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International Glaucoma Review

**VOLUME 23-1
2022**

The journal of the World Glaucoma Association

Abstracts and Review of Glaucoma Literature

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S I N C E 1 9 8 4

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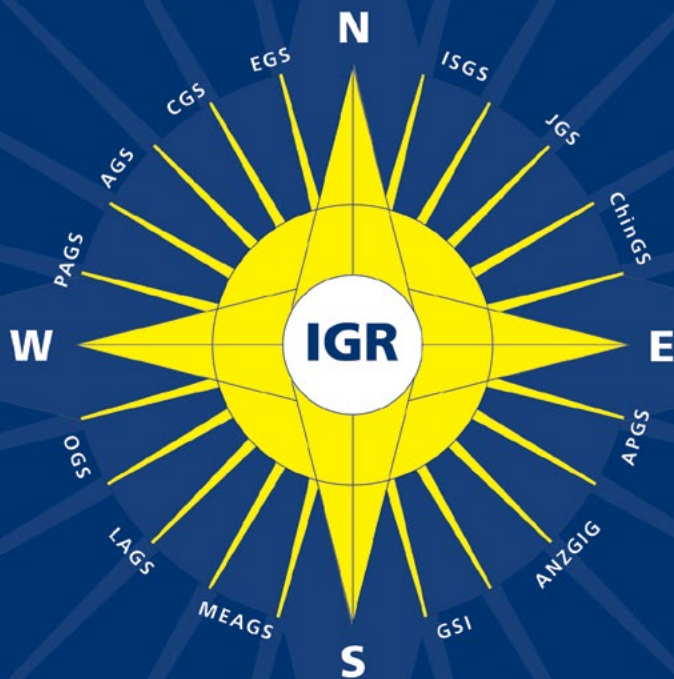
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A Quarterly Journal

Volume 23 no. 1



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Published by Kugler Publications, P.O. Box 20538, 1001 NM Amsterdam, The Netherlands, on behalf of the World Glaucoma Association.

Cover design: Cees van Rutten, The Hague, The Netherlands

Typesetting: 3bergen, www.3bergen.com

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From the WGA

Dear IGR readers,

We are happy to let you know that the WGA continues to expand our educational resources online and to develop numerous opportunities for remote learning by our members. Our collaborative work as a society helps our members to deliver the very best care to our glaucoma patients.

We planned another exciting WGA Global Webinar for you. On Saturday, November 5, we connected the entire glaucoma community once again, with free, high-quality education to all regions of the world with the 9th WGA Global Webinar, on **'All About Minimally Invasive Glaucoma Surgery'**.

On July 7, we held the third edition of the WGA Surgical Grand Rounds, which addressed 'Malignant Glaucoma' and 'Nanophthalmos with Glaucoma'. The recorded session is available to everyone with a WGA#One account on our website. The next edition of the Surgical Grand Rounds will be held in January 2023, and will cover the topics 'How to manage failing/failed filter' and 'Tube revisions to restore flow'. We invite you to join Drs. Pradeep Ramulu and Tanuj Dada for the discussion.

At the recent annual American Academy of Ophthalmology (AAO) meeting in Chicago (September 30–October 3), the WGA hosted the 39th Information and Planning Exchange (IPE) meeting in person, with many participants also calling in from around the world. Major stakeholders in glaucoma care and research, including our top industry members, met to collaborate and network with the concerted goal to defeat glaucoma. Additionally, thanks to all of you who attended the AAO meeting and stopped by the WGA booth. If you did not have the chance to get your copy of the WGA Patient Guide at our booth, you may download it [here](#).

The program of the 10th World Glaucoma Congress in Rome will feature over 70 sessions, including workshops, symposiums, and wet labs to advance your career.

The first preliminary program has been released on our congress website, and the WGA invites you to contribute to this very special, 10th edition of our congress by **registering and submitting an abstract. The registration and abstract submission sites are now open. Find out more about WGC-2023 in Rome (June 28–July 1, 2023): [WGC 2023 | 10th World Glaucoma Congress](#).**

Best wishes,

Shan Lin, MD

Executive Vice-President

Kaweh Mansouri, MD MPH

Associate Executive Vice-President

GET TO KNOW US!

Nkiru Kizor-Akaraiwe



My first time attending the World Glaucoma Congress that was held in Boston in 2009 will forever be a memorable trip. I found it very exciting and stimulating to be part of a network of glaucoma experts (specialists) around the world with a passion to share their experiences and knowledge in different aspects of glaucoma care. The **WGC**, subsequently, became a must-attend for me for updates as well as sharing of experiences and research in glaucoma/glaucoma care. I was thereafter privileged to be elected a member of the Board of Governors of the World Glaucoma Association in 2019.

Currently, I am an Associate Professor and the Head of Glaucoma services in Enugu State University of Technology Teaching Hospital Parklane (ESUTTHP), Nigeria. Together with other colleagues, I also work at The Eye Specialists Hospital (TESH) Enugu - Nigeria, a large referral super-specialists private practice with a huge glaucoma patient load. Previously, I was the Chairman of the Research, Education and Training committee/Director, Post Graduate Studies at ESUTTHP until 2021. And in 2009, I had the privilege of being the Faculty Secretary for the Faculty of Ophthalmology in the West African College of Surgeons. Not too long after, I became the founding Head of the Department of Ophthalmology in ESUTTHP after heading the Department of Surgery.

My research interests are centered around earlier glaucoma diagnosis in various communities, African glaucoma genetics and glaucoma surgical interventions (including lasers).

The silent blinding nature of glaucoma has always been a burden for me. Incidentally, the Southeastern part of Nigeria has the highest prevalence of glaucoma and glaucoma blindness in the country. And so, in 2002, I pioneered numerous glaucoma awareness campaigns in the South-Eastern region of Nigeria through the mass media and through religious, social, and secular organizations; alongside periodic free glaucoma screenings (three to five times a year). Over the years, my team has screened about half a million people.

When the first World Glaucoma Day was commenced by the WGA in 2008, it increased glaucoma awareness in no small measure globally; this further fueled my passion. Subsequently, in 2010, the WGA converted the World Glaucoma Day to the **World Glaucoma Week** which delightfully gave everyone a larger, official timeframe for awareness campaigns and screening exercises.

WGA continues to be a wonderful platform for constant positive change to our glaucoma care, providing great opportunities for networking and collaboration with outstanding glaucoma experts from all over the world. This has broadened my horizon. Personally, I am proud but mostly grateful to be a part of this organization through which I have collaborated with colleagues who have become friends across the continents. I am eager to see what great things the future holds for this organization as we rise above every challenge.



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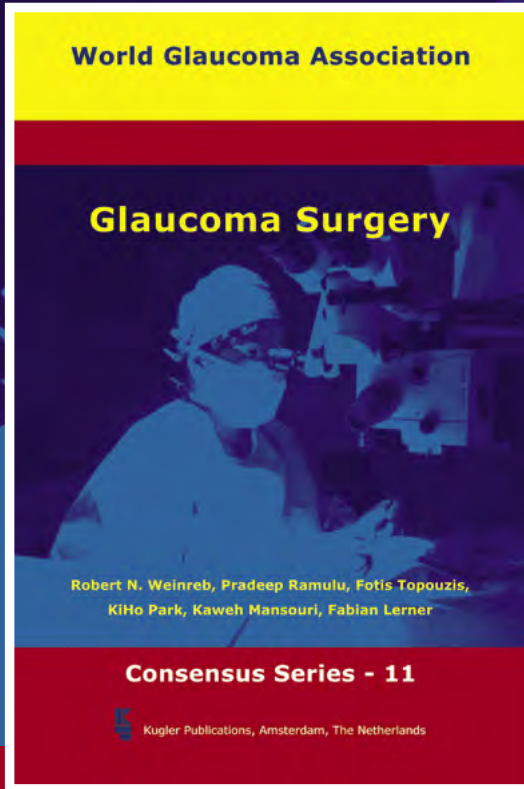
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Editor's Selection



With the multitude and variety of publications it seems almost impossible for the ophthalmologist to intelligently read all the relevant subspecialty literature. Even the dedicated glaucomatologist may have difficulty to absorb 1200+ yearly publications concerning his/her favorite subject. An approach to this confusing situation may be a critical selection and review of the world literature.

Robert N. Weinreb, Chief Editor

Screening and Detection

To screen or not to screen?



 Comment by **David Friedman**, Baltimore, MD, USA

100679 Screening for glaucoma in adults: Updated evidence report and systematic review for the US Preventive Services Task Force; Chou R, Selph S, Blazina I, Bougatsos C, Jungbauer R, Fu R, Grusing S, Jonas DE, Tehrani S; JAMA (Journal of the American Medical Association) 2022; 327: 1998-2012

The US Preventive Services Task Force (USPSTF) sets a high bar for recommending screening for medical conditions. They require high quality evidence that screening is better than not screening in terms of long-term outcomes, and this includes identifying possible harms of screening as well as benefits. This has often resulted in controversy surrounding USPSTF recommendations. The results of this current review and update of the literature are therefore not surprising: the USPSTF has once again determined that the evidence is insufficient to recommend screening for primary open-angle glaucoma (POAG).


The USPSTF has once again determined that the evidence is insufficient to recommend screening for primary open-angle glaucoma (POAG)

This article by Chou and colleagues updates the systematic review performed in 2013 to determine if screening is effective and to also assess the impact of treatment on outcomes. The focus for screening was on optical coherence tomography (SD-OCT) and visual fields (VF) for identifying individuals 40 years of age and older who do not have known POAG. Screening studies using case control designs were excluded as these are subject to bias. **Screening with SD-OCT had a pooled mean 79% sensitivity and 92% specificity while VF had sensitivity of 87% and specificity of 82%.** Treatment was also assessed, and IOP-lowering medications were associated with lower risk of progression (RR = 0.68), and treatment was not associated with increased risk of serious adverse events. Selective laser trabeculoplasty was also found to be safe and to provide outcomes similar to using medications. Overall, the authors conclude: 'Screening tests can identify persons with glaucoma and treatment was associated with a lower risk of glaucoma progression, but evidence of improvement in visual outcomes, quality of life, and function remains lacking.'

Clinical Examination Methods

Pulsatile Trabecular Motion and IOP Fluctuations



 Comment by **Clemens Strohmaier**, Linz, Austria and **Alex Huang**, San Diego, CA, USA

100738 Pulsatile Trabecular Meshwork Motion: An Indicator of Intraocular Pressure Control in Primary Open-Angle Glaucoma; Du R, Xin C, Xu J, Hu J, Wang H, Wang N, Johnstone M; *Journal of Clinical Medicine* 2022; 11(10): 2696. doi: 10.3390/jcm11102696

This cross-sectional study by Du *et al.* used phase-sensitive OCT to assess pulsatile trabecular meshwork motion (TM) in glaucomatous eyes compared to healthy individuals. **Their main finding is reduced motion (maximum velocity and cumulative displacement) in glaucoma subjects compared to controls.** Within the glaucoma group, they reported reduced motion in individuals with high IOP fluctuations ('fluctuant', 9.9 mmHg diurnal amplitude) compared to those with lower fluctuations ('stable', 4.0 mmHg diurnal amplitude). Furthermore, **regional differences between the quadrants of individual eyes have been found, with the nasal area showing increased motion compared to temporal.** This was seen in healthy individuals as well as glaucomatous eyes.

An important assessment for any new method is reliability and reproducibility, and the authors showed excellent results for their velocity and motion measures

However, it is unclear if this only included normal subjects. Imaging disease is often more difficult. Since the TM impacts IOP, IOP varies through the day, IOP behavior changes in glaucoma, and because the authors specifically compare IOP stable and IOP fluctuant subjects, very high reliability and reproducibility in glaucoma eyes might not be expected.

Nevertheless, the study is interesting in many aspects: **it demonstrates the clinical applicability of a non-invasive tool to assess the biomechanical properties of the trabecular meshwork.** Furthermore, it shows differences in these biomechanical properties between healthy individuals and patients with glaucoma. Lastly, it highlights the regional differences within the quadrants of each individual eye.

Overall, this study adds further evidence that the reduction of outflow facility to a single number – as modelled by the Goldmann equation – is not a precise characterization of aqueous humor outflow anymore. Instead, we need to consider the spatial differences within the eye, develop novel models and tools to assess biological properties adequately and lastly treat aqueous humor outflow as a dynamic system with changes over time.

Clinical Examination Methods

Pulsatile Trabecular Motion and IOP Fluctuations



 Comment by **Michael Girard**, Singapore

100738 Pulsatile trabecular meshwork motion: An indicator of intraocular pressure control in primary open-angle glaucoma; Du R, Xin C, Xu J, Hu J, Wang H, Wang N, Johnstone M; *Journal of Clinical Medicine* 2022; 11(10): 2696. doi: 10.3390/jcm11102696

In the proposed study, **the authors suggest that if one could fully characterize the biomechanical behavior of the trabecular meshwork (TM), one could potentially predict future IOP fluctuations in individual patients.** After all, the TM plays a major role in the control of IOP, and such a knowledge could have implication for the management of glaucoma. Specifically, in this study, **the authors were able to dynamically map the deformations of the TM in response to a change in IOP during the cardiac cycle** (also known as the ocular pulse). Those systole-to-diastole deformations are pulsatile in nature, and were locally mapped using phase-contrast optical coherence tomography (OCT), following a protocol already established by the same authors.¹

To test their main hypothesis, the authors recruited 20 normal and 30 glaucoma subjects. All subjects underwent biomechanical mapping (to assess diastole-to-systole TM movement). **The authors found that the TM of glaucoma eyes exhibited less TM displacement (and at a lower velocity) in response to the ocular pulse.** Regional variations were also observed in both groups. When glaucoma groups were further divided into two (according to their maximum diurnal IOP fluctuations; of less or more than 8 mmHg),

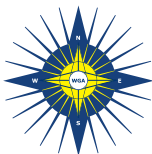
the group that exhibited the highest diurnal IOP fluctuations also exhibited the least TM displacements and velocities (nasal quadrant only). In other words, knowledge about TM biomechanics might tell us which patients would be more likely to exhibit transient IOP fluctuations.

Knowledge about TM biomechanics might tell us which patients would be more likely to exhibit transient IOP fluctuations

The proposed work has merit and several aspects can be discussed here for future improvements. First, **TM displacement is not necessarily directly related to TM stiffness**. TM displacement will be affected by the magnitude of the applied loads (including the ocular pulse) but also by surrounding tissues. For instance, the ocular pulse has been found to be different between normal and glaucoma patients. The ocular pulse is highly affected by a change in corneo-scleral stiffness, baseline IOP value, or in the choroidal pulse volume, all of which are known to change with the development and progression of glaucoma. Such variables would need to be very well controlled in future work. Second, TM stiffness can be assessed using techniques such as the 'inverse finite element'.¹ Such methods could complement the proposed analyses. Third, to gain a comprehensive knowledge of TM biomechanics, diastole-to-systole TM displacements should also be reported as full 3D vector fields. This is currently a technology limitation. Finally, to interpret their clinical data, it is worth noting that the authors would highly benefit from the use of a mathematical model that would model the biomechanics of drainage up to the episcleral vein. The authors have already conceptualized many aspects of the problem.²

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Clinical Examination Methods

IOP Temperature Measurements



 Comment by **Luciano Quaranta**, Brescia, Italy

100359 Measurement of intraocular temperature in glaucoma: week-day and seasonal fluctuations; Mansouri K, Gillmann K, Rao HL, Szurman P, Weinreb RN,; British Journal of Ophthalmology 2022; Apr 20;bjophthalmol-2021-320495. doi: 10.1136/bjophthalmol-2021-320495. (Online ahead of print)

This paper reports results on the evaluation of both the short-term and long-term variability of intraocular temperature (IOT) patterns in eyes with primary open-angle glaucoma (POAG) based on measurements collected with an intraocular pressure sensor the second generation eyemate-IO system (Implan-data Ophthalmic Products GmbH, Hannover, Germany) implanted in 22 patients during cataract surgery. The implant is powered externally by an electromagnetic field produced by the hand-held reader (Mesograph), which also acts as an antenna for the transmission of the reading signals emitted by the sensor. The mesograph also contains an ambient temperature sensor.

To obtain a measurement, the reader and the sensor implant need to be brought in close proximity with each other to activate the electromagnetic coupling sequence. During the sequence, ten measurements per second are made and averaged. The resulting IOP is recorded on the reader unit. Temperatures measured by the sensor and the mesograph on each occasion IOP measurement are also recorded.

The data collecting device was the abovementioned implanted sensor along with an external reading device able to provide power supply to the sensor via electromagnetic coupling as well as to perform as a data relay both via a cable connection or wireless into a web-based database.^{1,2} Patients were trained on how to measure their own IOP with the device and were instructed to carry out at least four measurement cycles per day. The 24-hour day duration was split into seven time periods, in which measurement cycles could take place. Twenty-two eyes of 22 patients underwent cataract surgery with implantation of the eyemate-IO sensor. Their mean age was 67.8 ± 6.8 years, and eight (36.4%) were women. A total of 132745 readings over 21102 measurement days were obtained from the sensor during the study period. The average number of measurements obtained from each study eye was 6.3 per day.

On average, **IOT was significantly higher on Sundays (34.57°C; 95% CI 34.37 to 34.78) than on any other day of the week (p < 0.001)**. Mean IOT on other weekdays ranged from 34.48°C to 34.51°C. Over the year, IOT followed a clear seasonal pattern, reaching its maximum in July (34.8°C; 95% CI 34.56 to 34.97) and its minimum in January (34.4°C; 95% CI 34.15 to 34.56; p < 0.001).

In my opinion, three aspects must be analyzed.

Firstly, as the authors correctly state in the paper, at present we do not have any normative data on IOT, to make a comparison with glaucoma patients. This is an important aspect to be further clarified in order also to understand if IOT has a potential role in glaucoma onset and progression (differences between normal and glaucoma patients).

Secondly, short-term IOT patterns. This finding is really intriguing. As a matter of fact, **IOT increase during the night-time could be correlated with the decrease of aqueous humor production during sleep**. In this prospect, if IOT increase should be considered a risk factor for glaucoma progression, further decrease of aqueous humor production during the night should be avoided or limited.

Thirdly, clinical meaning of IOT and its variations. The clinical meaning of increase of IOT is not completely understood. At the present only speculations can be drawn on the role of this variable on retinal ganglion cells vulnerability/apoptosis. Further pre-clinical and clinical investigations are warranted to understand the impact of IOT variations on glaucoma progression.

Overall, this is an outstanding job, based on an innovative and promising approach. Studies must go on, especially with regards to long-term variability for which the authors of this paper themselves claim there is a strong data paucity bias. Studies on short-term variability should consider and include different timeframes for both data collection and interpretation. The hours of the day should be covered more uniformly. These findings can have important implications both for clinical glaucoma management and clinical trials. We congratulate Kaweh Mansouri and coworkers for their so valuable contribution.

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Clinical Examination Methods

Optical Microangiography



 Comment by **Lucy Shen** and **Aimee C. Chang**, Boston, MA, USA

99667 Optical microangiography and progressive ganglion cell-inner plexiform layer loss in primary open-angle glaucoma; Rao HL, Dasari S, Puttaiah NK, Pradhan ZS, Moghimi S, Mansouri K, Webers CAB, Weinreb RN; American Journal of Ophthalmology 2022; 238: 36-44

In this prospective case series, Rao and colleagues evaluated the association between optical microangiography (OMAG) measurements and progressive ganglion cell-inner plexiform layer (GCIPL) loss in Indian patients with primary open-angle glaucoma (POAG). GCIPL loss rate of superior and inferior sectors was assessed in 63 eyes of 38 patients with mild-to-moderate POAG for a follow-up duration of 3.0 ± 0.8 years and with 4.1 ± 1.1 OCT examinations. The investigators reported an association between a faster rate of sectoral GCIPL loss and lower baseline quadrant peripapillary perfusion density (PD) and vessel density (VD). Specifically, **a 1% lower baseline peripapillary PD was associated with a 0.04 $\mu\text{m}/\text{year}$ faster rate of GCIPL loss in the corresponding sector**, and a $1 \text{ mm}/\text{mm}^2$ lower baseline peripapillary VD was associated with a $0.09 \mu\text{m}/\text{year}$ faster rate of GCIPL loss in the corresponding sector. **A potentially unexpected finding was the lack of association between baseline macular OMAG measurements and GCIPL thinning rate, suggesting that macular OCTA changes may not be as informative as peripapillary OCTA changes in predicting glaucoma progression.** Similar findings were reported by the same group when they assessed the association between rate of RNFL thinning and baseline OMAG measurements.¹ These findings suggest a clinical role for peripapillary OMAG measurements in predicting glaucoma progression in patients with mild-to-moderate POAG. As noted by the authors, this study is limited by its sample size, relatively short duration and potential confounding effects when assessing two sectors of the same eye and two eyes of the same patients, although statistical adjustment for potential correlations was performed. Additional studies in different ethnic groups with case and control subjects and other OCTA software are needed to confirm the findings of the study and further establish the clinical utility of peripapillary OCTA measurements in predicting glaucoma progression.


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Telemedicine

Home Monitoring



 Comment by **David Crabb** and **Peter Jones**, London, UK

100617 Home monitoring of glaucoma using a home tonometer and a novel virtual reality visual field device: Acceptability and feasibility; Hu GY, Prasad J, Chen DK, Alcantara-Castillo JC, Patel VN, Al-Aswad LA; *Ophthalmology Glaucoma*. 2022; May 14; S2589-4196(22)00081-3. doi: 1016/j.ogla.2022.05.001. (Online ahead of print)

Hu *et al.* (2022) report qualitative data from twenty confirmed/suspected glaucoma patients, asked to perform both tonometry and perimetry at home for a week. **The results highlight the strong desire among some glaucoma patients for home monitoring solutions**, as well as the ability of said patients to make astute observations (e.g., regarding potential sources of measurement error, or impediments to future use). Key unresolved controversies are highlighted (e.g., to what extent should patients have unfettered access to their data?). And various encouraging statistics are presented regarding adherence rates and patient acceptability ratings.

The results highlight the strong desire among some glaucoma patients for home monitoring solutions

We think the results from this report provide useful evidence regarding the feasibility of home assessments for monitoring glaucoma progression. However, while the messaging is resolutely upbeat, **attentive readers are also rewarded with telling insights into the current state of the art**. For example, 20% of VF tests were deemed 'anomalous', 25% of patients needed to contact the study authors for assistance, and 5% of patients were excluded due to 'an inability to demonstrate competence'. Such values are broadly consistent with previous studies, and without improvement threaten to render home monitoring unsustainable in practise.


Overall, as well as highlighting the considerable appetite for home monitoring among some glaucoma patients, **this study also serves as a timely reminder about how much remains unknown when it comes to ophthalmic home monitoring**. Thus, while it is encouraging that nearly all patients *felt* such data were useful, further research is required to demonstrate that they are in fact clinically useful and cost effective. And while in the present study a select group of trained individuals were willing and able to undergo home

monitoring for a week, **it still remains unclear how well home monitoring will perform in the 'real' real world**: where less motivated and less well supported individuals might be expected to adhere to home monitoring for months or years on end. As many long-suffering dentists will attest, the road to self-management is all too often paved with good intentions, but only transient resolve.

Telemedicine

Theranostic Contact Lenses



 Comment by **Kaweh Mansouri**, Lausanne, Switzerland and **Ewald Lindner**, Graz, Austria

100625 Intelligent wireless theranostic contact lens for electrical sensing and regulation of intraocular pressure; Yang C, Wu Q, Liu J, Mo J, Li X, Yang C, Liu Z, Yang J, Jiang L, Chen W, Chen HJ, Wang J, Xie X; Nature communications 2022; 13: 2556

Goldmann-Tonometry is still the gold standard of tonometry but it does not facilitate continuous pressure measurement. As intraocular pressure changes with activities and circadian rhythm, a snapshot measurement can miss pressure variations and spikes occurring during the daily course. As much as 80% of IOP peaks happen outside of scheduled appointments and frequently occur at night.¹ In recent years, contact lens-based IOP sensors have emerged. The possibility to integrate pressure measurement and therapy into a feedback-loop has been explored in other diseases, like diabetes mellitus, where novel devices measure glucose levels and apply insulin as needed,² which leads to a better disease control.

While most of the existing contact lens based applications for glaucoma focus on either sensing or delivery separately, **the study by Yang *et al.* presents a wireless theranostic contact lens, which is able to continuously measure intraocular pressure and to deliver anti-glaucoma drugs as needed.** The word 'theranostic' is a combination of 'therapeutics' and 'diagnostics'. As the space on a contact lens is curved and very limited the integration of a sensor and a delivery module is challenging. Increasing intraocular pressure leads to a deformation of the corneal curvature, which is transduced to the sensor circuit of the contact lens interfaced with the cornea. The displacement of capacitive plates induces significant electrical signals. **If the pressure reaches a certain threshold an electric field is built up, which leads to a migration of positively charged brimonidine through the cornea into the anterior chamber – a mechanism that is called iontophoresis. The sensory and the delivery module were tested *ex vivo*, using porcine eyeballs. The intraocular pressure was increased from 5 to 50 mmHg by controlled infusion of saline solution**

and the resonance frequency of the integrated reading coil was recorded. The relation between intraocular pressure and resonance frequency was analyzed. *In vivo* experiments were conducted on rabbits in order to determine the pressure lowering effects via iontophoresis. The power for the iontophoresis was applied by a wireless power transfer circuit.

The technology has to be significantly improved before human use as a sensing error of more than 40% has been mentioned

The wireless theranostic contact lens enables measurements of intraocular pressure and on-demand medicine administration without causing vision blockage. Separation of frequencies enables to have both pressure measurement and drug delivery on the same contact lens without cross-coupling. Still, the technology has to be significantly improved before human use as a sensing error of more than 40% has been mentioned. The paper describes the proof of concept of a promising new technology, but we have to see if it can be further developed for human trials.


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Risk Factors

Is Coffee a Risk Factor in Glaucoma?



 Comment by **Louis Pasquale** and **Kelsey Stuart**, New York, NY, USA

100555 Habitual coffee consumption increases risk of primary open-angle glaucoma: A mendelian randomization study; Li X, Cheng S, Cheng J, Wang M, Zhong Y, Yu AY; Ophthalmology 2022; 129(9): 1014-1021. doi: 10.1016/j.ophtha.2022.04.027

Mendelian randomization (MR) offers a complementary approach to epidemiology studies, substituting common genetic variants as instrumental variables (IVs) for exposures. The technique is analogous to a natural randomized controlled trial and, provided certain assumptions are met, allows for causal inferences from observational data.¹

Li and colleagues employ a two-sample MR approach to evaluate whether there is a link between coffee consumption and primary open-angle glaucoma (POAG). Using various IVs from the latest genome-wide association study of glaucoma, they show that **genetically predicted coffee consumption is adversely associated with POAG risk.**² Sensitivity analyses, using alternative MR methods, suggest these findings are robust, and they find no evidence for secondary genetic associations with traditional glaucoma risk factors, including intraocular pressure (IOP).

This is the first study using an MR approach to assess the relationship between coffee consumption and glaucoma risk. Recently, a large population-based study found that caffeine consumption was adversely associated with glaucoma, but only in participants with the strongest genetic predisposition to elevated IOP.³39-73 years The same study found no evidence for a causal role of coffee consumption on IOP in a MR analysis, findings that support the current study.

Despite the robust results, it is possible that the genetic variants used confer a risk of POAG through pleiotropic pathways

In MR studies, causal inferences are only possible when the IV assumptions are satisfied.¹ Despite the robust results, it is possible that the genetic variants used confer a risk of POAG through pleiotropic pathways (a violation of the exclusion restriction assumption). This is a particular possibility when using a statistically-driven approach to IV selection for complex traits, as the biological implications of the utilized genetic variants are not well understood. For example, a coffee consumption IV may be more reflective of an underlying genetic propensity to addiction, implicating alternative pathways unrelated to caffeine intake.

Further research is needed before dietary recommendations can be made to individuals with, or at risk of, glaucoma.

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Clinical Forms of Glaucoma

How frequent is post-mydriasis Acute Angle Closure?



 Comment by **Sasan Moghimi**, La Jolla, CA , USA

100595 Acute angle-closure attacks are uncommon in primary angle-closure suspects after pharmacologic mydriasis: The Zhongshan Angle-Closure Prevention Trial; Friedman DS, Chang DS, Jiang Y, Huang S, Kim JA, Munoz B, Aung T, He M, Foster PJ; Ophthalmology Glaucoma 2022; 11;S2589-4196(22)00082-5. doi: 10.1016/j.ogla.2022.04.003. (Online ahead of print)

Primary angle closure suspect (PACS) eyes are believed to be at high risk of developing acute angle-closure (AAC) attacks especially after pupillary dilation. One clinic-based study from the United States reported that AAC developed in 6% of subjects with angle closure or shallow anterior chambers over a mean period of 2.7 years of follow-up.¹

Despite the common clinical practice of deferring mydriatic drugs in patients with narrow angles, population-based epidemiologic studies have indicated low rates of AAC after dilation ranging from 0 to 2.2 cases per 100 000.²⁻⁴ Many of these participants who underwent dilation in these studies had wide, not narrow, anterior chamber angles and were White or African Americans. The risk of developing AAC after mydriasis in populations with much higher rates of PACSs, such as the Chinese population, remains largely unknown.

The landmark Zhongshan Angle Closure Prevention (ZAP) trial, was a randomized clinical trial that recruited 889 subjects with bilateral PACS, aged between 50 to 70 years, through community-based screening in Guangzhou, China and explored the benefit of treating PACS eyes with laser peripheral iridotomy (LPI). Bilateral PACSs were treated with LPI in one randomly selected eye, with the fellow eye serving as an untreated control. In the newest report from this large trial by Friedman *et al*, the incidence and risk of post-mydriasis AAC in LPI-treated and untreated, control eyes were documented in the participants who had their pupils pharmacologically dilated six times over the six years of follow-up with 5% phenylephrine and 0.5% tropicamide.

One bilateral AAC attack occurred after mydriasis at the two-week post-LPI visit. No other AAC events occurred in the LPI-treated eyes. In the untreated eyes, four additional attacks occurred: two occurred after dilation (one at 54 months and one at 72 months of follow-up), and two occurred spontaneously. **The risk of spontaneous AAC in the untreated eyes was 0.44 per 1000 eye-years** (95% confidence interval, 0.11-1.77 per 1000 eye-years).

The main limitation of the study is the generalizability of the results

They showed that the risk of incident AAC attacks in PACSs was extremely low, even in a higher-risk group that underwent repeated pharmacologic pupillary dilation over six years of follow-up. Prophylactic LPI reduced this small but real risk. Unfortunately, due to the small number of events, the study did not have the power for risk assessment of acute episodes.

The current report also confirms that laser peripheral iridotomy provided a protective effect, but did not completely eliminate the risk of developing AAC in primary angle-closure eyes

The main limitation of the study is the generalizability of the results. The study cohort was entirely comprised of Chinese subjects, and therefore, the results may not be fully generalizable to other racial and ethnic groups. They excluded participants with an IOP elevation of > 15 mmHg after a short darkroom prone provocative test, and provided acetazolamide, to all subjects who underwent dilation as well as other therapies to subjects who experienced a clinically significant IOP rise of > 8 mmHg after mydriasis. This may have also contributed to the reduction of the incidence of AAC in their study. Finally, they dilated the pupil using tropicamide 0.5% ; clinicians should not translate the results to their patients if they did not use tropicamide 1%.

The current report also confirms that laser peripheral iridotomy provided a protective effect, but did not completely eliminate the risk of developing AAC in primary angle-closure eyes.

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Clinical Forms of Glaucoma

How frequent is post-mydriasis Acute Angle Closure?



 Comment by **Shan Lin**, San Francisco, CA, USA

100595 Acute angle-closure attacks are uncommon in primary angle-closure suspects after pharmacologic mydriasis: The Zhongshan Angle-Closure Prevention Trial; Friedman DS, Chang DS, Jiang Y, Huang S, Kim JA, Munoz B, Aung T, He M, Foster PJ; Ophthalmology Glaucoma 2022; 11;S2589-4196(22)00082-5. doi: 10.1016/j.ogla.2022.04.003. (Online ahead of print)

In this study utilizing the results of the Zhongshan Angle-Closure Prevention (ZAP) Trial, the rates of acute angle-closure (AAC) attacks upon dilation were evaluated. **Among participants who were classified as primary angle-closure suspects (PACS), one eye was randomized to laser peripheral iridotomy (LPI) at the start of the study. There were 889 subjects enrolled in the ZAP Trial and dilation occurred at two weeks, six months, 18 months, 36 months, 54 months, and 72 months. There was a total of five patients who developed an AAC attack during the course of the study.** One case was a bilateral case (both a control eye and a LPI-treated eye) and four were unilateral cases (all control eyes). Among the five patients (six eyes) with AAC, the ones that occurred after dilation were one LPI-treated eye and two control eyes. From these results, **the risk of developing an attack after dilation was estimated to be 1 in 1587 among non-LPI eyes and 1 in 4762 among LPI-treated eyes.**

The authors conclude that it is extremely rare to develop an AAC attack after dilation in LPI-treated eyes, and that it is reasonably safe to do so when needed

The authors conclude that it is extremely rare to develop an AAC attack after dilation in LPI-treated eyes, and that it is reasonably safe to do so when needed. Among PACS eyes which have not received LPI, the risk with multiple dilations is small but should be considered. Patients who require routine dilation, such as those with diabetic retinopathy, may wish to consider LPI due to the additive risk with multiple dilations.

Patients who require routine dilation, such as those with diabetic retinopathy, may wish to consider LPI due to the additive risk with multiple dilations

Overall, the results of the present study are very helpful to clinicians as this scenario of whether to dilate in PACS eyes occurs commonly. The large population cohort and prospective nature of this study give credibility to the findings and recommendations. However, it should be noted that there are limitations due to the study design including the inclusion of only Chinese subjects, community recruitment causing potential selection bias, exclusion of very high-risk patients (eyes positive on the dark room prone provocative test), and the aggressive use of medications to prevent IOP elevation after LPI. Many of these issues may lead to underestimation of the true risk for AAC after dilation.

Clinical Forms of Glaucoma

Preventing Acute Angle Closure



 Comment by **Harrison Bennett** and **Christopher Teng**, New Haven, CT, USA

100577 Potentially missed opportunities in prevention of acute angle-closure crisis; Wu AM, Stein JD, Shah M; *JAMA ophthalmology* 2022; 140: 598-603; In this population-based retrospective cohort study, Wu *et al.* discuss the steps ophthalmologists can take to help prevent acute angle-closure crisis (AACC).

This study includes 1179 Medicare beneficiaries with a diagnosis of AACC, they discovered that only 796 (67.5%) had consulted with an ophthalmologist or optometrist at least once within the two-year interval prior to developing AACC. Of those 796 individuals, only 264 (33.2%) underwent gonioscopy in the two years prior to developing AACC, 113 (42.8%) of which received a diagnosis of anatomic narrow angles. The authors also discovered that of the original cohort, 414 patients (35.1%) received at least one medication associated with increased risk of AACC before developing the disease. In the two-year look-back period, 464 (39.4%) individuals were diagnosed with open-angle glaucoma (OAG) or suspected OAG.

The authors raise several good points about the state of ophthalmic care and the recognition of AACC risk factors. Firstly, **one-third of patients received no eye care in the two years prior to their AACC.** Secondly, **most patients (66.8%) who received eye care, did not undergo gonioscopy at any visit prior to the AACC.** Gonioscopy is a critical skill


for every ophthalmologist and appears to be underutilized. Furthermore, proper gonioscopic technique is necessary to assess for narrow angles. Anterior segment imaging techniques (optical coherence tomography and ultrasound biomicroscopy) show promise as an adjunct method for angle assessment. The authors call attention to newer studies demonstrating a relatively low rate or progression from suspected primary angle closure in Chinese patients, but note this may not be generalizable to the US population. The authors also suggest using electronic health record flags to prompt gonioscopic evaluation.

This study is limited by its retrospective nature and reliance on billing data, which may be missing data collected, but not billed at a visit. They also include only insured patients, so the data may not be generalized to uninsured persons.

Clinical Forms of Glaucoma

Glaucoma after Vitreoretinal Surgery



 Comment by **Taylor Nayman** and **Arthur Sit**, Rochester, MN, USA

100408 Risk of glaucoma after vitreoretinal surgery – Findings from a population-based cohort study; Loukovaara S, Gucciardo E, Korhonen A, Virtanen A, Harju M, Haukka J; *Acta Ophthalmologica* 2022; 100(6): 665-672. doi: 10.1111/aos.15161.

Vitrectomy has been linked to an increased risk of glaucoma.^{1,2} While vitrectomy leads to oxidative damage at the trabecular meshwork (TM) and likely increases outflow resistance,^{3,4} previous studies have also shown an increased risk of normal-tension glaucoma.²

Loukovaara and colleagues reported results from a longitudinal population-based study in Finland evaluating the risk of glaucoma following vitreoretinal surgery. In this case-control study of 261 individuals, of which 103 had glaucoma and 158 were age- and sex-matched controls, patients were separated into three groups based on the type of vitrectomy they had undergone. These were single vitrectomy (Vit), vitrectomy with a retinal procedure (VitRet), and phacoemulsification and/or lensectomy with/without intraocular lens implantation and vitrectomy (PhacoVit).

All three types of vitrectomies were associated with an increased risk of any subtype of glaucoma. The highest risk was associated with VitRet (OR 4.5), followed by Vit (OR 3.15), and PhacoVit (OR 2.7). Interestingly, risk of open-angle glaucoma (OAG) was increased after VitRet (OR 3.66), as well as Vit (OR 2.33), but not after PhacoVit. The risk of other types of glaucoma (unspecified or secondary) was highest with Vit (OR 5.37), followed by PhacoVit (OR 4.58), and VitRet (OR 4.06).

Authors suggest that VitRet induces more inflammation and oxidative stress, while membrane peeling may contribute to secondary glaucoma by directly damaging retinal ganglion cells. They also note the possible protective role of cataract extraction.

Diabetes was not associated with glaucoma. Five-year exposure to statins was associated with decreased risk of glaucoma (OR 0.86), and four- and five-year exposure decreased the risk of other subtypes (OR 0.87 and 0.81, respectively), but not OAG. Authors speculate that statins may play a role in mitigating inflammation that could affect outflow facility.

One limitation was the way glaucoma was defined without precise criteria (open-angle glaucoma with subtypes of exfoliation, normal tension, pigmentary, chronic primary OAG, and unspecified OAG; unspecified glaucoma or glaucoma secondary to other eye disorder).

This study confirms the increased risk of glaucoma post-vitrectomy and the need for increased monitoring of these patients

The authors discussed potential reasons why the risk may be different between groups, including internal limiting membrane peeling and increased inflammation causing higher rates in the VitRet group, while opening of the angle and TM decreased risk in the PhacoVit group. Unfortunately, they did not report the degree of vitrectomy, but it is possible that more complete vitrectomies in the VitRet group increased oxidative stress in the TM. While further studies are needed to better establish the pathophysiology, this study confirms the increased risk of glaucoma post-vitrectomy and the need for increased monitoring of these patients.

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Clinical Forms of Glaucoma

Glaucoma and Treated Diabetes



 Comment by **Rupert Bourne**, Cambridge, UK

100638 Association of diabetes medication with open-angle glaucoma, age-related macular degeneration, and cataract in the Rotterdam Study; Vergroesen JE, Thee EF, Ahmadizar F, van Duijn CM, Stricker BH, Kavousi M, Klaver CCW, Ramdas WD; *JAMA ophthalmology* 2022; 140(7):674-681. doi: 10.1001/jamaophthalmol.2022.1435

Long-term caloric restriction can reduce risk in some age-associated diseases such as cancer, diabetes, and cardiovascular disease. In this article by Vergroesen *et al.*, **metformin treatment was associated with a lower risk of primary open-angle glaucoma (POAG)**. This follows several cross-sectional and retrospective studies, for example, a medical claims database cohort of diabetic patients by Lin *et al.*,¹ who reported that metformin, a caloric restriction mimetic drug, was associated with a reduction in POAG risk. Indeed, **that study predicted that taking a standard dose of 2 mg metformin hydrochloride per day for two years would result in a 21% reduction in risk of POAG**. Further evidence is provided by Vergroesen *et al.*, involving the Rotterdam Study, a population-based cohort of 11,260 participants. Due to the nature of its prospective design and long follow-up (24 years), the authors were able to examine the association between untreated and treated Type-2 diabetes before the onset of POAG, and thereby determine cumulative lifetime risk of POAG. POAG was defined as glaucomatous visual field loss in at least one eye with reproducibility of the defect, independent of the intraocular pressure. Metformin treatment was associated with a lower POAG risk (OR, 0.18; 95% CI, 0.08-0.41, $P < 0.001$) compared with no treatment with diabetes medication.

Metformin treatment was associated with a lower POAG risk (OR, 0.18; 95% CI, 0.08-0.41, $P < 0.001$) compared with no treatment with diabetes medication

Additionally, the cumulative lifetime risk of POAG was lower for individuals taking metformin (1.5%; 95% CI, 0.01-3.1%) than for individuals without Type-2 diabetes (7.2%; 95% CI, 5.7%-8.7%). Longer periods of treatment and higher cumulative dose of metformin was associated with lower POAG risk.

This study has confirmed the association of metformin with reduced POAG risk and by assessing the association between POAG and Type-2 diabetes in persons without medication, the study has also addressed confounding by indication, a problem in the interpretation of previous studies. The analysis also adjusted for other confounders and offers the reader an interesting explanation of how they tested for a causal relationship using Bradford Hill criteria.² **As the authors point out in their discussion, the next step is external replication and functional proof, and the prospect of interventional randomized clinical trials.** To follow up on the latter, readers may like to read the editorial by Emily Eton and Paula Newman-Casey that directly follows Vergroesen *et al.*'s report, which discusses how such trials may be designed and the ethical implications therein.³

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Laser Treatment

Post-iridotomy Cataract



 Comment by **Sirisha Senthil**, Hyderabad, India

100468 Cataract progression after Nd:YAG laser iridotomy in primary angle-closure suspect eyes; Chang DS, Jiang Y, Kim JA, Huang S, Munoz B, Aung T, He M, Foster PJ, Friedman D; *British Journal of Ophthalmology* 2022; May 2;bjophthalmol-2021-320929. doi: 10.1136/bjophthalmol-2021-320929. (Online ahead of print)

Chang *et al.*, in a prospective Zhongshan Angle Closure Prevention Trial, evaluated the rate and type of cataract progression following laser peripheral iridotomy (LPI). Among 889 participants with bilateral primary angle-closure suspect (PACS), one randomly selected eye underwent LPI and the contralateral eye of the participant served as untreated control. Post LPI, they were followed up for 72 months and progression in cataract was compared between the LPI and controls using LOCS III grading system. Progression was defined as increase in grade of cataract by at least two units or cataract surgery.

LPI does not increase the risk for cataract formation

The study conclusion that **LPI does not increase the risk for cataract formation** is sound and is supported by a prospective study design with long follow-up and ideal (fellow eye) comparative group. The following is an important clinically relevant result of the study. Nine eyes in each group received cataract surgery with five participants receiving surgery in both eyes. The total cumulative probability of reaching pre-defined cataract progression was 21.2% in LPI-treated eyes and 19.4% in control eyes ($p = 0.401$). The differences in the average nuclear grades and cortical grades were not clinically significant, although there was statistically significant difference. The average nuclear grades were slightly higher at 72 months among LPI-treated eyes (both NO and NC: 2.9 vs 2.8, $p < 0.001$, table 2). However, the average cortical grades were lower in LPI-treated eyes (0.76 vs 0.82, $p = 0.030$, table 2). This significant difference in p-value is possibly due to large sample size.

The authors also mentioned that **the total energy used for LPI was not associated with greater risk of cataract progression in a multivariate analysis among treated eyes** ($p = 0.072$). This possibly suggests that there is no biological causal relationship between LPI and cataract progression.

The following two results of 10% for overall cataract and 50% for NC progression risk are 'relative risk' and need to be interpreted along with the absolute risk of 21.2% vs 19.4% for overall cataract and 4.61% vs 3.04% for NS. The overall risk of cataract progression in LPI-treated eyes appeared 10% higher compared with controls (HR = 1.10 (95% CI 0.88 to 1.36) (table 3, figure 1), this was not statistically significant. The risk of cortical and PSC progression remained unchanged between eyes, and while the risk of nuclear sclerosis progression was approximately 50% higher in LPI-treated eyes, this was not statistically significant (HR = 1.49 (95% CI 0.91 to 2.42).

The incidence rate of cataract progression was 3.7 per 100 eye-years in LPI-treated eyes and 3.4 per 100 eye-years in control eyes. This considers the follow-up period of individual participants during the study period. While interpreting this result, one also needs to consider the fact that the number of events were small and about 30% participants dropped out by the end of the study, that possibly has resulted in wide confidence interval of Hazard ratios.

The studies by Lim¹ and Vijaya² show increased risk of cataract with LPI.

The main issue with these studies is no control group in the Lim *et al.* study and an inappropriate control group in the Vijaya *et al.* study.

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Surgical Treatment

Does Phaco de-regulate functioning Filtration Surgeries?



 Comment by **Jose-Maria Martinez de la Casa**, Madrid, Spain

100522 Glaucoma control after phacoemulsification in eyes with functioning glaucoma filtration surgeries: trabeculectomies versus glaucoma drainage devices; Purohit M, Mohite AA, Sung VCT; Graefe's Archive for Clinical and Experimental Ophthalmology 2022; 260(11):3597-3605. doi: 10.1007/s00417-022-05680-z

There is ample evidence about the deleterious effect of cataract surgery on a functioning glaucoma filtering surgery. Less evidence exists, however, on the effect of cataract surgery on patients with a glaucoma drainage device (GDD).

Purohit *et al.* conducted a retrospective comparative study to evaluate the effect of cataract surgery in patients with trabeculectomies (n = 15) and GDD (n = 23), analysing intraocular pressure (IOP), visual field and retinal nerve fiber layer (RNFL) over 24 months.

The authors found that **the increase in IOP over the follow-up period was greater in the GDD group than in the trabeculectomy group.** In addition, **in the GDD group there was a significant worsening of the mean visual field defect while this difference was not significant in the trabeculectomy group.** Regarding the RNFL, the changes were also greater in the GDD group.

These results may have been influenced by some differences between the groups. First of all, in 40% of the trabeculectomy eyes a 5-fluorouracil injection was given at the time of cataract surgery while no antimetabolites were used in the GDD group. Other differences between the groups at baseline were mean age (lower in the GDD group), race (lower percentage of Caucasians in the GDD group) and type of glaucoma (more secondary glaucoma in the GDD group). These differences may have also influenced the results.

The present study therefore shows that cataract surgery can affect the function of a previously implanted GDD. However, the differences at baseline and the different use of antimetabolites make comparison between the two groups difficult.

Surgical Treatment

Phaco and Ab-interno Surgery



 Comment by **Robert Feldman** and **Ruchi Shah**, Houston, TX, USA

100458 Canaloplasty and trabeculotomy combined with phacoemulsification for glaucoma: 12-month results of the GEMINI Study; Gallardo MJ, Pyfer MF, Vold SD, Sarkisian SR, Campbell A, Singh IP, Flowers B, Dhamdhare K.; Clinical Ophthalmology 2022; 16: 1225-1234

The GEMINI study by Gallardo and colleagues aims to determine the **12-month effectiveness of 360 degree canaloplasty and 180 degree trabeculotomy using the OMNI surgical system in conjunction with cataract extraction** for patients with mild to moderate open angle glaucoma. This is a follow-up study from their six-month data which showed a mean IOP reduction of 38% and a medication reduction of 67%. **This prospective study included 120 adult patients with intraocular pressure \leq 33 mmHG on glaucoma medication who also had unmediated post-washout diurnal IOP of \geq 21 and \leq 36 in their final effectiveness analysis.** They found that patients who underwent canaloplasty and trabeculotomy with OMNI surgical system during their cataract extraction had a lower unmedicated mean diurnal IOP at 12 months with minimal adverse events. **The unmedicated mean diurnal IOP was reduced by 34%, and 84% of eyes achieved 20% or more reduction. Eighty percent of patients were medication-free at 12 months.**


Drawbacks of this study include no control arm. This study had a high portion of Caucasian patient (82%) so this data may not be generalizable to other demographics. **Patients had very mild glaucoma with a MD of -3.7. It is also unclear if the patients' fellow eyes were receiving any glaucoma treatment as some glaucoma medications such as b-blockers may affect the fellow eye.**

In glaucoma we are always trying to find safe and effective methods to help decrease intraocular pressure and medication burden for our patients. Results from this study show that OMNI canaloplasty and trabeculotomy are worth further study for select patients to decrease their pressure and medication burden for at least 12 months after surgery. It will be interesting to see long-term results from controlled studies to see if there are real and lasting effects of the procedure.

Surgical Treatment

Filtering Surgery in Neovascular Glaucoma



 Comment by **Steve Mansberger** and **Alexander Robin**, Portland, OR, USA

100657 Comparing surgical outcomes in neovascular glaucoma between tube and trabeculectomy: A multicenter study; Iwasaki K, Kojima S, Wajima R, Okazaki T, Yokoyama Y, Inoue T, Higashide T, Miki A, Nakazawa T, Inatani M; *Ophthalmology*. Glaucoma 2022; May 20;S2589-4196(22)00084-9. doi: 10.1016/j.ogla.2022.05.003. (Online ahead of print)

Ophthalmologists use trabeculectomy or glaucoma tube shunt surgery to control intraocular pressure in patients with neovascular glaucoma (NVG). There is debate about which type of incisional glaucoma surgery is the most successful in this situation. **Iwasaki *et al.* conducted a retrospective clinical cohort study to investigate the outcomes of Baerveldt glaucoma implants (BGI) versus trabeculectomy for the treatment of NVG. The study population included 304 eyes (100 BGI, 204 trab) from patients treated for NVG at five different sites in Japan between 2012 and 2019.**

The authors used Kaplan-Meier survival curves extending out to five years to compare procedures. **Failure was defined as meeting any of the following requirements on two consecutive visits after three months postoperatively: < 20% reduction in IOP, loss of light perception, hypotony with IOP < 5, or IOP > 21 (criteria A), IOP > 17 (criteria B), or IOP > 14 (criteria C).**


The results of the study demonstrated that **BGI had a lower failure rate than trabeculectomy at timepoints up to five years for criteria A and B while the groups had equivalent success for criteria C.** Additionally, the number of early post-operative complications was not significantly different between the groups. Finally, the **BGI-group had less reoperations for glaucoma.**

The data provides a compelling argument for BGI over trabeculectomy for the treatment of NVG in patients with a goal IOP > 21 with a five-year success rate (criteria A) of about 80%. There are some limitations to the study. The groups in this retrospective analysis were not equally matched in many important categories including lens status, previous intraocular surgeries, use of intravitreal anti-VEGF agent, and neovascularization of the iris or angle. Most of us would not attempt a trabeculectomy in an NVG eye with active neovascularization because of the high risk of hyphema and scarring. Active NVG that is not controlled by laser or intravitreal injections will usually require a glaucoma tube implant. The authors provide compelling evidence for when to choose a BGI over trabeculectomy. However, a randomized controlled study with similar preoperative characteristics might provide further evidence about the best surgical options for patients with NVG.

Prognostic factors

Race and Ethnicity as Prognostic Factors



 Comment by **Kelsey V. Stuart** and **Anthony Khawaja**, London, UK

100791 Race and ethnicity differences in disease severity and visual field progression among glaucoma patients; Halawa OA, Jin Q, Pasquale LR, Kang JH, Lorch AC, Sobrin L, Miller JW, Li Y, Eslami M, Wang M, Zebardast N, Elze T; American Journal of Ophthalmology 2022; 242: 69-76. doi: 10.1016/j.ajo.2022.05.023. Epub 2022 May 30.

From both a clinical and an epidemiological perspective, ethnicity is an important consideration in glaucoma, with well-documented ethnic variation in the prevalence, diagnosis, severity, progression and treatment of the disease.^{1,2} While these differences may reflect variation in genetic susceptibility to glaucoma across population groups, there is increasing recognition of the non-genetic factors driving these disparities.³

Is glaucoma simply more aggressive in some ethnic groups, or are there addressable socioeconomic and healthcare access issues that explain the observed differences?

In **this large retrospective cohort study (1998–2020) from a single tertiary eyecare center in the United States**, Halawa and colleagues aimed to explore ethnic and language preference differences in the presenting severity and subsequent progression rate of glaucoma, by using visual field (VF) test data as a functional measure of the disease.

Overall, they found that **Black/African American, Asian, and Hispanic patients presented at a younger age and with more severe disease than their White/Caucasian counterparts**. While Asian and Hispanic patients had a higher frequency of VF testing, Black/African American patients, despite their worse severity at presentation, were monitored less frequently and had greater progression of VF loss over time, compared to White/Caucasian patients. Similarly, non-English-speakers presented at an older age and with worse glaucoma severity than English-speakers.

Interestingly, language preference was found to partially explain the observed differences between ethnic groups, particularly among Asian and Hispanic patients.

Language preference may act as a significant barrier to timely access to healthcare

These results are an important contribution to the growing body of literature demonstrating ethnic disparities across various fields of medicine, and suggest that language preference may act as a significant barrier to timely access to healthcare. The role of other potential mediating factors, including socioeconomic status, medical comorbidities, environmental exposures, physician implicit bias, and structural racism, remain unclear. Additionally, the study design may limit generalizability to other geographic regions or specific glaucoma subtypes. Nevertheless, the study should motivate all those involved in glaucoma care to consider how ethnicity may influence both patient- and clinician-related factors relevant to the management of the disease. Halawa and colleagues have demonstrated that **differences in glaucoma metrics and outcomes between ethnic groups may not just be pre-destined in the genetic code, but may be due to addressable differences such as English language proficiency**. This offers hope that future interventions addressing these differences can reduce social inequalities that exist in glaucoma care.

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Prognostic factors

Prognostic Factors in Advanced Glaucoma



 Comment by **Sasan Moghimi**, La Jolla, CA, USA

99664 Factors threatening central visual function of patients with advanced glaucoma: a prospective longitudinal observational study; Sugisaki K, Inoue T, Yoshikawa K, Kanamori A, Yamazaki Y, Ishikawa S, Uchida K, Iwase A, Araie M,; *Ophthalmology* 2022; 129: 488-497

Eyes with advanced glaucoma have little residual reserve and small amounts of progression have important consequences affecting a patient's visual function and quality of life. Investigation of risk factors for further deterioration of functional damage in these patients is of clinical importance. This is especially true for changes in central vision as studies have shown that the visual field (VF) close to the fixation^{1,2} is more strongly associated with quality of life in glaucoma patients. However, information on the risk factors for further deterioration of central visual function in a large cohort of patients with advanced glaucoma is relatively scarce.

Sugisaki *et al.* published the results of a five-year prospective, observational study to identify risk factors for further deterioration of visual function in patients with advanced glaucoma whose IOP was clinically well controlled, paying particular attention to the changes in the central 10-2 VF. At baseline, all the patients had best corrected visual acuity (BCVA) of better than 20/40 and 24-2 VF of worse than -20 dB. Deterioration of 10-2 VF was defined by the presence of the same ≥ 3 points with negative total deviation slope -1 dB/year at $P < 0.01$ on ≥ 3 consecutive tests, deterioration of HFA 24-2 results by an increase ≥ 2 in the Advanced Glaucoma Intervention Study score on ≥ 2 consecutive tests, and deterioration of BCVA by an increase of ≥ 0.2 logarithm of the minimum angle of resolution (logMAR) on ≥ 2 consecutive tests.

A total of 175 eyes of 175 patients with a mean 24-2 VF and 10-2 VF of -25.9 and -22.9 dB, respectively, were included. **After five years, lower BCVA at baseline was associated significantly with further deterioration of 10-2 VF. Greater β -peripapillary atrophy (β -PPA) area-to-disc area ratio, use of systemic antihypertensive agents and lower BCVA were associated significantly with further deterioration of BCVA.**

Interestingly, **although the mean IOP during follow-up was 13.0 mmHg over the course of five years, 26.9% of the eyes showed deterioration of VF within the central 10, and 19.4% of the eyes showed VA deterioration attributable to glaucoma progression, which resulted in blindness in 4.6% of eyes.** The use of systemic antihypertensive agents and lower diastolic blood pressure were risk factors for further VA or 10-2 VF

deterioration in advanced glaucoma in the current report, which is consistent with prior studies that reported compromised local circulation as an important prognostic factor for central visual function in advanced glaucoma.^{3,4}

There are some limitations to this study. It should be noted that these results would not be applicable to eyes with advanced glaucoma whose VA was impaired to worse than 20/40 because of glaucomatous damage. Also, the mean IOP of Japanese population is lower than many other ethnic groups. In fact, despite the low mean IOP in this study, only 13 eyes from this cohort had undergone trabeculectomy, which shows that the results might not be generalizable to other ethnicities. Finally, the eyes in this cohort were very advanced with a mean 24-2 VF of worse than -25 dB. At this level, visual fields have a significant amount of variability and this limits the ability to detect progression.⁵ However, the specificity of the criteria they used was sufficiently high (99.99%) for the simulated stable HFA 10-2 VF series of eyes with advanced glaucoma.

Greater β -PPA area-to-disc ratio and lower BCVA could be used as simple prognostic factors for the central VA of eyes with advanced glaucoma

Overall, the present study suggests that greater β -PPA area-to-disc ratio and lower BCVA could be used as simple prognostic factors for the central VA of eyes with advanced glaucoma and that a medical history of hypertension should also be considered in the management of advanced glaucoma.

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News Flashes

- ★ The USPSTF has once again determined that the evidence is insufficient to recommend screening for primary open-angle glaucoma (POAG)
- ★ An important assessment for any new method is reliability and reproducibility, and the authors showed excellent results for their velocity and motion measures
- ★ Knowledge about TM biomechanics might tell us which patients would be more likely to exhibit transient IOP fluctuations
- ★ The results highlight the strong desire among some glaucoma patients for home monitoring solutions
- ★ The technology has to be significantly improved before human use as a sensing error of more than 40% has been mentioned
- ★ Despite the robust results, it is possible that the genetic variants used confer a risk of POAG through pleiotropic pathways
- ★ The main limitation of the study is the generalizability of the results
- ★ The current report also confirms that laser peripheral iridotomy provided a protective effect, but did not completely eliminate the risk of developing AAC in primary angle-closure eyes
- ★ The authors conclude that it is extremely rare to develop an AAC attack after dilation in LPI-treated eyes, and that it is reasonably safe to do so when needed
- ★ Patients who require routine dilation, such as those with diabetic retinopathy, may wish to consider LPI due to the additive risk with multiple dilations
- ★ This study confirms the increased risk of glaucoma post-vitrectomy and the need for increased monitoring of these patients
- ★ Metformin treatment was associated with a lower POAG risk (OR, 0.18; 95% CI, 0.08-0.41, $P < 0.001$) compared with no treatment with diabetes medication
- ★ LPI does not increase the risk for cataract formation
- ★ Language preference may act as a significant barrier to timely access to healthcare
- ★ Greater β -PPA area-to-disc ratio and lower BCVA could be used as simple prognostic factors for the central VA of eyes with advanced glaucoma

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Kugler Publications, Amsterdam, The Netherlands