Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY, AJO,* AND *JAMA OPHTHALMOLOGY*

Ophthalmology

Reduced Cerebrovascular Reactivity in Primary Open-Angle Glaucoma

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Zhang et al. evaluated hemodynamics and vasoreactivity in the posterior cerebral arteries (PCAs) of patients with primary open-angle glaucoma (POAG). They found that vascular insufficiency in the PCAs—the main vessels supplying the visual pathway posterior to the lateral geniculate ganglion—may be associated with POAG. Moreover, they found that this insufficiency may contribute to the onset and progression of glaucomatous neuropathy and may precede central visual field loss.

The researchers evaluated 13 POAG patients and matched them with a control group of 12 participants; all were between the ages of 40 and 60 years. The POAG patients had marked visual field loss; a preserved, mostly central visual field of at least 5 degrees; and best-corrected visual acuity of at least 20/40. Transcranial Doppler sonography was used to measure PCA hemodynamics and vasoreactivity, and these measurements were then correlated with parameters of visual function and retinal nerve fiber layer thickness in the POAG patients.

Sonography revealed disturbed hemodynamics in the PCAs of POAG patients at baseline, after visual stimulation, and under hyperventilation. Within the glaucoma group, measurements of the hemodynamic parameters were significantly associated with the visual field parameters; however, a similar association did not emerge with regard to measurements of retinal nerve fiber layer thickness.

According to the authors, these findings suggest a widespread involvement of the cerebrovascular system in glaucoma. The exact mechanism, however, remains unclear. The vasoreactivity changes may be secondary to the glaucoma-related central neurodegeneration and abnormal glial activation in the central visual pathway; or alternatively, they may be the result of pathologic impairments in the vessels themselves.

Safety and Efficacy of IOL Scaffold Surgery

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Narang et al. evaluated the safety and one-year outcome of the intraocular lens (IOL) scaffold technique in eyes that had soft to moderate nuclear remnants following intraoperative posterior capsule rupture. They found that the technique provided a good visual outcome and a favorable complication rate and offered an effective, relatively noninvasive means of emulsifying the remnants.

In this retrospective consecutive case series, the researchers evaluated the outcomes of the scaffold technique in 20 eyes of 20 patients. All of the surgeries were carried out by a single surgeon, who performed the technique by implanting a three-piece acrylic, foldable IOL with a 6-mm optic and a modified C-loop haptic configuration in all eyes. The IOL served as a temporary scaffold or barrier to compartmentalize the anterior and posterior chambers, thereby preventing vitreous prolapse, vitreous hydration, and nucleus drop.

Outcome measures included uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), intraocular pressure (IOP), and anterior and posterior segment inflammation.

After a mean follow-up of 12 months, the researchers found a significant improvement in UDVA. A mean postoperative CDVA of 20/20 and 20/30 was achieved in 15 and five eyes, respectively. No significant change in IOP was noted. Although clinical macular edema was observed in one eye, there were no cases of postoperative endophthalmitis, retinal tears, or

retinal detachments. Repeat surgery was not required in any of the eyes.

Despite the promising outcomes, the researchers noted that there is a considerable risk of complications, particularly in hyperopic eyes with short anterior chamber depth and eyes with hard cataract. They therefore emphasized the need for careful patient selection and adequate follow-up and suggested further long-term studies to evaluate the safety profile of the technique.

Mixed Results on Fibrin Glue in Strabismus Surgery

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In an Academy *Ophthalmic Technology Assessment*, **Yang et al.** evaluated the safety and efficacy of fibrin glue for the closure of conjunctival incisions in strabismus surgery. They found that, compared with sutures, use of the glue resulted in less postoperative inflammation and required shorter operating time; however, fibrin glue also increased the percentage of wounds that needed follow-up repair with sutures.

The authors evaluated five studies for this assessment. In total, fibrin glue was used to seal the incisions in 68 eyes; sutures were used in 74 eyes. All incisions were limbal; no studies were found that evaluated fornix incisions.

One study showed significantly less postoperative inflammation and patient discomfort during one- to three-week follow-up for eyes treated with fibrin glue. In two studies comparing the surgical time necessary for both closure techniques, fibrin glue required one to five minutes less time in one study and 55 percent less time in the second. And in three studies evaluating wound apposition, 4 percent of the incisions that were initially closed with the glue subsequently developed a wound gap that required suture repair. None of the reports evaluated the cost-effectiveness of, or the potential risk of viral transmission with, use of the fibrin glue.

All five of the studies were rated level II (defined as a low-quality trial) because of lack of randomization, lack of masking, or both. In addition, all five had small sample sizes. The authors concluded that future research can improve the quality of the evidence by appropriately randomizing patients to treatment groups, using masked observers, and using standard scales for rating postoperative signs and symptoms of ocular inflammation.

American Journal of Ophthalmology

Echographic Surveillance of Choroidal Nevi

September *AJO*

Both decreased internal reflectivity on standardized A-scan echography and acoustic hollowness on B-scan examination have been reported as risk factors for malignant transformation of choroidal nevi. In this retrospective cohort study, **Doro et al.** reported the outcomes of choroidal nevi monitoring using these detection methods. They found no long-term changes in echographic features or thickness of choroidal nevi elevated up to 1.5 mm and noted a strong agreement between the two methods, as the vast majority of choroidal nevi with initially atypical standardized A-scan features also showed ultrasonographic hollowness.

The authors focused on the detection of echographic signs of malignant transformation and growth in choroidal nevi that were elevated at least 1.5 mm, as this elevation allows for more distinct differentiation from other lesions. As such, they performed standardized A- and B-scan echography and ophthalmoscopy in a group of 358 consecutive patients in which 51 patients presented with a baseline choroidal nevus higher than 1.5 mm, and 307 presented with a nevus lower than 1.5 mm.

No growth or changes in echographic or ophthalmoscopic features were found in the 307 nevi lower than 1.5 mm (median elevation, 0.9 mm). However, the authors detected both decreased internal reflectivity on standardized A-scan and ultrasonographic hollowness on B-scan in seven of the 38 typical highly reflective choroidal nevi higher than 1.5 mm (median elevation, 1.98 mm); two of these grew into melanoma 15 years after the first observation. In the 13 remaining choroidal nevi higher than 1.5 mm (median thickness, 2.75 mm), the authors detected atypical medium to high reflectivity on standardized A-scan and hollowness on B-scan; six were treated with radioactive plaque therapy six to 15 months later because of the presence of multiple risk factors.

The authors conclude that B-scan hollowness is strongly related to decreased internal reflectivity on standardized A-scan, which is considered the gold standard. They also note that choroidal nevi that are elevated up to 1.5 mm carry a very low risk of malignant transformation; however, annual follow-up to monitor the lesion is recommended.

Intravitreal Bevacizumab vs. Ranibizumab for the Management of Diabetic Macular Edema

September *AJO*

Nepomuceno et al. examined visual acuity and spectral-domain optical coherence tomography outcomes of intravitreal bevacizumab and ranibizumab treatment for diabetic macular edema. They found that both treatments were associated with significant improvement in best-corrected visual acuity (BCVA) and central subfield thickness when compared with baseline values.

In this prospective randomized trial, the authors assigned 48 patients with center-involved diabetic macular edema to receive 1.5 mg bevacizumab or 0.5 mg ranibizumab at baseline and monthly thereafter if central subfield thickness was greater than 275 µm. Forty-five of these patients completed 48 weeks of follow-up.

The authors observed a significant improvement in mean BCVA in both groups at all study points; this improvement was significantly greater in the ranibizumab group compared

with the bevacizumab group at weeks 8 and 32. A significant reduction in mean central subfield thickness was also detected in both groups at all study points compared with baseline. And although the bevacizumab group was treated with a significantly higher number of injections compared with the ranibizumab group, they found no significant difference in the magnitude of macular thickness reduction between the two groups.

The authors noted that this is the first report comparing bevacizumab and ranibizumab for the treatment of diabetic macular edema. Because this study was limited by a small sample size, they called for larger prospective studies to confirm these preliminary findings.

Surgery for Retained Lens Fragments After Cataract Surgery

September *AJO*

In this retrospective case series, **Modi et al.** compared visual acuity outcomes and adverse events in patients with retained lens fragments who underwent either same-day or later pars plana vitrectomy (PPV) and found no differences in visual acuity or rates of complications.

In this single-center study, the authors evaluated all patients with retained lens fragments who underwent PPV from 1990 to 2011. For their analysis, the researchers included 569 eyes of 568 patients with a mean age of 74.6 years at the time of surgery and a median follow-up of eight months. Of the eyes, 117 (21 percent) underwent same-day vitrectomy, 131 (23 percent) underwent PPV within one week, and 321 (56 percent) underwent PPV more than one week later. Median time to vitrectomy in the same-week group was five days, compared with 22 days in the delayed group.

At the last examination, 61 percent, 63 percent, and 56 percent of eyes undergoing PPV on the same day, within one week, and more than one week later, respectively, achieved best-corrected visual acuity (BCVA) of 20/40 or better. Sixteen percent, 15 percent, and 21 percent, respectively, had BCVA of 20/200 or worse. There were no differences between groups in the occurrence of cystoid macular edema, retinal detachment, elevated intraocular pressure, or suprachoroidal hemorrhage.

The authors concluded that although same-day surgery may be attractive logistically in many cases, these retrospective results suggest equivalent outcomes regardless of surgical timing.

Interferon vs. Methotrexate in Intermediate Uveitis With Macular Edema

September *AJO*

In this prospective randomized controlled trial, **Mackensen et al.** compared interferon (IFN) beta with methotrexate (MTX) for the treatment of intermediate uveitis with macular edema and demonstrated the superiority of IFN beta with regard to visual acuity and resolution of macular edema.

The authors enrolled 19 patients who had either primary intermediate uveitis or uveitis associated with multiple sclerosis and who had visual acuity of 20/30 or worse and macular edema of more than 250 µm. The patients were then randomized into one of two groups: an IFN beta group (10 patients) in which 44 µg was administered subcutaneously three times weekly or an MTX group (nine patients) in which 20 µg was administered subcutaneously once weekly. At three months, visual acuity had improved by a mean 0.31 logMAR in the IFN beta group versus a mean 0.09 logMAR in the MTX arm. Macular thickness decreased by a mean of 206 µm in the IFN arm but increased by 47 µm in the MTX group.

Although the sample size was small, the authors concluded that the results of this trial support the superiority of IFN beta over MTX in the treatment of macular edema in the setting of intermediate uveitis. Nonetheless, they called for further studies with larger numbers of patients to confirm these findings.

JAMA Ophthalmology

Effect of Intravitreal Ranibizumab vs. Triamcinolone on Worsening of Diabetic Retinopathy

August *JAMA Ophthalmology*

Because of the destructive nature of panretinal photocoagulation, therapeutic alternatives that might safely obviate or substantially delay its use are desirable. In this study, **Bressler et al.** evaluated the effects of intravitreal ranibizumab and triamcinolone acetonide—administered to treat diabetic macular edema—on worsening of diabetic retinopathy. They found that ranibizumab was associated with a reduced risk of worsening of diabetic retinopathy in eyes with or without proliferative diabetic retinopathy (PDR), while intravitreal triamcinolone was associated with a reduced risk in eyes with PDR only.

This study included patients with diabetic macular edema causing visual acuity impairment. The authors randomly assigned eyes to sham intravitreal injection with prompt focal/grid macular laser, 0.5 mg of intravitreal ranibizumab with prompt or deferred laser, or 4 mg of intravitreal triamcinolone acetonide with prompt laser. For eyes without PDR at baseline, the three-year cumulative probabilities for worsening of retinopathy were 23 percent using sham with prompt laser, 18 percent with ranibizumab with prompt laser, 7 percent with ranibizumab with deferred laser, and 37 percent with triamcinolone with prompt laser. For eyes with PDR at baseline, the three-year cumulative probabilities for worsening of retinopathy were 40 percent, 21 percent, 18 percent, and 12 percent, respectively.

The authors concluded that use of these drugs to prevent worsening of diabetic retinopathy may be feasible. However, given the risk of endophthalmitis following intravitreal injections and the fact that intravitreal triamcinolone can cause cataract or glaucoma, they cautioned that use of these treatments for these effects does not seem warranted at this time.

Plus Disease in Retinopathy of Prematurity

August *JAMA Ophthalmology*

Plus disease is the most important parameter that characterizes retinopathy of prematurity (ROP) requiring intensive treatment. Yet there is discrepancy even among experts in recognizing plus disease, and the characteristics they use in establishing the diagnosis are unclear. In this study, **Hewing et al.** addressed these gaps and examined the diagnostic reasoning process of a panel of international ROP experts. The authors found that experts differed in their reasoning process, the retinal features that they focused on, and interpretations of the same features.

Six physicians were videotaped while independently reviewing seven wide-angle retinal images from infants with ROP. The physicians were then asked to explain their diagnostic procedure in detail, mark findings relevant to their reasoning, and diagnose each image.

Using research methods from cognitive informatics, the authors found that five of the six physicians agreed on the same diagnosis in the first three study images; four of six agreed on the fourth image; and three of six agreed on the last three images. The mean correlation coefficient between pairs of physicians was 0.33. All physicians considered arterial tortuosity and venous dilation while reviewing each image. Some considered venous tortuosity, arterial dilation, peripheral retinal features, and other factors. When physicians were asked to review the images again to diagnose plus disease based strictly on definitions of sufficient arterial tortuosity and venous dilation, all but one changed their diagnosis.

Ophthalmology *summaries are written by Jean Shaw and edited by John Kerrison, MD.* American Journal of Ophthalmology *summaries are edited by Thomas J. Liesegang, MD.* JAMA Ophthalmology *summaries are written by the lead authors.*

ROUNDUP OF OTHER JOURNALS

Oncogenic Mutations Unrelated to Patient Survival in Uveal Melanoma

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Koopmans et al. examined the extent to which oncogenic mutations in *GNAQ* and *GNA11* could be correlated with survival in uveal melanoma patients. The authors found that although these mutations occur frequently in most cases of the disease, they were not associated with patient outcome.

This study involved a total of 92 patients, 48 of whom were male. The median age was 62 years, and the mean follow-up was 74.9 months. Only tumors located in the ciliary body and choroid were included; the mean tumor thickness was 13.3 mm. The authors classified 15 tumors as epithelioid, 38 as mixed, and 39 as spindle cell. Tumors were then analyzed for *GNAQ* and *GNA11* mutations and for chromosomal aberrations in chromosomes 1, 3, 6, and 8. Mutation status was also correlated with disease-free survival and other parameters.

The authors reported that mutations occurred mutually exclusively in the majority of tumors (up to 93.4 percent). Moreover, their occurrence had no correlation with the rate of tumor growth. Because of these findings, the researchers hypothesized that the mutations may be an early event in melanoma development, and they noted that therapeutic strategies that target the downstream pathway may hold the greatest promise for stabilizing the disease process.

Femtosecond Cataract Surgery Outperforms Conventional Approach

Clinical and Experimental Ophthalmology
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Abell et al. compared the safety and efficacy of femtosecond laser–assisted cataract surgery with that of conventional cataract surgery and found that the two approaches had comparable safety rates. However, use of the femtosecond laser may provide a better opportunity to reduce complications and unexpected refractive outcomes, as it significantly lowered effective phacoemulsification time (EPT) and allowed for accurate scanning and defining of critical safety zones for the iris and the posterior capsule.

For this prospective case-control study, the researchers enrolled 400 patients and divided them equally into two groups: a control group undergoing conventional cataract surgery and a treatment group undergoing femtosecond laser capsulotomy with the Catalys femtosecond laser system followed by conventional cataract surgery.

The researchers found no statistically significant difference in intraoperative complications between the two groups. There was one case of posterior capsule rupture in each; both cases occurred during hydrodissection and were managed successfully with pars plana vitrectomy and removal of retained lens fragments the same day without complication. Mean EPT was 70 percent lower in the femtosecond group than in controls, with 26 patients in the femtosecond group receiving no phacoemulsification versus one patient in the control group.

The researchers also reported a reduction in total vacuum time with the second 100 cases in the treatment group—a result of the surgical learning curve.

Despite these positive short-term outcomes, the authors called for further long-term studies to evaluate the cost-effectiveness and operating efficiency of this new technology.

Roundup of Other Journals *is written by Jean Shaw and edited by Deepak P. Edward, MD.*