

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Insurance Coverage and Disparities in Glaucoma Care

October 2017

Elam et al. compared the receipt of glaucoma care between patients with Medicaid and those with commercial health insurance. They found that, regardless of race or ethnicity, patients with commercial plans received substantially more monitoring.

For this longitudinal study, records were reviewed for 18,372 commercial plan (managed care) members and 3,394 Medicaid members with newly diagnosed open-angle glaucoma (OAG). The proportion of patients who received the following exams within 15 months of diagnosis was documented: visual field (VF) testing, fundus photography (FP), and other ocular imaging (OOI). Odds ratios (OR) were calculated, and multivariable logistic regression was applied to determine the extent to which race/ethnicity and type of health insurance affected the odds of having a glaucoma monitoring test.

The proportions of patients with commercial plans who underwent VF testing, FP, and OOI were 63%, 22%, and 54%, respectively. In comparison, those percentages for Medicaid members were 35%, 19%, and 30%. Patients with Medicaid were 234% more likely to not receive any glaucoma-related test within 15 months of diagnosis.

With regard to race and ethnicity, after adjusting for confounders, the

odds of white Medicaid members having no glaucoma test were found to be 198% greater than for whites with commercial health insurance. Black Medicaid members were even less likely to be tested; the odds of no testing were 291% higher among those with Medicaid.

The findings emphasize the profound impact of race and type of health plan on the care of patients with OAG, the authors said, and they concluded that considerable efforts are needed to improve the quality and timeliness of glaucoma care for Medicaid recipients, especially those who are black and/or are members of other minority groups. (See related commentary by Eve J. Higginbotham, SM, MD, in the same issue.)

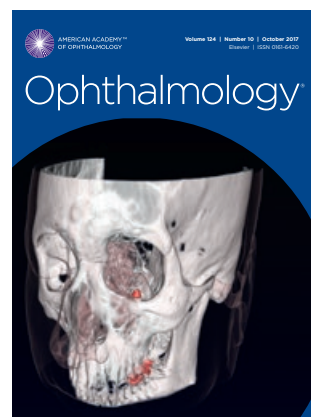
Second-Eye Cataract Surgery, Vision, and Quality of Life

October 2017

Second-eye cataract surgery is common in developed countries and is expected to grow in popularity, despite reports indicating that its benefits may be inferior to those of first-eye surgery. Shekawat et al. determined that visual function and quality of life (QOL) improve substantially after surgery on the second eye.

For this multicenter study, the researchers included 328 patients (mean age, 70.4 years) who underwent separate first- and second-eye cataract

surgeries in the United States. Comprehensive ophthalmic exams were performed pre- and postoperatively for both procedures. Best-corrected visual acuity (BCVA) was measured and patients completed the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) 30-90 days pre- and postoperatively. NEI-VFQ scores were calculated



using a traditional subscale scoring algorithm and the Rasch-refined approach, each yielding separate data for socioemotional impact (QOL) and visual function. Primary outcome measures were postoperative NEI-VFQ scores and the differences between these scores for the 2 procedures.

Relative to the second eyes, first eyes had poorer mean preoperative BCVA (0.55 vs. 0.36 logMAR), greater improvement in mean BCVA after surgery (-0.50 vs. -0.32 logMAR), and slightly worse postoperative BCVA (0.06 vs. 0.03 logMAR). Second-eye surgery resulted in higher postoperative NEI-VFQ scores for nearly all traditional subscales and for the visual function and socioemotional subscales (visual function, -3.85 vs. -2.91 logits; socio-economic, -2.63 vs. -2.10 logits).

The authors concluded that, in general, second-eye cataract surgery

appears more beneficial than first-eye surgery, especially with respect to QOL. They recommend that, during consultation for potential surgery on the second eye, patients be asked about their current level of satisfaction with visual function and QOL.

U.S. Multicenter Trial of CXL for Keratoconus

September 2017

Hersh et al. studied data from 2 multicenter trials of corneal collagen cross-linking (CXL) for keratoconus and noted beneficial effects on disease progression.

In the concurrent studies, 205 patients with keratoconus (mean age, 33 years) were assigned randomly to either standard ultraviolet A–riboflavin 0.1% CXL treatment (n = 102 eyes) or sham treatment (riboflavin 0.1% with dextran, no epithelial removal or irradiation; n = 103 eyes). The primary efficacy endpoint was the between-group difference in maximum keratometry change over 1 year. Secondary endpoints were corrected and uncorrected distance visual acuity (CDVA and UDVA, respectively), manifest refraction spherical equivalent (MRSE), endothelial cell count, and adverse events.

Ninety CXL eyes and 76 control eyes were followed for 12 months. The mean decrease in maximum keratometry value in the CXL group was 1.6 ± 4.2 D during the 1-year period; a decrease of ≥ 2.0 D occurred in 28 eyes (31.5%) and an increase of ≥ 2 D occurred in 5 eyes (5.6%). In contrast, the control group had a mean increase of 1.0 ± 5.1 D. The difference in maximum keratometry change between the study groups was 2.6 D. CDVA in the CXL group improved by 5.7 logMAR letters, with 23 of 83 eyes (27.7%) gaining and 5 eyes (6%) losing ≥ 10 letters. UDVA improved by 4.4 logMAR letters in the CXL group. Corneal haze was the most common adverse effect of CXL. The endothelial cell count did not change significantly during the year following treatment, and the between-group differences in MRSE changes were not significant.

The authors concluded that CXL treatment effectively and safely halts the progression of keratoconus, findings supported by several international studies. The benefits include reduced corneal steepness, better visual acuity, and improved subjective functioning.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Ocriplasmin for Symptomatic Vitreomacular Adhesion

September/October 2017

Lim et al. evaluated the anatomic and visual outcomes in patients with symptomatic vitreomacular adhesion (VMA) who were treated with ocriplasmin. They found that VMA had resolved with ocriplasmin alone in 83 of 191 eyes (43%) by week 12 and in 148 of 200 eyes (74%) by the last visit, including eyes that underwent pars plana vitrectomy (PPV).

For this retrospective chart review, the authors surveyed members of the Macula Society online. Participating clinicians provided information for each eligible patient in their practice, data collection was open for 6 months, and no limit was placed on the length of follow-up. Information was collected on demographics, visual acuity (VA), extent of VMA, presence or absence of macular hole, and spectral-domain optical coherence tomography (SD-OCT) findings before and after treatment.

All told, 31 investigators participated, contributing data on 208 patients (208 eyes). Of these, 52 (25%) had diabetes, 143 (69%) were female, and 175 (84%) were non-Hispanic whites. At baseline, all patients had symptomatic VMA, 75 (36%) had a full-thickness macular hole, and 41 (20%) had a lamellar hole. Mean VA at baseline was 20/63. The median follow-up was 166 days (range, 21–704 days).

Release of VMA—regardless of whether the eye underwent subsequent PPV—was observed as follows: 1) by the first week, in 70 of 161 eyes (44%); 2) by week 4, in 94 of 190 eyes (49%); 3) by week 12, in 111 of 191 eyes (58%); and 4) by the patient's final

visit, in 148 of 200 eyes (74%). In eyes treated with ocriplasmin alone, those results were 85 of 190 eyes (45%) at 4 weeks, 83 of 191 eyes (43%) at 12 weeks, and 90 of 200 eyes (45%) at the final visit.

For eyes with a macular hole at baseline, closure was achieved with ocriplasmin alone in 35 of 64 eyes (55%) by the first week, 42 of 73 (58%) by 4 weeks, and in 30 of 75 (40%) by the last visit. With regard to VA, it had improved by ≥ 2 lines at the final visit in 69 eyes (35%) and by ≥ 3 lines in 54 eyes (27%)—but had decreased by ≥ 2 lines in 35 eyes (18%) and by ≥ 3 lines in 27 eyes (14%).

Complications included photopsias (15%), dimness of vision (14%), decreased color vision (10%), and macular hole development (5%).

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Pediatric Nystagmus: Incidence and Types

October 2017

Estimates of the incidence of pediatric nystagmus, including its subtypes, are limited. Nash et al. addressed this by compiling information from a large epidemiologic database. They found that developmental delays are common among young patients with nystagmus, as are associations with retinal and optic nerve pathology, and that malignancy of the central nervous system appears to be rare.

For this study, the authors reviewed medical records for all children younger than 19 years of age in Olmsted County, Minnesota, who were diagnosed as having nystagmus during a 30-year period. Of particular interest were data from the exam in which nystagmus was first observed and from the most recent follow-up evaluation.

The incidence of nystagmus among the study population was 6.72 per 100,000 (N = 71). The median age at diagnosis was 12.7 months (range, 0–18.6 years), and 42 (59.2%) were male. Sixty-two (87.3%) of the 71 chil-

dren had infantile nystagmus, defined as onset by 6 months of age; this represents a birth prevalence of 1 in 821. Nystagmus occurred bilaterally in 64 cases (90.1%), in only the right eye in 2 cases (2.8%), and in just the left eye in 3 cases (4.2%). The most common type of nystagmus was that associated with retinal/optic nerve disease (n = 23; 32.4%), followed by idiopathic or congenital motor nystagmus (n = 22; 31.0%) and latent forms of nystagmus (n = 17; 24.0%). Less common were associations with Chiari malformation, medication use, or a tumor of the central nervous system (n = 2.8 each).

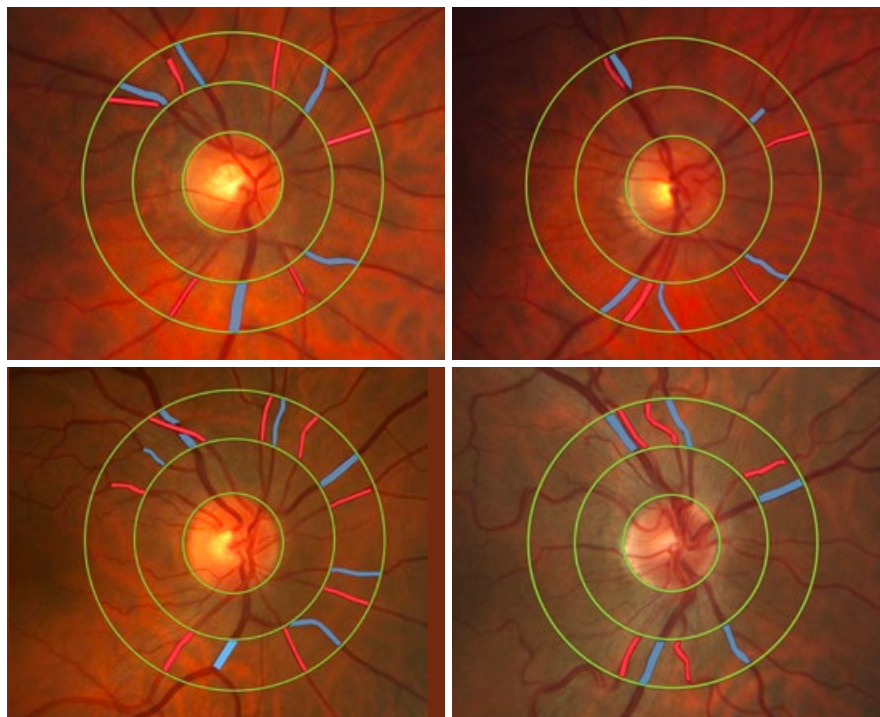
Thirty-one children (43.7%) had a developmental delay, 25 (35.2%) had strabismus, and 10 (14.1%) had amblyopia. Of the 60 patients (84.4%) whose visual acuity was assessed at presentation, 48 (80.0%) had 20/40 vision or better in at least 1 eye.

Sleep Apnea and Retinopathy

October 2017

Obstructive sleep apnea (OSA) is linked to ocular conditions caused by vascular dysregulation, including optic disc edema and nonarteritic anterior ischemic optic neuropathy. Advances in retinal imaging have enabled noninvasive accurate detection of retinal microvascular pathology, which may long precede clinical evidence of disease. **Tong et al.** examined the quantitative relationship between both static and dynamic retinal vascular caliber and the severity of OSA and found an independent association between retinal arteriolar narrowing and attenuated vascular pulsation amplitude.

For this prospective cross-sectional study, the researchers performed a quantitative analysis of retinal vascular caliber among patients with OSA, who were recruited from adult patients who planned to undergo diagnostic polysomnography at a private tertiary sleep unit in Australia. OSA severity was defined by the apnea-hypopnea index (AHI), as follows: ≥ 30 = severe; ≥ 15 to < 30 = moderate; ≥ 5 to < 15 = mild; and < 5 = control. Of the 115 final participants (mean age, 58 years; 73 males), OSA was severe in 41, moderate



INCREASING SEVERITY. In this group of male patients, changes similar to mild hypertensive retinopathy became more apparent with increasing OSA severity. (Top left) No OSA; the patient's apnea-hyponea index (AHI) was 3.0 per hour. (Top right) This patient had mild OSA and an AHI of 14.4/hr. (Bottom left) An example of moderate OSA; the patient's AHI was 21.4/hr. (Bottom right) An example of severe OSA; the patient's AHI was 40.6/hr.

in 35, and mild in 25; the remaining 14 patients served as controls.

Static retinal vascular caliber was calculated as the average diameter of retinal arterioles and venules and summarized as the arteriovenous ratio (AVR). Dynamic retinal vascular caliber was defined as the average pulsation amplitude of retinal arterioles and venules. Groups were compared using multivariate linear regression analysis. Results were adjusted for age, body mass index, and arterial pressure.

Increasing AHI was significantly associated with decreasing AVR and decreasing central retinal arteriolar equivalent. Also significant was the relationship between increasing AHI and attenuated retinal vascular pulsation amplitude. Qualitative grading of fundus photographs demonstrated that retinal vascular changes resembling mild hypertensive retinopathy were more common in patients with moderate and severe OSA than in controls.

The investigators concluded that OSA severity is independently associ-

ated with retinal arteriolar narrowing and attenuated vascular pulsation amplitude. Retinal vasculature is easily imaged and may be a surrogate biomarker of cerebral and systemic vascular risk in patients with OSA requiring extensive evaluation.

—Summaries by Lynda Seminara

JAMA Ophthalmology

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

Maternal Preeclampsia, Risk of Premature Birth, and ROP

September 2017

Studies of the effect of preeclampsia on premature birth and retinopathy of prematurity (ROP) have produced conflicting results. In research aimed at clarifying this relationship and explaining the discrepancies, **Shulman et al.** found that preeclampsia was associated with elevated risk of ROP in an unrestricted cohort, but it reduced the risk of ROP in a preterm-only cohort.

For this study, the researchers reviewed records of 290,992 live births that occurred during a 10-year period (January 2001–December 2010). They used generalized estimating equations for logistic regression, with covariate adjustment, to determine the relationship between ROP and maternal preeclampsia among 2 cohorts: the entire study population and the preterm subgroup with very low birth weight born before 31 weeks' gestation (n = 2,015). Infants in the latter group weighed < 1,500 g.

In the full (unrestricted) cohort, preeclampsia was associated with an increased risk of all ROP, severe ROP, infant death, and having a premature/low birth weight baby. In the premature/low birth weight cohort, preeclampsia was inversely associated with all ROP, severe ROP, and infant death.

In conclusion, these findings suggest an overall adverse effect of preeclampsia on ROP and are consistent with evidence of a protective effect of preeclampsia on infants born prematurely. However, it is unclear whether the latter denotes a true direct protective effect, collider bias, and/or another form of uncontrolled confounding.

Laser Vitreolysis for Symptomatic Floaters

September 2017

Vitreous floaters, which become more common with age, often are bothersome and can hamper visual quality. **Shah and Heier** performed a trial of Nd:YAG laser vitreolysis, a potential but understudied treatment for Weiss ring floaters, and found that it produced subjective improvement in symptoms and objective improvement in appearance.

The single-center, randomized clinical trial involved 52 patients (35 females) with symptomatic Weiss ring floaters secondary to posterior vitreous detachment. Participants were assigned randomly (2:1) to receive either unilateral treatment with Nd:YAG laser vitreolysis (n = 36; mean age, 61.4 years) or sham laser treatment (n = 16; mean age, 61.1 years). All procedures were performed by the same physician.

Outcomes were evaluated 6 months postoperatively and included subjective change measured on a 10-point visual disturbance scale, a 5-level qualitative scale, and the National Eye Institute Visual Functioning Questionnaire 25 (NEI VFQ-25). Secondary outcomes included objective change assessed by masked grading of color fundus photographs and by measuring visual acuity.

At the 6-month follow-up exam, self-reported improvement in floater-related visual disturbance was greater in the treatment group (54% vs. 9%). Improvement in the 10-point visual disturbance score also was superior for the treatment group (3.2 vs. 0.1). On the 5-level qualitative scale, 19 (53%) of the 36 patients treated actively and none (0%) of the sham controls reported substantial or complete improvement in symptoms. NEI VFQ-25 responses showed that laser treatment yielded better general and peripheral vision, fewer role difficulties, and less dependency. Grading of masked wide-angle photographs demonstrated that 34 (94%) of the 36 patients with active treatment experienced significant or complete resolution of floaters, compared with none (0%) of the patients in the sham group. No clinically relevant adverse events were noted.

The authors concluded that Nd:YAG laser vitreolysis produces moderate improvement in floater symptoms. However, they cautioned that larger studies are needed to confirm long-term stability of outcomes and to fully capture adverse events.

Course of Gamma-Irradiated Corneal Patch Grafts After Drainage Device Placement

September 2017

Although surgically implanted aqueous drainage devices (ADDs) lower intraocular pressure in patients with glaucoma, the devices often become exposed through the conjunctiva over time. **de Luna et al.** hypothesized that the thinning of gamma-irradiated sterile cornea (GISC) patch grafts commonly used to cover the tube of ADDs contributes to this exposure. They found that the risk of a GISC patch

graft becoming undetectable increases substantially each year after ADD surgery, and their use does not ensure long-term tube coverage.

This cross-sectional study involved 107 patients (120 eyes) who underwent ADD surgery with a GISC patch graft at Wilmer Eye Institute in Baltimore between July 2010 and October 2016. Of these, 49 were male, and 43 were African American. The patients' mean age was 64 years (range, 24–96 years), and the mean time since surgery was 1.7 years (range, 1 day to 6 years). Primary outcomes were graft thickness over time and risk factors for undetectable grafts. Measurements were obtained by anterior segment optical coherence tomography (AS-OCT) during follow-up exams.

The linear regression model used to evaluate time after ADD surgery (with graft thickness as the outcome) demonstrated that thinner grafts were observed as time passed (β regression coefficient, $-60 \mu\text{m}$ per year since surgery). Moreover, in 16.6% of eyes, no GISC patch graft could be discerned. Each year after ADD surgery, the odds ratio of the graft being undetectable by AS-OCT increased by 2.1. No correlation was found between graft presence/absence and age, sex, race, type of ADD, position of ADD, previous conjunctival surgery, or diagnosis of uveitis or dry eye syndrome.

—*Summaries by Lynda Seminara*

OTHER JOURNALS

Selected by Deepak P. Edward, MD

Screening for Congenital Zika Virus Infection

JAMA Pediatrics

Published online July 17, 2017

According to current guidelines, screening eye exams are recommended for infants with microcephaly or laboratory-confirmed infection with the Zika virus (ZIKV) but not for all infants potentially exposed to the virus in utero. To assess the adequacy of this recommendation, **Zin et al.** examined ophthalmic findings of infants whose mothers were infected with ZIKV during pregnancy. They found that eye

abnormalities may occur in the absence of microcephaly and may be the sole initial sign of congenital ZIKV infection.

For this descriptive case series, the researchers examined 112 mothers and their infants at a facility for high-risk pregnancies in Brazil. During gestation, the mothers were confirmed to be infected with the virus by real-time polymerase chain reaction (PCR) testing. The infants were evaluated from birth to 1 year of age by a multidisciplinary team. Median age at the first eye exam was 31 days (range, 0-305 days). Eye abnormalities were documented, and their relationship to microcephaly, central nervous system (CNS) findings, and the timing of maternal infection was explored.

Ocular defects were observed in 24 (21.4%) of the 112 infants born to ZIKV-infected mothers, with abnormalities of the retina and optic nerve the most common findings. Of these 24 infants, 10 (41.7%) did not have microcephaly, and 8 (33.3%) had normal CNS findings.

With regard to the timing of maternal infection, 14 of the 24 infants with an eye abnormality (58.3%) were born to mothers who contracted ZIKV in their first trimester, 8 (33.3%) to those infected during the second trimester, and 2 (8.3%) to those infected in the third trimester.

As eye abnormalities may be the only initial indicator of congenital ZIKV infection, the authors recommended that screening eye exams be given to all infants potentially exposed to the virus at any point during gestation, regardless of CNS findings or laboratory confirmation of infection.

Gene Replacement for *RPE65*-Mediated Inherited Retinal Dystrophy

Lancet

Published online July 13, 2017

Building on evidence of the potential benefit of gene replacement for *RPE65*-mediated inherited retinal dystrophy, Russell et al. evaluated voretigene neparvovec in patients whose retinal dystrophy would cause complete blindness if untreated. They found that gene

replacement with the AAV2 vector was safe and effective.

For this open-label, randomized phase 3 trial, the researchers enrolled 31 patients who were ≥ 3 years of age at 2 sites in the United States. Participants had a best-corrected visual acuity (BCVA) of 20/60 or worse in each eye and/or a visual field < 20 degrees in any meridian as well as a confirmed genetic diagnosis of biallelic *RPE65* mutations. All participants were required to have sufficient viable retinal cells and to perform a standardized multiluminance mobility test (MLMT) within the luminance range evaluated.

Of the 31 patients, 21 were randomly assigned to the intervention arm; the remaining 10 were assigned to the control arm. Treatment consisted of bilateral subretinal injection (1.5×10^{11} vector genomes of voretigene neparvovec in 0.3 mL total volume). The primary efficacy outcome was the 1-year change in MLMT performance, with functional vision measured at specified light levels.

The mean bilateral change in MLMT score from baseline to one year was 1.8 light levels in the intervention group and 0.2 light levels in the control group. Thirteen (65%) of the 20 intervention participants and none of the controls passed the MLMT at 1 lux, demonstrating that maximum possible improvement was achieved in those 13 patients. No serious adverse events related to the study treatment occurred, and there were no deleterious immune responses. Most adverse ocular events were mild.

—Summaries by Lynda Seminara

Assessing Practice Preferences in Glaucoma Surgery

Journal of Glaucoma

2017;26(8):687-693

How have practice patterns changed among glaucoma surgeons during the past 20 years? Vinod et al. set out to assess glaucoma surgical trends, as reported by members of the American Glaucoma Society (AGS). The results confirm that the trend away from trabeculectomy and toward the use of glaucoma drainage devices (GDDs) continues in most clinical settings.

For this study, the researchers created an anonymous online survey and distributed it via email to AGS members who subscribe to the AGS-net. Participants were asked about their practice location and date of glaucoma fellowship training; in addition, they were asked to report on their preferred approach for a set of common clinical scenarios. The data were then compared with the results from previous surveys (conducted in 1996, 2002, and 2008).

All told, 252 (23%) of the 1,091 subscribers to the AGS-net participated in this survey. A majority (59%) reported that they are in private practice, while the remainder practice in an academic setting. Most had completed their fellowship training either ≥ 20 years ago (33%) or ≤ 5 years ago (29%).

When the results were analyzed by practice setting, no significant differences emerged between surgeons in private and academic settings regarding any given surgical technique in any clinical scenario. However, differences did emerge when years of surgical experience were factored in: Older surgeons were more likely to use trabeculectomy with mitomycin-C (MMC) in several clinical scenarios, while their younger counterparts preferred GDDs.

Overall, the respondents preferred to use GDDs in 7 of the 8 clinical scenarios presented. This represents nearly a complete reversal from the results of the 1996 survey, in which trabeculectomy was selected most frequently to manage glaucoma in all clinical scenarios presented, the authors noted. The results also indicate that GDDs are being used more frequently in eyes at low risk for filtration failure.

A new question—on combined cataract/glaucoma surgery and minimally invasive glaucoma surgery (MIGS)—was added to this iteration of the survey. When given the scenario of a patient with cataract and primary open-angle glaucoma, 44% of the respondents reported that they would use phacoemulsification alone, 24% would combine phaco with trabeculectomy/MMC, 22% would perform phaco with MIGS, and 9% would perform phaco and implant a GDD.

—Summary by Jean Shaw