

# Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

## Ophthalmology

### Glaucoma Progression in American and Korean Cohorts

April 2016

Konstanyan et al. set out to compare the structural and functional progression of glaucoma among U.S. and Korean cohorts. They found differences in type of glaucoma, retinal nerve fiber layer (RNFL) thickness at baseline, and rates of RNFL thinning.

In this retrospective longitudinal study, the investigators examined 313 eyes from 189 glaucoma patients and suspects. Participants were followed for a median of 38 months and examined semiannually using visual field (VF) testing and spectral-domain optical coherence tomography. Each subject had 5 or more documented office visits.

The main outcome measures included rates of change in RNFL thickness, cup-to-disc (C/D) ratios, and VF mean deviation. For each of these parameters, the researchers evaluated the possible effects of a number of variables, including ethnicity, refraction, baseline age, disease severity, disease subtype (high-tension versus normal-tension glaucoma), and clinical diagnosis (glaucoma versus glaucoma suspect).

The Korean cohort, which was composed entirely of Asians participants, predominantly had normal-tension glaucoma. In contrast, the U.S. cohort, which included both white and black participants, was more likely to have high-tension glaucoma. Although both cohorts had similar VF parameters at

baseline, the eyes in the Korean cohort had significantly thicker mean RNFL and larger cups than the U.S. cohort. The Korean eyes with glaucoma also demonstrated more rapid RNFL thinning (mean,  $-0.71 \mu\text{m}$  per year versus  $-0.24 \mu\text{m}$  per year;  $p < .01$ ).

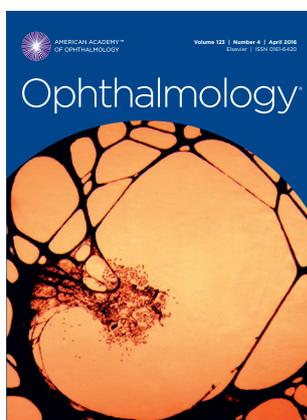
The researchers found no detectable differences in the rate of change between the glaucoma cohorts for C/D ratios and VF mean deviation.

However, when assessing the entire study group (i.e., not comparing the 2 cohorts) for rate of change, the researchers determined that ethnicity, baseline severity, disease subtype, and clinical diagnosis in different combinations had a significant effect on progression. Thus, they concluded that these factors should be considered when comparing glaucoma studies.

### Intravitreal Aflibercept in DME Patients With and Without Prior Anti-VEGF Treatment

April 2016

As treatment evolves for diabetic macular edema (DME), researchers are continuing to assess response to laser versus anti-VEGF therapy. Do et al. compared outcomes of intravitreal aflibercept injections (IAI) versus laser treatment



in DME patients with or without prior anti-VEGF therapy. They found that IAI produced better outcomes than laser both in patients who had prior anti-VEGF treatment and those who were treatment naive.

The current study is a post hoc analysis of eyes with center-involving DME from 2 randomized controlled double-masked phase 3 trials: VISTA (n = 461) and VIVID (n = 404). In those

studies, patients were randomized to 3 groups: 2 mg of IAI every 4 weeks (2q4); 2 mg of IAI every 8 weeks after 5 monthly doses (2q8); or macular laser photocoagulation at baseline with sham injections at study visits.

Of the patients with prior anti-VEGF therapy, a large majority had received only bevacizumab, and treatment ranged from 28 days to 3.9 years. In these patients, the changes in mean best-corrected visual acuity from baseline to 100 weeks in the 3 study groups were as follows: IAI 2q4, +10.9 letters; IAI 2q8, +10.8 letters; and laser,  $-0.8$  letters. For patients without prior anti-VEGF treatment, the changes at week 100 were as follows: IAI 2q4, +12.0 letters; IAI 2q8, +11.3 letters; and laser, +2.1 letters.

Among patients with prior anti-VEGF treatment, mean reductions in central retinal thickness for the 3 study groups were 180.1  $\mu\text{m}$ , 196.4  $\mu\text{m}$ , and 94.1  $\mu\text{m}$  at week 100. Corresponding reductions among patients without

prior anti-VEGF treatment were 200.0  $\mu\text{m}$ , 186.7  $\mu\text{m}$ , and 76.9  $\mu\text{m}$  at week 100.

The researchers concluded that IAI yielded better visual anatomic results over laser regardless of prior anti-VEGF treatment status. They also noted that eyes with DME that had been initially treated with anti-VEGF therapy, particularly bevacizumab, had the potential to achieve further improvements after being switched to IAI.

### **Treatment of Presbyopia With a Shape-Changing Corneal Inlay**

March 2016

**Whitman et al.** reported the 1-year safety and clinical outcomes of a novel shape-changing corneal inlay designed to treat presbyopia. Their study was a prospective nonrandomized multicenter U.S. FDA Investigational Device Exemption clinical trial.

The 373 emmetropic presbyopic study participants (mean age, 51.3 years), underwent implantation of the Raindrop Near Vision Inlay (ReVision Optics) in their nondominant eye. The corneal inlay was implanted under a corneal flap created with a femtosecond laser centered on the light-constricted pupil. The inlay itself has no refractive power. Rather, it biomechanically raises the stroma and epithelium over the inlay and alters the anterior corneal surface.

Of the initial participants, 340 completed the 1-year follow-up. Main outcome measures were monocular and binocular visual acuity (VA), refractive stability, contrast sensitivity, symptoms, satisfaction questionnaire results, and adverse events.

At 1 year, uncorrected near VA in the participants' treated eye had improved by 5.1 lines; uncorrected intermediate VA improved by 2.5 lines; and uncorrected distance VA decreased by 1.2 lines. From 3 months through 1 year, 93% of the study participants had uncorrected near VA of 20/25 or better; 97% had an uncorrected intermediate VA of 20/32 or higher; and 95% had uncorrected distance VA of 20/40 or better. Binocularly, the mean uncorrected distance visual acuity exceeded 20/20 from 3 months through 1 year. The re-

searchers noted that contrast sensitivity loss occurred only at the highest spatial frequencies and only in the treated eye.

Visual symptoms (glare, halos, double vision, and fluctuations in vision), were rated as absent or mild in 96% of the participants. Pain, light sensitivity, and discomfort were reported as absent or mild by 99% of subjects. For dry eye symptoms, 95.3% of subjects reported absent or mild dryness, and 4.1% reported moderate dryness; additionally, 1 subject reported marked dryness, and 1 reported severe dryness.

The researchers noted that adverse events were treatable and resolved over time. Eighteen inlays were exchanged, mainly because of decentration; and 11 inlays were explanted, for reasons including patient dissatisfaction with vision, flap problems, or corneal haze. After explantation, the uncorrected distance acuity, on average, returned to within 1 line of preoperative status.

### **American Journal of Ophthalmology**

#### **Dissociations of the Fluocinolone Acetonide Implant in the MUST Trial**

April 2016

The purpose of the Multicenter Uveitis Steroid Treatment (MUST) trial was to compare outcomes of treatment with systemic corticosteroids versus a fluocinolone implant (Retisert) in patients with noninfectious uveitis. In this current follow-up study, **Holbrook et al.** describe the rate of dissociation—defined as the detachment of the drug pellet from its supporting strut—in patients who received the implant.

In the MUST trial, 250 eyes (146 patients) received at least 1 implant between December 2005 and December 2008. Median follow-up time after placement was 6 years (range, 0.5–9.2 years). There were 34 dissociations reported in 30 participants; of these, 22 events (in 22 participants) were classified as spontaneous, meaning that they were identified or confirmed on clinical examination. The 12 others were found during implant removal or replacement surgery (39 procedures), and it was

unknown whether the event occurred before or during the surgery.

The 6-year cumulative risk of a spontaneous dissociation was low (4.8%), and risk increased over time. The earliest spontaneous event occurred 4.8 years after placement. (By that time, the device would not have been therapeutically active.) Nine of 22 eyes with data available had a decline in visual acuity  $\geq 5$  letters temporally related to the dissociation.

The researchers concluded that there is an increasing risk of dissociation of fluocinolone implants during follow-up and that the risk is greater with removal or exchange surgeries. They found that in 22% of affected eyes, visual acuity declined by 15 or more letters. However, they commented that this rate is not unexpected in eyes with years of moderate to severe uveitis and that it is often impossible to disentangle the effect of implant dissociation from the effects of uveitis or its treatments.

#### **Incorporating HRQOL Into Outcomes Assessment After Strabismus Surgery**

April 2016

The success or failure of strabismus surgery is currently assessed by standard motor and diplopia criteria. **Hatt et al.** studied health-related quality of life (HRQOL) after strabismus surgery in adults and found that more than half of the patients classified as surgical failures reported improved quality of life.

This prospective cohort outcomes study included 227 adult patients who had strabismus surgery at a single clinical practice and had completed Adult Strabismus-20 HRQOL questionnaires preoperatively and at 1 year after surgery. Motor and diplopia criteria were used to classify surgical outcomes as success, partial success, or failure; in 40 patients (18%) the outcome was classified as a failure. For the cases assessed as failures, the researchers reviewed the medical record from the 1-year examination to determine whether the patient had reported any subjective improvement.

The researchers also looked at improvement in HRQOL in at least 1 of

the 4 Adult Strabismus-20 domains, and then compared that with the proportion of patients reporting subjective improvement versus those who did not. Of the 40 “failed” patients, 39 had reliable HRQOL tests. Overall, 21 of these 39 (54%) showed improved HRQOL. Twenty-five patients (64%) reported subjective improvement; and, of these, 16 (64%) had improved HRQOL.

The researchers concluded that many patients who were considered surgical failures according to standard criteria nevertheless reported subjective improvement, which was often reflected in improved HRQOL scores. Thus, they propose incorporating quantitative HRQOL criteria into the assessment of strabismus surgery outcomes to define success as either meeting motor and diplopia criteria or showing improvement in HRQOL.

## **JAMA Ophthalmology**

### **Association of Obesity With Diabetic Retinopathy**

March 2016

The association between obesity and diabetic retinopathy (DR) is equivocal, perhaps because of the interrelationship between generalized and abdominal obesity, which may have a confounding effect. **Man et al.** investigated the associations of generalized obesity (assessed by body mass index [BMI]) and abdominal obesity (assessed by waist to hip ratio [WHR]) with DR in a clinical sample of Asian patients.

This cross-sectional clinic-based study, conducted at the Singapore National Eye Centre, included 420 patients (mean age, 57.8 years; 67.9% men) with type 2 diabetes. The presence and severity of DR were graded from retinal images into the following groups: none, mild-moderate, and severe DR. The associations of BMI and WHR with DR were assessed using multinomial logistic regression models adjusting for age, sex, traditional risk factors, and mutually for BMI and WHR.

Among these patients, the median (interquartile range) for BMI and WHR were 25.7 (5.7) and 0.94 (0.08), respectively. In multivariable models, BMI was

inversely associated with mild-moderate and severe DR (odds ratio [OR], 0.90 and 0.92, respectively, per 1-unit increase), while WHR was positively associated with mild-moderate and severe DR (OR, 3.49 and 2.68, respectively, per 0.1-unit increase) in women. No sex-specific associations were found between BMI and DR.

The researchers concluded that in this group of patients, a higher BMI appeared to confer a protective effect against DR, while higher WHR was associated with the presence and severity of DR in women. The results may inform future clinical trials to determine whether WHR is a more clinically relevant risk marker than BMI for individuals with type 2 diabetes.

### **Survey of Patients on Marijuana Use to Treat Glaucoma**

March 2016

Little is known regarding glaucoma patients’ perceptions about using marijuana for glaucoma and their intentions to try this therapeutic alternative. **Belyea et al.** conducted a cross-sectional survey among glaucoma patients and suspects to identify factors that might affect intentions to use marijuana for treatment.

This study was conducted at an academic-based glaucoma clinic in Washington, D.C. (where medical marijuana use is legal), between Feb. 1 and July 31, 2013. Of the 334 patients invited to participate, 204 completed a self-administered survey assessing demographics, perceived severity of glaucoma, prior knowledge about marijuana use in glaucoma, past marijuana use, perceptions on marijuana use (including legality, effectiveness, and safety), satisfaction with current glaucoma management, relevance of treatment costs, and intentions to use marijuana for glaucoma. About half the participants were women (51.0%), and 40.2% were white.

The main outcome was patients’ intentions to use marijuana for glaucoma; overall, the intentions were generally modest (mean score, 2.36 on a scale of 1-5). Multiple linear regression analysis was conducted to identify factors associated with patients’ intentions to use marijuana for glaucoma. This analysis

indicated that perceptions of legality of marijuana use ( $\beta$  coefficient, 0.378), false beliefs regarding marijuana ( $\beta$ , 0.323), satisfaction with current glaucoma care ( $\beta$ , -0.222), and relevance of marijuana and glaucoma treatment costs ( $\beta$ , 0.127) were significantly associated with intentions to use marijuana for glaucoma after controlling for demographic variables, disease severity, and previous marijuana use.

The American Glaucoma Society has recommended against the use of marijuana in the treatment of glaucoma because of its short duration of action, its documented adverse effects, and the lack of scientific evidence that its use could alter the course of glaucoma. Given the legality and growing public acceptance of the use of medical marijuana, this study’s findings suggest a need for more education on this topic so that ophthalmologists can help protect their patients by counteracting false perceptions on the therapeutic value of marijuana in treating glaucoma.

### **Geographic Variation in Cataract Surgery**

March 2016

**Kauh et al.** sought to assess the extent of geographic variation in patient age at initial cataract surgery and the age-standardized cataract surgery rate in a large group of insured U.S. patients. They found considerable variation in these parameters in different communities.

The researchers undertook a retrospective cross-sectional study of 1,050,815 beneficiaries older than 40 years of age with cataracts who were enrolled in a nationwide managed-care network during the period from 2001 to 2011. The main outcomes and measures were median age at initial cataract extraction, age-standardized cataract surgery rate, and time from initial diagnosis to first surgery for patients with cataracts in 306 communities.

A total of 243,104 patients with cataracts (23.1%) underwent 1 or more surgical procedures. Communities with the youngest and oldest patients at initial surgery showed an age difference of nearly 20 years (59.9-60.1 years in Lansing, Mich., and Aurora, Ill., vs.

77.0-79.6 years in Marquette, Mich., Rochester, N.Y., and Binghamton, N.Y.). The highest age-standardized cataract surgery rate (37.3% in Lake Charles, La.) was 5-fold higher than the lowest (7.5% in Honolulu). The median time from initial cataract diagnosis to date of first surgery ranged from 17 days (Victoria, Texas) to 367 days (Yakima, Wash.).

Multivariable regression modeling generated hazard ratios (HRs) with 95% CIs identifying factors associated with patients' likelihood of undergoing cataract surgery. Compared with white patients, black patients had a 15% decreased hazard of surgery (HR, 0.85), while Latino patients (HR, 1.08) and Asian patients (HR, 1.09) had an increased hazard. For every 1-degree higher latitude, the hazard of surgery decreased by 1% (HR, 0.99). For every additional optometrist per 100,000 enrollees in a community, the hazard of surgery increased 0.1% (HR, 1.001).

These data indicate that in recent years, patient age at first cataract surgery and the age-standardized surgery rate have varied considerably among some U.S. communities; these findings contrast with studies in the 1980s, which showed little geographic variation. The authors recommend that future studies should explore the underlying causes for such variation and its effect on patient outcomes.

## OTHER JOURNALS

### Initial Clinical Experience With the CyPass Micro-Stent

*Journal of Glaucoma*  
2016;25(1):106-112

The CyPass Micro-Stent (Transcend Medical) is a novel device implanted in the supraciliary space in conjunction with cataract surgery in order to facilitate suprachoroidal aqueous outflow and reduce intraocular pressure (IOP). **Hoeh et al.** evaluated the device's efficacy and safety and found that it yielded a reduction in IOP and in medication use. The procedure is ab interno and minimally invasive.

The study included 142 patients with open-angle glaucoma and cataract who

underwent a combined procedure of phacoemulsification, intraocular lens implantation, and stent implantation. Patients were divided into 2 cohorts: those with baseline medicated IOP  $\geq 21$  mm Hg (group 1) and those with medicated IOP  $< 21$  mm Hg (group 2). The main outcome measures were adverse events, changes in IOP, and the number of IOP-lowering medications required.

Mean (SD) follow-up was 294 (121) days, and no serious intraoperative or postoperative complications occurred. Group 1 had a 35% decrease in mean IOP and a 49% reduction in mean glaucoma medication usage, and group 2 had a 75% reduction in mean medication usage while maintaining a mean IOP of  $< 21$  mm Hg. For all eyes, mean IOP at 12 months was  $15.9 \pm 3.1$  mm Hg (a 14% reduction from overall baseline). There were no sight-threatening intraoperative complications. The most common postoperative adverse event was transient IOP fluctuation during the first 4 weeks after surgery; 14% of eyes had transient early hypotony, but all cases resolved by 1 month.

The researchers concluded that the 1-year safety profile and clinical outcomes from this study indicate that suprachoroidal outflow through this novel implantable device may be a promising approach for glaucoma management.

### Phenytoin for Neuroprotection in Acute Optic Neuritis

*Lancet Neurology*

Published online Jan. 25, 2016

Acute demyelinating optic neuritis (ON) is common among patients with multiple sclerosis and damages the optic nerve and its fibers in the retina. **Kapoor et al.** studied whether sodium-channel inhibition with phenytoin, an antiseizure drug, might be neuroprotective in ON, and their findings support this concept of neuroprotection.

The researchers conducted a randomized placebo-controlled double-blind phase 2 trial at 2 academic hospitals in the United Kingdom. The study participants ranged in age from 18 to 60, had documented acute ON, and presented within 2 weeks of onset with a visual acuity of 6/9 or worse.

A total of 86 participants were randomly assigned to either oral phenytoin (42) or placebo (44) for 3 months. Patients assigned to phenytoin received a loading dose of 15 mg/kg of body weight for 3 days, after which 29 of them were assigned to a maintenance dosage of 4 mg/kg per day and 13 to 6 mg/kg per day (depending on date of assignment). The participants were also stratified by time from onset, medical center, previous multiple sclerosis diagnosis, use of disease-modifying treatment, and use of corticosteroids for acute ON.

The primary study outcome was retinal nerve fiber layer (RNFL) thickness in the affected eye at 6 months. This was adjusted for fellow-eye RNFL thickness at baseline and analyzed in a modified intention-to-treat population of all randomized participants who were followed up at 6 months. The investigators analyzed safety in the entire population, including 5 subjects who were lost to follow-up.

The mean RNFL thickness in the affected eye at 6 months was 81.46  $\mu$ m in the phenytoin group versus 74.29  $\mu$ m in the placebo group. This finding corresponds to a 30% reduction in the extent of RNFL loss with phenytoin compared to placebo. The most common adverse event was skin rash, which led to withdrawal of 10 patients from the phenytoin group.

The researchers concluded that their results support the concept of neuroprotection using phenytoin to inhibit voltage-gated sodium channels in patients with acute ON results and should encourage larger, phase 3 trials of sodium-channel inhibitors in ON and other relapses of multiple sclerosis.

*Ophthalmology* summaries are written by Marianne Doran and edited by Susan M. MacDonald, MD. *American Journal of Ophthalmology* summaries are written by Peggy Denny and edited by Richard K. Parrish II, MD. *JAMA Ophthalmology* summaries are based on authors' abstracts, as edited by senior editor(s). *Other Journals* summaries are written by Marianne Doran and edited by Deepak P. Edward, MD.



**MORE ONLINE.** See this article at [www.eyenet.org](http://www.eyenet.org) for additional summaries.