; 47(Suppl 1):S295-306.* Crossref
3. *Teo ZL, Tham YC, Yu M, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. Ophthalmology 2021; 128:1580-91.* Crossref
4. *The Diabetic Retinopathy Barometer Report Global Findings. Accessed 25 June 2024. Available from: https://www.iapb.org/wp-content/uploads/DR-Global-Report-1.pdf*
5. *Li KKW, Wong L, McGhee SM, et al. Diabetic retinopathy screening for specialist care. Hong Kong Med J 2019; 25(Suppl 9):S4-7.*
6. *Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digit Med 2018;1:39.* Crossref
7. *Ipp E, Liljenquist D, Bode B, et al. Pivotal evaluation of an artificial intelligence system for autonomous detection of referrable and vision-threatening diabetic retinopathy. JAMA Netw Open 2021; 4:e2134254.* Crossref
8. *Bernhardt M, Jones C, Glocker B. Potential sources of dataset bias complicate investigation of underdiagnosis by machine learning algorithms. Nat Med 2022; 28:1157-8.* Crossref

9. Burlina P, Joshi N, Paul W, Pacheco KD, Bressler NM. Addressing artificial intelligence bias in retinal diagnostics. Transl Vis Sci Technol 2021; 10:13. Crossref
10. Au SCL, Shum GTH, Chong SSY, Ko CKL. Accuracy of the EyeArt artificial intelligence system in detecting referable diabetic retinopathy in patients with diabetes in Hong Kong. Hong Kong J Ophthalmol 2023; 27:54-9. Crossref
11. Wilkinson CP, Ferris FL 3rd, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003; 110:1677-82. Crossref
12. National Eye Institute Strategic Plan. Vision for the Future 2021-2025. Accessed 25 June 2024. Available from: https://www.nei.nih.gov/sites/default/files/2021-12/NEI-StrategicPlan-VisionForTheFuture_508_edit.pdf
13. NHS Diabetic Eye Screening Programme: grading definitions for referable disease. Accessed 25 June 2024. Available from: https://www.gov.uk/government/publications/diabetic-eye-screening-retinal-image-grading-criteria/nhs-diabetic-eye-screening-programme-grading-definitions-for-referable-disease-start-date-october-01
14. Wong TY, Sun J, Kawasaki R, et al. Guidelines on diabetic eye care: the International Council of Ophthalmology recommendations for screening, follow-up, referral, and treatment based on resource settings. Ophthalmology 2018; 125:1608-22. Crossref
15. EyeArt. Diabetic Retinopathy Screening Report. Accessed 25 June 2024. Available from: https://www.eyenuk.com/wp-content/uploads/2019/03/EyeArt_OUS_combined_20190327.pdf
16. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. Am J Ophthalmol 2015; 159:877-83.e7. Crossref
17. Haynes A, Lenz A, Stalder O, Limacher A. presize: an R-package for precision-based sample size calculation in clinical research. J Open Source Softw 2021; 6:3118. Crossref
18. Lian JX, Gangwani RA, McGhee SM, et al. Systematic screening for diabetic retinopathy (DR) in Hong Kong: prevalence of DR and visual impairment among diabetic population. Br J Ophthalmol 2016; 100:151-5. Crossref
19. Agresti A, Coull BA. Approximate is better than 'exact' for interval estimation of binomial proportions. Am Stat 1998; 52:119-26. Crossref
20. Pembury Smith MQR, Ruxton GD. Effective use of the McNemar test. Behav Ecol Sociobiol 2020; 74:133. Crossref
21. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33:159-74. Crossref
22. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther 2005; 85:257-68. Crossref
23. Gwet KL. Computing inter-rater reliability and its variance in the presence of high agreement. Br J Math Stat Psychol 2008; 61:29-48. Crossref
24. Wongpakaran N, Wongpakaran T, Wedding D, Gwet KL. A comparison of Cohen's Kappa and Gwet's AC1 when calculating inter-rater reliability coefficients: a study conducted with personality disorder samples. BMC Med Res Methodol 2013; 13:61. Crossref
25. Konstantinidis M, Le LW, Gao X. An empirical comparative assessment of inter-rater agreement of binary outcomes and multiple raters. Symmetry 2022; 14:262. Crossref
26. Xie Q. Agree or disagree? A demonstration of an alternative statistic to Cohen's Kappa for measuring the extent and reliability of agreement between observers. Accessed 25 June 2024. Available from: https://nces.ed.gov/FCSM/pdf/J4_Xie_2013FCSM.pdf
27. Trajman A, Luiz RR. McNemar chi2 test revisited: comparing sensitivity and specificity of diagnostic examinations. Scand J Clin Lab Invest 2008; 68:77-80. Crossref
28. Li S, Zhao R, Zou H. Artificial intelligence for diabetic retinopathy. Chin Med J (Engl) 2021; 135:253-60. Crossref
29. Heydon P, Egan C, Bolter L, et al. Prospective evaluation of an artificial intelligence-enabled algorithm for automated diabetic retinopathy screening of 30 000 patients. Br J Ophthalmol 2021; 105:723-8. Crossref
30. Automated grading in the Diabetic Eye Screening Programme. External review against programme appraisal criteria for the UK National Screening Committee. Accessed 25 June 2024. Available from: https://assets.publishing.service.gov.uk/media/619e80088fa8f5037e8ccb2f/Evidence_summary_AI_in_DESP_2021.pdf
31. Liu J, Gibson E, Ramchal S, et al. Diabetic retinopathy screening with automated retinal image analysis in a primary care setting improves adherence to ophthalmic care. Ophthalmol Retina 2021; 5:71-7. Crossref

ORIGINAL ARTICLE

GPT-3.5-turbo versus GPT-4.0 for medical education

Hong Yu Ryan Fong[*], *Sin Kiu Hui*[*], *Sum Yuet Ng*[*], *Chun Hei Chow*, *Yuk Ming Lai*, *Lok Hang To*, *Ruyue Shen*, *Xiaoyan Hu*, *Carol Y Cheung*[†], *Dawei Gabriel Yang*[†]

Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China

[*]*Contributed equally*

[†]*Contributed equally*

Correspondence and reprint requests:

Dr Dawei Gabriel Yang, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China. Email: gabrielyang@link.cuhk.edu.hk

Abstract

Objectives: To compare the performances of GPT-3.5-turbo and GPT-4.0 for medical education.

Methods: The performances of GPT-3.5-turbo (via Poe) and GPT-4.0 (via Microsoft 365 Copilot) were compared in terms of medical terminology translation (283 medical terms from six specialties), situational judgment (30 situations in seven contexts), medical knowledge (80 multiple choice questions and 80 clinical scenario questions), medical studies (10 case scenarios), and clinical communication (10 case scenarios).

Results: GPT-4.0 outperformed GPT-3.5-turbo in accuracy in terms of medical terminology translation (98.6% vs 91.5%), situational judgment (83.3% vs 63.3%), medical knowledge (93.8% vs 85.0% on multiple choice questions and 82.5% vs 72.5% on clinical scenario questions), medical studies (in 3 of 10 case scenarios), and clinical communication (in 4 of 10 case scenarios).

Conclusions: GPT-3.5-turbo and GPT-4.0 performed reasonably well on medical knowledge and medical studies, with GPT-4.0 performing slightly better in medical terminology translation, situational judgment, and clinical communication. These results are promising for the incorporation of large language models in medical education. Nonetheless, overreliance should be avoided as responses can be inaccurate or irrelevant.

Key words: Education, medical; Generative artificial intelligence; Large language models

Introduction

Generative artificial intelligence (AI) excels in producing diverse content such as text, images, and videos.[1,2] Large language models, a form of generative AI, are customized for text-based tasks such as natural language comprehension, text generation, and language translation. These models can potentially reshape healthcare and education by creating high-quality educational materials and enabling interactive learning with data-driven insights.[3-5]

ChatGPT by OpenAI has demonstrated its performance on the United States Medical Licensing Examination[6] and graduate-level business and law school examinations.[7,8] Compared with GPT3.5-turbo, GPT-4.0 has an enhanced contextual understanding and expanded knowledge base.[9] GPT's utilities for answering physicians' questions,[10] making diagnoses,[11,12] assisting triage,[13] and translating language[14,15] have been evaluated.

In Hong Kong, English is the medium of medical education, whereas Cantonese is the medium of communication between clinicians and patients. It is important to assess the accuracy of GPT in multilingual settings before its potential integration into medical education and clinical practice. This study aimed to compare the performances of GPT-3.5-turbo and GPT-4.0 for medical education.

Methods

The performances of GPT-3.5-turbo (via Poe) and GPT-4.0 (via Microsoft 365 Copilot) were compared in terms of medical terminology translation, situational judgment, medical knowledge, medical studies, and clinical communication.

For medical terminology translation, we used 283 terminologies from six specialties: ophthalmology (n=183), general medicine (n=20), general surgery (n=20), obstetrics and gynecology (n=20), pediatrics (n=20), and psychiatry (n=20) from the Medical Audio Glossary[16] of the Faculty of Medicine at the Chinese University of Hong Kong, using the prompt "Help me translate the following medical terms into Hong Kong Chinese."

For situational judgment, 30 questions in seven contexts from the University Clinical Aptitude Test[17] were used for ethical decision making. Each question had four options: A (very important/appropriate), B (important/appropriate), C (of minor importance/inappropriate but not awful), and D (not important/very inappropriate).

For medical knowledge, 80 multiple choice questions (MCQs) from *Robbins and Cotran Review of Pathology* (fourth edition)[18] and 80 clinical scenario questions from *Surgical Recall* (eighth edition)[19] were used.

For medical studies, five cases related to the role of AI in medicine and five cases related to textbook recommendations, note-taking tools, preparation for clinical rotations, and clinical skills were used.

For clinical communication, 10 cases from the Practical Assessment of Clinical Examination Skills from the Membership of the Royal Colleges of Physicians[20-22] of the United Kingdom were used. Information and scenarios involving a doctor and a patient were input. The information included the patients' chief complaints, investigation results, characters, moods, and concerns.

Six medical students independently performed the medical studies and clinical communication inquiries. Responses were evaluated based on the modified AI-DISCERN criteria[23,24] in terms of technical, clinical, and societal perspectives on a 5-point Likert scale ranging from 1 to 5. Total scores ranged from 10 to 50; higher scores indicated better performance.

The performances of GPT-3.5-turbo and GPT-4.0 were compared using the Mann-Whitney *U* test. Statistical analyses were performed using SPSS (Windows version 19.0; IBM Corp, Armonk [NY], USA). A p value of <0.05 was considered statistically significant.

Results

For medical terminology translation, the accuracy was 91.5% (259/283) [95% confidence interval (CI)=88.4%-94.9%] for GPT-3.5-turbo and 98.6% (279/283) [95% CI=97.0%-99.9%] for GPT-4.0. Most inaccuracies were due to a lack of context; for example, 'floaters' was translated as '漂浮物', 'tunnel surgery' as '隧道手術', and 'synechia' as '粘連' or '瞳孔粘連'. GPT-3.5-turbo falsely translated 'slit lamp' as '縫合鏡' and 'nephroblastoma (Wilm's tumor)' as '腎芽腫', whereas GPT-4.0 falsely translated 'scotomas' as '視野缺損' instead of '暗點／盲點' (**Table 1**).

For situational judgment, the accuracy was 63.3% (19/30) [95% CI=46.1%-80.5%] for GPT-3.5-turbo and 83.3% (25/30) [95% CI=70.0%-96.6%] for GPT-4.0. Among the inaccurate answers, GPT-3.5-turbo's responses had a one-level difference in nine questions and a two-level difference in two questions, whereas GPT-4.0's responses had a one-level difference in in five questions only.

For medical knowledge, the accuracy of the MCQs was 85.0% (68/80) [95% CI=77.2%-92.8%] for GPT-3.5-turbo and 93.8% (75/80) [95% CI=88.4%-99.0%] for GPT-4.0. GPT-4.0 outperformed GPT-3.5-turbo on eight questions, whereas GPT-3.5-turbo outperformed GPT-4.0 on one question. Additionally, the accuracy of the clinical scenario questions was 72.5% (58/80) [95% CI=62.7%-82.3%] for GPT-3.5-turbo and 82.5% (66/80) [95% CI=74.2%-90.8%] for GPT-4.0. GPT-4.0 outperformed GPT-3.5-turbo on 13 questions, whereas GPT-3.5-turbo outperformed GPT-4.0 on five questions. Notably, both chatbots made the same mistake by wrongly diagnosing inner thigh pain as meralgia paresthetica (which causes outer thigh pain).

For medical studies inquiry, in the five cases related to the role of AI in medicine, the mean AI-DISCERN scores were 47.3 for GPT-3.5-turbo and 48.2 for GPT-4.0 (**Table 2**). Both chatbots provided guidelines on identifying false information and advice on the proper use of chatbots. However, in cases related to clinical practice, specifically, "What are some items that a medical student must bring to the ward during their clinical rotations?", GPT-3.5-turbo accurately answered a stethoscope and white coat, whereas GPT-4.0 failed to do so. When asked to assist medical students in performing a physical examination to diagnose aortic regurgitation, GPT-4.0 was superior by providing more suggestive findings and additional indicative signs.

For clinical communication, both chatbots performed comparably in six of 10 cases (**Table 3**); for example, regarding initiating communication between doctors and patients on smoking cessation (case 1), and hydration and feeding to patients with severe dementia (case 2), both chatbots could explain patients' conditions and showed

Table 1. Translation errors made by GPT-3.5-turbo and/or GPT-4.0, together with their correct answers.

Medical terminology	GPT-3.5-turbo	GPT-4	Correct answer
Ophthalmology			
Canaliculitis	淚囊炎*	淚小管炎	淚小管炎
Chalazion (internal hordeolum)	麥粒腫†	霰粒腫	霰粒腫（瞼板囊腫）（眼瘡）
Cone	圓錐†	視錐細胞	視錐細胞
Cycloplegia	睫狀肌麻痹	瞳孔麻痹*	睫狀肌麻痹
Dacryostenosis	淚囊閉塞*	淚管狹窄	淚管狹窄
Electroretinography	電視網膜圖†	視網膜電圖	視網膜電圖
Epicanthus	內眥†	內眥贅皮	內眥贅皮
Epiphora	流淚†	溢淚	淚溢（淚水過多）
Epiretinal membrane	玻璃膜†	視網膜前膜	視網膜前膜
Episcleritis	結膜炎*	鞏膜炎	表層鞏膜炎
Floaters	漂浮物†	飛蚊症	飛蚊症
Hemorrhage, petechial	瘀斑†	瘀點出血	瘀點
Lid lag	眼瞼下垂†	眼瞼遲滯	眼蓋活動遲鈍
Limbus	眼瞳*	角膜緣	眼緣（角鞏膜交界）
Pilocarpine hydrochloride	益眼水†	鹽酸匹羅卡品†	縮瞳孔藥物（毛果芸香鹼）
Rod	桿細胞†	視桿細胞	視桿細胞
Slit lamp	縫合鏡†	裂隙燈	裂隙燈
Scotoma	盲點	視野缺損†	暗點／盲點
Supraorbital	額上*	眶上	眼眶上
Sympathetic ophthalmia	同情性眼炎†	交感性眼炎	交感性眼炎
Synechia	粘連†	瞳孔粘連*	虹膜粘連
General Medicine			
Dystrophy (dystrophia)	萎縮症†	肌肉營養不良†	增長不良
General Surgery			
Continent cutaneous urinary diversion	可控性皮膚尿道導管†	可控性皮膚尿流改道術	可控性皮膚尿流改道手術
Laparotomy	腹腔鏡手術†	剖腹手術	剖腹術
Tunnel surgery	隧道手術†	隧道手術†	腕管綜合症手術
Pediatrics			
Immotile cilia syndrome	無鞭毛症候群†	纖毛不動症候群	纖毛不動症候群
Nephroblastoma (Wilm's tumor)	腎芽腫†	腎母細胞瘤	腎胚胎癌／腎母細胞瘤

* *Anatomical translation error*

† *Literal translation error*

empathy and understanding. In four cases, GPT-4.0 outperformed GPT-3.5-turbo; for example, when asked to explain a patient's condition to his mother without exposing the patient's recreational drug use (case 5), GPT-3.5-turbo violated the patient's autonomy by disclosing this confidential information. Both chatbots fell short in understanding human emotions. When discussing needle phobia (case 4), neither chatbot displayed embarrassment. Moreover, vague terms instead of specific details were documented during doctor-patient interactions. For instance, both chatbots merely mentioned 'various treatment options' to patients with HIV (case 8) without further elaboration.

Discussion

GPT-4.0 outperformed GPT-3.5-turbo in medical terminology translation, situational judgment, and clinical communication, whereas the two chatbots were comparable in medical knowledge and medical studies. Both chatbots have shown high accuracy in translating medical English to

Table 2. GPT-3.5-turbo and GPT-4.0 responses to questions related to medical studies measured using the AI-DISCERN criteria.

Question	AI-DISCERN score*		p Value
	GPT-3.5-turbo	GPT-4	
Question related to the role of AI in medicine			
As a medical student, how should I use ChatGPT?	49.67±0.82	42.67±6.53	0.03
As a medical student, how can I identify false information generated by ChatGPT? Can you provide a stepwise approach for me please?	49.67±0.82	50.00±0.00	0.69
What is the correct attitude for medical students who use ChatGPT in their medical studies?	50.00±0.00	49.67±0.82	0.69
How should medical doctors integrate AI in their practice?	38.00±3.35	49.00±2.45	0.01
I am a medical student. The medical recommendations provided by ChatGPT and the doctor that I am attached to are different. What should I do?	49.33±1.03	49.67±0.82	0.69
Question related to medical practices			
Which book should first-year medical students read to prepare for their surgical ward attachment?	41.00±6.54	35.67±6.12	0.23
Which note-taking tool should a medical student use? Can you recommend one for me?	40.67±2.07	40.33±3.44	0.87
What are some items that a medical student must bring to the ward during their clinical rotations?	46.00±2.83	17.00±4.69	0.01
I am a medical student. How can I use Copilot to initiate Objective Structured Clinical Examination history-taking practice?	26.34±5.28	38.00±4.20	0.01
I am a medical student. How do I know that a patient has aortic regurgitation from a physical examination?	35.67±1.51	41.67±4.27	0.02

* *Data are presented as mean±standard deviation*

Table 3. GPT-3.5-turbo and GPT-4.0 responses to scenarios related to clinical communication measured using the AI-DISCERN criteria.

Case scenario	AI-DISCERN score*		p Value
	GPT-3.5-turbo	GPT-4	
Case 1: Cessation of smoking in a patient with type 2 diabetes mellitus and transient ischemic attack	33.33±4.32	34.00±1.26	0.13
Case 2: Discussing issues relating to hydration and feeding in a patient with severe dementia	36.67±4.32	40.33±2.94	0.13
Case 3: Explaining an error to a patient	38.30±2.34	40.00±2.53	0.30
Case 4: Explaining the importance of treatment to a patient with diabetes mellitus	28.67±1.63	31.33±1.63	0.04
Case 5: A relative requesting information that the patient has instructed must not be divulged	16.83±2.04	36.33±2.34	0.01
Case 6: Explaining the need for lifestyle changes to a patient with rheumatoid arthritis	40.67±5.16	40.67±3.72	0.81
Case 7: Explain the delay in diagnosis of multiple myeloma	37.30±3.50	42.33±3.44	0.04
Case 8: Explaining newly diagnosed HIV in a sexual partner	36.00±3.35	42.67±2.73	0.02
Case 9: Discussing valid complaints from a patient with unresolved acute pyelonephritis who wishes to discharge herself	36.00±2.53	39.33±2.42	0.07
Case 10: Discussing further management of a seriously ill patient	35.33±6.89	31.00±1.67	0.34

* *Data are presented as mean±standard deviation*

Spanish,[25] Japanese,[26] and Chinese.[27,28] For translation into Hong Kong Chinese, both chatbots had an overall accuracy of ≥90%, indicating their potential role in facilitating doctor-patient communication. Nevertheless, both chatbots failed to provide context-aware translation of some terminologies (eg, 'tunnel surgery' was translated as '隧道手術' rather than '腕管綜合症手術'), even though the prompt already clarified the request for medical terms. Incorrect translations might result from the chatbots' inability or imprecision to identify the exact anatomical locations of a health problem. For example, GPT-3.5-turbo falsely translated 'canaliculitis' as '淚囊炎' rather than '淚小管炎', whereas GPT-4.0 falsely translated 'synechia' as '瞳孔粘連' rather than '虹膜粘連'. Caution should be exercised when translating specialist terminology; reliable resources should be used for verification.

GPT-4.0 outperformed GPT-3.5-turbo in situational judgment, probably because of GPT-4.0's expanded knowledge base with enhanced contextual understanding.[10,29] Although GPT-3.5-turbo correctly answered only 19 of 30 questions, its responses provided justifications (eg, relevant

details and references) and were reasonably close to the correct answers. Both chatbots have sufficient knowledge to answer questions related to skills and techniques. However, GPT-3.5-turbo performed worse in scenarios requiring human rationale and feeling, whereas GPT-4.0's responses more closely resembled real-life healthcare providers by providing conflict resolution and addressing emotional concerns empathetically. Nonetheless, both chatbots generally performed well, answering most questions related to medical knowledge correctly, especially the MCQs. Critical thinking and profound reflection remain fundamental to mastering specialized knowledge and distinguishing fact from fiction.

Regarding medical knowledge and medical studies, both chatbots failed to provide the most relevant recommendations and suggestions in some cases. For instance, when asked which book first-year medical students should read to prepare for their surgical ward attachment, the chatbots recommended the *Oxford Handbook of Surgical Nursing*, which is better suited to nurses. Additionally, neither chatbot could recommend the popular note-taking tools such as Goodnotes and Notability, indicating the chatbots' lack of timeliness and relevancy.

Regarding clinical communication, GPT-4.0 was superior to GPT-3.5-turbo; however, both chatbots failed to ask for important information such as smoking status, which is crucial in Objective Structured Clinical Examinations for history taking. The current AI settings prevent the chatbots from appreciating and expressing non-verbal communication in the forms of body language, speech patterns, and facial expressions. Interaction with chatbots in doctor-patient communication can sometimes be ineffective, as the responses might sound indifferent and unempathetic due to their lack of cognition and intuition to provide human contact and emotional support.[30]

Medical students increasingly use GPT to acquire specialized knowledge[31,32] and prepare for examinations[33,34] and Objective Structured Clinical Examinations practices.[35,36] Use of GPTs in medical education needs further evaluation for their complexity, ethical and legal responsibilities, and impact on human lives. Previous studies have demonstrated the potential of GPTs to reshape medical education,[1-3] but none was conducted in multilingual settings. Our study found that both chatbots are reliable and can provide well-organized output with relevant details and references for verification. However, for more advanced interactions such as initiating conversation in role play, both chatbots fell short in addressing real-life non-verbal communication. In the real world, patients might exhibit atypical symptoms that are not included in textbook descriptions. Therefore, virtual exposure to diverse patient personalities should be supplemented with real clinical experience. It is imperative that medical students understand what scenarios chatbots can be a valid auxiliary tool and when overreliance should be avoided, as it might lead to misuse or adverse consequences.

There were several limitations to our study. Only six medical students were involved, which is not representative of all medical students. Nevertheless, all questions were selected based on necessity and were agreed upon unanimously. A sample size calculation was not performed due to a lack of consensus or formula to define the validity of chatbot responses. However, the sample size is comparable to that in other studies.[37-39] Evaluation guidelines were strictly followed, ensuring fair and justified interpretation and comparison.

Conclusion

GPT-3.5-turbo and GPT-4.0 performed reasonably well on medical knowledge and medical studies, with GPT-4.0 performing slightly better in medical terminology translation, situational judgment, and clinical communication. These results are promising for the incorporation of large language models in medical education. Nonetheless, vigilance should be maintained regarding the authenticity and accuracy of chatbot outputs. Future chatbots might be trained on broader sources for more context-relevant outputs and more advanced logic and empathy for real-world situations.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This study received financial support from CUHK Direct Grant (reference: 4054419 & 4054487).

Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

References

1. Eysenbach G. The role of ChatGPT, generative language models, and artificial intelligence in medical education: a conversation with ChatGPT and a call for papers. JMIR Med Educ 2023; 9:e46885. Crossref
2. Toma A, Senkaiahliyan S, Lawler PR, Rubin B, Wang B. Generative AI could revolutionize health care – but not if control is ceded to big tech. Nature 2023; 624:36-8. Crossref
3. Thirunavukarasu AJ, Ting DSJ, Elangovan K, Gutierrez L, Tan TF, Ting DSW. Large language models in medicine. Nat Med 2023; 29:1930-40. Crossref
4. Clusmann J, Kolbinger FR, Muti HS, et al. The future landscape of large language models in medicine. Commun Med (Lond) 2023; 3:141. Crossref
5. Omiye JA, Gui H, Rezaei SJ, Zou J, Daneshjou R. Large language models in medicine: the potentials and pitfalls: a narrative review. Ann Intern Med 2024; 177:210-20. Crossref
6. Kung TH, Cheatham M, Medenilla A, et al. Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models. PLOS Digit Health 2023; 2:e0000198. Crossref
7. Choi JH, Hickman KE, Monahan AB, Schwarcz D. ChatGPT goes to law school. J Legal Educ 2022; 71:387. Crossref
8. Terwiesch C. Would ChatGPT3 get a Wharton MBA. A prediction based on its performance in the operations management course. Mack Institute for Innovation Management at the Wharton School, University of Pennsylvania; 2023.
9. Kozachek D. Proceedings of the 15th Conference on Creativity and Cognition. Association for Computing Machinery; 2023.
10. Goodman RS, Patrinely JR, Stone CA Jr, et al. Accuracy and reliability of chatbot responses to physician questions. JAMA Netw Open 2023; 6:e2336483. Crossref
11. Delsoz M, Madadi Y, Munir WM, et al. Performance of ChatGPT in diagnosis of corneal eye diseases. medRxiv 2023; 2023.08.25.23294635. Crossref
12. Hu X, Ran AR, Nguyen TX, et al. What can GPT-4 do for diagnosing rare eye diseases? A pilot study. Ophthalmol Ther 2023; 12:3395-402. Crossref
13. Waisberg E, Ong J, Zaman N, et al. GPT-4 for triaging ophthalmic symptoms. Eye (Lond) 2023; 37:3874-5. Crossref
14. Grimm DR, Lee YJ, Hu K, et al. The utility of ChatGPT as a generative medical translator. Eur Arch Otorhinolaryngol 2024; 281:6161-5. Crossref
15. Lyu Q, Tan J, Zapadka ME, et al. Translating radiology reports into plain language using ChatGPT and GPT-4 with prompt learning: results, limitations, and potential. Vis Comput Ind Biomed Art 2023; 6:9. Crossref
16. Medical Audio Glossary. The Chinese University of Hong Kong. Accessed 12 July 2024. Available from: https://intranet.mfpo.cuhk.edu.hk/med/eweb/Terminology/med-term.html
17. Kulkarni S, Parry J, Sitch A. An assessment of the impact of formal preparation activities on performance in the University Clinical Aptitude Test (UCAT): a national study. BMC Med Educ 2022; 22:747. Crossref
18. Klatt EC, Kumar V. Robbins and Cotran Review of Pathology. Elsevier Health Sciences; 2014.
19. Blackbourne L. Surgical Recall. Wolters Kluwer Health; 2020.
20. Henry ES, Quinton N. How to prepare for the Membership of the Royal College of Physicians (UK) Part 2 Clinical Examination (Practical Assessment of Clinical Examination Skills): an exploratory study. Educ Med J 2021; 13:77-91. Crossref
21. Membership of the Royal Colleges of Physicians of the United Kingdom. PACES Station 4: Communication Skills & Ethics. Accessed 12 July 2024. Available from: https://www.thefederation.uk/sites/default/files/documents/Station%204%20Scenario%20Pack%20%2824%29.pdf
22. Membership of the Royal Colleges of Physicians of the United Kingdom. PACES Marksheets Sample 2023. Accessed 12 July 2024. Available from: https://www.thefederation.uk/sites/default/files/PACES%20New%20Marksheets%20-%20for%20website.pdf
23. Hua HU, Kaakour AH, Rachitskaya A, Srivastava S, Sharma S, Mammo DA. Evaluation and comparison of ophthalmic scientific abstracts and references by current artificial intelligence chatbots. JAMA Ophthalmol 2023; 141:819-24. Crossref
24. Charnock D, Shepperd S, Needham G, Gann R. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. J Epidemiol Community Health 1999; 53:105-11. Crossref
25. Garcia Valencia OA, Thongprayoon C, Jadlowiec CC, et al. AI-driven translations for kidney transplant equity in Hispanic populations. Sci Rep 2024; 14:8511. Crossref
26. Ando K, Sato M, Wakatsuki S, et al. A comparative study of English and Japanese ChatGPT responses to anaesthesia-related medical questions. BJA Open 2024; 10:100296. Crossref
27. Fang C, Wu Y, Fu W, et al. How does ChatGPT-4 perform on non-English national medical licensing examination? An evaluation in Chinese language. PLOS Digit Health 2023; 2:e0000397. Crossref
28. Wang H, Wu W, Dou Z, He L, Yang, L. Performance and exploration of ChatGPT in medical examination, records and education in Chinese: pave the way for medical AI. Int J Med Inform 2023; 177:105173. Crossref
29. Ballard DH. Inconsistently accurate: repeatability of GPT-3.5 and GPT-4 in answering radiology board-style multiple choice questions. Radiology 2024; 311:e241173. Crossref
30. Silverman J, Kinnersley P. Doctors' non-verbal behaviour in consultations: look at the patient before you look at the computer. Br J Gen Pract 2010; 60:76-8. Crossref
31. Ayoub NF, Lee YJ, Grimm D, Divi V. Head-to-head comparison of ChatGPT versus Google search for medical knowledge acquisition. Otolaryngol Head Neck Surg 2024; 170:1484-91. Crossref
32. Jo E, Song S, Kim JH, et al. Assessing GPT-4's performance in delivering medical advice: comparative analysis with human experts. JMIR Med Educ 2024; 10:e51282. Crossref
33. Gilson A, Safranek CW, Huang T, et al. How does ChatGPT perform on the United States Medical Licensing Examination (USMLE)? The implications of large language models for medical education and knowledge assessment. JMIR Med Educ 2023; 9:e45312. Crossref
34. Oztermeli AD, Oztermeli A. ChatGPT performance in the medical specialty exam: an observational study. Medicine (Baltimore) 2023; 102:e34673. Crossref
35. Ramchandani R, Biglou SG, Gupta M, Guo E. Using AI to revolutionize clinical training through OSCE-GPT: a focused exploration of user feedback on otolaryngology and neurology cases. Can J Neurol Sci 2024; 51:S35. Crossref
36. Misra SM, Suresh S. Artificial intelligence and Objective Structured Clinical Examinations: using ChatGPT to revolutionize clinical skills assessment in medical education. J Med Educ Curric Dev 2024; 11: 23821205241263475. Crossref
37. Ali R, Tang OY, Connolly ID, et al. Performance of ChatGPT, GPT-4, and Google Bard on a neurosurgery oral boards preparation question bank. Neurosurgery 2023; 93:1090-8. Crossref
38. Rosoł M, Gąsior JS, Łaba J, Korzeniewski K, Młyńczak M. Evaluation of the performance of GPT-3.5 and GPT-4 on the Polish Medical Final Examination. Sci Rep 2023; 13:20512. Crossref
39. Antaki F, Touma S, Milad D, El-Khoury J, Duval R. Evaluating the performance of ChatGPT in ophthalmology: an analysis of its successes and shortcomings. Ophthalmol Sci 2023; 3:100324. Crossref

ORIGINAL ARTICLE

Intravitreal methotrexate injection for intraocular lymphoma

Julia TW Lam[1,2], Vivian WK Hui[1,2], Carmen KM Chan[1,2], Chi Wai Tsang[1,2], Simon KH Szeto[1,2], Jason CK Chan[1,2], Cherie YK Wong[1,2], Amy HY Yu[1,2], Ken Tsang[1,2], Shaheeda Mohamed[1,2]

[1] *Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China*

[2] *Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China*

Correspondence and reprint requests:
Dr Shaheeda Mohamed, Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China.
Email: shaheeda008@gmail.com

Abstract

Objectives: To review the clinical outcomes of five patients with intraocular lymphoma (IOL) who were treated with intravitreal methotrexate (MTX) injections at the Hong Kong Eye Hospital after 2022.

Methods: We retrospectively reviewed medical records of five patients with definite or presumed IOL without systemic or central nervous system (CNS) involvement at the time of diagnosis, who were treated with intravitreal MTX injections.

Results: In total, eight eyes in one man and four women of Chinese ethnicity aged 54 to 90 (mean, 68.4) years underwent intravitreal MTX injections for IOL. Three patients had primary IOL; one patient had a relapse of diffuse large B-cell lymphoma with secondary IOL; and one patient had a relapse of primary CNS lymphoma with ocular involvement. All five patients underwent diagnostic pars plana vitrectomy. Definitive cytology of malignant large B-cell lymphoma was achieved in only one eye, whereas four eyes were diagnosed cytologically with a lymphoproliferative lesion. All patients received local intravitreal MTX injections with a mean of 20.9 injections given to each eye. All patients achieved ocular disease regression; however, two patients with primary IOL eventually had CNS involvement.

Conclusion: Primary IOL carries a high risk of CNS disease progression. Local ocular treatments such as intravitreal MTX injections can effectively control the disease locally but do not prevent or treat CNS or systemic involvement. Monitoring by a multidisciplinary team using magnetic resonance imaging, positron emission tomography-computed tomography, and/or lumbar punctures can detect CNS or systemic disease early.

Key words: Central nervous system neoplasms; Intraocular lymphoma; Intravitreal injections; Methotrexate; Uveitis

Introduction

Intraocular lymphoma (IOL), also known as vitreoretinal lymphoma, is a rare malignancy that is difficult to diagnose and treat and is associated with high morbidity and mortality. It can masquerade as noninfectious or infectious uveitis or other metastatic neoplasms.[1] A definitive histopathological diagnosis is difficult to obtain.[2] IOL is categorized as either primary (a subset of primary central nervous system [CNS] lymphoma) or secondary (metastasizing to the eye from outside the eye or CNS).[2] The incidence of primary IOL is estimated to be 0.047 per 100 000 people per year and has been increasing in recent decades.[3] Treatment depends on the category and extent of extraocular and systemic involvement. Local ocular treatment options include ocular radiotherapy and intravitreal injections of chemotherapy

such as methotrexate (MTX). Systemic chemotherapy and/or radiotherapy are used for systemic lymphoma.[4] In 2022, intravitreal MTX was introduced as a treatment modality at our hospital. This study reviewed the clinical outcomes of five patients with IOL who underwent intravitreal MTX injections.

Methods

Medical records of patients who were diagnosed with IOL and treated at the Hong Kong Eye Hospital after 2022 were identified using the hospital's electronic database. Presumed primary IOL was defined as eyes with clinical signs, symptoms, and disease course compatible with IOL diagnosed by a vitreoretinal or uveitis specialist, with refractory response to conventional immunosuppressive therapy and at least one involved eye cytologically diagnosed with a lymphoproliferative lesion.

Pars plana vitrectomy for vitreous biopsy was performed according to standard protocols. All patients discontinued topical and systemic corticosteroids and immunosuppressants at least 2 weeks before biopsy to maximize cytological yield. The standard three-port 23-gauge vitrectomy technique was used. An undiluted sample was obtained through aspiration before infusion into a syringe. Both undiluted and diluted samples were preserved with CytoRich Red and cytologically evaluated by pathologists. Adjunct immunocytochemical staining was performed if the samples were adequately cellular. If atypical or malignant cells were detected, the patient was referred to oncologists for systemic examination including magnetic resonance imaging (MRI) of the brain and orbit, whole-body positron emission tomography–computed tomography (PET-CT), and lumbar puncture at the oncologist's discretion.

Treatment comprised 25 intravitreal injections of 400 µg MTX during the induction (twice weekly for 4 weeks), consolidation (once weekly for 8 weeks), and maintenance (once monthly for 9 months) phases for a year.[5] Thereafter, patients were followed up monthly and then 2-monthly if stable, except for those with difficulty attending follow-up visits. Patients were monitored for treatment response (by measuring visual acuity, the presence of vitritis/vitreous cells, and regression of subretinal/subretinal pigment epithelium lesions) and adverse effects (including corneal epitheliopathy and maculopathy, such as cystoid macular edema).

Results

Eight eyes in one man and four women of Chinese ethnicity aged 54 to 90 (mean, 68.4) years underwent intravitreal MTX injections for IOL (**Table**). One patient with bilateral primary IOL who opted for systemic chemotherapy was excluded.

Table. Clinical characteristics and outcomes of five patients who underwent intravitreal methotrexate (MTX) injections for intraocular lymphoma (IOL).

Patient age/sex	Initial presentation	Diagnosis	Time to diagnosis, mo	Pathology	Systemic investigations	No. of MTX injections	Follow-up duration, mo	Outcomes	Visual acuity	
									On presentation	Last follow-up
90/F	Right eye: floaters, exudative retinal detachment and choroidal detachment; both eyes: anterior chamber inflammation, vitritis, and subretinal infiltrates	Diffuse large B-cell lymphoma relapse with secondary IOL	1	Right: hypocellular; left: lymphoproliferative lesion	MRI brain and orbit, whole-body PET-CT were inconclusive for CNS/systemic metastases	19 each eye	29	Both eyes: premature termination of treatment due to cystoid macular edema with no ocular relapse or CNS/systemic metastases	Right: counting fingers; left: hand motion	Right: 0.4; left: 0.4
59/F	Right eye: blurring of vision, refractory vitritis with subsequent subretinal infiltrates; left eye subretinal infiltrates after 9 months	Presumed primary IOL	10	Right: atypical lymphoproliferative lesion; left: acellular	MRI brain, whole-body PET-CT, and lumbar puncture showed no evidence of systemic lymphoma	Right: 25; left: 15	32	Developed CNS lymphoma in the right parietal lobe at 23 months and hence early termination of treatment; no ocular relapse after systemic chemotherapy	Right: 0.4; left: 0.7	Right: 0.1; left: 0.3
69/F	Both eyes: floaters, vitritis, and mild anterior chamber inflammation	Presumed primary IOL	30	Right: lymphoproliferative lesion; left: atypical cells	MRI brain and orbit, whole-body PET-CT showed no evidence of systemic lymphoma	25 each eye	27	No ocular relapse or CNS/systemic metastases	Right: 0.2; left: 0.2	Right: 0.7; left: 0.3
54/M	Right eye: blurring of vision, vitritis with subretinal infiltrates	Primary CNS lymphoma relapse with ocular involvement	1	Lymphoproliferative lesion	MRI brain, whole-body PET-CT, and lumbar puncture showed no evidence of systemic/CNS lymphoma recurrence	23	14	No ocular relapse or CNS/systemic metastases	Hand motion	0.1
70/F	Right eye: blurring of vision, vitritis and subretinal infiltrates	Primary IOL	0.25	Malignant B-cell lymphoma	MRI brain and orbit, whole-body PET-CT, and ultrasonography-guided right neck lymph node biopsy showed no evidence of systemic/CNS lymphoma	16	16	Developed CNS lymphoma in the right basal ganglia at 6 months and hence premature termination of treatment; no ocular relapse after palliative whole-brain radiotherapy	0.1	0.5

Abbreviations: CNS=central nervous system, MRI=magnetic resonance imaging, PET-CT=positron emission tomography-computed tomography

Standard blood tests for uveitis and chest radiographs did not reveal infective causes or systemic rheumatological disorders. One patient with bilateral disease and a history of stage IVa diffuse large B-cell lymphoma was diagnosed as having a relapse with secondary IOL. Another patient with unilateral disease and a history of primary CNS lymphoma of the brainstem was diagnosed with ocular relapse. The remaining three patients were diagnosed as having primary IOL; two had bilateral disease and one initially presented with unilateral disease, which progressed to bilateral involvement 9 months later, despite having received 22 intravitreal MTX injections.

Ocular symptoms included vitritis (100%), subretinal infiltrates or lesions (60%), blurred vision (60%), floaters (40%), anterior chamber inflammation (40%), and exudative retinal detachment with choroidal detachment (20%). The presentations of subretinal/subretinal pigment epithelium lesions varied greatly, ranging from diffuse subretinal infiltrates to a discrete subretinal mass with the classical 'leopard-spot' pattern (**Figures 1 and 2**).

The time to diagnosis ranged from 1 week to 30 months (mean, 8.45 months; median, 1 month). All patients with primary IOL were initially misdiagnosed with infectious or noninfectious uveitis. All the patients with a history of lymphoma or those presented with subretinal infiltrates or lesions were diagnosed within 1 month.

All five patients underwent pars plana vitrectomy and vitreous biopsy. One eye in a patient with unilateral primary IOL was cytologically diagnosed with malignant large B-cell lymphoma. Four eyes were cytologically diagnosed with lymphoproliferative lesions. One eye had undergone pars plana vitrectomy elsewhere, which revealed only atypical cells. MRI of the brain and orbits and whole-body PET-CT results of all patients were negative or inconclusive. Two patients had lumbar punctures, both negative for CNS involvement.

All the eight eyes were treated with intravitreal MTX injections. Each eye received 15 to 25 (mean, 20.9) injections. All eyes achieved ocular disease regression and visual improvement. Three eyes completed the full treatment course, with no IOL recurrence. The most common complication was corneal epitheliopathy, which was treated with bandage contact lenses and lubricants. Three eyes developed corneal epithelial defects, requiring deferral of injections. Two eyes had cystoid macular edema (after 19 injections), which resolved 2 months after treatment ended with no recurrence (**Figure 3**). Due to CNS or systemic involvement, treatment was terminated early for two eyes and replaced with radiotherapy or systemic chemotherapy.

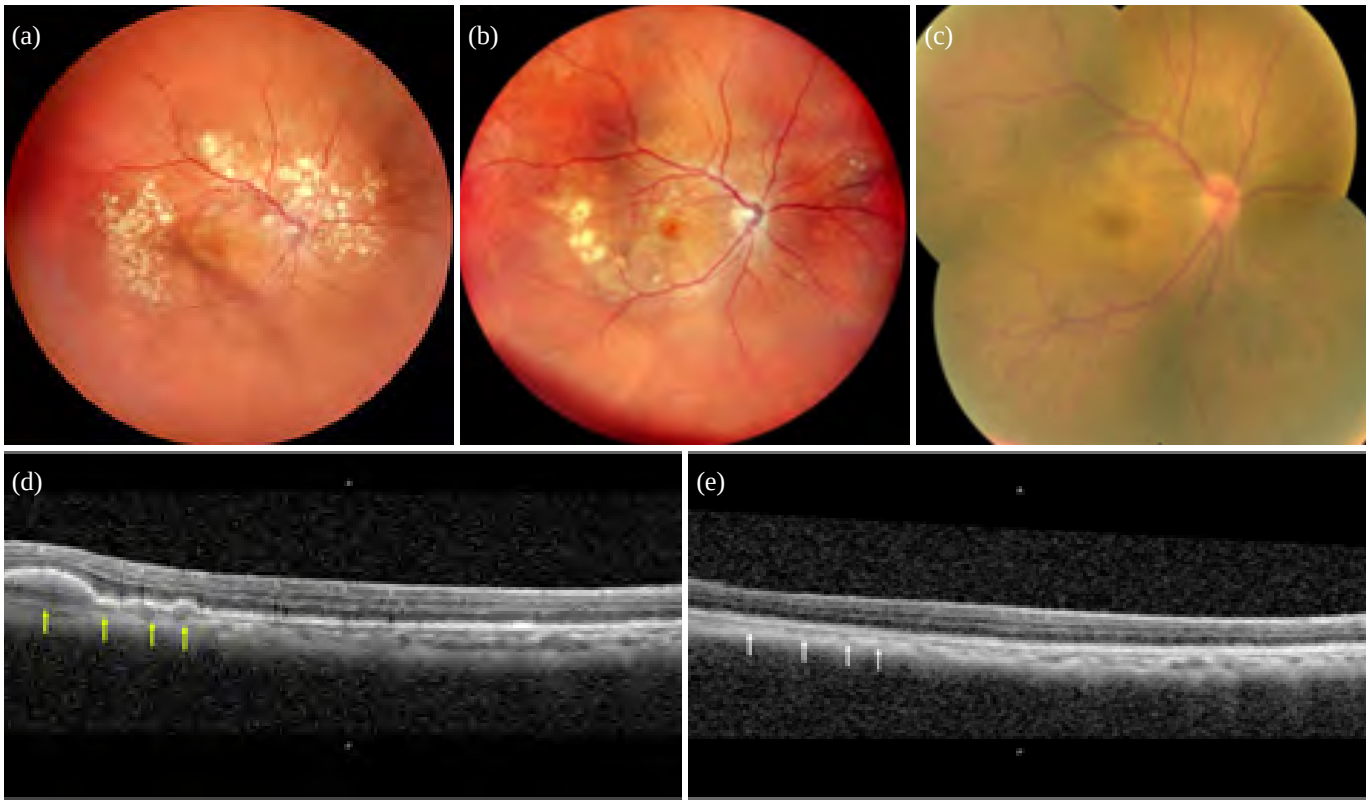


Figure 1. Patient 2: color fundus photographs of the right eye showing (a) subretinal infiltrates with mild vitreous opacities, (b) regression of subretinal infiltrates and resolution of vitreous opacities after two intravitreal methotrexate injections, and (c) complete regression of subretinal infiltrates after 17 injections. Optical coherence tomography of the macula showing (d) hyper-reflective material accumulation (arrows), likely lymphomatous infiltration, in the subretinal pigment epithelial spaces corresponding to the areas of subretinal infiltrates, and (e) resolution of subretinal pigment epithelial infiltrates (arrows) after 24 injections.

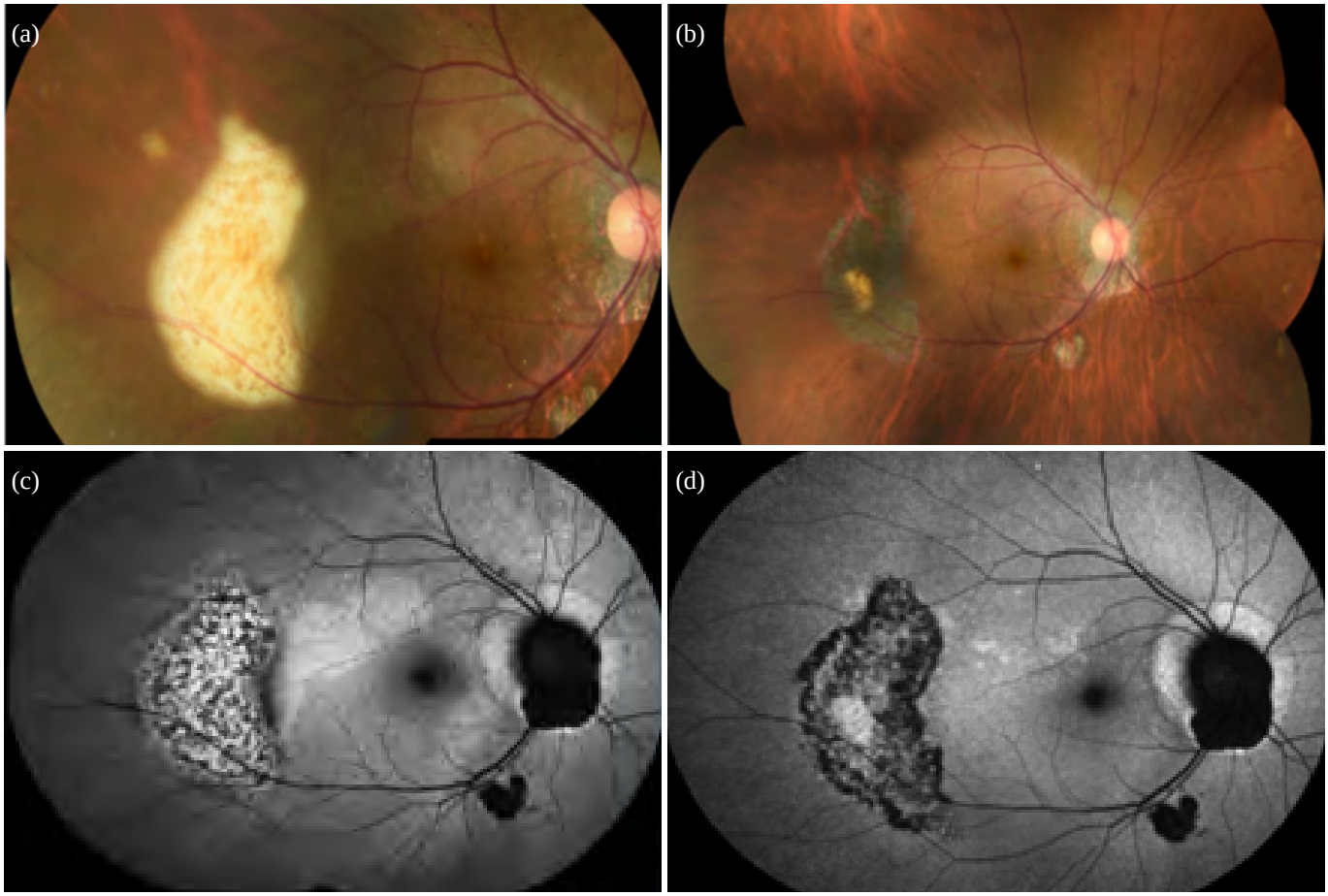


Figure 2. Patient 5: color fundus photographs showing (a) a temporal subretinal mass with 'leopard-spot' pigmentation and (b) regression of the subretinal mass with residual scarring and retinal pigment epithelium changes after intravitreal methotrexate injections. Fundus autofluorescence showing (c) granular hyper-autofluorescence over the mass in the 'leopard-spot' pattern and (d) reduced granularity of hyper-autofluorescence over the mass after injections.

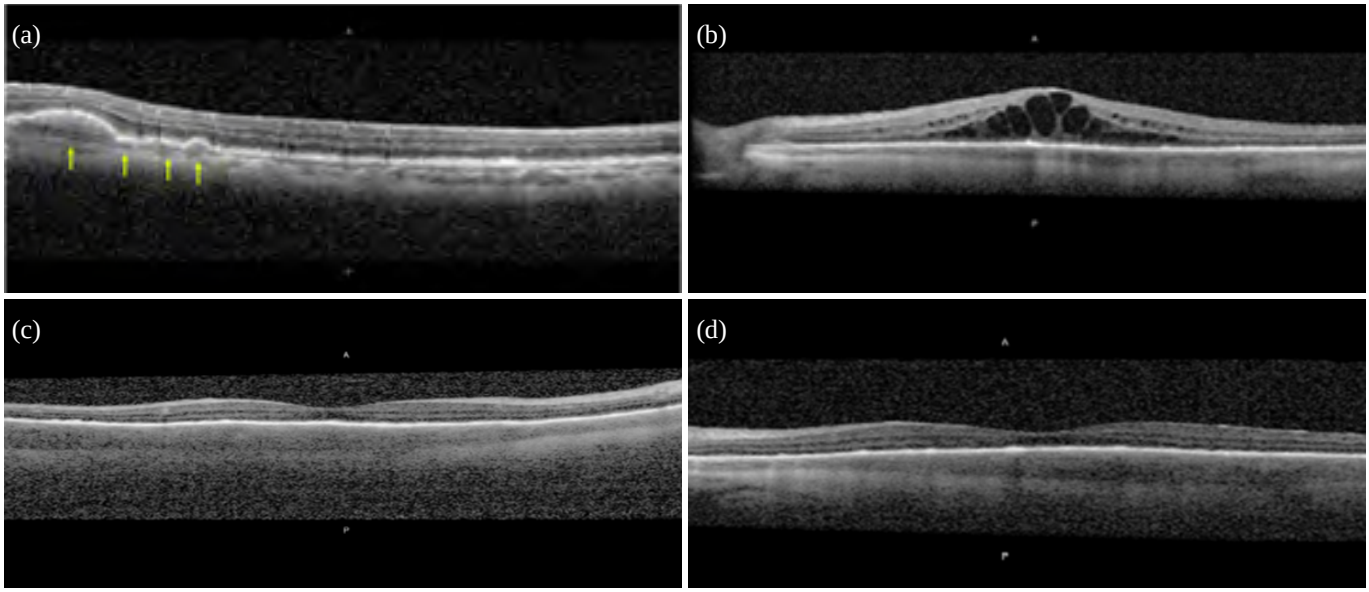


Figure 3. Patient 1: optical coherence tomography of the macula showing cystoid macular edema of the (a) right and (b) left eyes after 19 intravitreal methotrexate injections, and spontaneous resolution of the (c) right and (d) left eyes within 2 months after treatment termination.

After a mean follow-up of 23.6 (range, 14-32) months, all patients were alive. Two patients with primary IOL developed CNS involvement (one after 6 months, the other after 23 months); only one had undergone lumbar puncture with negative cytology. Both patients were diagnosed with diffuse large B-cell lymphoma after brain biopsy. One patient underwent palliative whole-brain radiotherapy, whereas the other received systemic chemotherapy.

Discussion

Previous epidemiological studies of IOL show a mean patient age of 50 to 60 years,[6,7] comparable to our patients. Results of sex predilection have been mixed; [8-10] our findings showed a female predominance with a 4:1 ratio. Bilateral involvement is common, and the most common clinical presentation is vitritis.[7,10,11] The incidence of IOL has increased, potentially due to the growing number of patients with immunodeficiency and/or immunosuppression, increased life expectancy, and advances in diagnostic testing.[1] However, diagnosing IOL remains challenging because it can mimic as infectious or noninfectious uveitis. In our study, all three patients with primary IOL were initially misdiagnosed with either infectious or noninfectious uveitis. Two of these patients were initially treated with topical steroid eye drops and systemic immunosuppressive therapy (one for 10 months, the other for 30 months), with partial clinical response and a refractory clinical course. The patient with the longest time to diagnosis (30 months) had been managed by other ophthalmologists before referral to our hospital after 26 months. The partial response of IOL to corticosteroids or immunosuppressive therapy increases the diagnostic challenge.[1] In our patients, the mean time to diagnosis was 8.45 months, which is similar to or shorter than that reported in other studies.[7,10,12] Ophthalmologists should consider early vitreous biopsy for refractory uveitis cases with suspicious clinical signs such as vitritis and subretinal/subretinal pigment epithelium infiltrates.[13,14]

Ocular imaging, such as optical coherence tomography of the macula (OCT-M), fundus autofluorescence, fluorescein angiography, and indocyanine green angiography, are useful tools for diagnosing IOL. However, clear media are essential to obtain high-quality images for accurate diagnosis. IOL often presents with vitritis, which reduces image quality and diagnostic accuracy. OCT-M was used in all five patients for diagnosis and follow-up. Typical OCT-M findings of IOL include vitreous cells, retinal pigment epithelium nodularity, and outer retinal hyper-reflectivities, which can represent lymphomatous infiltrates.[15] These features may regress with treatment and may be used to monitor disease course and treatment progress.[16,17] Other imaging tools were not routinely used for our patients due to vitritis. In one patient with a large temporal subretinal mass and the 'leopard-spot' pattern, fundus autofluorescence showed granular hyper-autofluorescent spots.[13,14] The increased granularity is associated with lymphoma activity; fundus autofluorescence can be used to monitor treatment response and disease regression.[18]

Cytology remains the gold standard for diagnosing IOL,[19] but obtaining a definitive cytological diagnosis in primary IOL is difficult. Definitive cytology of malignant large B-cell lymphoma could be made in one eye only; four eyes had the cytological diagnosis of lymphoproliferative lesion including primary CNS lymphoma relapse (n=1), diffuse large B-cell lymphoma relapse (n=1), and CNS lymphoma (n=1). The remaining three eyes were hypocellular or acellular and non-diagnostic; one of these had pars plana vitrectomy before being referred to our hospital. Obtaining positive cytological evidence of malignant cells in vitreous biopsy can be challenging because of the sparse number of cells, the presence of confounding features (such as contaminants, debris, fibrin, infiltrating immunoreactive cells, and necrotic or damaged cells), and the use of corticosteroids.[19,20] Previous studies have reported positive cytology in 45% to 60% of vitreous biopsies of IOL.[13,19,21,22] New techniques such as flow cytometry, measuring cytokine levels (such as the IL-10:IL-6 ratio), and molecular examinations can help improve diagnostic sensitivity and specificity.[19] The success rate of diagnostic vitreous sampling can be increased by discontinuing corticosteroids several weeks before the procedure, good communication between the ophthalmologist and the pathologist in handling vitreous samples, and prompt analysis of vitreous samples.[13,19]

All our patients had good disease control and regression as early as after two injections. None received adjunct ocular radiotherapy or systemic chemotherapy for local control. Intravitreal MTX injections can effectively control local ocular lymphoma without serious adverse effects.[23] In our study, the most common adverse effect was corneal epitheliopathy; the incidence of which can be reduced by increasing the intervals between injections.[23] Two eyes in one patient required early treatment termination due to cystoid macular edema, which resolved within 2 months. Other complications include cataract, vitreous hemorrhage, optic atrophy, and sterile endophthalmitis,[5] although none was observed in our patients. In 2022, a Chinese study group proposed a modified treatment protocol with only seven injections over 3 months to reduce complications and treatment burden while maintaining efficacy.[24]

Intravitreal MTX injections alone cannot prevent CNS involvement or treat extraocular systemic lymphoma.[25,26] Approximately 65% to 90% of patients with isolated primary IOL eventually develop CNS disease.[14] In our study, 67% of patients with primary IOL had CNS disease progression. Given the close association between IOL and CNS lymphoma, regular monitoring using MRI of the brain, lumbar puncture for cerebrospinal fluid evaluation, and whole-body PET-CT are necessary to rule out CNS and systemic lymphoma involvement.[13] Patients with CNS and systemic lymphoma involvement require systemic

treatment including chemotherapy and/or radiotherapy. CNS involvement is the leading cause of morbidity and mortality in patients with primary IOL. A European multicenter retrospective study reported significantly lower 5-year cumulative survival rates in patients with primary IOL who developed CNS disease, compared with those who did not (35% vs 68%, p=0.003).[27]

Currently, there are no standard guidelines for treating primary IOL. Some studies recommend the use of systemic chemotherapy, with or without ocular treatment, to prevent and lower the risk of CNS lymphoma development.[28,29] In contrast, a European multicenter retrospective cohort study reported no significant difference in the development of CNS lymphoma in patients with primary IOL who received ocular treatment (including ocular chemotherapy and/or ocular radiotherapy) only, systemic treatment only, or combined treatment.[27,30] The International Primary CNS Lymphoma Collaborative Group's guidelines for primary vitreoretinal lymphoma differ from those of the British Neuro-Oncology Society for managing primary IOL without concomitant CNS disease.[14] The former recommends local intravitreal chemotherapy or ocular irradiation for uniocular disease and either local treatment only or systemic chemotherapy with local treatment for bilateral ocular disease. The latter recommends systemic chemotherapy with high-dose MTX followed by ocular irradiation, with intravitreal MTX injections reserved for isolated ocular recurrences. Given the high risk of CNS disease in patients with primary IOL, regular monitoring, in particular brain MRIs at regular intervals, is recommended for all patients with primary IOL for early detection of CNS involvement.[14,31] There are currently no guidelines for the recommended interval of brain MRI for primary IOL; however, the International Primary CNS Lymphoma Collaborative Group recommendation for primary CNS lymphoma can be taken into consideration: upon completion of treatment, regular MRI scans every 3 months for 2 years, then every 6 months for 3 years, and then annually for 5 years with complete neurological examination and optional lumbar puncture for cerebrospinal fluid analysis if indicated.[32]

Conclusion

IOL is a systemic disease that requires multidisciplinary collaboration involving ophthalmologists, pathologists, physicians, and oncologists. In particular for primary IOL, ocular symptoms may be the first presentation, and ophthalmologists must maintain a high index of suspicion, especially in cases of refractory uveitis. Local ocular treatments such as intravitreal MTX injections are effective in controlling local disease but cannot prevent CNS involvement or treat extraocular systemic lymphoma. Given the high risk of developing CNS disease in patients with primary IOL, good communication with oncologists is essential, as CNS disease progression is the greatest prognostic factor for survival. Regular monitoring of systemic symptoms with neurological examinations, together with regular brain MRIs, PET-CT scans, and lumbar punctures is crucial for early detection of CNS disease and facilitate prompt treatment.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As editors of the journal, CKMC and SKHS were not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics approval

This study was approved by the Hospital Authority Central Institutional Review Board (reference: KC/KE-19-0061/ER-4). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures.

References

1. *Tang LJ, Gu CL, Zhang P. Intraocular lymphoma. Int J Ophthalmol 2017; 10:1301-7.* Crossref
2. *Buggage RR, Chan CC, Nussenblatt RB. Ocular manifestations of central nervous system lymphoma. Curr Opin Oncol 2001; 13:137-42.* Crossref
3. *Levasseur SD, Wittenberg LA, White VA. Vitreoretinal lymphoma: a 20-year review of incidence, clinical and cytologic features, treatment, and outcomes. JAMA Ophthalmol 2013; 131:50-5.* Crossref
4. *Plotkin SR, Batchelor TT. Primary nervous-system lymphoma. Lancet Oncol 2001; 2:354-65.* Crossref
5. *Smith JR, Rosenbaum JT, Wilson DJ, et al. Role of intravitreal methotrexate in the management of primary central nervous system lymphoma with ocular involvement. Ophthalmology 2002; 109:1709-16.* Crossref
6. *Cho BJ, Yu HG. Risk factors for intraocular involvement in patients with primary central nervous system lymphoma. J Neurooncol 2014; 120:523-9.* Crossref
7. *Cassoux N, Merle-Beral H, Leblond V, et al. Ocular and central nervous system lymphoma: clinical features and diagnosis. Ocul Immunol Inflamm 2000; 8:243-50.* Crossref

8. Berenbom A, Davila RM, Lin HS, Harbour JW. Treatment outcomes for primary intraocular lymphoma: implications for external beam radiotherapy. Eye (Lond) 2007; 21:1198-201. Crossref
9. Qualman SJ, Mendelsohn G, Mann RB, Green WR. Intraocular lymphomas. Natural history based on a clinicopathologic study of eight cases and review of the literature. Cancer 1983; 52:878-86. Crossref
10. Hoffman PM, McKelvie P, Hall AJ, Stawell RJ, Santamaria JD. Intraocular lymphoma: a series of 14 patients with clinicopathological features and treatment outcomes. Eye (Lond) 2003; 17:513-21. Crossref
11. Peterson K, Gordon KB, Heinemann MH, DeAngelis LM. The clinical spectrum of ocular lymphoma. Cancer 1993; 72:843-9. Crossref
12. Grimm SA, Pulido JS, Jahnke K, et al. Primary intraocular lymphoma: an International Primary Central Nervous System Lymphoma Collaborative Group Report. Ann Oncol 2007; 18:1851-5. Crossref
13. Soussain C, Malaise D, Cassoux N. Primary vitreoretinal lymphoma: a diagnostic and management challenge. Blood 2021; 138:1519-34. Crossref
14. Chan CC, Rubenstein JL, Coupland SE, et al. Primary vitreoretinal lymphoma: a report from an International Primary Central Nervous System Lymphoma Collaborative Group symposium. Oncologist 2011; 16:1589-99. Crossref
15. Xu LT, Huang Y, Liao A, Anthony CL, Voloschin A, Yeh S. Multimodal diagnostic imaging in primary vitreoretinal lymphoma. Int J Retina Vitreous 2022; 8:58. Crossref
16. Liu TY, Ibrahim M, Bittencourt M, Sepah YJ, Do DV, Nguyen QD. Retinal optical coherence tomography manifestations of intraocular lymphoma. J Ophthalmic Inflamm Infect 2012; 2:215-8. Crossref
17. Zhao H, Wang X, Mao Y, Peng X. Longitudinal observation of OCT imaging is a valuable tool to monitor primary vitreoretinal lymphoma treated with intravitreal injections of methotrexate. BMC Ophthalmol 2020; 20:10. Crossref
18. Ishida T, Ohno-Matsui K, Kaneko Y, et al. Fundus autofluorescence patterns in eyes with primary intraocular lymphoma. Retina 2010; 30:23-32. Crossref
19. Tan WJ, Wang MM, Ricciardi-Castagnoli P, Chan ASY, Lim TS. Cytologic and molecular diagnostics for vitreoretinal lymphoma: current approaches and emerging single-cell analyses. Front Mol Biosci 2021; 7:611017. Crossref
20. Akpek EK, Ahmed I, Hochberg FH, et al. Intraocular-central nervous system lymphoma: clinical features, diagnosis, and outcomes. Ophthalmology 1999; 106:1805-10. Crossref
21. Davis JL, Miller DM, Ruiz P. Diagnostic testing of vitrectomy specimens. Am J Ophthalmol 2005; 140:822-9. Crossref
22. Kimura K, Usui Y, Goto H; Japanese Intraocular Lymphoma Study Group. Clinical features and diagnostic significance of the intraocular fluid of 217 patients with intraocular lymphoma. Jpn J Ophthalmol 2012; 56:383-9. Crossref
23. Frenkel S, Hendler K, Siegal T, Shalom E, Pe'er J. Intravitreal methotrexate for treating vitreoretinal lymphoma: 10 years of experience. Br J Ophthalmol 2008; 92:383-8. Crossref
24. Zhou N, Xu X, Liu Y, Wang Y, Wei W. A proposed protocol of intravitreal injection of methotrexate for treatment of primary vitreoretinal lymphoma. Eye (Lond) 2022; 36:1448-55. Crossref
25. Akiyama H, Takase H, Kubo F, et al. Systemic following intravitreal MTX administration prevents CNS infiltration of primary intraocular lymphoma. Blood 2014; 124:3053. Crossref
26. de Smet MD. Management of non Hodgkin's intraocular lymphoma with intravitreal methotrexate. Bull Soc Belge Ophtalmol 2001; 279:91-5.
27. Riemens A, Bromberg J, Touitou V, et al. Treatment strategies in primary vitreoretinal lymphoma: a 17-center European Collaborative Study. JAMA Ophthalmol 2015; 133:191-7. Crossref
28. Dalvin LA, Pulido JS, Shields CL, et al. Vitreoretinal lymphoma: central nervous system lymphoma risk with unilateral or bilateral ocular tumour. A multicentre collaboration. Eye (Lond) 2023; 37:54-61. Crossref
29. Akiyama H, Takase H, Kubo F, et al. High-dose methotrexate following intravitreal methotrexate administration in preventing central nervous system involvement of primary intraocular lymphoma. Cancer Sci 2016; 107:1458-64. Crossref
30. Davis JL. Intraocular lymphoma: a clinical perspective. Eye (Lond) 2013; 27:153-62. Crossref
31. Sagoo MS, Mehta H, Swampillai AJ, et al. Primary intraocular lymphoma. Surv Ophthalmol 2014; 59:503-16. Crossref
32. Abrey LE, Batchelor TT, Ferreri AJ, et al. Report of an international workshop to standardize baseline evaluation and response criteria for primary CNS lymphoma. J Clin Oncol 2005; 23:5034-43. Crossref

ORIGINAL ARTICLE

Myopia prevention practices among ophthalmologists in Hong Kong: a cross-sectional survey

CL Yim[1,2,3], YZ Zhang[1], SSL Cheung[2,3], JC Chuang[2,3], W Tang[2,3], YT Ho[2,3], ESH Wong[1,2], PC Chow[2,3], TC Ko[3,4]

[1] *Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China*

[2] *Hong Kong Eye Hospital, Hong Kong SAR, China*

[3] *Department of Ophthalmology, Hong Kong Children's Hospital, Hong Kong SAR, China*

[4] *TWGHs Lo Ka Chow Memorial Ophthalmic Centre, Hong Kong East Cluster, Hong Kong SAR, China*

Correspondence and reprint requests:
Dr CL Yim, 3/F, Hong Kong Eye Hospital, 147K Argyle Street, Kowloon, Hong Kong SAR, China.
Email: charleneclyim@cuhk.edu.hk

Abstract

Objectives: To explore the preferred pharmacological, optical, and behavioral interventions for myopia control among private-sector ophthalmologists in Hong Kong.
Methods: Between July and August 2025, a survey was distributed electronically to private-sector ophthalmologists in Hong Kong. Ophthalmologists working exclusively in the public sector were excluded because interventions to control myopia, such as low-dose atropine, optical interventions, and red-light therapy, are only available in the private sector. Data collected included participants' demographics, years of clinical experience, and interventions used including pharmacological, optical, behavioral, and red-light therapies. All responses were aggregated for analysis.
Results: In total, 118 private-sector ophthalmologists were included in analysis. In terms of preferred treatment modality, 91.5% preferred pharmacological, 5.1% preferred optical, and 3.4% preferred behavioral interventions although many used a combination of modalities. Most (97.5%) respondents had prescribed eye drops, typically atropine, and the most common concentrations were 0.05% and 0.01%. However, there was no consensus on the criteria for initiation and discontinuation of eye drop treatment. The most frequently prescribed optical intervention was peripheral defocus spectacle lenses (86.5%). Behavioral recommendations were also commonly provided. Only 5.1% of respondents prescribed red-light therapy.
Conclusion: Among private-sector ophthalmologists in Hong Kong, low-dose atropine is the most frequently used pharmacological intervention for myopia. However, there is no consensus on the criteria for initiating and discontinuing treatment. Optical intervention (particularly peripheral defocus spectacle lenses) and behavioral recommendations are also commonly used.

Key words: Atropine; Health surveys; Myopia; Ophthalmologists

Introduction

Myopia is a major public health concern across Asia, with prevalence rising sharply over the past two decades.[1] The Chinese government has prioritized childhood myopia prevention, implementing policies aimed at early detection and intervention.[2] Without timely and effective control, children with myopia are at risk of progressing to high or pathological myopia, which significantly increases the risk of developing vision-threatening complications (such as myopic maculopathy, choroidal neovascularization, and retinal detachment),[3] impairs quality of life, and increases the healthcare burden.[4]

Myopia is potentially preventable,[5,6] and its progression can be slowed by behavioral, optical, and pharmacological interventions.[7-9] Behavioral interventions include spending more time outdoors in natural light and avoiding excessive near work. Optical interventions include wearing glasses with defocus incorporated multiple segments (DIMS)

or highly aspherical lenslet target (HALT) lenses, orthokeratology, and other specialized contact lenses. Pharmacological interventions, particularly low-dose atropine eye drops, have gained attention for their efficacy and safety profile.[10]

The LAMP (Low-Concentration Atropine for Myopia Progression) studies in Hong Kong support treatment with low-dose atropine to slow the progression of myopia.[11,12] There is a concentration-dependent effect; atropine 0.05% (compared with lower concentrations) shows the most significant reduction in myopic progression with minimal adverse effects. We conducted a cross-sectional survey to explore the preferred pharmacological, optical, and behavioral interventions for myopia control among private-sector ophthalmologists in Hong Kong.

Methods

Between July and August 2025, a survey was distributed electronically through ophthalmology communication networks to private-sector ophthalmologists. Ophthalmologists working exclusively in the public sector were excluded because interventions to control myopia, such as low-dose atropine, optical interventions, and red-light therapy, are only available in the private sector.

Data collected included participants' demographics, years of clinical experience, and interventions used including pharmacological, optical, behavioral, and red-light therapies. All responses were aggregated for analysis.

Results

In total, 118 private-sector ophthalmologists in Hong Kong were included in the analysis. In terms of clinical experience, 36.4% had practiced for 25 years, 22.0% for 20 to 25 years, 20.3% for 15 to 20 years, and 21.2% for 10 to 15 years. In terms of experience in myopia control, 29.7% had >10 years, 28.0% had 6 to 10 years, 29.7% had 3 to 5 years, and 12.7% had 1 to 2 years. In terms of preferred treatment modality, 91.5% preferred pharmacological, 5.1% preferred optical, and 3.4% preferred behavioral interventions although many used a combination of modalities. Most (97.5%) respondents had prescribed eye drops, typically atropine, and the most common concentrations (multiple options can be selected) were 0.05% (93.9%) and 0.01% (79.1%), followed by 0.025% (35.7%), 0.125% (20.0%), and 1% (10.4%). No respondents reported using cyclopentolate, pirenzepine, or tropicamide.

Regarding criteria for initiation of eye drops (multiple options could be selected), 41.7% of respondents started prescribing eye drops to those with any myopia aged >4 years, 37.4% waited for the progression to exceed 1.00 D per year, 33.9% started prescribing as soon as myopia was identified regardless of age, 18.3% initiated treatment when myopia exceeded -1.00 D, and 13.9% used other criteria.

Regarding the age of treatment discontinuation, 31% of respondents discontinued atropine therapy after patients aged 17 years, 20.4% after 16 years, 17.7% after 14 years, 10.6% after 15 years, 3.5% after 13 years, and 0.9% after 12 years. Notably, 16.1% did not discontinue treatment in any patient. After treatment discontinuation, 28.6% of respondents reported rebound cases, 49.1% did not, and 22.3% had not discontinued treatment.

The most frequently prescribed optical intervention (multiple options could be selected) was peripheral defocus spectacles (including DIMS/HALT, 86.5%), followed by contact lenses with peripheral defocus (35.6%), orthokeratology (33.1%), full correction spectacles (27.1%), progressive addition lenses (11.0%), bifocal spectacle lenses (6.8%), and optical undercorrection (5.9%). Less commonly used options included bifocal soft contact lenses (1.7%), single vision gas permeable lenses (1.7%), monofocal soft contact lenses (0.8%), and single vision soft contact lenses (0.8%).

The most common behavioral recommendations (multiple options can be selected) were decreasing smartphone use (85.6%), reducing screen time (82.2%), maintaining a reading distance of ≥34 cm (75.4%), encouraging outdoor activities (64.4%), and reading in natural light (55.1%). Less common recommendations included visual therapy (1.7%) and biofeedback (1.7%). Red-light therapy was rarely used; only 5.1% of respondents prescribed it.

Discussion

Among private-sector ophthalmologists in Hong Kong, 99.2% engaged in myopia management, reflecting awareness and responsiveness to the growing prevalence of myopia. Myopia control has become a widely practiced component of ophthalmic care. Atropine eye drops were the preferred pharmacological intervention, particularly concentrations of 0.05% and 0.01%, consistent with findings from the Low-concentration Atropine for the Treatment of Myopia 2 study[10] and the LAMP studies,[11,12] which demonstrated that atropine 0.05% eye drops most effectively slow the progression of myopia with minimal adverse effects on pupil size, accommodation, and near visual function.

Most respondents adopted early intervention with eye drops for patients starting at age 4 years, but there is no consensus. Early-onset myopia is associated with faster progression and a higher risk of pathological outcomes.[13] The age of treatment discontinuation also varied, ranging from 12 to >17 years; 28.6% of respondents reported rebound effects, underscoring the importance of tapering strategies and long-term follow-up.[14] Further research is required to establish evidence-based guidance on optimal tapering protocols.

Peripheral defocus spectacle lenses (DIMS/HALT) are effective optical interventions,[15,16] and 86.5% of respondents prescribed them. Orthokeratology and contact lenses with peripheral defocus were also commonly prescribed by approximately one-third of respondents.

Behavioral recommendations (reducing screen time, increasing outdoor activities, and maintaining proper reading habits) are supported by epidemiological studies.[9,17] Visual therapy and biofeedback show limited evidence.[18] Red-light therapy was rarely used, likely owing to concerns about safety, accessibility, or insufficient clinical validation.[19]

One limitation of our study was inclusion of private-sector ophthalmologists only, whose practices may not reflect those in public institutions. Our findings may not be generalizable to ophthalmologists working solely in the public sector. Additionally, voluntary participation potentially introduces self-selection bias, as those with stronger views or greater involvement in myopia control may be more likely to respond. Results of the survey may be subject to self-reporting bias, recall bias, and social desirability bias.

Conclusion

Among Hong Kong private-sector ophthalmologists, low-dose atropine is the most frequently used pharmacological intervention for myopia. However, there is no consensus on the criteria for initiating and discontinuing treatment. Optical intervention (particularly peripheral defocus spectacle lenses) and behavioral recommendations are also commonly used. Our findings underscore the need for a consensus in myopia management, including initiation criteria, treatment duration, and discontinuation protocols, particularly in light of concerns about rebound effects. Red light therapy is an emerging option; ongoing research is essential to ensure its safe and effective use.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an advisor of the journal, TCK was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics approval

The study was conducted in accordance with the tenets of the Declaration of Helsinki. The participants provided written informed consent for publication.

Acknowledgment

We thank the Hong Kong Association of Private Eye Surgeons for their assistance in survey dissemination and participant outreach.

References

1. *Liang J, Pu Y, Chen J, et al. Global prevalence, trend and projection of myopia in children and adolescents from 1990 to 2050: a comprehensive systematic review and meta-analysis. Br J Ophthalmol 2025; 109:362-71.* Crossref
2. *Jan C, Li L, Keay L, Stafford RS, Congdon N, Morgan I. Prevention of myopia, China. Bull World Health Organ 2020; 98:435-7.* Crossref
3. *Haarman AEG, Enthoven CA, Tideman JWL, Tedja MS, Verhoeven VJM, Klaver CCW. The complications of myopia: a review and meta-analysis. Invest Ophthalmol Vis Sci 2020; 61:49.* Crossref
4. *Sankaridurg P, Tahhan N, Kandel H, et al. Impact of myopia. Invest Ophthalmol Vis Sci 2021; 62:2.* Crossref
5. *Chen Y, Mueller A, Morgan I, et al. Best practice in myopia control: insights and innovations for myopia prevention and control: a round table discussion. Br J Ophthalmol 2024; 108:913-4.* Crossref
6. *Wang B, Watt K, Chen Z, Kang P. Predicting the child who will become myopic – can we prevent onset? Clin Exp Optom 2023; 106:815-24.* Crossref
7. *Saw SM, Matsumura S, Hoang QV. Prevention and management of myopia and myopic pathology. Invest Ophthalmol Vis Sci 2019; 60:488-99.* Crossref
8. *Zhang XJ, Zaabaar E, French AN, et al. Advances in myopia control strategies for children. Br J Ophthalmol 2025; 109:165-76.* Crossref
9. *Biswas S, El Kareh A, Qureshi M, et al. The influence of the environment and lifestyle on myopia. J Physiol Anthropol 2024; 43:7.* Crossref
10. *Chia A, Chua WH, Cheung YB, et al. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology 2012; 119:347-54.* Crossref
11. *Yam JC, Jiang Y, Tang SM, et al. Low-concentration atropine for myopia progression (LAMP) study: a randomized, double-blinded, placebo-controlled trial of 0.05%, 0.025%, and 0.01% atropine eye drops in myopia control. Ophthalmology 2019; 126:113-24.* Crossref
12. *Yam JC, Zhang XJ, Zhang Y, et al. Effect of low-concentration atropine eyedrops vs placebo on myopia incidence in children: the LAMP2 randomized clinical trial. JAMA 2023; 329:427-81.* Crossref
13. *Myopia: Causes, Prevention, and Treatment of an Increasingly Common Disease. DC: National Academies Press; 2024.*
14. *Lee SH, Tsai PC, Chiu YC, Wang JH, Chiu CJ. Myopia progression after cessation of atropine in children: a systematic review and meta-analysis. Front Pharmacol 2024; 15:1343698.* Crossref
15. *Bao J, Huang Y, Li X, et al. Spectacle lenses with aspherical lenslets for myopia control vs single-vision spectacle lenses: a randomized clinical trial. JAMA Ophthalmol 2022; 140:472-8.* Crossref
16. *Lam CSY, Tang WC, Tse DY, et al. Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol 2020; 104:363-8.* Crossref
17. *Ha A, Lee YJ, Lee M, Shim SR, Kim YK. Digital screen time and myopia: a systematic review and dose-response meta-analysis. JAMA Netw Open 2025; 8:e2460026.* Crossref
18. *American Academy of Ophthalmology. Complementary Therapy Assessment: Visual Training for Refractive Errors. Accessed 29 August 2025. Available from: https://www.aao.org*
19. *Chang DJ, Sriram PL, Jeong J, Saw SM, Sevdalis N, Najjar RP. Light therapy for myopia prevention and control: a systematic review on effectiveness, safety, and implementation. Transl Vis Sci Technol 2024; 13:31.* Crossref

CASE REPORT

Combined excision and punch punctoplasty for peripunctal nevus: a report of three cases

Stella Weng Chi Sio[1,2], *MBBS; Andre Ma*[1,2], *MBBS, BA(Cantab), AFCOphth (HK); Hunter Kwok Lai Yuen*[1,2], *MBChB, FRCOphth, FRCS(Ed), FCOphth (HK), FHKAM (Ophthalmology), DipClinDerm (London)*
[1] *Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China*
[2] *Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China*

Correspondence and reprint requests:
Dr Hunter Kwok Lai Yuen, Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China.
Email: hunterklyuen@gmail.com

Abstract

We describe a safe, effective, and minimally invasive procedure that combines excision and punch punctoplasty for treatment of peripunctal nevi in three patients. The peripunctal lesions are removed, and the punctal opening and canaliculus are expanded using a standardized Kelly punch, while minimizing the risk of postoperative punctal stenosis. No temporary stents are needed, eliminating the risk of related complications. At the 2-month follow-up, all three patients had fully recovered and had visibly well-patent puncta.

Key words: *Conjunctival neoplasms; Nevus*

Introduction

Peripunctal nevi, also known as circumpunctal nevi, are a rare type of conjunctival nevi. However, they are the most common peripunctal lesion, with an incidence of 38% to 79%.[1-3] These benign, pigmented, dome-shaped lesions predominantly affect the lower puncta and have no evidence of melanoma transformation. Their swollen punctal lips create a slit-like punctal orifice.[4] Peripunctal nevi differ from juxtapunctal nevi, which develop at the eyelid margin and adjacent to, rather than surrounding, the punctum. Differential diagnoses include papillomas, cysts, pyogenic granulomas, malignant melanomas, basal cell carcinomas, and oncocytomas. Most patients present with a long history of an asymptomatic, gradually enlarging mass that has not affected the lacrimal drainage system. However, some develop epiphora due to punctal displacement, distortion, or intracanalicular extension.[5,6]

Although the treatment goal is to remove the lesion with a clear margin and maintain a sufficient punctal opening for tear drainage, there is no consensus on the optimal approach in the literature (Table).[1,3-9]

Excision alone can lead to epiphora and punctal stenosis from the healing wound, potentially requiring a follow-up punctoplasty. Shave excision with the temporary placement of a silicone punctal plug[4] and ablation with a CO_2 laser and the use of a temporary stent[3] have been suggested to prevent scarring and stenosis. At the Hong Kong Eye Hospital, we primarily use punch punctoplasty with a Kelly punch, which is a successful first-line treatment for epiphora associated with punctal stenosis and eliminates the need for temporary intubation.[10] We describe a combination of excision and punch punctoplasty for treatment of peripunctal nevi in three patients.

Case presentations

Patient 1: In July 2019, a 58-year-old Asian woman presented with a peripunctal mass on the lower lid of her left eye. The mass had not changed in size or color for 10 years. Slit-lamp examination revealed a lightly pigmented, raised mass surrounding the punctum, measuring 3×4 mm, with an elongated, slit-like punctal opening (**Figure 1a**).

It was initially misdiagnosed as a papilloma by her family doctor, but histopathology confirmed the mass to be a nevus, characterized by an intradermal cyst with proliferated nevus cells and occasional melanin pigments. No significant nuclear pleomorphism or mitotic figures were observed.

Patient 2: In March 2022, a 55-year-old Asian woman presented with a peripunctal mass on the lower lid of her right eye. The mass had not changed in size for over 20 years. The raised, dome-shaped, moderately pigmented mass, measuring 3×5 mm, encircled the punctum (**Figure 1b**).

Patient 3: In May 2024, an 81-year-old Asian woman

Table. Literature review of peripunctal nevi treatments.

Study	No. of patients	Patient sex/age, y	Surgical technique	Stent removal	Location of nevus	Follow-up
Scott et al,[4] 1989	6	M (n=2), F (n=4)/12-75	Shave excision with silicone punctal plug insertion	3 weeks	RLL (n=3), LLL (n=3)	3 months to 5 years
Rumelt et al,[6] 2005	7	M (n=6), F (n=1)/54-76	Excision only or with silicone tube insertion	-	RLL (n=2), LLL (n=3), LUL+LLL (n=1), RUL (n=1)	3 to 5 years
Hwang et al,[9] 2011	1	M/37	Shave excision only	-	LLL	1 month
Chang et al,[7] 2013	1	-	Excision with perforated plug insertion	2 months	RLL	2 months
Nair et al,[1] 2022	19	12-76	Excision only or with mini-Monoka stent insertion	3 months	-	3 months to 10 years
Chen et al,[3] 2022	17	-	CO_2 laser ablation with silicone stent insertion	1 month	-	1 to 3 months
Ali and Jakati,[5] 2024	1	M/62	Excision only	-	LUL	-
Custer and Council,[8] 2024	13	-	Shave excision only	-	UL (n=5), LL (n=8)	No routine follow-up

Abbreviations: LL=lower lid, LLL=left lower lid, LUL=left upper lid, RLL=right lower lid, RUL=right upper lid, and UL=upper lid

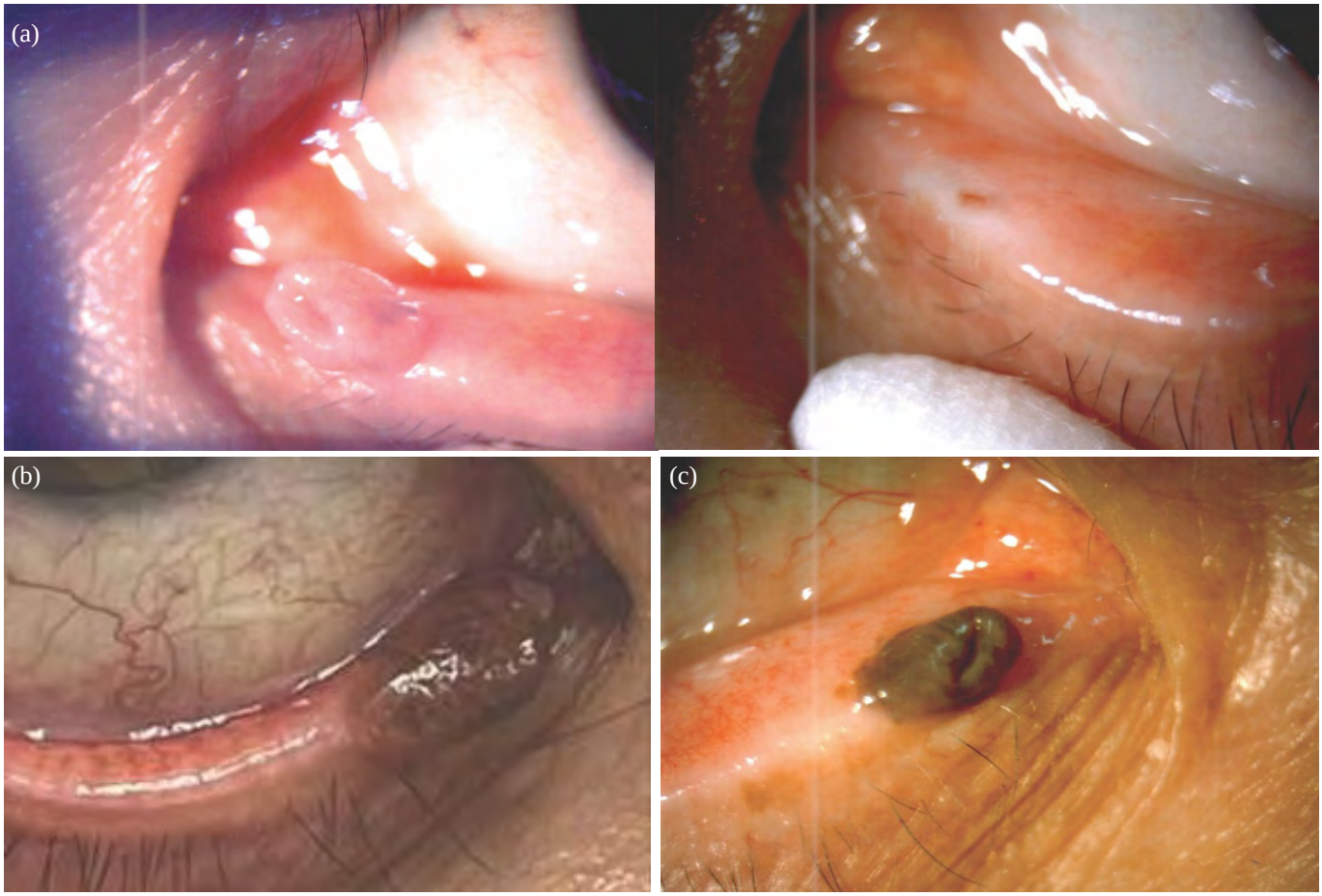


Figure 1. (a) Patient 1: an elevated, lightly pigmented peripunctal nevus surrounding the left lower punctum with an elongated, slit-like punctal opening (upper). At 3.5 years postoperatively, a visibly well-patent punctum and smooth lid margin are seen (lower). (b) Patient 2: a raised, dome-shaped, moderately pigmented mass encircling the right lower punctum. (c) Patient 3: a raised, heavily pigmented mass encircling the right lower punctum with puffy lips at the surface.

presented with a peripunctal mass on the lower lid of her right eye. The mass had developed 5 years earlier and had been growing gradually over the past 2 years. The raised, heavily pigmented mass, measuring 2.5×3.5 mm, encircled the punctum and had puffy lips on the surface (**Figure 1c**).

None of these patients reported epiphora, bleeding, discharge, redness, or pain. Preoperative syringing confirmed patent lacrimal systems in all cases.

The three patients underwent combined excision and punch punctoplasties between July 2021 and July 2024. Before surgery, topical antibiotics and anesthetic eye drops were given. Then, 2 mL of 2% lidocaine with adrenaline (1:200 000) was injected into the affected eyelid, and a corneal protector was inserted. The peripunctal lesion was carefully excised using forceps and curved scissors (**Figure 2**). We aimed to completely excise the mass with a clear border, while minimizing depression in the eyelid margin. Next, the punctal opening was expanded circumferentially using a punctal dilator. A prophylactic punch punctoplasty was performed using a standardized Kelly Descemet's membrane punch, which was inserted into the ampulla to undertake posterior ampullectomy. The punctal tissue was generally resected up to 2 to 3 mm beyond the vertical segment into the horizontal segment of the canaliculus to enlarge both the punctal opening and canaliculus to counteract subsequent wound contraction. Cotton buds soaked in 2.5% phenylephrine eye drops were used to compress the wound and reduce bleeding and scarring. An irrigation test was carried out using a syringe to ascertain the patency of the lacrimal drainage system. After surgery, topical antibiotic ointment was applied, and the patients were discharged with 2-week supply of steroid and antibiotic eye drops.

Histopathological examination of the excised lesions revealed intradermal nevi. At the 2-month follow-up, all three patients had patent puncta and nasolacrimal drainage systems, with smooth eyelid margin contours; they were satisfied with the aesthetic outcome. Throughout the mean follow-up duration of 17 (range, 2-42) months, there was no recurrence or any malignant transformation or punctal stenosis. None of the patients reported epiphora or dry eyes.

Discussion

Peripunctal nevi are often misdiagnosed clinically as papillomas, malignant melanomas, or basal cell carcinomas, particularly when the lesion presents as an amelanotic nevus. In Asian populations, 59% to 79% of all peripunctal lesions are peripunctal nevi,[2,3] which differ from benign eyelid tumors, of which squamous papilloma is the most common. Incidence of peripunctal nevus is similar among men and women, consistent with the overall prevalence of melanocytic nevus. Indications for excision include epiphora secondary to displaced and everted puncta, lacrimal pump failure, or cosmetic concerns. It is essential to remove any elevated pigmented conjunctival lesions to rule out potential malignancies such as melanoma.[4] Instances of nevus extension into the canaliculus causing obstruction or recurrence are rare, particularly when clear margins are excised.

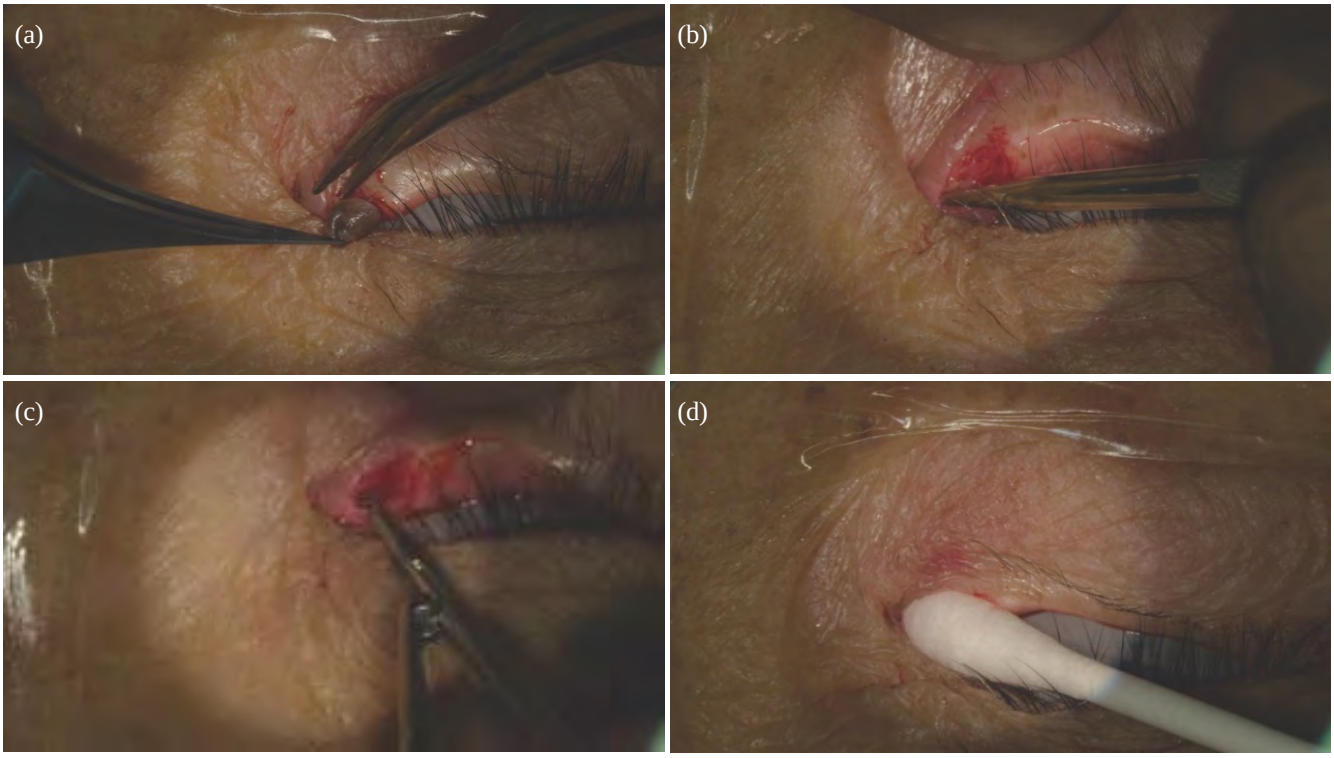


Figure 2. (a) The peripunctal lesion is excised using forceps and curved scissors. (b) The punctal opening is expanded circumferentially using a punctal dilator. (c) A punch punctoplasty is performed using a standardized Kelly Descemet's membrane punch. (d) A cotton bud soaked in 2.5% phenylephrine eye drops compresses the wound to stop any bleeding.

Removing growths around the punctum can result in acquired punctal stenosis and epiphora. Reportedly, 10.3% of patients who underwent excision without stent placement lost punctal visibility after the procedure.[1] The success rate is higher when excision is combined with intubation, compared with excision alone.[1] However, complications associated with stent placements may occur, including stent displacement or dislodgement, patient discomfort, chronic irritation, and infection.[3,7] Moreover, the follow-up for stent removal is an additional burden on patients. CO_2 laser ablation with silicone stent intubation for treatment of benign peripunctal tumors has a high success rate and satisfactory aesthetic outcomes. However, this approach requires intraoperative pathological examination, which prolongs the operating time and requires additional equipment and costs.

Using a Kelly punch for punctoplasty in patients with symptomatic punctal stenosis is effective.[11] For our three patients, excision followed by punch punctoplasty resulted in minimal blood loss and hemostasis by compression with a cotton bud soaked in phenylephrine. There was no need for cauterization to minimize the risk of punctal stenosis and eyelid notching. The punctal opening and canaliculus were expanded to counteract punctal stenosis during the subsequent healing and contraction. Should a Kelly punch be unavailable, other punctoplasty techniques such as three-snip punctoplasty can be used to create a similar wedge excision extending 2 to 3 mm into the horizontal canalicular segment. Our approach eliminates the need for stent insertion and removal, thus avoiding stent-related complications while reducing the risk of additional surgery. The combined excision and punch punctoplasty produced favorable short-term anatomical and functional outcomes. Nonetheless, the long-term outcomes regarding lacrimal system patency and the optimal management strategy remain to be determined.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an advisor of the journal, HKLY was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics approval

The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

References

1. *Nair AG, Mukherjee B, Kamal S, et al. Peripunctal mass lesions: clinicopathological analysis and surgical outcomes: a multicentric series. Ophthalmic Plast Reconstr Surg 2022; 38:154-9.* Crossref
2. *Zhao Y, Hui JW, Yang LL, Zhao H, Lin JY, Pan Y. Clinical and pathological analysis of 64 patients with primary neoplasms of the lacrimal drainage system [in Chinese]. Zhonghua Yan Ke Za Zhi 2020; 56:364-9.* Crossref
3. *Chen C, Lee YK, Lai CC. Outcomes of lacrimal punctal tumors treated with a superpulse CO_2 laser. Lasers Med Sci 2022; 37:2287-91.* Crossref
4. *Scott KR, Jakobiec FA, Font RL. Peripunctal melanocytic nevi. Distinctive clinical findings and differential diagnosis. Ophthalmology 1989; 96:994-8.* Crossref
5. *Ali MJ, Jakati S. Punctal nevus with intracanalicular extension. Ophthalmic Plast Reconstr Surg 2024; 40:360.* Crossref
6. *Rumelt S, Pe'er J, Rubin PA. The clinicopathological spectrum of benign peripunctal tumours. Graefes Arch Clin Exp Ophthalmol 2005; 243:113-9.* Crossref
7. *Chang M, Ahn SE, Baek S. The effect of perforated punctal plugs in the management of acquired punctal stenosis. J Craniofac Surg 2013; 24:1628-30.* Crossref
8. *Custer PL, Council ML. Clinical features and management of eyelid margin nevi. Orbit 2024; 43:8-15.* Crossref
9. *Hwang CS, Lee S, Yen MT. Peripunctal melanocytic nevus. Int Ophthalmol 2011; 31:497-9.* Crossref
10. *Wong ES, Li EY, Yuen HK. Long-term outcomes of punch punctoplasty with Kelly punch and review of literature. Eye (Lond) 2017; 31:560-5.* Crossref
11. *Carrim ZI, Liolios VI, Vize CJ. Punctoplasty with a Kelly punch. Ophthalmic Plast Reconstr Surg 2011; 27:397-8.* Crossref

Acknowledgements

The Editor-in-Chief is grateful to the following individuals who acted as reviewers for the Journal during the past year.

Sunny Chi Lik Au
Carmen KM Chan
CK Jason Chan
Guy Chen
Jonathan Ho
Mary Ho
Wing Lau Ho
Andrew Kuk
Alvin Kwan Ho Kwok
Stephanie Hiu-wai Kwok
Connie Lai
Frank Lai
Tracy Lai
Winne Lau
Peter Leung
Danny Ng
Wing Sang Ngai
Emily Tang
Emily Suhan Wong
Macy Wu
Wilson Yip
Hunter Yuen
Xiujuan Zhang

Winners of HKJO Best Original Articles Awards 2024

HKJO Best Original Article Award 2024 (Fellow)
Topic: Prognostic factors in Chinese patients with acute non-infectious optic neuritis treated with intravenous methylprednisolone and oral prednisolone
Awardee: Dr LAM Chun Wah

HKJO Best Original Article Award 2024 (Trainee)
Topic: Micropulse transscleral laser therapy for glaucoma: a retrospective study
Awardee: Dr CHAN Yin Yung Alison

ELEVATE
THE EVERYDAY

enVista™ HYDROPHOBIC ACRYLIC IOL ASPIRE™

Transcend the boundaries of standard monofocals and deliver your patients an IOL designed for the modern world.

BROADER DEPTH OF FOCUS
COMPARED TO THE AO MONOFOCAL OPTIC [1]

3C CONTROLLED CURVATURE CHANGE TECHNOLOGY

Uncompromised distance contrast sensitivity compared to the AO monofocal optic.[1]

A 1.5mm central zone on the posterior surface designed to create a broader depth of focus.[1]

The original glistening-free optic material.[2]

enVista ASPIRE
HYDROPHOBIC ACRYLIC IOL

References:
1. enVista Aspire Directions for Use, Bausch & Lomb. 2. enVista Directions for Use, Clinical Data [May 2017].

Bausch & Lomb (HK) Ltd.
Suites 3901 & 3912-14, 39/F, Tower 6, The Gateway, 9 Canton Road,
Tsim Sha Tsui, Kowloon, Hong Kong Tel: +852 2213 3333 HK-SU-2024-11-010

BAUSCH+LOMB

VYZULTA™
(latanoprostene bunod ophthalmic solution),0.024%

20 YEARS
OF BREAKTHROUGH IN GLAUCOMA TREATMENT

Indication

VYZULTA™ (latanoprostene bunod ophthalmic solution), 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.[1]

One molecule, two pathways

Lowers IOP by increasing outflow through both the trabecular meshwork and uveoscleral pathway[1]

Remarkable efficacy

Reduced the mean IOP up to 9.0 mmHg from baseline[2*]

Demonstrated safety

<1% discontinuation rate due to ocular adverse effects[1]

***VOYAGER study design:** a randomized, parallel-group, phase 2 study, which compared the efficacy and safety of 4 doses of VYZULTA™ and latanoprost 0.005% in 413 patients with open-angle glaucoma or ocular hypertension. Primary endpoint was the change of mean diurnal IOP at day 28 from baseline. The mean IOP at baseline was 26.0 mmHg in the VYZULTA™ 0.024% group and 26.2 mmHg in the latanoprost 0.005% group.[2]

IOP=intraocular pressure.

References: 1. VYZULTA Hong Kong prescribing information. **2.** Weinreb RN, Ong T, Scassellati Sforzolini B, et al. A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study. Br J Ophthalmol 2015; 99(6): 738-45.

INDICATION VYZULTA™ (latanoprostene bunod ophthalmic solution), 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. **DOSAGE AND AMINISTRATION** The recommended dosage is one drop in the conjunctival sac of the affected eye(s) once daily in the evening. Do not administer VYZULTA™ (latanoprostene bunod ophthalmic solution), 0.024% more than once daily since it has been shown that more frequent administration of prostaglandin analogs may lessen the intraocular pressure lowering effect. If VYZULTA™ is to be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure, administer each drug product at least five (5) minutes apart. **IMPORTANT SAFETY INFORMATION** • Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent. • Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation. • Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA™ should generally not be used in patients with active intraocular inflammation. • Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema. • There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients. • Contact lenses should be removed prior to the administration of VYZULTA™ and may be reinserted 15 minutes after administration. • The most common ocular adverse reactions observed in patients treated with latanoprostene bunod were: conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%). Approximately 0.6% of patients discontinued therapy due to ocular adverse reactions including ocular hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis and foreign body sensation. Please refer to full package insert for the detail.

For healthcare professional only.
Please refer to full Prescribing Information and additional Important Safety Information for VYZULTA™.

BAUSCH + LOMB
See better. Live better.

Bausch & Lomb (H.K.) Ltd.
Suites 3901 & 3912-14, 39/F
Tower 6, The Gateway, 9 Canton Road
Tsim Sha Tsui, Kowloon, Hong Kong
Tel: (+852) 2213 3333

Transform how you lower IOP

POWER WITHOUT PRESERVATIVES

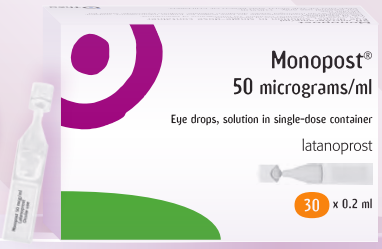
IOP REDUCTION FOR OPEN-ANGLE GLAUCOMA & OCULAR HYPERTENSION IN ADULTS

EFFECTIVE
IOP Reduction [1,2]

SATISFACTORY
Tolerability Profile [1,2]

CONTINUOUS
Persistence [1,2]

1st CHOICE
In 1st line Treatment



1st CHOICE
In 2nd line Treatment

US FDA APPROVED

Stored at room temperature, below 25°C

0.2ML X 30's Single-dose Containers

Monopost®
Latanoprost 50MCG/ML

No.1 PROSTAGLANDIN IN EUROPE [3]

FixaPost®
Latanoprost 50MCG/ML + Timolol 5MG/ML

1. Bacharach J, et al. Clin Ophthalmol. 2023;2575-88.
2. Aptel F, et al. J Glaucoma. 2019;28:498-506.
3. Market data, August 2025 (SU and values).

HMS WORLD'S LOCAL PARTNER

For further information:
Hongkong Medical Supplies Ltd.
Tel: 2806 3112 Fax: 2887 3425
E-mail: sales@hkmedsup.com.hk
Website: www.hongkongmedical.com.hk

Théa let's open our eyes

FOR PATIENTS WITH DRY EYES

THEALOZ® DUO

TREHALOSE 3% | HYALURONIC ACID 0.15%

PROTECTION, HYDRATION AND LUBRICATION OF THE EYE, FOR TREATMENT OF MODERATE TO SEVERE DRY EYE SYNDROME

NO.1 PRODUCT IN EUROPE [1]
IQVIA DRY EYE MARKET 2024

- Increases tear film thickness and tear break-up time[2,3]
- Provides greater improvements in dry eye symptoms[3]
- Reduces tear film inflammatory biomarkers[4]
- Allows a better recovery after cataract surgery[5]

Properties

- **Preservative-free**

tfos DEWS III

TFOS DEWS III Report recommended preservative-free preparations when patients need frequent instillation of eye drops[6]

- **Phosphate-free**
- **Hypotonic formulation**
- **Multidose ABAK® bottle**
  Up to 6 months of use after opening

Suitable for

- Adults and children
- Pregnant or breastfeeding women
- Contact lens wearers

HMS WORLD'S LOCAL PARTNER

For further information:
Hongkong Medical Supplies Ltd.
Tel: 2806 3112 Fax: 2887 3425
E-mail: sales@hkmedsup.com.hk
Website: www.hongkongmedical.com.hk

Théa let's open our eyes

References: 1. Internal analysis by Laboratoires Théa using monthly data from the IQVIA Consumer Health Customized Insights for the period 2024 2. Thealoz® Duo clinical study for CE mark file 2012. 3. Mateo-Orobia AJ. et al. A Preservative-Free Combination of Sodium Hyaluronate and Trehalose Improves Dry Eye Signs and Symptoms and Increases Patient Satisfaction in Real-Life Settings: The TEARS Study. Ophthalmol Ther. 2024 Dec;13(12):3123-3134. 4. Fariselli C. et al. Trehalose/hyaluronate eyedrop effects on ocular surface inflammatory markers and mucin expression in dry eye patients. Clinical Ophthalmology 2018:12 1293–1300. 5. Balta, Ö. & Telek, H. H. Effect of a Hyaluronate-Trehalose Solution on Ocular Comfort and Tear-Film Instability After Cataract Surgery. İzlek Akademik Dergi 2020;3(1):34-43. 6. Jones, Lyndon, et al. "TFOS DEWS III Management and Therapy Report." American Journal of Ophthalmology (2025).

NOW
AVAILABLE
TO ORDER

Prefilled Syringe

VABYSMO®
faricimab injection 6 mg

DELIVER THE DIFFERENCE WITHIN

DUAL-PATHWAY • DRYING • DURABILITY

START FIRST | WITH VABYSMO® (faricimab)

Vabysmo is indicated for the treatment of adult patients with:
- neovascular (wet) age-related macular degeneration (nAMD),
- visual impairment due to diabetic macular oedema (DME),
- visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).

Call for Reporting: If you have a suspected side effect or problem to report regarding one of our products, please contact or send the information to the Roche Patient Safety team via: (a) Email: hong_kong.drug_safety@roche.com, or (b) Phone: +852 2733 4711.

***For VABYSMO product information, please scan the QR code. Full product information will be provided upon request.**
Reference: VABYSMO Hong Kong Prescribing Information

Roche

Roche Hong Kong Limited
Unit 1-2, 24/F, Central Plaza, 18 Harbour Rd, Wan Chai, Hong Kong
Tel: (852) 2723 2832

M-HK-00002278 approved in November 2025 is valid for 2 years or until change is required in accordance with regulatory requirements, whichever comes first.