

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Natural History of Geographic Atrophy Secondary to AMD

June 2020

Despite termination of the phase 3 lampalizumab clinical studies in 2017 due to insufficient efficacy, the Proxima A and B portions of the trials have yielded important data on the relationship between visual function and worsening geographic atrophy (GA) from age-related macular degeneration (AMD). In a comparative analysis, **Holekamp et al.** found that the natural history studies spotlight the major functional loss and rapid progression that are common with GA, even in early stages of the disease.

Between May 2015 and February 2017, three cohorts were involved in these prospective studies:

- patients with bilateral GA and no choroidal neovascularization (CNV) in either eye (Proxima A cohort; 295 participants)
- patients with GA but no CNV in the study eye plus CNV in the other eye with or without GA (Proxima B/fellow-eye cohort; 168 participants)
- patients with GA only in the study eye and no CNV in either eye (Proxima B/fellow-eye intermediate AMD cohort; 32 participants)

Follow-up duration varied because

of early termination of studies. The primary outcome was the mean change in GA lesion area in the study eyes.

At 24 months, the adjusted mean (standard error) change in lesion area was 3.87 (0.15) mm² in the Proxima A cohort, 3.55 (0.16) mm² in the fellow-eye CNV cohort of Proxima B, and 2.96 (0.25) mm² in the fellow-eye intermediate AMD cohort of Proxima B. In

all three groups, visual function decreased from baseline to month 24. Adjusted mean changes in corrected visual acuity (VA) were –13.88 (1.40) in Proxima A, –9.49 (1.29) in the fellow-eye CNV cohort of Proxima B, and –11.48 (3.39) in the fellow-eye intermediate AMD cohort. Mean changes in low-luminance VA were –7.65 (1.20), –7.57 (1.26), and –8.37 (3.02), respectively. In the intermediate AMD cohort, 30% of patients had conversion to GA in the fellow eye, and 6.7% had conversion to CNV by 12 months.

The authors cautioned that the difference in progression rates between Proxima A and B at 24 months may relate to the variability in GA area at baseline. The high rate of conversion from unilateral to bilateral GA within 12 months underscores the stealth of the disease and suggests it may be more

rapid—and have greater effects on quality of life—than previously thought.

LASIK Versus SMILE for Myopic Conditions

June 2020

LASIK remains the most popular refractive treatment for myopia and myopic astigmatism, but small-incision lenticule extraction (SMILE) is increasing in popularity. **Ang et al.** performed a paired-eye noninferiority trial to compare the two procedures objectively. They found that both had good refractive predictability and similar safety indices at three and 12 months.

This prospective masked study was conducted at the Singapore National Eye Centre. Consecutive patients (recruited from May 2014 to November 2016) were assigned randomly to receive SMILE in one eye and LASIK in the other, with both procedures provided on the same day by a single surgeon. The prespecified primary outcome was refractive predictability three months after surgery; secondary outcomes included efficacy and safety results.

Ultimately, 70 eligible patients were assessed (mean age, 28 years; all Asian; 64% female). Preoperatively, there was little difference in spherical equivalence (SE) between eyes (-05.3 ± 1.8 D vs. -5.2 ± 1.7 D; $p = .87$). Both procedures had high three-month predictability: 99% of SMILE eyes and 97% of LASIK eyes achieved SE within ± 1 D of attempted correction. However, the high performance of both procedures suggested that a noninferiority margin



of ± 1 D was too great to offer a meaningful distinction. Additional analysis looking at a margin of ± 0.5 D indicated that at three months, 87% of SMILE eyes and 92% of LASIK eyes achieved SE within ± 0.5 D of attempted correction.

Uncorrected distance visual acuity (UDVA) of 20/40 or better was achieved in 100% of both groups, and UDVA of 20/20 or better was attained in 84% of SMILE eyes, versus 87% of LASIK eyes. Through 12 months, similarity was sustained in predictability (SE within ± 1 D of attempted correction: 99% for both SMILE and LASIK), efficacy (UDVA of 20/20 or better: 85% vs. 83%), and safety (index: 1.15 ± 0.20 for both).

The authors noted that neither procedure resulted in major complications. Nevertheless, they emphasize that SMILE is a challenging procedure that necessitates additional surgical training. (Also see related editorial by Thomas M. Lietman, MD, in the same issue.)

Selective Laser Trabeculoplasty Outcomes in the United Kingdom

June 2020

Selective laser trabeculoplasty (SLT) successfully reduces intraocular pressure (IOP) in patients with open-angle glaucoma and ocular hypertension, especially those who are treatment-naïve. To determine whether these results translate to clinical practice, Khawaja et al. analyzed electronic health records gathered from five U.K. ophthalmology teaching centers. They found that although most eyes with elevated IOP responded to SLT in the short term, treatment failed in three-quarters of eyes within two years, and many patients eventually needed more glaucoma medication or another procedure.

For this study, the researchers de-identified medical records and reviewed them for demographics, procedures, outcomes, and factors linked to treatment success. The main outcomes were changes from baseline in IOP and number of glaucoma medications. A Kaplan-Meier probability analysis was used to determine treatment success. Failure was defined as any of the following: need for another procedure

(including repeat SLT), two consecutive visits with IOP > 21 mm Hg or IOP reduction $< 20\%$, or two consecutive visits with a higher number of glaucoma medications than at baseline.

Altogether, 831 patients met the eligibility criteria. The mean follow-up time was 19.4 months (range, 3-67 months). In the 12- to 18-month window (439 eyes), the mean change in IOP was -4.2 mm Hg; in the subsequent 12 months (243 eyes), it was -3.4 mm Hg (both $p < .0001$). The mean increases in glaucoma medications per eye were 0.13 ($p = .007$) and 0.20 ($p = .005$), respectively. The probability of treatment success was 70% at six months but declined to 45%, 34%, 27%, and 18% by months 12, 18, 24, and 36, respectively. IOP > 21 mm Hg at baseline was associated with a 33% reduction in the risk of failure (hazard ratio, 0.67; $p < .001$). Age, sex, baseline visual field mean deviation, and use of IOP-lowering drugs had no association with successful outcomes.

Although the success rate for SLT was 70% at six months, it dropped to 27% by 24 months. The decline in visual field mean deviation in the later timeframes supports common wisdom that the effects of treatment typically slow and may lead to disease progression. The authors ascribed the link between baseline IOP and treatment success to a likely floor effect with SLT, indicating that the procedure may be better suited for ocular hypertension or high-tension primary open-angle glaucoma than for normal-tension glaucoma.

—Summaries by Lynda Seminara

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MHS

Evaluation of Micropulse Cyclophotocoagulation

May/June 2020

Kaba et al. set out to evaluate whether micropulse cyclophotocoagulation (MP-CPC) is a safe and effective treatment for treating ocular hypertension (OHT) and glaucoma. They found that it is, with patients experiencing a mean reduction in intraocular pressure (IOP)

of 20% or more over baseline at the one-year mark. However, they also found that patients in certain subgroups— notably those with normal-tension glaucoma or a baseline IOP of ≤ 21 mm Hg—had a more limited response.

The researchers assessed the results of 399 MP-CPC surgeries (399 eyes of 214 patients) performed between May 2016 and May 2018 in Canada. The main outcome measure was IOP; secondary outcomes included use of glaucoma medications and ocular adverse effects.

Patients were evaluated at four points postoperatively. At baseline, mean IOP was 19.8 ± 7.4 mm Hg; reductions in IOP were 22.7%, 20.2%, 20.7%, and 23.7% at the one-, three-, six-, and 12-month evaluations, respectively ($p < .0001$ for all timepoints). All told, 68% of the study eyes achieved a $\geq 20\%$ mean reduction in IOP from baseline. However, the mean IOP reduction in eyes with normal-tension glaucoma was 7.6% from baseline. In addition, a subanalysis based on IOP stratification found that mean IOP reduction was 32% at post-op month 1 for those eyes with a baseline IOP of > 21 mm Hg, versus 17.1% for those with a baseline IOP ≤ 21 mm Hg.

With regard to secondary outcomes, more than two-thirds of the eyes were being treated with topical glaucoma medications preoperatively. This stayed roughly the same throughout the study. However, of the 25 patients initially on oral glaucoma medications, 18 (72%) were able to discontinue their use by the 12-month mark. The most common adverse events were vision loss, IOP spike, and cataract. Eight patients needed a minimally invasive glaucoma surgery procedure during the study.

—Summary by Jean Shaw

Ophthalmology Retina

Selected by Andrew P. Schachar, MD

Safety of FA in Children

June 2020

Chee et al. evaluated the safety of fluorescein angiography (FA) in pediatric patients. They found that FA was not associated directly with systemic or

ocular adverse events. In addition, they found that younger children were more likely to undergo inpatient FA examinations, while those older than age 4 were more likely to be evaluated in an outpatient setting.

For this retrospective study, the researchers reviewed the charts of 115 patients who were treated between January 2010 and December 2015. Patients with fewer than 24 hours of documented follow-up were excluded.

A total of 214 FA exams were performed. Of these, 129 took place in 60 outpatients, and 85 occurred in 65 inpatients. (Ten patients underwent both in- and outpatient exams.) The researchers reviewed a number of intra- and perioperative physiological parameters, including heart rate, blood pressure, and oxygen saturation. Peri-injection effects of FA were evaluated by a two-tailed paired t-test comparison of mean five-minute pre- and postinjection physiological data.

The results showed a significant difference in patient age for inpatient exams (mean, 2.5 years; range, 4 weeks to 16.2 years) and outpatient evaluations (mean, 10.7 years; range, 3.8 to 18.4 years). No significant systemic or ocular adverse events were noted within 24 hours of FA, whether it was given on an in- or outpatient basis.

—*Summary by Jean Shaw*

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Ocular Outcomes of Alcohol Exposure in Utero

June 2020

Alcohol exposure in utero has been linked to growth and learning deficits, facial abnormalities, and organ damage. It also can cause eye problems such as optic nerve hypoplasia (ONH) and abnormal retinal configuration, although few studies of fetal alcohol spectrum disorder (FASD) have fully described the ocular aspects of the disorder. Gyllencreutz et al. examined individuals with FASD; they found that refractive errors, strabismus, and fundus abnormalities persisted from

childhood through to early adulthood.

The authors enrolled 30 children who were adopted from Eastern European countries by families in Sweden. The children were diagnosed with FASD at a mean age of 7.9 years and examined by a multidisciplinary team between 2000 and 2002. Thirteen to 18 years later, the same team performed follow-up exams; at this point, the patients' mean age was 22 years.

Visual acuity (VA) and refractive results were as follows:

- During childhood, median VA was 20/32 in the right eye and 20/32 in the left (0.2 logMAR for both). Median refraction was +0.88 D in the right eye (range, -8.75 to +4.75) and +1.25 D (range, -9.38 to +5.25) in the left.
- During adulthood, median VA was 20/22 in the right eye and 20/20 in the left (0.05 logMAR in the right and 0.0 in the left). Median refraction was -0.25 D in both eyes (right eye range, -12 to +2.75; left eye range, -13.25 to +2.63).
- Thirteen children (40%) and 14 adults (47%) had astigmatism ≥ 1 D.

In other results, defective stereoacuity (>60 arc second) was apparent in 20 children (67%) and 22 adults (73%); and 12 children (40%) and 13 adults (43%) had heterotropia. Also noted was ONH persistence over time (three children, four adults) and increased tortuosity of retinal vessels (eight children, 11 adults). Nine of the 11 adults with increased tortuosity were born preterm and/or were small for their gestational age. (Data were unavailable for the other two.) The findings reinforce the need for ongoing follow-up of patients with FASD.

Assessing Photoreceptors After Repair of Macula-Off RD

June 2020

Macula-off retinal detachment (RD) can be repaired by pars plana vitrectomy with gas tamponade, but visual outcomes often are disappointing. Clinical factors such as macula-off duration and detachment height are known to affect prognosis after RD. Using a multimodal approach, Reumueller et al. explored the role of another factor—retinal

regeneration—in RD outcomes. They found that even though cone morphology and function improved by 56 weeks postoperatively, structural and functional impairment remained.

This prospective fellow-eye comparison case series took place in an outpatient clinic at the Medical University of Vienna. Using a combination of spectral-domain optical coherence tomography (SD-OCT), adaptive-optics OCT (AO-OCT), and micropertometry (MP), the authors examined five eyes of five patients at six weeks (baseline) and 56 weeks (follow-up) after vitrectomy with gas tamponade for macula-off RD. They also evaluated the patients' five healthy fellow eyes. The same eight corresponding regions at foveal eccentricities of 2.5 and 6.5 degrees were analyzed in each eye. Main outcome measures were cone density, cone pattern regularity, signal attenuation, and retinal sensitivity.

The patients' mean age was 59.8 years, and their macula-off duration ranged from 0.5 to 5.5 days. Morphologic assessment with AO-OCT at baseline showed severe pattern irregularity, and SD-OCT showed attenuated outer retinal bands with severely reduced signal intensity in RD eyes compared with healthy fellow eyes.

Although cone pattern regularity improved from baseline to follow-up in the RD eyes ($p < .001$), irregularity persisted in 63% of AO-OCT images at follow-up, and severe signal reduction was observed in 45.5% of SD-OCT B-scans. Mean cone density at the inner-outer segment junction and cone outer segment tips was approximately 20,000/mm² (2.5 degrees) and 16,000/mm² (6.5 degrees), respectively, for healthy fellow eyes at baseline and follow-up. In contrast, cone density was much lower for RD eyes at baseline (range, 200-15,600/mm²; $p < .001$)—and although improvement was observed at follow-up ($p < .001$), mean density was lower in RD eyes at the inner-outer segment junction and cone outer segment tips (range, 7,790-9,555/mm²; $p < .001$).

Functional assessment with MP in healthy fellow eyes showed mean retinal sensitivity of 18 dB at baseline and

follow-up; it was much lower in RD eyes (14.30 dB and 14.64 dB, respectively) and did not improve substantially. Overall, SD-OCT grading and MP sensitivity correlated strongly with AO-OCT grading and cone density (ρ values $> .750$).

The combination of AO-OCT, SD-OCT, and MP provides helpful insight into cone regeneration after vitreoretinal procedures. Despite evidence that cone morphology improves, there can be ample functional and morphologic distortion of cones, along with reduced retinal sensitivity, a year after successful reattachment. Hence, successful repair “does not equal restoration of the outer photoreceptor segment,” said the authors. —*Summaries by Lynda Seminara*

JAMA Ophthalmology

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

Use of Eye Care by Adults at High Risk of Vision Loss

May 2020

Saydah et al. compared the number of U.S. adults at high risk for vision loss and the use of eye care services in 2002 and 2017. They found that more adults were at high risk for vision loss in 2017 than in 2002. However, while more adults received eye care in 2017, the percentage who could not afford eyeglasses was higher in 2017.

For this study, the authors gathered data from two National Health Interview Surveys. Covariates included demographics, health insurance status, vision or eye problems (age-related macular degeneration, cataract, diabetic retinopathy, glaucoma, or an eye injury), and the presence of diabetes. Main outcome measures were self-reports of having done the following in the preceding 12 months: 1) visiting an eye care professional, 2) undergoing a dilated eye exam, and 3) needing eyeglasses but being unable to afford them. Respondents who were unable to see or were younger than 18 years of age were excluded from the analysis.

Participants who were deemed at high risk for vision loss were those ≥ 65 years of age and those with a diabetes

diagnosis or eye/vision problem. Assessment methods included multivariable logistic regression and temporal comparisons (2002 vs. 2017) derived from estimates standardized to the 2010 census population.

In 2017, more than 93 million U.S. adults were at high risk for vision loss, up from almost 65 million in 2002. For this study, of the 30,920 eligible respondents in 2002, 16% were at least 65 years old, compared with 20% of the 32,886 respondents in 2017. Fifty-two percent of both samples were female.

Although use of eye care services was greater in 2017 than in 2002 (visit: 56.9% vs. 51.1%; dilated exam: 59.8% vs. 52.4%), so was the percentage of individuals who could not afford eyeglasses (8.7% vs. 8.3%). This finding was more pronounced for low-income participants.

Gender Disparities in Leadership Positions and Publication Rates

May 2020

Women make up 25.3% of ophthalmologists in the United States and comprise 28% of academic ophthalmology faculty members. To better understand gender inequality in ophthalmology, Camacci et al. looked at sex composition of the boards of ophthalmic journals and societies; they also compared publication productivity. Their analysis showed that the sex composition of the boards mirrors that of the ophthalmology profession, but high-level positions such as society president and editor-in-chief are heavily dominated by men.

For this cross-sectional study, the authors used the SCImago Journal Rank indicator to determine the 20 highest-ranked ophthalmology journals. Highly influential ophthalmology societies were identified via a faculty survey. The 2018 board members of each journal and society were identified from the relevant official websites, and the sex of each individual was noted. The Scopus database was used to obtain each member's h-index and m-quotient. (The h-index is designed to take both authors' productivity and the impact of their papers into account.

The m-quotient accounts for different durations of academic careers and is calculated by dividing the h-index by the number of years since an author's first publication.)

Among the 1,077 members of ophthalmic journal and society boards, 797 (74%) were men. Of the 24 journal editors-in-chief, 23 (95.8%) were male. Thirteen (86.7%) of the 15 presidents of professional societies were men. The median h-index was significantly higher for men (journals: 34 vs. 28, $p < .001$; societies: 27 vs. 17, $p = .006$). The median number of publications was 157 for men and 109 for women ($p < .001$). Likewise, more society board members were male (109 vs. 58, $p = .001$), and median citations favored men (4,027 vs. 2,871, $p < .001$). The m-quotients for board members were comparable (journal boards: 1.2 [male] vs. 1.1 [female], $p = .54$; society boards: 1.0 [male] vs. 0.9 [female], $p = .32$).

In summary, the sex distribution of society and journal boards is consistent with that of U.S. ophthalmologists.

Career length seems to have no bearing on publication productivity. If journals and societies want their leadership to fully reflect the demographics of ophthalmologists, it may help to consider early-career personnel for new openings, which may give women greater opportunity to fill these positions, the authors said. (*Also see related commentary by Kathryn Colby, MD, PhD, in the same issue.*)

AI May Help Identify Candidates for Refractive Surgery

May 2020

Xie et al. evaluated the utility of deep learning as an adjunct to tomographic imaging for identifying high-risk corneas. Their artificial intelligence (AI) system appeared useful for classifying images, providing important details about the cornea, and identifying potentially at-risk corneas.

This cross-sectional analysis was performed at the Zhongshan Ophthalmic Center in Guangzhou, China. The researchers included patients throughout China who wanted refractive surgery, had a primary diagnosis of

keratoconus, and had a stable post-op refractive state. Data were collected using a Pentacam HR system, and four-map composite refractive images were used to determine the overall profile of the cornea. Altogether, data for 6,465 de-identified corneal tomographic images (1,385 patients) were used to generate the AI model, which was based on the Pentacam InceptionResNetV2 Screening System (PIRSS). Images were analyzed independently by 20 individuals (including 10 senior ophthalmologists) and by the AI model.

The overall accuracy rate of the PIRSS model was 94.7% (95% confidence interval [CI], 93.3%-95.8%) on the validation dataset. Most areas under the receiver operator characteristic curves were above 0.99. For an independent test dataset, the model achieved similar accuracy (95% [95% CI, 88.8%-97.8%]), comparable to that of five senior ophthalmologists who perform refractive surgery (92.8% [95% CI, 91.2%-94.4%]; $p = .72$). The PIRSS model was superior to human classifiers for identifying corneas that would be unsuitable for refractive surgery (95% vs. 81%; $p < .001$).

Larger samples and other refinements are needed to improve the performance of PIRSS, said the authors, who emphasized that technology cannot replace human clinical expertise. They suggested that biochemical assessment may improve screening for keratoconus and that combining it with

AI could help guide clinical decisions. (Also see related commentary by Travis K. Redd, MD, MPH, J. Peter Campbell, MD, MPH, and Michael F. Chiang, MD, MA, in the same issue.)

—Summaries by Lynda Seminara

OTHER JOURNALS

Selected by Prem S. Subramanian, MD, PhD

Assessing Fear of Falling in Patients With POAG

Investigative Ophthalmology & Visual Science
2020;61(3):52

Previous research has correlated visual field loss with reduced activity levels in patients with primary open-angle glaucoma (POAG), and there is a need to explore the role of falls and fear of falls in patient behaviors. Yuki et al. set out to determine which factors drive the fear of falling among patients with POAG and to explore the relationship between this fear and visual field (VF) loss. They found that fear of falling was more pronounced for older adults, women, and those patients who have damage to the inferior peripheral VF.

For this cross-sectional observational study, the authors evaluated 273 patients with POAG (average age, 64.2 years), using the Fall Efficacy Scale–International (FES-I) questionnaire during face-to-face interviews. Multivariable linear regression was used to

explore relationships between the total FES-I score and age, sex, and level of best-corrected visual acuity as well as other factors, such as time spent walking each day, total deviation (TD) in four VF areas, and number of previous falls.

Results showed that fear of falling increased with age and was higher for women. Reduced inferior peripheral VF sensitivity and increased inferior central VF sensitivity correlated with greater fear of falling. No meaningful associations were observed for other variables, including the number of previous falls. Only four of the 13 study variables were included in the optimal model for total FES-I score: age (coefficient, 0.23; standard error [SE], 0.04; $p < .001$), sex (coefficient, 1.79 for women; SE, 0.84; $p = .034$), and mean TD in the inferior central area (coefficient, 0.92; SE, 0.22; $p < .001$) and the inferior peripheral area (coefficient, -0.86 ; SE, 0.21; $p < 0.001$).

The authors believe that this study is the first to use the FES-I questionnaire to assess fear of falling in patients with glaucoma. In addition to being aware of the demographic factors linked to greater fear, they said, additional attention should be paid to patients with damage in the inferior peripheral VF.

—Summary by Lynda Seminara

MORE ONLINE. For a study on undiagnosed HIV in ocular syphilis patients, see this section at aao.org/eyenet.

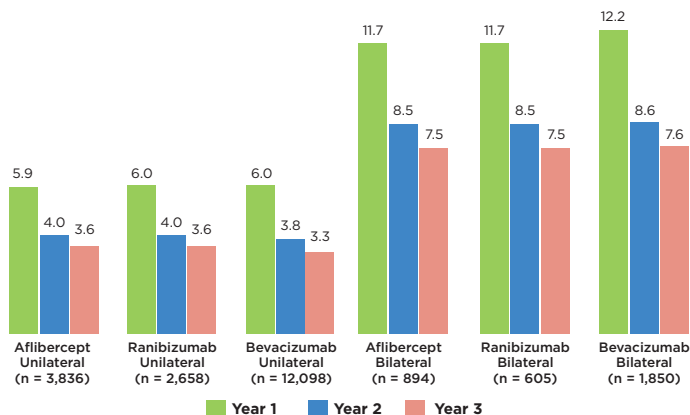
IRIS Registry Snapshot: Intravitreal Injections for AMD

Real-world treatment often differs from standard-of-care practices. In a study sponsored by Janssen Global Services, Verana Health analyzed data from the Academy's IRIS Registry (Intelligent Research in Sight) to assess changes in anti-VEGF treatment frequency in patients with neovascular age-related macular degeneration (AMD).

The three-year study involved 18,596 patients; of these, 3,034 had bilateral wet AMD. The findings (right) suggest that a large proportion of individuals discontinue treatment within the first year, regardless of treatment type, and they underscore some of the known challenges in treatment of patients with wet AMD.

Note: The Academy has partnered with Verana Health to curate and analyze IRIS Registry data.

Mean Anti-VEGF Injections Per Year, By Treatment Type



SOURCE: Verana Health