Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Bicanalicular Silicone Stents in Endonasal DCR

October 2016

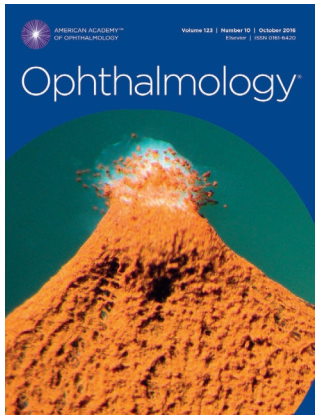
Fayers et al. compared the long-term success rates in endonasal dacryocystorhinostomy (EN-DCR) between surgeries performed with versus without use of a temporary silicone stent. They found a higher rate of success in the stent surgeries.

This prospective randomized controlled trial included 300 adults who underwent primary EN-DCR for nasolacrimal duct obstruction performed by the senior author of the study; 152 patients were randomized to surgery with a stent, and 148 without a stent. The primary end point was subjective symptoms of epiphora at 12 months, reported as resolved; significantly improved; partially improved; or no change or worse. The secondary, objective, end point was anatomic patency and reflux as assessed on nasolacrimal syringing.

Complete success was defined as having resolved or significantly improved symptoms of watering and minimal or no reflux on nasolacrimal syringing. Partial success was defined as symptoms partially improved with a combination of patency and reflux on syringing. Failure was categorized as no change or worse symptoms of watering and 50% to 100% reflux on syringing.

Overall success, both subjectively and objectively, was 94.7% in the stented group and 87.8% in the nonstented group ($p = .034$). The most common complications of stents were canalicular cheese-wiring and tube prolapse (approximately 4% each).

The authors noted that the use of tubes in EN-DCR is associated with higher cost and longer surgical time, as well as minor complications. However, they concluded that the significantly higher success rate achieved with tubes justifies their use.



2-Year Results From the OASIS Randomized Trial

October 2016

Dugel et al. reported the 2-year results from the Ocriplasmin for Treatment of Symptomatic Vitreomacular Adhesion Including Macular Hole (OASIS) trial. This trial evaluated the long-term efficacy and safety of intravitreal ocriplasmin for the treatment of symptomatic vitreomacular adhesion (VMA), including full-thickness macular hole (FTMH). They found that ocriplasmin yielded a higher success rate of resolution of VMA and macular hole compared with sham.

This phase 3b randomized controlled double-masked clinical trial included 220 participants (146 assigned to ocriplasmin and 74 to sham), who were assessed at 12 visits over 24 months. Among the inclusion criteria were the presence of symptomatic VMA and best-corrected visual acuity (BCVA) of 20/32 or worse in the study eye. Patients with FTMH >400 µm, presence of epiretinal membrane, or aphakia in the study eye were excluded.

The primary efficacy end point was the proportion of subjects with VMA resolution at day 28. Secondary efficacy end points were assessed at month 24 and included the proportion of subjects with BCVA improvement from baseline, nonsurgical FTMH closure, vitrectomy, and Visual Function Questionnaire 25 (VFQ-25) outcomes.

The researchers found that the rate of VMA resolution at day 28 was significantly higher in the ocriplasmin group (41.7%) compared with the sham group (6.2%) and that the treatment effect was maintained until the end of the study.

BCVA improvement of ≥2 lines from baseline was seen in 50.5% of the ocriplasmin group versus 39.1% of subjects in the sham group. The nonsurgical FTMH closure rate was 30.0% for the ocriplasmin group compared with 15.4% for the sham group. All other secondary end points also favored ocriplasmin over sham treatment. Regarding safety, most adverse events were mild to moderate, had a short onset time, and were transient,

with no new safety signals identified.

The authors stated that the OASIS trial provides the largest sample size to date for the analysis of the long-term effects of ocriplasmin assessed in a prospective, standardized manner over a 2-year period. They concluded that this trial demonstrates the long-term efficacy and safety of ocriplasmin and shows a higher rate of pharmacological resolution of symptomatic VMA compared with previous phase 3 trials.

Orbital Angiogenesis and Lymphangiogenesis in Thyroid Eye Disease

September 2016

In a study designed to assess the role of vascular growth factors in thyroid eye disease (TED), **Wong et al.** analyzed the composition of orbital fat from patients with acute TED or chronic TED and from individuals without thyroid disease (controls). They also investigated the tenet that orbital adipose tissue lacks lymphatic vessels. They found that in acute TED, there is a greater vascular density and a paucity of lymphatic vessels compared with either chronic TED or controls.

This retrospective cohort study included fat specimens removed during orbital decompression from 26 orbits of 15 patients with TED. Orbital fat specimens from patients without TED, as well as cadaveric orbital fat, served as controls. Tissue specimens were processed for use in immunohistochemistry and for reverse-transcriptase polymerase chain reaction (RT-PCR). These samples were examined for a variety of vascular and lymphatic molecular markers, as well as for mRNA levels of vascular endothelial growth factor (VEGF) and VEGF receptors.

Clinicopathologic correlations in patients with TED were also assessed. In samples from patients with acute TED with a clinical activity score of more than 4, there was increased staining of CD31-positive blood vessels, as well as rare staining of podoplanin-positive lymphatic vessels within acutely inflamed orbital fat tissue. In addition, RT-PCR demonstrated increased expression of VEGF receptor 2 as well as VEGF signaling molecules VEGF-A, VEGF-C, and VEGF-D.

The researchers concluded that the inflamed orbits in acute TED, as compared with chronic TED and control orbits, exhibit increased blood vessels, likely mediated by VEGFR-2 and increased VEGF-A signaling. They also established the presence of some lymphatic vessels. These findings imply that orbital edema in acute TED may be mediated, in part, by both the formation of new, immature blood vessels and the formation of lymphatic capillaries that are functionally incapable of draining interstitial fluid.

American Journal of Ophthalmology

Optimizing Recruitment in Clinical Trials of CRVO

October 2016

The investigators in the SCORE-CRVO trial had found timely recruitment of adequate numbers of patients to be challenging. Thus, to improve recruitment for the subsequent study (SCORE2), **Scott et al.** evaluated recruitment in other trials of intravitreal pharmacotherapy for central retinal vein occlusion (CRVO) and implemented techniques to optimize enrollment. They found that the recruitment rate in SCORE2 was higher than that in SCORE-CRVO (0.39 vs. 0.10 participants/month/site, respectively) and that it compared favorably to rates in previous clinical trials of intravitreal pharmacotherapy for macular edema associated with CRVO.

In addition to calculating recruitment rates, the researchers conducted a survey of the SCORE2 principal investigator and primary clinical coordinator at each study site as to the perceived impact of 4 study design features related to recruitment. These features were rated on a 5-point scale (ranging from 1 = major hindrance to 5 = major positive impact). The utility of specific communication methods also were ranked on a 5-point scale (ranging from "not at all" to "extremely" helpful/useful).

Of the 75 sites, 69 (92%) completed at least 1 survey. Mean scores showed that principal investigators and site coordinators felt positively about all 4 design features evaluated. Of these, provision of standard-of-care active treatment to all patients (i.e., no placebo group) received the highest rating (4.76), followed by SCORE supply of the study drug (4.53), ability to screen and randomize in 1 day (4.53), and allowing enrollment of patients with previous anti-VEGF treatment (4.15).

The most effective tools to aid enrollment goals included a monthly e-newsletter to site staff and congratulatory/motivational communications by physician members of the SCORE2 Executive Committee to site investigators and coordinators upon site activation and randomization.

The authors concluded that study design factors, methods of communication with sites, and recruitment techniques implemented in SCORE2 were well received by investigators and coordinators and may be helpful in optimizing recruitment in future clinical trials.

Endothelial vs. Penetrating Keratoplasty: Practice Patterns and Long-Term Outcomes

October 2016

Although endothelial keratoplasty (EK) has largely replaced penetrating keratoplasty (PK) as the treatment of choice for Fuchs' endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK), the superiority of EK for these indications was questioned in 2 recent registry studies. Thus, **Dickman et al.** compared long-term graft survival, best-corrected visual acuity (BCVA), endothelial cell density (ECD), and astigmatism after PK versus EK for FED and PBK. They found that, at 5 years postoperatively, graft survival and ECD were comparable for PK and EK, and BCVA and astigmatism were better with EK.

The researchers analyzed data from the Netherlands Organ Transplant Registry of all patients with FED or PBK who underwent keratoplasty in the Netherlands between 1998 and 2014 (2,725 EK and 2,390 PK). They

found that during the first 2 years, graft survival was significantly lower for EK than PK in patients with FED (95.2% vs. 97.4%) or PBK (88.7% vs. 94.5%). However, between 2 and 5 years, it was significantly better for EK than PK in patients with FED (98.2% vs. 95.2%) or PBK (97.2% vs. 85.9%). By year 5, graft survival had improved significantly in patients who underwent EK and had remained stable in those treated by PK.

They also found that BCVA was significantly better following EK in patients with FED until 36 months postoperatively; the difference was not significant after that time. Among patients with PBK, EK resulted in significantly better BCVA throughout the study. Refractive astigmatism was substantially higher for PK for both conditions throughout the study period. At 1 year, ECD was significantly lower for EK for both conditions; at 3 years, there was no statistical difference between PK and EK in this outcome.

The authors concluded that long-term graft survival is better after EK, whereas short-term survival is better after PK. Moreover, EK graft survival increased over the course of the study, suggesting a learning curve and improved technique. Visual recovery is faster after EK compared with PK and is associated with minimal postoperative astigmatism and a mild hyperopic shift.

Choriocapillaris Flow Features Follow a Power Law Distribution

October 2016

Spaide hypothesized that the pattern of flow voids seen in the choriocapillaris during in vivo optical coherence tomography angiography (OCT-A) could be related to ocular and even systemic microvascular disease states. However, there are technical limitations that make it difficult to image the choriocapillaris in vivo: light scattering within the overlying tissue, and inadequate lateral resolution in both fluorescein angiography and OCT. In this paper, the author presents a method that allows analysis of the structure and pattern of the flow signal in the choriocapillaris.

OCT-A and subsequent analysis were performed on 104 eyes of 80 patients ranging in age from 24 to 99 years (median, 71 years) to mathematically model blood flow in the choriocapillaris. The choriocapillaris was sampled as a 10-µm-thick section starting 31 µm or 34 µm posterior to the segmentation of the retinal pigment epithelium and Bruch's membrane complex.

Although OCT-A cannot resolve individual choriocapillary vessels, a visible pattern of bright and dark areas suggests their structure, with the bright areas representing blood flow; and the dark areas, flow voids. Evaluation of the distribution of the number of flow voids reveals a potential mathematical relationship that could be used to grade choriocapillaris flow.

Flow voids were identified with the Phansalkar method of thresholding and were measured, counted, and binned by size. The log-transformed data were fit to a slope-intercept equation. Results showed that the occurrence of flow voids in the choriocapillaris is a fractal process that follows a power-law distribution, with many small flow voids and progressively fewer larger flow voids.

In the choriocapillaris, capillary branches are organized as discrete lobules, and blood flow is segmented. In this study, flow voids generally were smaller than the lobules, suggesting that flow abnormalities occur sublobularly. The power law distribution implies that the presence of numerous low-flow segments in the microvasculature increases the likelihood that flow abnormalities will occur in neighboring segments.

The author concluded that this study has a number of new findings, which consequently suggest new research possibilities. In particular, the blood flow in the choriocapillaris has been found to have a mathematically defined structure that has been implicated, but not shown, in living tissue before. Flow voids in the choriocapillaris may be predictive of systemic microvascular abnormalities and may contribute to macular diseases such as late AMD.

JAMA Ophthalmology

Assessment of the ABO's Maintenance of Certification Part 4

September 2016

Improvement in Medical Practice is Part 4 of the Maintenance of Certification (MOC) program established by the American Board of Ophthalmology (ABO). **Wiggins and Etz** assessed the effectiveness of MOC Part 4 in helping ophthalmologists to improve their practice. They analyzed the performance of ophthalmologists before and after completing the activities and found significant improvement in a number of designated areas and outcomes.

The authors conducted a retrospective analysis of the performance of 1,046 ABO diplomates on MOC Practice Improvement Modules (PIMS) completed between Sept. 1, 2012, and Dec. 31, 2014. The mean scores for each process or outcome measure on a medical record abstraction were calculated at baseline and after the diplomate completed the activity, and paired *t* tests were used to assess the improvement. Diplomates' comments and ratings of the usefulness of the activity were also reviewed.

The authors analyzed improvement on those measures that were selected by at least 20 diplomates: Improvement was seen in 24 of the 30 (80%) individual process measures, and in 7 of the 18 (38.9%) individual outcome measures. Analysis of the mean results for each diplomate on process measures chosen for improvement showed gains occurring in 9 of 12 modules. In outcomes measures chosen for improvement, mean results showed gains in 6 of 12 modules. Diplomates rated 826 of 1,115 modules (74.1%) as good to excellent; positive comments outnumbered negative ones by a ratio of 5 to 1.

The authors concluded that the ABO's MOC Part 4 can help diplomates improve quality in process measures and, to a lesser extent, in outcome measures. However, the authors also noted that about one-quar-

ter of the diplomates did not find the process useful, and they suggested that the results of this study could provide insights on how to improve this activity.

Surveillance Tools Emerging From Search Engines and Social Media Data

September 2016

To explore whether social media use and Internet searches can provide a valuable source of information on epidemiologic factors in eye diseases, **Diener et al.** studied the correlation of diagnoses of conjunctivitis with data from keyword searches and Tweets. They found a strong association between these data and clinically diagnosed conjunctivitis in electronic medical records (EMRs).

The authors analyzed data from 5,816 clinical encounters of 4,143 patients diagnosed with conjunctivitis from June 3, 2012, to April 26, 2014, at the University of California San Francisco (UCSF) Medical Center and used Spearman rank correlation of each weekly observation to compare demographics and seasonality of nonallergic conjunctivitis with allergic conjunctivitis.

The authors found that the seasonality of clinical diagnoses of nonallergic conjunctivitis correlated strongly with results of Google searches in the United States for the term *pink eye* (ρ, 0.68) and correlated moderately with Twitter results about pink eye (ρ, 0.38) and with clinical diagnosis of influenza (ρ, 0.33) but did not correlate significantly with seasonality of clinical diagnoses of allergic conjunctivitis at UCSF or with results of Google searches in the United States for the term *eye allergy*. Seasonality of clinical diagnoses of allergic conjunctivitis at UCSF correlated strongly with results of Google searches in the United States for the term *eye allergy* (ρ, 0.44) and *eye drops* (ρ, 0.47).

The authors noted that the clinical data, Google search results, and Twitter posts showed a common pattern: Clinical diagnoses of conjunctivitis detected through EMRs appear to be seasonal and are highly correlated with results of Google searches and correlated with relevant Tweets. In keeping with prior studies of allergic rhinitis, they found that searches related to allergic conjunctivitis peaked in the spring. In addition, EMR data on influenza were also correlated with both EMR data on nonallergic conjunctivitis data and search results for pink eye (probably owing to similar seasonality of the underlying infections).

In conclusion, the authors stated that the information that people post and search for online—and the timing of those activities—can be leveraged to promote better understanding of the epidemiologic factors related to conjunctivitis.

Current and Future Status of Diversity in Ophthalmologist Workforce

September 2016

Because an increase in level of diversity among ophthalmologists may help reduce disparities in eye care, **Xierali et al.** assessed the current ophthalmology workforce—and also estimated future diversity based on medical students who said they wanted to enter ophthalmology residency—by sex, race, and ethnicity between 2005 and 2015. They found that women and ethnic minorities are still underrepresented and will remain so, at least in the near future.

To study the demographic trends and characteristics among ophthalmologists, the researchers used the 2005-2015 annual AMA Physician Masterfile. To estimate the demographics of future ophthalmologists, they looked at ophthalmology residents and analyzed the responses of medical school graduates who, on the Medical School Graduation Questionnaire, indicated plans to specialize in ophthalmology.

Among the key results, the authors found that both women and minority groups traditionally underrepresented in medicine (URM)—black, Hispanic, and Native American—were underrepresented as practicing ophthalmologists (22.7% and 6%, respectively), ophthalmology faculty (35.1% and 5.7%, respectively), and ophthalmology residents (44.3% and 7.7%, respectively), compared with the U.S. population (50.8% and 30.7%, respectively). Although there had been a modest increase in the proportion of female practicing ophthalmologists over the last decade, no increase was identified in URM ophthalmologists.

A similar pattern was seen for residents, with an increase in the proportion of female residents (from 35.6% to 44.3%; $p = .001$) and a slight decrease in the proportion of URM residents (from 8.7% to 7.7%; $p = .04$). The proportion of URM groups among ophthalmology faculty also slightly decreased during the study period (from 6.2% to 5.7%; $p = .01$). However, a higher proportion of URM ophthalmologists practiced in medically underserved areas ($p < .001$).

The authors concluded that, given the prevalent racial/ethnic disparities in eye care and an increasingly diverse society, future research and training efforts should intentionally focus on increasing the level of diversity among ophthalmology residents to benefit from the full range of talent that exists in the United States.

OTHER JOURNALS

Risk Factors for Bacterial Conjunctival Flora in Preoperative Cataract Patients

Eye

Published online July 15, 2016

Hoshi et al. investigated the types of aerobic bacterial conjunctival flora present in preoperative cataract patients and the impact of these pathogens on endophthalmitis. They found that bacterial colonization varied by patient demographic and medical factors.

This study, conducted in Japan, included 990 cataract surgery patients. Data on factors including age, sex, diabetes, hypertension, and use of oral steroids or glaucoma eye drops were obtained from medical records. Lacrimal drainage was assessed via irrigation. Conjunctival specimens were obtained by swabbing and were cultured, and risk factors for 7 typical

bacteria were analyzed by univariate and multivariate analyses.

The investigators found that the detection rate of alpha-hemolytic *Streptococci* and *Enterococcus faecalis* increased with age. They also noted that the detection rate of gram-negative bacilli was higher among patients who had used oral steroids (odds ratio [OR], 3.29) or who had experienced lacrimal duct obstruction (OR, 4.75). *Corynebacterium* species were detected more frequently among older patients and men, and less frequently among patients who used glaucoma eye drops.

Among other findings, the detection rate of methicillin-susceptible coagulase-negative *Staphylococcoci* was higher among men and lower among patients with a history of surgery in other hospital departments; while the rate of methicillin-resistant coagulase-negative *Staphylococci* (MR-CNS) was higher among patients with oral steroid use (OR, 3.65), a history of visits to ophthalmic facilities (OR, 1.65), or a surgical history in other departments (OR, 2.80).

The researchers concluded that risk factors for each type of conjunctival bacteria and for endophthalmitis varied according to patient characteristics. Elderly patients, men, people with lacrimal duct obstruction, or immunosuppressed individuals were more likely to be colonized by pathogens that cause postoperative endophthalmitis. In particular, the presence of MR-CNS in the conjunctival flora was linked with health care–associated infection. To prevent the spread of MR-CNS in ophthalmology departments, strict observance of standard precautions is critically important.

In Vivo Cellular-Resolution Retinal Imaging in Infants and Children

Nature Photonics
2016;10:580-584

Adaptive optics has made possible the viewing of retinal photoreceptor cells in vivo and has led to a better understanding of retinal structure and function. But until now, the necessary equipment has been bulky and required the patient to sit upright and fixate for a considerable time; thus, its use was limited to cooperative adult patients. **LaRocca et al.** describe a handheld probe they designed that performs both scanning laser ophthalmoscopy (SLO) and optical coherence tomography (OCT) of the parafoveal photoreceptor structure in infants and children without the need for adaptive optics.

The new probe, tested in children aged 14 months through 12 years, weighs only 94 g, which is substantially lighter than previous handheld SLO and/or OCT probes. Three innovations made possible the significant reduction in size: 1) a novel telescope design that employs converging rather than collimated light on a scanner to decrease the length; 2) a single high-speed micro-electromechanical scanner system that can be used for both SLO and OCT imaging, rather than 2 sets of larger galvanometer-based optical scanners; and 3) custom lens designs to correct for monochromatic and chromatic aberrations in the optical system, while minimizing device size.

The researchers demonstrated that their ultracompact SLO/OCT handheld probe is capable of imaging the parafoveal cone mosaic in infants, toddlers, and older children. It quantifies packing densities of parafoveal cone photoreceptors and allows the user to visualize cross-sectional photoreceptor substructure. They concluded that, with further clinical development and research, this novel device will benefit pediatric research by increasing our understanding of retinal development and pathogenesis.

Comparison of Peristat Online Perimetry With Clinic-Based Humphrey Perimetry

Translational Vision Science & Technology
2016;5(4):4

Because open-angle glaucoma lacks symptoms in its early stages, only 34% and 8% of cases are diagnosed in the developed and developing world, respectively. Issues of access and cost may create barriers for some patients to in-office perimetry. A possible solution is use of in-home testing; thus, **Lowry et al.** assessed the correlation between Peristat, a free online perimetry test, and clinic-based Humphrey visual field (HVF) testing.

Peristat online perimetry (POP) is a novel web-based virtual suprathreshold system that allows self-testing on any 17-inch or larger computer monitor. It sequentially tests a visual field of 24 degrees from fixation horizontally and 20 degrees vertically using 4 levels of standardized threshold stimuli. This allows patients to be tested for characteristic glaucomatous irregularities in fewer than 5 minutes per eye. It is available at www.keepyoursight.org for free unlimited home access.

In this study, the researchers compared POP with HVF to assess the correlations between the 2 methods in 1 eye each of 93 participants (63 with glaucoma; 30 controls). Both types of perimetry were performed by all participants in random order from August 2013 to February 2014. The researchers compared the points missed between the 2 methods, and generated receiver operating characteristics (ROC) curves for detection of mild to moderate and severe glaucoma. They found that the areas under the ROC curve with POP were generally comparable to those generated with HVF testing.

The authors concluded that POP exhibits a reasonable ROC curve without use of specialized equipment and showed significant correlation with the conventional 24-degree HVF testing. They noted that it could be a useful complement to traditional clinic-based testing in reducing cost and travel burdens. They cautioned, however, that if used only once, as the sole screening method, POP would miss at least 14% of moderate or worse glaucoma and up to 46% of early glaucoma.

Ophthalmology summaries are written by Marianne Doran and edited by Susan M. MacDonald, MD. *American Journal of Ophthalmology* summaries are written by Lynda Seminara and edited by Richard K. Parrish II, MD. *JAMA Ophthalmology* summaries are written by Peggy Denny and edited by Neil M. Bressler, MD. *Other Journals* summaries are written by Marianne Doran and edited by Deepak P. Edward, MD.