Journal Highlights

Ophthalmology

Selected by Russell N. Van Gelder, MD, PhD

Demographics Affect Outcomes of Amblyopia Treatment February 2023

Using data from the IRIS Registry, **Repka et al.** previously reported on the residual VA deficits caused by amblyopia. In a follow-up study, they performed multivariable analysis of their findings to explore success rates for amblyopia treatment, adjusted for age, race/ethnicity, and type of health insurance. Although treatment was successful in more than 77% of young children and 55% of older children, the success rates were disproportionately lower for Black patients and for those covered by Medicaid.

For this work, the authors gathered IRIS Registry data for 3- to 12-year-old children who were new to the registry from 2013 through 2019. The main outcome was IRIS-50, a composite endpoint representing the effectiveness of amblyopia treatment. The IRIS-50 measure helps to capture denser amblyopia at baseline and accounts for unilateral amblyopia associated with strabismus and/or refractive error. Although it was designed for younger children, the authors also utilized it for 8- to 12-year-olds. Types of insurance were categorized as private, military, or Medicaid.

Prior to analysis, VA was converted to logMAR units. IRIS-50 success was defined as satisfying at least one of three criteria: 1) corrected interocular VA difference of <.23 logMAR within three to 12 months of initial amblyopia diagnosis; 2) corrected VA improvement of at least 3 lines (\geq .30 logMAR) in the amblyopic eye in the same period; or 3) final VA of 20/30 or better (\leq .18 logMAR) in the amblyopic eye.

Among the younger cohort (n = 18,841), amblyopia was treated successfully in 77.3%. Outcomes were successful in 55.5% of the 8- to 12-year-olds (n = 9,762). Multivariable analyses of the younger cohort showed that, relative to White patients, the likelihood of treatment success was substantially lower for Black children (OR, .71). The ORs for Hispanic/Latino and Asian children were .93 and .97, respectively.

Compared with private insurance, Medicaid conferred significantly lower odds of treatment success (OR, .65). Among 8- to 12-yearolds, the odds of treatment success were lower for Blacks (OR, .81) and higher for Hispanics (OR, 1.16) than for

Whites. As in the younger cohort, older children with Medicaid were less likely to have a successful outcome (OR, .84). For both cohorts, military insurance was comparable to private insurance with respect to treatment outcomes.

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noteworthy given that nearly 50% of U.S. children are covered by Medicaid, said the authors. They recommend developing strategies to improve the success of amblyopia treatment, especially for children who are Black and/or covered by Medicaid.

Alcohol Consumption Raises Risk of Exfoliation Glaucoma February 2023

Studies of the relationship between alcohol and exfoliation glaucoma are limited by their small size and inconsistent findings. **Hanyuda et al.** set out to address the knowledge gap and determine if alcohol consumption affects the risk of confirmed or suspected exfolia-

> tion glaucoma (XFG/XFGS). They found that both shortand long-term consumption of alcohol raised the risk of exfoliation glaucoma.

> This prospective longitudinal study included nearly 200,000 people who had participated in the Nurses' Health Study (1980-2018), the Health Professionals Follow-Up Study (1986-2018), and the Nurses' Health Study II (1991-2019). All had completed follow-up

questionnaires biennially; data were collected on diet, lifestyle, and disease outcomes, including glaucoma. At each two-year observation interval, only the participants who were at least 40 years old, free of glaucoma, and had available data for eye exams and diet were permitted to contribute person-time to later periods of the study. Cumulative averages were determined for total alcohol intake (primary exposure) and intake of specific beverages (beer, wine, and liquor) at intervals of two to four years. The main outcome measure was incident XFG/XFGS, confirmed by medical records. Per-eye Cox proportional hazards models, accounting for inter-eye correlations, were applied to estimate multivariate-adjusted relative risks (MVRRs) and 95% CIs.

During the 6,877,823 eye-years of follow-up, 705 eyes of 507 patients were found to have XFG/XFGS, and high levels of total alcohol consumption significantly boosted an individual's risk. The MVRR for XFG/XFGS status for cumulatively averaged alcohol consumption of ≥ 15 g/day (vs. nondrinking) was 1.55 (95% CI, 1.17-2.07; p = .02 for trend). Both short- and longterm alcohol intake significantly raised the risk of XFG/XFGS. The strongest associations with cumulatively averaged alcohol intake were within the four years preceding documentation of XFG/XFGS (MVRR \geq 15 g/day vs. nondrinking; relative risk, 1.65; 95% CI, 1.25-2.18; p = .002 for trend).

The type of alcoholic beverage also affected XFG/XFGS risk. Relative to participants who abstained from alcohol, risk was elevated for those with weekly intake of at least 3.6 beverages of beer (MVRR, 1.26; 95% CI, 0.89-1.77), wine (MVRR, 1.30; (95% CI, 1.00-1.68), or liquor (MVRR, 1.46; 95% CI, 1.15-1.85). There was no apparent link between XFG/XFGS status and age, residential latitude, or intake of folate or vitamin A.

Although the underlying mechanism between alcohol consumption and exfoliation glaucoma remains unclear, the researchers speculated that folate deficiency may play a role, as suggested by previous smaller investigations.

Uveitis Risk After COVID-19 Vaccination

February 2023

Some evidence suggests that a temporal relationship exists between uveitis and common vaccinations, including those for influenza, hepatitis B, and measles/mumps/rubella. Although the immunopathologic mechanisms of vaccine-associated uveitis (VAU) are unknown, it has been proposed that the immune response stems from vaccine adjuvants, molecular mimicry between vaccine-peptide fragments and uveal self-peptides delayed hypersensitivity, or subsequent immune complex deposition. Reports of uveitis after SARS-CoV-2 have been climbing; as of June 2022, more than 70 studies had been published. To learn more, Singh et al. analyzed data from the CDC's Vaccine Adverse Event Reporting System (VAERS). Overall, they found that the rates of postvaccine uveitis were low for all three COVID vaccines approved for use in the United States.

For this research, the authors mined VAERS data to identify people who received a uveitis diagnosis after inoculation with the Pfizer-BioNTech, Moderna, or Janssen vaccines during the 17-month study period. They performed descriptive analyses of demographic and clinical data, then looked for correlations between each vaccine and continuous and categorical variables. Post hoc one-way analysis of variance was applied to explore the postvaccine time to uveitis in relation to age, vaccine type, and vaccine number. They also calculated 30-day VAU risk.

Main outcome measures were the estimated global crude reporting rate, observed-to-expected ratio of VAU, ocular and systemic presentations, and the interval between inoculation and uveitis onset.

More than 2 billion COVID-19 vaccines were administered worldwide during the study period (80.7% Pfizer-BioNTech, 16.8% Moderna, 2.5% Janssen). The overall rate of adverse vaccine-related events was .06%. There were 1,094 cases of VAU; the rates were .57, .44, and .35 per million vaccine doses with the Pfizer-BioNTech, Moderna, and Janssen vaccines, respectively. The observed-to-expected VAU ratio was comparable for Pfizer-BioNTech (.023), Moderna (.025), and Janssen (.027). The mean age of patients with VAU was 46.2 years, and 68.7% were women. Most cases of VAU were reported after the initial dose (41.32%) and within one week of initial vaccination (54.02%). The mean interval between vaccination and uveitis onset was significantly longer (p < .0001) for recipients of the Moderna vaccine (21.22 days; vs. 11.42 days for Pfizer-BioNTech and 12.69 days for Janssen). Post hoc work showed that VAU onset was much faster after Pfizer-BioNTech, and the 30-day risk also was highest with this vaccine.

The authors note that the VAERS reporting mechanism is passive and may underreport events. Nonetheless, these results suggest that absolute VAU risk is low after COVID-19 vaccination, said the authors. Although the findings corroborate a possible temporal association between VAU and the vaccines studied, the authors emphasized that more research is needed to determine the relevant immunologic mechanisms.

-Summaries by Lynda Seminara

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MHS

Ab Interno Versus Ab Externo Placement of the Xen45 Gel Stent

January/February 2023

Ruda et al. set out to compare the effectiveness of ab interno versus ab externo placement of Xen45 gel stents in patients with refractory open-angle glaucoma (OAG). They found that the off-label ab externo approach produced comparable outcomes to the more established ab interno placement.

For this single-center retrospective comparative case series, the researchers evaluated 89 patients (89 eyes) with OAG. Group 1 (n = 29) underwent ab interno positioning of the stent, while group 2 (n = 60) had ab externo placement. All were treated by the same surgeon between 2017 and 2020. Outcomes were recorded at each follow-up visit from post-op day 1 up to 24 months (median follow-up, 12 and eight months for group 1 and 2, respectively). The primary outcome measure



At eight months, success rates were 72% in group 1 and 74% in group 2. There was no difference in the median time to failure between the groups (p = .98). Complication rates and bleb revision rates were comparable between both groups, with approximately one-third of patients developing complications and one-fourth requiring bleb needling, regardless of group.

With regard to IOP and medication usage, the findings were as follows:

• Mean baseline IOPs were 22.8 ± 7.5 mm Hg on $3.8 \pm .9$ medications in group 1 and 25.3 ± 10.7 mm Hg on 3.7 ± 1 medications in group 2.

• At the last follow-up among eyes with surgical success, the mean IOPs were $12.5 \pm 3.8 \text{ mm Hg on } 2.2 \pm 1.4 \text{ medications in group 1 and } 12.2 \pm 2.1 \text{ mm Hg on } 1.8 \pm 1.3 \text{ medications in group 2.}$

The researchers noted limitations of the study, including its retrospective design, with some patients lost to follow-up. In addition, the surgeon started with the ab interno approach and adopted the ab externo technique later on, thus introducing the possibility of bias. Finally, given the sample size, this study was underpowered for direct comparison in surgical success rates between the two approaches. Larger studies with longer follow-up are needed. —Summary by Jean Shaw

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Extramacular Drusen and AMD Progression

February 2023

Domalpally et al. set out to assess the prevalence of extramacular drusen and their role in the progression of age-related macular degeneration (AMD).

They found that extramacular drusen are commonly observed in eyes with AMD and are more frequent with an increased drusen load within the macula. However, in eyes with intermediate AMD, extramacular drusen do not confer any additional risk of progression to late AMD.

For this retrospective analysis of data from the Age-Related Eye Disease Study 2 (AREDS2), the researchers evaluated 4,168 eyes of 2,998 participants. All had intermediate AMD in one or both eyes. The presence of drusen outside the macular grid was documented at all study visits via three-field 30-degree color photographs. The characteristics of the extramacular drusen were then compared with those of drusen within the macula. The main outcome measure was the rate of progression to late AMD (both geographic atrophy and neovascular AMD).

All told, extramacular drusen were observed in 3,634 eyes (87%). There was no difference in participant age, sex, smoking status, diabetes, hypertension, angina, statin use, and AREDS2 randomization arm between those with and without extramacular drusen (all p > .05), and the mean VA was similar at 79.5 and 78.4 letters, respectively. With regard to drusen area (DA), as based on drusen circles, this was small (<.5 mm²) in 50.3% of affected eyes and ≥1 DA in only 14.5% of affected eyes. Pigment changes were observed in only 3.6% of eyes in the extramacular region.

During five years of follow-up, progression to late AMD was observed in 1,259 eyes (35.8%) with and in 178 eyes (33.3%) without extramacular drusen. Progression to GA, central GA, and neovascular AMD in eyes with and without extramacular drusen was 19.4% versus 17%, 9.7% versus 8.2%, and 19.1% versus 19.9%, respectively.

In their discussion, the authors noted that, in eyes with intermediate AMD, extramacular drusen "are not an independent risk factor in and do not provide added risk to previously identified risk factors for progression to late AMD. The role of drusen in the midperiphery and peripheral retina remains to be studied."

—Summary by Jean Shaw

Ophthalmology Science

Selected by Emily Y. Chew, MD

Predicting Conjunctivitis Outcomes via Genome Sequencing and Machine Learning December 2022

To what degree do genetic variants determine clinical outcomes in adenoviral conjunctivitis? Nakamichi et al. explored this question via whole-genome viral sequencing and found that adenovirus (AdV) type D8 has three prevalent molecular substrains that predispose to varying risk of developing subepithelial infiltrates (SEIs), a complication of viral conjunctivitis.

For this study, the researchers evaluated banked conjunctival swab samples collected during the BAYnovation Study, a previously conducted study of a compound to treat adenoviral keratoconjunctivitis. They purified DNA from the swabs of 96 patients with AdV D8positive samples and subjected it to viral sequencing. Viral variants were identified and correlated with clinical outcomes. Two machine learning models were independently trained to predict clinical outcomes using polymorphic sequences. The main outcome measures were viral DNA sequence and development of SEIs.

Full genome reconstructions were obtained for 71 AdV D8–positive samples. A total of 630 single-nucleotide variants were identified, including 156 missense mutations. Sequence clustering revealed three previously unappreciated viral clades within the AdV D8 type. The likelihood of developing SEIs differed between the clades, ranging from 46% to 83%. With regard to the two machine learning models, using a newly sequenced validation set of 16 cases, the models proved capable of predicting SEI development with >97% accuracy.

These findings add to prior evidence that sequence variants influence disease severity in adenoviral conjunctivitis, the researchers said. In addition, they noted, the use of machine learning may be applicable to other questions in viral pathogenesis—including the "determination of oncogenic potential of human papilloma viruses, understanding risks for reactivation of varicella zoster causing shingles, or understanding determinants of outcomes from SARS-CoV2." —Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

PCP Familiarity and Compliance With Guidelines for Eye Exams February 2023

Moustafa et al. explored the degree of familiarity that primary care physicians (PCPs) possess in regard to the Academy's *Preferred Practice Pattern* (*PPP*) guidelines on the frequency of comprehensive eye examinations. They also looked at PCP opinions and practices pertaining to counseling and referring of patients for eye exams. They found that the levels of familiarity and compliance varied widely.

For this research, a survey to be completed anonymously was emailed to clinicians who had earned an MD, DO, physician assistant (PA), or nurse practitioner (NP) degree. Residents with an MD or DO were included. The survey was designed to be self-administered electronically. Its overarching domains were knowledge of the 2015 PPP guidelines regarding comprehensive eye exams, attitudes toward the guidelines, and counseling/referral practices for eye exams. Also included were five clinical scenarios for which respondents noted when the patient should see an eve specialist.

Of the 336 PCPs invited, 216 completed the survey (response rate, 64.3%). Only 10.6% of PCPs could state some of the guidelines, and nearly 64% were completely unaware of them. In regard to counseling patients about comprehensive eye exams, 15.4% "always" did so, 48.1% "usually" did so, and 36.5% replied "seldom" or "never." With regard to patients with diabetes, nearly 91% of PCPs correctly referred those with type 2 diabetes for a comprehensive eye exam at the time of diagnosis, and 77.8% of PCPs prematurely referred patients with newly diagnosed type 1 diabetes. Approximately one in seven PCPs would refer a patient with family history of glaucoma only if visual or other ocular symptoms developed.

Overall, PAs and NPs were most likely to recommend unnecessary comprehensive eye exams for low-risk individuals (p = .009). Relative to other providers, residents counseled patients less often (p = .003) and were less likely to be familiar with the practice guidelines (p = .026) or to recommend appropriate follow-up for patients with a family history of glaucoma (p = .004).

The primary care workforce is a key partner in accurately identifying patients who need specialized eye care. Boosting awareness of practice guidelines among PCPs may help improve the referral process, said the authors.

Cataract Surgery Improves BCVA in Patients With RP February 2023

The photoreceptor loss that occurs with

retinitis pigmentosa (RP) may cause night blindness, concentric loss of peripheral visual fields, and loss of central vision. The most common RP-related anomaly of the anterior segment is cataract, which forms at a relatively young age in patients with RP. Although the usual treatment is surgical cataract extraction plus IOL implantation, the visual prognosis following surgery is uncertain for these patients. Moreover, patients with RP are susceptible to intraoperative phototoxic retinal damage, cystoid macular edema (CME), and weakened lens zonules-all of which can adversely affect vision and raise the risk of complications. Even so, exploring factors that influence visual outcomes in patients with RP who undergo cataract surgery may help physicians to select candidates who are most likely to benefit from the procedure. Nguyen et al. retrospectively explored outcomes of cataract surgery in patients with RP. They found that BCVA improved significantly in most patients.

For this work, the authors gathered data from European academic centers with expertise in performing cataract surgery for RP. They extracted relevant clinical data from patients' medical records, including pre-, intra-, and post-op information. Excluded from the analysis were patients who did not receive an IOL or whose surgery involved both the anterior and posterior segment (e.g., phacovitrectomy). The main outcome measure was change in BCVA from pre-op status.

Overall, 295 eyes (226 patients) met the inclusion criteria. The mean age at first-eye surgery was 56.1 ± 17.9 years. Mean BCVA improved significantly after the surgery, from 1.03 to .81 log-MAR (20/214 to 20/129) in the first eye (p < .001) and from .80 to .56 logMAR (20/126 to 20/73) in the second eve (p < .001). Marked BCVA improvement, defined as a BCVA change from baseline of $\geq 0.3 \log MAR$, occurred in 39% of patients. Patients with poorer vision preoperatively had the best odds for marked improvement. The most common intraoperative complications were zonular dialysis (n = 15; 5%) and CME exacerbation (n = 14; 5%). Postop posterior capsular opacification was observed in 38% of eyes.

The authors recommend that pre-op evaluations include identifying CME and the potential for zonular insufficiency. They hope that spectral-domain OCT and patient-reported outcomes will be included in future studies because the findings may be useful adjuncts to assess visual outcomes.

-Summaries by Lynda Seminara

JAMA Ophthalmology

Selected and reviewed by Neil M. Bressler, MD, and Deputy Editors

Perceptions of Parental Leave Among Practicing Ophthalmologists

January 2023

Once ophthalmologists have finished training, how do they handle parental leave? **Kalra et al.** set out to evaluate perceptions of parental leave policy among North American ophthalmologists currently in practice. They found mixed awareness of and support for what are commonly known as "stopthe-clock" policies.

For this study, the researchers used a 19-item anonymous nonvalidated



A convenience sample of practicing ophthalmologists was obtained using social media, residency program coordinators, and listservs. Data were collected from May to June 2022. Of 186 respondents, 105 (56.5%) identified as female, 110 (59.1%) were in private practice, 156 (83.9%) had children, and 133 (71.5%) were one to 20 years out from training. Awareness of stop-the-clock policies varied: for instance, among academic physicians, 56 (73.7%) and 49 (64.5%) were unaware if their institution had a policy for tenure review or promotion review, respectively. Support varied as well: of 171 participants who indicated their attitudes about these policies, 78 (45.6%) thought the policies should be optional, 39 (22.8%) thought they should be required, 31 (18.1%) thought they should be removed, and 23 (13.5%) indicated "other."

Comfort levels with taking parental leave varied: for instance, among 155 respondents, 33 (21.3%) were concerned about negative workplace reactions when taking leave, 88 (56.8%) were not, and the remainder were neutral. All female respondents (n = 105) either would choose to take leave or were not sure, versus 58 of the 71 male respondents (81.7%). Primary stressors associated with taking leave were patient care/coverage and salary concerns, followed by peer perception, referrals, promotions, and research.

In their discussion, the authors noted several limitations of this study, including small sample sizes. Nonetheless, they said, the results provide an overview of some of the concerns and considerations inherent in taking parental leave from active practice. (Also see related commentary by Julia A. Haller, MD, in the same issue.)

Ganglion Cell Complex Thinning and Central VF Loss January 2023

Mahmoudinezhad et al. set out to investigate the association between ganglion cell complex (GCC) thinning and the rate of central visual field (VF) loss. They found that rapid GCC thinning during a follow-up period of 4.7 years was associated with faster rates of central VF decline.

This retrospective cohort study involved 139 patients (202 eyes) who had primary open-angle glaucoma (POAG; n = 154 eyes) or who were glaucoma suspects (n = 48 eyes). All had participated in the Diagnostic Innovations in Glaucoma Study and the African Descent and Glaucoma Evaluation Study and were followed from June 18, 2014, to Jan. 11, 2019.

Data analysis for this study occurred in March 2022. Initial rates of GCC thinning were obtained from global GCC thickness values of the first three OCT scans during the original studies. To quantify rates of central VF loss, the researchers used univariable and multivariable linear mixed-effects models to assess the change in central (10-2) VF mean deviation (MD) during follow-up. Eyes were categorized as slow or fast progressors based on rates of GCC thinning.

During the first 1.8 years of followup, the rate of GCC change was -.56µm per year (95% CI, -.66 to -.46 µm/ year). All told, 163 eyes (80.7%) were slow progressors, and 39 (19.3%) were fast progressors, with GCC rates of thinning of -.3 µm/year and -1.6 µm/ year, respectively. Rapid initial GCC deterioration was associated with faster subsequent rates of central VF MD worsening: the rates of worsening among slow and fast progressors were -.10 dB/ and -.34 dB/year, respectively.

As all of the patients were participating in clinical trials, the results of this analysis may be conservative—that is, the fast progressors may have preferentially received intensified IOP-lowering treatment. Nonetheless, the authors said, these results support the use of macular imaging for monitoring patients at the time of diagnosis as well as for monitoring the rate of GCC thinning.

Ophthalmic Burden of Mpox

January 2023

In a primer on the 2022 outbreak of Mpox, **Kaufman et al.** compiled clinically relevant information regarding Mpox and its ophthalmic manifestations. They report that Mpox-related ophthalmic disease (MPXROD) may be associated with severe ocular and visual morbidity, and they note that ophthalmologists may play an important role in the diagnosis and management of the viral disease.

Highlights of the primer include the following:

• Virology. The Mpox virus (MPXV) is a member of the genus *Orthopoxvi-rus*, which includes the variola, vaccinia, and cowpox viruses. The incubation period of MPXV is typically seven to 14 days but may be up to 21 days.

• Clinical presentation. MPXV infection typically begins with a prodromal fever, followed two to three days later by skin and oropharyngeal/mucosal eruptions. Lymphadenopathy may be noted. The number of skin lesions varies widely, from fewer than 25 to more than 500. Other complications include bronchopneumonia, gastroenteritis, and encephalitis.

• Ophthalmic manifestations. Ocular findings may include external and ocular surface lesions. Eyelid margin lesions occurring in association with conjunctivitis have been reported. Corneal disease in the setting of MPXV can include ulcerative keratitis, immune stromal keratitis, and neurotrophic keratitis. Persistent MPXROD may be present as late as six weeks from the onset of MPXV and can be severe.

• **Ophthalmic treatment.** There is no FDA-approved topical ophthalmic antiviral agent specific for MPXV infection, although the CDC recommends considering topical trifluridine use in cases of MPXROD. Generous topical lubrication remains an important component of supportive ocular therapy, and topical antibiotics for corneal ulceration and epithelial defects may be important to prevent bacterial superinfection.

• Corneal transplantation concerns. There are no reported cases of Mpox transmission by corneal transplant to date. However, patients with active Mpox conjunctivitis can shed virus, and the Eye Bank Association of America has developed recommendations regarding corneal transplantations.

—Summaries by Jean Shaw

Other Journals

Selected by Prem S. Subramanian, MD, PhD

RNA Profiling of TAO Orbital Connective Tissue

Investigative Ophthalmology & Visual Science 2022;63(12):27

Ye et al. looked at the molecular mechanisms of two clinical subtypes of thyroid-associated ophthalmopathy (TAO): type I (mainly fat) and type II (mainly muscle). Using high-throughput RNA sequencing (RNA-seq), they explored the expression profiles of circular RNAs (circRNAs). They found differences between the two subtypes and identified signaling pathways that may contribute to TAO pathogenesis and thus could be promising diagnostic and therapeutic targets.

In this study, the high-throughput RNA-seq was performed on six pairs of type I and type II samples of orbital connective tissue from patients with TAO. In another three pairs of type I and type II samples, the expression levels of circRNA and messenger RNA (mRNA) were measured by quantitative real-time polymerase chain reaction (qRT-PCR). Bioinformatics predictions were used to construct a circRNA-microRNA (miRNA) network. Subsequently, a protein-protein interaction network was constructed based on differential mRNA expression, and hub genes were determined from Cytoscape software. To determine circRNA function, pathway and functional enrichment analyses were performed. Western blotting was applied to evaluate lentiviral-mediated overexpression of hsa_circ_0007006 and the relationship between hsa_circ_0007006 and COL1A1 or MMP2. It also was used to identify differential pathways.

Findings demonstrated that RNAseq predicted 7,489 circRNAs and 15,803 mRNAs, which included 94 upregulated and 76 downregulated circRNAs and 488 upregulated and 138 downregulated mRNAs. The RNA-seq data were validated by qRT-PCR analysis of seven dysregulated circRNAs and two major mRNAs. The competing endogenous RNA network comprised seven circRNAs, 23 mi-RNAs, and 262 mRNAs. Functional analysis showed that overexpression of hsa_circ_0007006 led to decreased expression of COL1A1 and MMP2. It also revealed differences in the activation level of the relaxin signaling pathway between the TAO subtypes, which was significantly higher in type II.

According to the authors, the competing endogenous RNA analysis of potential target genes emphasizes the relationship between dysregulated circRNAs and the clinical subtype of TAO, which may provide a new perspective for research on TAO. The authors have begun exploring the indepth mechanism and overall effect of hsa_circ_0007006 and relaxin signaling in TAO, which could be potential biomarkers and therapeutic targets for future studies, they said.

Measuring Vascular Health via Al Retinal Vasculometry

British Journal of Ophthalmology 2022;106(12):1722-1729

Rudnicka et al. developed and validated risk models based on artificial intelligence (AI) analysis of retinal vessel images and found that AI-enabled retinal vasculometry (RV) is an effective noninvasive method to predict circulatory mortality, stroke, and heart attack. Its performance was on par with that of current risk-scoring systems. Future formal assessment with experimental evidence will help determine the clinical utility, said the authors, who emphasized that the advantages of RV, including the low cost, could make it attractive for community screening programs.

For this work, retinal vessel analysis was performed on images from records of patients listed in the U.K. Biobank and from participants of the European Prospective Investigation into Cancer-Norfolk (EPIC-Norfolk). Data extracted from images included retinal arteriolar and venular width, area, and tortuosity. Predictive models were developed from the Biobank dataset, using multivariable Cox proportional hazards regression for circulatory mortality, incident stroke, and myocardial infarction (MI), which were validated in the EPIC-Norfolk dataset. The authors compared the performance of a simple model based on RV, age, smoking status, and medical history with that of the Framingham risk score system for incident stroke and incident MI. They also looked at the utility of adding RV to the Framingham system.

Altogether, they developed prognostic models from 65,144 U.K. Biobank participants (mean age, 56.8 years; median follow-up, 7.7 years), which they validated by data for 5,862 EPIC-Norfolk participants (mean age, 67.6 years; median follow-up, 9.1 years). To determine model performance, they applied optimism-adjusted calibration, C statistics, and R2 statistics. The primary outcome measure was circulatory mortality as defined by ICD-10 codes.

The prediction models for circulatory mortality had optimism-adjusted C statistics ranging from .75 to .77 and R2 statistics ranging from .33 to .44. For stroke and MI, adding RV to the Framingham score system did not improve the model's performance. However, the simple RV model performed at least as well as the Framingham system.

The authors emphasize that their system is focused on the retinal tree and offers detailed quantification of vasculometry, making it suitable for large populations. With further research, this simple low-cost method could become a key adjunct or standalone assessment tool.

— Summaries by Lynda Seminara