

Journal Highlights

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

Ophthalmology

VEGF and Retinal Nonperfusion in Diabetic Macular Edema

Ophthalmology

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Campochiaro et al. investigated the effect of the neutralization of vascular endothelial growth factor (VEGF) on posterior retinal nonperfusion (RNP) in patients with diabetic macular edema (DME). They found that monthly injections of the anti-VEGF drug ranibizumab can slow, but not completely prevent, retinal capillary closure in patients with DME.

The authors retrospectively analyzed data from 666 patients from two phase 3 clinical trials. These trials, known by the acronyms RISE and RIDE, were designed to assess the efficacy and safety of ranibizumab in patients with DME. In these trials, patients were randomly assigned to receive 0.3 mg or 0.5 mg of ranibizumab or sham injections for 24 months; at that point, those in the sham group had the option to cross over and receive monthly injections of 0.5 mg of ranibizumab for an additional 12 months.

For this analysis, the primary outcome measure was the percentage

of patients with no posterior RNP, as measured by fluorescein angiography. Patients in all three cohorts experienced DME and RNP that worsened over time, with faster progression occurring in the sham group. However, as soon as the sham group crossed over and started treatment with ranibizumab, the progression of RNP slowed.

These data support the hypothesis that macular edema and worsening of RNP are both consequences of high intraocular levels of VEGF, the researchers said. However, the analysis further suggests that VEGF-induced worsening of retinal perfusion in DME is superimposed on another, more gradual, cause of worsening, possibly glucotoxicity.

Thus, even though monthly injections of ranibizumab may slow disease progression, they do not stop it altogether.



Differentiating Compressive From Glaucomatous Optic Neuropathy

Ophthalmology

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Danesh-Meyer et al. compared optic disc topography in eyes with compressive optic neuropathy (CON) and open-angle glaucoma (OAG). Using spectral-domain optical

coherence tomography (SD-OCT) and confocal scanning laser ophthalmoscopy with Heidelberg retinal tomography, they found distinctive patterns of retinal nerve fiber layer (RNFL) loss and changes in optic nerve head morphology between CON and OAG discs.

For this cross-sectional observational study, the researchers evaluated 200 eyes (123 patients). Of these eyes, 69 had CON and 58 had OAG, while 73 eyes served as controls. Both CON and OAG discs showed cup enlargement and RNFL thinning; however, they differed in that the eyes with CON demonstrated proportionally more thinning nasally and temporally compared with OAG, while the inferior RNFL was thinner in OAG eyes when adjusted for the level of visual field damage. Notably, the temporal optic nerve sector, specifically the 3 o'clock position as measured by SD-OCT, emerged as particularly useful in differentiating between CON and OAG discs. However, Heidelberg retinal tomography was unable to distinguish between eyes with CON and eyes with normal discs.

The researchers cautioned that neither Heidelberg retinal tomography nor SD-OCT can be used in isolation to discriminate between CON and OAG discs, given the substantial overlap in the appearance of these two types of optic neuropathies. However, a pattern of temporal and nasal RNFL thinning is highly suspicious of a compressive

lesion, particularly when there is preservation of the inferior RNFL.

Fungal Keratitis and Susceptibility Testing

Ophthalmology

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Sun et al. addressed the role of susceptibility testing in guiding therapy for fungal keratitis by assessing the link between minimum inhibitory concentration (MIC) and clinical outcomes in cases of filamentous fungal keratitis in South India. They found a correlation between decreased in vitro susceptibility and poor clinical outcomes in cases treated with natamycin. However, they found no association between susceptibility to voriconazole and outcomes.

This study included 221 patients with reported MIC values from the randomized double-masked Mycotic Ulcer Treatment Trial 1. The primary outcome was best-corrected visual acuity; secondary outcomes included three-month infiltrate or scar size, corneal perforation and/or therapeutic penetrating keratoplasty (PK), and time to re-epithelialization.

Decreased susceptibility to natamycin correlated with larger three-month infiltrate or scar size and increased odds of perforation and/or PK, the researchers reported. With regard to specific fungal species, 92 percent (55 of 60) of *Fusarium* cases treated with natamycin had successful outcomes versus 59 percent (39 of 66) of those treated with voriconazole. For *Aspergillus flavus*, 50 percent (7 of 14) of cases treated with natamycin had successful outcomes versus 56 percent (10 of 18) of those treated with voriconazole.

Conbercept Holds Promise for Neovascular AMD

Ophthalmology

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Li et al. assessed the safety and efficacy of conbercept, a new anti-VEGF drug, in patients with neovascular age-related macular de-

generation (AMD). They found that intravitreal injections of conbercept improved BCVA in the 12-month study and that the drug was generally safe and well tolerated.

This randomized double-masked phase 2 study (known by the acronym AURORA) was divided into a three-month loading phase and a nine-month maintenance phase. The researchers enrolled 122 patients who were randomized 1:1 to receive either 0.5 or 2.0 mg of conbercept for three consecutive monthly doses. After the third dose, they were randomly reassigned to receive injections on either a monthly or an as-needed (PRN) basis.

Conbercept produced significant improvements in BCVA in all treatment groups at both the three- and 12-month marks. For example, at 12 months, in the 0.5-mg group, 50 percent of those treated PRN and 31 percent of those receiving monthly injections gained 15 letters or more. Similarly, in the 2.0-mg group, 42.3 percent treated PRN and 46.7 percent of those treated monthly gained 15 letters or more.

Improvements also were noted in central retinal thickness, lesion area, and leakage; and the incidence of ocular and systemic adverse events was low.

The researchers noted that this study was limited by the relatively small number of participants and the absence of a control group.

American Journal of Ophthalmology

Markers of Ocular Surface Dysfunction in Video Display Terminal Workers

July *AJO*

Fenga et al. compared the Ocular Surface Disease Index (OSDI) questionnaire and tear osmolarity as ways to screen for ocular surface alterations in video display terminal (VDT) users in Italy. Their cross-sectional study found that tear osmolarity is the more reliable screening test in VDT users.

VDT use is a frequent cause of ocular discomfort. Sixty-four VDT

workers were screened for ocular surface alterations using OSDI and tear osmolarity. Additionally, tear film break-up time (TBUT), fluorescein corneal staining, and meibomian gland function were evaluated. The alteration of two or more of these parameters was considered a sign of ocular surface dysfunction. Data for the statistical analysis were obtained from the eyes with the worst tear osmolarity score. For the statistical analysis, the receiver operating characteristic (ROC) curves and Spearman correlation coefficient were used. The area under the ROC curve (AUC) for tear osmolarity showed, for all the classification variables considered, significantly higher values than those obtained with OSDI. Furthermore, tear osmolarity showed a direct correlation with corneal staining and ocular surface dysfunction and an inverse correlation with TBUT. No correlation was found between OSDI and the parameters considered.

Tissue Alteration and Post-LASIK Ectasia

July *AJO*

Santiago et al. investigated the association of a novel metric—percent tissue altered (PTA)—with the occurrence of ectasia after laser in situ keratomileusis (LASIK) in eyes with normal preoperative corneal topography and compared this metric with other recognized risk factors in a retrospective case-control study. The study found that the PTA was a more robust indicator of risk than other recognized risk factors.

The study included 30 eyes from 16 patients with bilateral normal preoperative Placido-based corneal topography that developed ectasia after LASIK (ectasia group) and 174 eyes from 88 consecutive patients with uncomplicated LASIK and at least three years of postoperative follow-up. The following metrics were evaluated: age, preoperative central corneal thickness, residual stromal bed, Ectasia Risk Score System, and PTA. (The formula for determining PTA is ablation depth plus

flap thickness, divided by preoperative central corneal thickness.)

In the ectasia group, a PTA of 40 or higher was the most prevalent risk factor (97 percent), followed by age less than 30 years (63 percent), residual stromal bed of 300 μ m or less (57 percent), and ectasia risk score of 3 or higher (43 percent). PTA of 40 or more had the highest odds ratio (223), followed by residual stromal bed of 300 μ m or less (74), and ectasia risk score of 4 or higher (8). Stepwise logistic regression revealed PTA of 40 or more as the single most significant independent variable.

Visual Field Improvement in the CIGTS

July *AJO*

Musch et al. analyzed visual field (VF) improvement among patients in the Collaborative Initial Glaucoma Treatment Study (CIGTS), a randomized clinical trial that compared trabeculectomy and topical medications in treating open-angle glaucoma (OAG). VF improvement occurred frequently over extended periods in this study, and the authors designed a comparative case series to determine whether it was due to chance variation, learning effects, or other influences.

A total of 607 subjects with newly diagnosed OAG were identified for study. Baseline and follow-up VF tests were obtained, and mean deviation (MD) change from baseline over follow-up was analyzed. Clinically substantial change (loss or improvement) was defined as change from baseline of 3 or more decibels in MD. Baseline factors were inspected to determine their association with VF improvement in repeated-measures regression models.

The authors found that the percentage of patients showing substantial VF improvement over time was similar to that showing VF loss through five years after initial treatment, after which time VF loss became more frequent. Measures of better IOP control during treatment were significantly predictive of VF improvement, including a

lower mean IOP, a lower minimum IOP, and lower sustained levels of IOP over follow-up. Other predictive factors included female sex, visits one year prior to cataract extraction, and an interaction between treatment and baseline MD wherein surgically treated subjects with worse baseline VF loss were more likely to show VF improvement. The researchers concluded that approximately half of the observed VF improvement was real rather than attributable to other factors and was related to IOP control.

JAMA Ophthalmology

Superior Rectus Transposition vs. Medial Rectus Recession for Esotropic Duane Syndrome

June *JAMA Ophthalmology*

Yang et al. compared the safety and efficacy of superior rectus transposition (SRT), with or without medial rectus recession (MRc), to MRc alone in the treatment of esotropic Duane syndrome in a retrospective medical record review. This study included all patients who had surgery for this condition from Jan. 1, 2006, through Dec. 31, 2012, in a multispecialty hospital-based pediatric ophthalmology/adult strabismus practice at Boston Children's Hospital. Patients in the SRT group underwent SRT with or without MRc; those in the non-SRT group underwent unilateral or bilateral MRc.

The medical record review identified 36 patients who underwent 37 procedures, including 19 procedures in the SRT group (13 SRT + MRc and 6 SRT alone) and 18 in the non-SRT group (11 unilateral MRc and 7 bilateral MRc). When performed with SRT, the mean MRc was smaller (3.3 versus 5.3 mm; $p = .004$). Although the initial deviation was larger in the SRT group, both groups had similar improvement in esotropia and head turn. Abduction improved by at least 1 unit in 15 of 19 patients in the SRT group (79 percent) compared with 5 of 18 in the non-SRT group (28 percent). In 24 patients followed for more than six months,

mean esotropia decreased from 8.2 to 6.1 prism diopters (PD) in the SRT group ($n = 12$) but increased from 7.2 to 10.9 PD in the non-SRT group ($n = 12$).

The authors concluded that the combination of SRT and MRc may be more effective than unilateral or bilateral MRc alone at improving abduction while allowing for a smaller recession to align the eyes and eliminate a compensatory head turn. Although in theory any surgery on the vertical rectus muscles increases the risk for vertical or torsional complications, this theory was not borne out in the group studied. Moreover, patients treated with SRT appear to have a reduced likelihood of long-term undercorrection.

Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma

June *JAMA Ophthalmology*

The treatment of juxtapapillary choroidal melanoma is challenging because of the proximity of the tumor to visually important structures. **Sagoo et al.** reported on the complications of plaque radiotherapy for this condition in a retrospective case series of patients from an ocular oncology service. The authors studied 650 consecutive eyes with juxtapapillary choroidal melanoma (located 1 mm or less from the optic disc) treated with plaque radiotherapy from Oct. 1, 1974, through Nov. 30, 2005.

The main outcome measures were Kaplan-Meier analysis of rates of radiation complications, secondary enucleation, and visual acuity outcomes. Following are the rates of complications at five years (and 10 years): nonproliferative retinopathy, 66 percent (75 percent); proliferative retinopathy, 24 percent (32 percent); maculopathy, 56 percent (65 percent); papillopathy, 61 percent (77 percent); cataract, 66 percent (80 percent); neovascular glaucoma, 15 percent (22 percent); vitreous hemorrhage, 35 percent (42 percent); and secondary enucleation, 16 percent (26 percent). Visual acuity of 20/200 or worse

occurred in 54 percent (87 percent), and loss of more than five lines of Snellen visual acuity occurred in 45 percent (78 percent).

The authors concluded that plaque radiotherapy for juxtapapillary choroidal melanoma commonly leads to retinopathy and papillopathy and

that vision loss should be anticipated in 45 percent of eyes by five years. However, the rate of globe retention remained high—84 percent—at five years. The authors stated that plaque radiotherapy continues to be a suitable choice for the treatment of juxtapapillary choroidal melanoma.

Ophthalmology summaries are written by Jean Shaw and edited by Susan M. MacDonald, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. JAMA Ophthalmology summaries are based on authors' abstracts as edited by senior editor(s).

ROUNDUP OF OTHER JOURNALS

Microstent Effective for Combined Cataract-Glaucoma Surgery

Klinische Monatsblätter für Augenheilkunde

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Höh et al. evaluated the clinical outcomes seen with the CyPass Micro-Stent for patients who had open-angle glaucoma (OAG) and needed cataract surgery. They found that the stent was implanted successfully in all eyes, was associated with minimal complications, provided long-lasting control of IOP, and reduced the need for IOP-lowering drugs.

For this multicenter, prospective consecutive case series, the researchers enrolled 136 patients with OAG. All subjects were on glaucoma medication at baseline; these medications were stopped postoperatively but could be restarted if the investigator deemed it necessary. During the cataract surgery, the stent was implanted into the supraciliary space through a clear corneal incision. In the immediate postsurgical period, patients were followed with the typical cataract surgery protocol at one day, one week, and one month.

At the two-year mark, 82 patients remained in the study. Results indicated a sustained effect on both need for glaucoma medications and IOP measurements, with a 50 percent reduction in the need for IOP-lowering drugs and a more than 35 percent reduction of IOP in those patients whose IOPs were not controlled below 21 mmHg before surgery. No sight-threatening complications or device-related adverse events were noted.

Safety of Air Travel After Scleral Buckle

British Journal of Ophthalmology

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Noble et al. investigated the safety of air travel for patients with a scleral buckle and small amounts of intravitreal gas. They found that although these eyes experience significant changes in intraocular pressure (IOP) in a simulated flight, the presence of a scleral buckle limits the magnitude of IOP change, suggesting that typical air travel is likely to be safe for these patients.

For this consecutive case series of 12 eyes (12 patients), the researchers used a hypobaric chamber to simulate the atmospheric depressurization that occurs during commercial air travel. All patients had undergone pars plana vitrectomy, and six of the 12 eyes had scleral buckles. Testing took place four to six weeks after surgery, when intravitreal gas volumes were estimated to be approximately 10 percent.

During the ascent phase, non-buckled eyes had significantly higher peak IOPs than did buckled eyes (mean peaks of 32 ± 8 mmHg versus 20 ± 5 mmHg, respectively). In addition, non-buckled eyes showed higher absolute increases in IOP than did buckled eyes (19 ± 7 mmHg versus 7 ± 1 mmHg, respectively). IOP dropped in both groups during the cruising phase, stabilizing to a mean of 18 to 19 ± 5 mmHg. Finally, during descent, nonbuckled eyes experienced IOPs significantly lower than baseline, while the IOPs in buckled eyes did not differ significantly from baseline.

Macular Changes and Anterior Segment Inflammation in Femtosecond-Treated Eyes

Journal of Refractive Surgery

Published online April 4, 2014

Conrad-Hengerer et al. evaluated the incidence of postoperative macular edema (ME) and the correlation between macular thickness and postoperative intraocular inflammation in cataract surgery patients who had undergone laser-assisted surgery or standard phacoemulsification. They found that the use of the femtosecond laser did not influence the incidence of postoperative ME.

For this prospective trial, 208 eyes of 104 patients were evaluated; the final analysis covered 202 eyes. The patients underwent standard phacoemulsification in one eye and femtosecond laser-assisted surgery in the fellow eye; all procedures were performed by a single surgeon. Laser flare photometry was measured preoperatively and at two hours, three to four days, one month, three months, and six months postoperatively. Retinal thickness was measured by spectral-domain optical coherence tomography.

Two hours after surgery, laser photometry showed higher levels of flare in the eyes that had been treated with standard phacoemulsification. However, this was the only significant difference noted between the two groups at any time point; there were no apparent differences in macular thickness or ME.

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