

# Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

## Ophthalmology

### Pediatric IIH: Age, Gender, and Anthropometric Features

November 2016

In a retrospective international study, **Sheldon et al.** examined anthropometric and maturational characteristics at diagnosis in children with idiopathic intracranial hypertension (IIH). The researchers defined 3 subgroups of IIH patients based on measures of body mass index (BMI), height and weight Z-scores, and sexual maturation.

IIH cases among pediatric patients aged 2 to 18 years were identified retrospectively based on diagnostic code, pediatric neuro-ophthalmologist databases, or both; of these, 233 cases were confirmed according to updated diagnostic criteria (2013).

The researchers found that boys ( $n = 72$ ) had a moderate association between age and BMI Z-scores (Pearson's correlation coefficient [PCC], 0.50;  $p < .001$ ). Among girls ( $n = 161$ ), a weak association was noted (PCC, 0.34;  $p < .001$ ). The age threshold at which the average patient was more likely to be overweight at diagnosis was 6.7 years in girls and 8.7 years in boys, while the age threshold for obesity at diagnosis was 12.5 years in girls and 12.4 years in boys. Compared with age- and gender-matched reference values, early adolescent patients were taller for age (girls,  $p = .002$ ; boys,  $p = .02$ ). Data on pubertal status were available for 57 of the patients (25%). Prepubertal participants ( $n = 12$ ) had lower

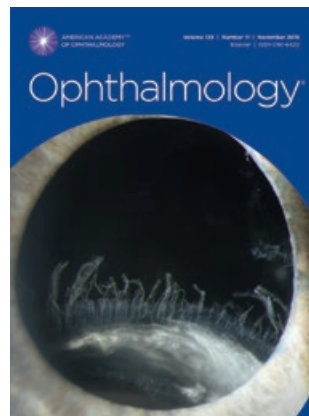
average BMI Z-scores ( $0.95 \pm 1.98$ ) compared with pubertal participants ( $n = 45$ ;  $1.92 \pm 0.60$ ). However, this result did not reach statistical significance.

The researchers noted that through the use of updated criteria and pediatric-specific assessments, their study identified 3 subgroups of pediatric IIH: a young group that is not overweight, an early adolescent group that is either overweight or obese, and a late adolescent group that is mostly obese. Their data also suggest that the early adolescent group with IIH may be taller than age- and gender-matched reference values. They concluded that understanding these features may help to illuminate the complex pathogenesis of pediatric IIH.

### 12-Month Outcomes of Ranibizumab vs. Aflibercept for Neovascular AMD

December 2016

Although the VIEW I and II randomized controlled studies compared ranibizumab and aflibercept for neovascular age-related macular degeneration (nAMD), **Gillies et al.** sought to compare the visual acuity (VA) outcomes between the 2 drugs as used in routine



clinical practice. At 12 months, they found no significant difference in the VA outcomes nor in the number of injections between these anti-VEGF agents.

This was an observational database study of 394 treatment-naïve eyes with nAMD in the Fight Retinal Blindness outcome registry. Anti-VEGF therapy was started with ranibizumab ( $n = 197$ ) or aflibercept ( $n = 197$ ) between Dec.

1, 2013, and Jan. 31, 2015. Eyes were matched at baseline for VA, age, and choroidal neovascular membrane (CNV) size. The main outcome measures were change in mean VA, number of injections and visits, and proportion of eyes with inactive CNV over 12 months.

The mean (standard deviation) VA of ranibizumab-treated eyes increased from 58.6 (20.3) letters at baseline to 62.3 (23.9) for a gain of 3.7 letters, compared with 58.9 (19.2) letters at baseline to 63.1 (21.5) for a gain of 4.26 letters in aflibercept-treated eyes. The difference in change in the crude VA of 0.6 letters between the 2 groups was not statistically significant, nor was the difference in adjusted mean VA of the 2 groups. Among participants who completed the study, the mean numbers of injections (8.1 vs. 8.0;  $p = .27$ ) and visits (9.6 vs. 9.5;  $p = .15$ ) did not differ between the ranibizumab and aflibercept groups, respectively. Similarly, there was no significant difference in the proportion of eyes in which the

CNV was graded as inactive (ranibizumab, 74%; aflibercept, 77%;  $p = .63$ ).

The researchers concluded that both ranibizumab and aflibercept delivered similar, good outcomes after 12 months of treatment for nAMD in routine clinical practice and that there was no difference in treatment frequency between the 2 drugs. They acknowledged that the lack of prospective randomization is a weakness of this study but said that their data were likely to reflect real-world practice and outcomes.

## *American Journal of Ophthalmology*

### **Gevokizumab for Treatment of Autoimmune, Non-Necrotizing Anterior Scleritis**

December 2016

Targeting the various cells and cytokines implicated in the pathogenesis of noninfectious non-necrotizing scleritis has proved beneficial for treating this vision-threatening condition. In a small phase 1/2 study, **Knickelbein et al.** investigated the efficacy of gevokizumab, an anti-interleukin 1 $\beta$  (IL-1 $\beta$ ) monoclonal antibody, in the treatment of noninfectious anterior scleritis. The drug appeared to be effective and well tolerated in their study.

Eight patients (9 eyes) with active, noninfectious, non-necrotizing anterior scleritis (scleral inflammatory grade of +1 to +3 in at least 1 eye) were enrolled in this nonrandomized prospective single-arm trial.

Each patient received a subcutaneous injection of 60 mg of gevokizumab at baseline and at 4-week intervals for 12 weeks. Complete physical and ocular examinations were performed regularly throughout the study. The primary outcome was defined as reduction of at least 2 steps in the inflammatory grade or reduction to grade 0. Secondary outcomes included changes in visual acuity and intraocular pressure. Patients whose eyes met the primary outcome were eligible for an extension study of up to 52 weeks, during which safety was evaluated at weeks 40 and 52.

Seven eyes (7 patients) achieved the primary outcome within 2 weeks

(median) of the first gevokizumab injection. No definitive change in visual acuity or intraocular pressure was identified, and no serious adverse events were attributed to the study drug.

In conclusion, these promising results suggest that IL-1 $\beta$  blockage with gevokizumab is well tolerated and effective for treating active, noninfectious anterior scleritis. The authors noted that large randomized trials are warranted to confirm their findings.

### **Malignancy Status and Features of 5,002 Conjunctival Tumors**

December 2016

There are many types of conjunctival neoplasms, and differential diagnosis can be challenging. **Shields et al.** performed a statistical analysis of conjunctival tumor types and clinical features for a large series of patients. The authors identified properties that differentiate malignant tumors from their benign/premalignant counterparts and found that certain clinical characteristics are associated with specific conjunctival tumors.

The retrospective review included 4,625 patients (5,002 tumors) with a conjunctival tumor who presented to the ocular oncology service of Wills Eye Hospital from 1974 to 2015. Diagnoses were compared among age brackets, races, sexes, and tumor findings (e.g., color, size, predominant localization). Features of malignant conjunctival tumors were compared with those of benign/premalignant counterparts because malignancies usually originate from or resemble the corresponding benign versions.

The most common lesion was nevus (23%). A majority of tumors (52%) were benign; 30% were malignant and 18% were premalignant. Malignant tumors included melanoma (12%), squamous cell carcinoma (9%), and lymphoma (7%).

Compared with primary acquired melanosis, conjunctival melanoma was significantly associated with advanced age, Caucasian race, male gender, larger lesion size, and specific location and vascular hallmarks. Squamous cell carcinoma generally was larger, more

diffuse, and more commonly pigmented than conjunctival intraepithelial neoplasia. Compared with benign reactive lymphoid hyperplasia, lymphoma was more likely to be larger, exhibit specific localization patterns, and occur in elderly patients.

The authors concluded that malignant conjunctival tumors generally exceed benign tumors in diameter and thickness and occur more frequently in older patients. The identification of statistical associations for conjunctival neoplasms can inform clinical and surgical decision making and can improve clinical recognition of malignancy. However, the authors cautioned that their results may reflect overrepresentation of serious malignancies and of tumors common to Caucasians.

### **OCT-Assisted DSAEK: Residual Fluid and Patient Outcomes**

December 2016

**Hallahan et al.** used intraoperative optical coherence tomography (iOCT) to measure graft-host interface fluid during Descemet stripping automated endothelial keratoplasty (DSAEK). Despite the advantages of DSAEK, there is risk for postoperative graft dislocation and failure, which may be a function of residual fluid at the graft-host interface. The authors validated iOCT for measurement of residual interface fluid during DSAEK and found that greater amounts of interface fluid correlate with early graft nonadherence.

In this study, known as PIONEER, 173 patients (178 eyes) who underwent DSAEK were evaluated prospectively. After each graft was positioned, adherence was facilitated by either manual pressurization of the anterior chamber or an active air infusion system. Serial iOCT images were obtained during DSAEK and were analyzed with an automated algorithm to quantify interface fluid. Patients were followed for up to 1 year postoperatively. Study endpoints included graft nonadherence or the need for reintervention.

Fluid measurements from final iOCT images (i.e., obtained immediately after the last surgical maneuver) included total fluid volume, largest vol-

ume in 1 fluid pocket, maximum fluid area, mean fluid thickness, and maximum fluid thickness. These measurements correlated positively with graft nonadherence in the first postoperative week. Both techniques for promoting graft adherence significantly decreased interface fluid, and reintervention rates were similar. Final iOCT images of the 21 grafts that exhibited partial nonadherence or complete dislocation during postoperative follow-up showed significant elevation of total fluid volume, largest volume in 1 fluid pocket, and maximum fluid area.

This study is the first to correlate iOCT measurements of residual graft-host interface fluid with graft nonadherence in the early postoperative period. The authors concluded that more fluid at completion of surgery is predictive of early graft nonadherence and, further, that iOCT can differentiate fluid dynamics during DSAEK.

## **JAMA Ophthalmology**

### **Patient Adherence to Follow-up Care After DR Screening in a Public Health Setting**

November 2016

The success of public health screening programs for diabetic retinopathy (DR) depends on patients' adherence to the recommended follow-up schedules.

**Keenum et al.** determined the adherence rate for patients screened at a public county-funded clinic and examined factors associated with attaining follow-up eye care. The majority of their largely African American study population did not observe the recommended follow-up schedules. Those most likely to adhere were older and aware of their glycated hemoglobin level.

This prospective study included 949 adults (aged 21-95 years) who had been diagnosed with diabetes type 1 or 2. The mean duration of diabetes at DR screening was 9.6 years. Most participants were African American (85%), and many lacked health insurance (72%). However, county residents have access to the clinic's services regardless of their ability to pay or their insurance status.

Although all enrollees had been cautioned that the screening program is not a substitute for comprehensive examination by an ophthalmologist, only 30% observed their recommended schedule for follow-up eye care. Within 2 years of the screening, 51% had not received a subsequent eye exam.

Factors associated with adherence were advanced age (odds ratio [OR], 1.02; 95% CI, 1.01-1.04) and knowing one's glycated hemoglobin level (OR, 2.00; 95% CI, 1.34-2.97). However, agreeing to assistance in making follow-up appointments was associated with nonadherence (OR, 0.67; 95% CI, 0.45-0.99). Younger adults, who were more likely to be employed than older adults, were less likely to adhere to the recommended follow-up regimens, perhaps due to inconvenience or concerns about lost wages on days of follow-up care.

The authors concluded that even when cost and accessibility barriers are minimized, DR screening programs are unlikely to meet their goals without the incorporation of eye health education initiatives that promote adherence to the comprehensive care required to prevent vision loss. Combining such efforts is especially important in light of the soaring prevalence of diabetes.

### **Use of Alleviating Maneuvers for Periocular Facial Dystonia**

November 2016

Patients with periocular facial dystonia may seek treatment with botulinum toxin (BTX) and may perform alleviating maneuvers such as touching their face or coughing to minimize symptoms. **Kilduff et al.** conducted a prospective cross-sectional observational study to determine whether self-performed alleviating maneuvers are associated with BTX treatment or dystonia severity. They noted that performing such maneuvers correlated significantly with more severe facial dystonia and that BTX use was similar between patients who did and did not employ these maneuvers.

Dystonia severity was assessed from questionnaires completed by 74 patients with benign essential blepharospasm (BEB) and 56 patients with

hemifacial spasm (HFS). Patients with BEB completed the Jankovic Rating Scale and the Blepharospasm Disability Index. Patients with HFS completed the 7-item HFS Quality of Life Scale and the SMC Severity Grading Scale. All participants underwent clinical examination.

Thirty-nine patients with BEB (53%) and 25 patients with HFS (45%) affirmed that they utilized sensory and motor stimulatory techniques to manage dystonia. Touching specific regions of the face was the most common alleviating maneuver described, followed by covering the eyes, singing, and yawning. Regardless of spasm type, patients who used alleviating maneuvers scored higher on grading scales than those who did not, denoting more severe dystonia in maneuver users. The alleviating maneuvers reduced at least 50% of involuntary movement for 65% of patients with BEB and 46% of patients with HFS. The dose and frequency of BTX were similar for patients who did and did not utilize the maneuvers.

The authors concluded that use of alleviating maneuvers is associated with more severe disease but not with greater use of BTX. Initiating the maneuvers may indicate worsening of the dystonia. However, by performing these maneuvers, patients with BEB or HFS may be able to maintain a specific BTX dosage even if their condition worsens. These findings may aid in the development of new therapies for periocular facial dystonia. (See also invited commentary by Lee AG and Miller NR.)

## **OTHER JOURNALS**

### **Subfoveal Choroidal Thickness as a Predictor for CSC**

*Eye*

Published online Sept. 30, 2016

Central serous chorioretinopathy (CSC) remains poorly understood, despite its high prevalence. **Ambiya et al.** analyzed data from enhanced depth imaging optical coherence tomography (EDI-OCT) to evaluate the role of subfoveal choroidal thickness (CT) in the course of the disease. They found that a thinner CT ( $\leq 356 \mu\text{m}$ ) was more likely

to indicate chronic disease requiring treatment.

In this retrospective chart review, the authors analyzed 38 treatment-naïve eyes of 33 patients (26 men, 7 women; mean age of  $44.3 \pm 8.8$  years). Ocular history, demographics, laterality, and comorbidities were recorded; clinical examination included visual acuity, slit-lamp biomicroscopy, ophthalmoscopy, and—at the discretion of the investigator—digital fluorescein angiography with or without indocyanine green angiography. All eyes were examined with OCT, and EDI-OCT was used to measure subfoveal CT. Univariate and multivariate analyses for association of baseline features with need for treatment were performed.

On multivariate regression analysis, the authors found that only baseline subfoveal CT had a statistically significant association with the need for treatment. Specifically, the mean baseline subfoveal CT was significantly lower ( $307.07 \mu\text{m}$ ) in eyes that required treatment with laser photocoagulation, photodynamic therapy, or both, compared with eyes that were managed with observation ( $420.48 \mu\text{m}$ ). Based on their analyses, the authors hypothesized that  $356 \mu\text{m}$  was a possible critical CT value for deciding whether to treat or observe; and they classified eyes with  $\text{CT} \leq 356 \mu\text{m}$  as Group A and those with  $\text{CT} > 356 \mu\text{m}$  as Group B.

The authors concluded that eyes in Group A were more likely to have chronic CSC that required treatment (12 of 22 eyes; 54.55%) compared with those in Group B (3 of 16 eyes; 18.75%). They also commented that EDI-OCT is an important tool for monitoring the course of CSC.

### Ophthalmic Presentation of GCA in African Americans

Eye

Published online Sept. 16, 2016

Garrity et al. compared the presenting characteristics of giant cell arteritis (GCA) between African Americans and Caucasians. The researchers found that the features were not markedly distinct, but they did identify a few significant differences.

In this multicenter retrospective case series, neuro-ophthalmologists at 10 institutions provided data on biopsy-proven GCA in a total of 32 patients who self-identified as African American. These cases were compared against a previously published cohort of 84 Caucasian patients with GCA. Characteristics that were compared included age, sex, erythrocyte sedimentation rate, C-reactive protein level, ophthalmic symptoms, and ischemic lesions.

The researchers found that the mean age of the African American cohort was slightly lower than that of the Caucasian cohort (72.6 years vs. 76.1 years); notably, 1 of the African Americans was 46 years old, which is younger than any previously reported cases. There was no difference in sex distribution between the groups, with women comprising more than two-thirds of the patients in both groups.

The most common presentation of giant cell arteritis in both groups was acute vision loss, though it was less common in African Americans (78% vs. 98% of Caucasians,  $p < .001$ ). Eye pain was more common in African Americans (28% vs. 8% of Caucasians,  $p < .01$ ). With regard to systemic signs and symptoms, headache, neck pain, and anemia were more frequent in African Americans, while jaw claudication was noted to be less frequent ( $p$  values  $< .01$ ,  $< .001$ ,  $< .02$ , and  $< .03$ , respectively).

The researchers concluded the similarities in presentation of GCA between African Americans and Caucasians outnumber the differences. They recommended that GCA should be part of the differential diagnosis for any patient, regardless of race, who has suggestive signs or symptoms.

### 5-Year Results of Small Incision Lenticule Extraction

*British Journal of Ophthalmology* 2016;100(9):1192-1195

In 2008/2009, the first group of patients underwent a new procedure, refractive lenticule extraction (ReLEx), with the small incision lenticule extraction (SMILE) technique for treatment of myopia and myopic astigmatism. Blum

et al. performed a 5-year follow-up study among these original patients and found that the procedure was effective, stable, and safe in the long term.

In this study, 56 eyes (30 patients) out of 91 eyes in the original treatment group volunteered to be reexamined 5 years after surgery. Average age at follow-up was 42 years (range, 26-61). Uncorrected and corrected distance visual acuity and objective and manifest refractions were measured, and the interface and corneal surface were examined at the slit lamp. Late side effects such as corneal scars, corneal ectasia, persistent dry eye symptoms, or cataract were documented.

The researchers found no significant changes in the data recorded 6 months postoperatively and the 5-year results. Spherical equivalent was  $-0.375 \text{ D}$  (which represents  $0.48 \text{ D}$  long-term regression), remaining close to target refraction (emmetropia). There was a trend toward improvement between 6 months and 5 years, but it was not statistically significant. No eyes lost 2 or more lines over the 5-year period.

In terms of safety, all patients were routinely treated for dry eye symptoms in the first 3 months after SMILE, but none needed further treatment after 3 months. No patients reported any associated side effects at the 5-year follow-up. Furthermore, no signs of corneal ectasia, cataract formation, or other ocular pathology were found in any of the eyes.

In conclusion, the researchers stated that this first long-term study of SMILE demonstrates that it is an effective, stable, and safe procedure for treatment of myopia and myopic astigmatism.

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