

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Comparing Accuracy of Modern Toric IOL Formulas

November 2020

Kane and Connell compared the accuracy of six toric IOL formulas and found that the Kane formula outperformed the others in predicting astigmatism outcomes following cataract surgery.

This retrospective review included 823 patients (823 eyes) who underwent insertion of an Alcon SN6AT(2-9) IOL by the same surgeon during uncomplicated cataract surgery. The six toric formulas evaluated were Abulafia-Koch, Barrett, EVO 2.0, Holladay 2 (with total surgical-induced astigmatism), Kane, and Naeser-Savini. The dataset used in the study was not part of the development of any of the formulas.

Both pre- and postoperative biometry were measured with the IOL-Master 500 or 700. All calculations were performed using vector addition, and the predicted postoperative refractive astigmatism was determined for each formula. The post-op refractive prediction error was calculated as the vector difference between the predicted and actual refractive astigmatism. Main outcome measures were the mean and standard deviation of the prediction error and the percentage of eyes with a prediction error within ± 0.50 D.

According to post-op keratometry and measurement of the IOL axis, the Kane formula had the highest proportion (65.6%) of eyes with predic-

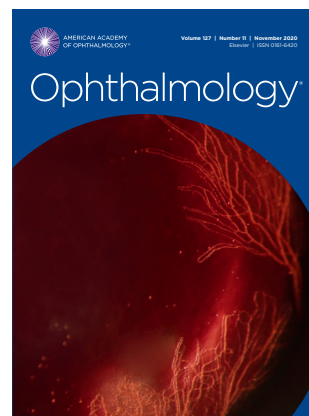
tion errors not exceeding ± 0.50 D. The next-best performers were Barrett (59.9%) and Abulafia-Koch (59.5%). Compared with the five other formulas, the Kane formula had a significantly lower absolute prediction error ($p < .001$) and variance in prediction error ($p < .01$). The percentage of prediction errors did not differ substantially for the Barrett (59.9%), Abulafia-Koch (59.5%), and EVO 2.0 (58.9%) formulas.

This research is one of the largest published comparative studies of toric formulas and is among the first to include three newer formulas (EVO 2.0, Holladay 2, and Kane). Although the Kane formula compared favorably to the others, the authors encourage further comparisons of these and other toric IOL formulas.

Benefits of Standardized Opioid Prescribing Guidance

November 2020

Although an ophthalmologist generally writes fewer than a dozen opioid prescriptions each year, cumulative reduction could help limit the abuse and diversion of unused narcotics that may result from overprescribing. In a study of opioid prescribing patterns



at an academic ophthalmology department, Starr et al. looked at the effect of implementing standard prescribing guidelines for acute postoperative pain. They found that the new guidelines led to reductions in both quantity and frequency of opioid prescriptions.

For their study, the authors searched electronic health records (EHRs) of patients with no history of long-term opioid use and with no opioids prescribed from 90 to seven days before surgery. All prescriptions for an opioid agonist, opioid partial agonist, or opioid combination were counted. The quantity of opioids prescribed for post-op use was converted to oral morphine equivalents (OME, in milligrams), and three target prescribing categories were defined based on the type of surgery (i.e., level 0 = no OME; level 1 = ≤ 40 OME; level 2 = ≤ 80 OME). Assessments of the existing opioid prescribing practices were made during a six-month period. After this point, standardized prescribing guidelines and information on pain management and alternatives were disseminated throughout the department. In addition, electronic flags were built into the EHR system. Prescribing patterns during the subsequent six months were reviewed.

More than 5,300 surgeries are represented in this study (2,613 in the first period, 2,736 in the latter period). After implementing the guidelines, 3.0% of

patients received opioid prescriptions compared with 4.4% previously ($p < .005$). The mean OME was significantly lower overall (42 vs. 93 mg; $p < .001$) and for level 0 and 1 procedures. Of the surgeries in the first six months, 96% would not have exceeded the maximum recommendation (≤ 80 OME); this increased to 99% once the guidelines were in place. The number of refills did not increase.

The authors recommend a review of prescribing practices and consideration of guidelines that would reduce overprescribing yet effectively manage patients' pain after surgery. They emphasized that ongoing education of prescribers will be crucial to improve adherence to any new guidelines.

Anatomic Outcomes for PPV and PPV Plus Scleral Buckle

November 2020

During the past 15 years, the standard of care for rhegmatogenous retinal detachment (RRD) has shifted from scleral buckle (SB) to pars plana vitrectomy (PPV). However, despite this trend, researchers have conducted few comparisons of PPV and the combination of PPV and SB (PPV-SB) across multiple sites and with multiple surgeons. To address this gap, Joseph et al. performed a multicenter study and found that, relative to PPV alone, the PPV-SB combination produced superior single-surgery anatomic success. Visual acuity (VA) outcomes were similar for the two cohorts.

This retrospective study included six retina practices and 61 surgeons. Only patients with at least 90 days of follow-up were considered. Among the 893 pseudophakic eyes that met inclusion criteria, 23% received the PPV-SB combination, and 77% had PPV alone. Collected data included macula status; RRD location; and the size, type, and number of retinal breaks. Main outcomes were VA and anatomic success; the latter was defined as retinal attachment without ongoing tamponade or another RRD surgery within 90 days of primary repair.

Anatomic success was achieved in 84% of vitrectomy-only cases and in

92% of combination procedures ($p = .0093$). Post-op VA outcomes did not differ substantially between the two study groups ($p = .8581$). Anatomic success was not affected by the type of gas tamponade or the gauge of instrumentation. Although PPV-SB was performed in more eyes with inferior detachments, the buckle addition seemed beneficial for RRDs of various anatomic configurations. In both macula-on and macula-off eyes, as well as inferior and superior detachments, PPV-SB outperformed PPV with respect to anatomic success.

The superior anatomic success of PPV-SB in this study may relate to the buckle's ability to close small tears that could have been missed otherwise, the authors said. However, they also acknowledged the possibility of chance, given the study's retrospective nature. Adding the buckle to all PPVs for RRD would not necessarily improve anatomic success, they said. "To prove cause and effect, we need a randomized controlled prospective study powered to test this hypothesis."

—*Summaries by Lynda Seminara*

Ophthalmology Retina

Selected by Andrew P. Schachar, MD

Hyperreflective Foci and Hyperreflective Specks Linked to Impaired Dark Adaptation

November 2020

In longitudinal studies of age-related macular degeneration (AMD), the presence of hyperreflective foci (HRF) at baseline signals risk for progression to advanced disease. Echols et al. assessed the impact of HRF on rod- and cone-mediated function in the macula. They also explored the association of hyperreflective specks (HRS) with visual dysfunction. They found that both HRF and HRS are strongly associated with delayed rod-mediated dark adaptation, which has been found to be accentuated as AMD progresses.

For this cross-sectional study, the researchers evaluated 101 eyes of 101 patients with healthy maculae ($n = 34$), early AMD ($n = 26$), and intermediate AMD ($n = 41$). Vision tests were used

to assess cones, mixed cones and rods, and rods. HRF and HRS were counted manually in optical coherence tomography (OCT) scans.

All told, HRF and HRS were found in 25 and 95 eyes, respectively. HRF were present but sparse in healthy eyes, infrequent in eyes with early AMD, and frequent but highly variable in eyes with intermediate AMD—the mean \pm standard deviation (SD) number per eye for these three groups was 0.1 ± 0.2 , 0.2 ± 0.5 , and 1.9 ± 3.4 , respectively. HRS were present in all eyes, increasing from a mean SD of 4.5 ± 3.2 in healthy eyes to that of 19.4 ± 22.4 in eyes with intermediate AMD.

With regard to impact on vision, HRF were associated with worse low-luminance visual acuity (VA), and HRS were associated with worse contrast sensitivity, low-luminance VA, low-luminance deficit, and mesopic and scotopic sensitivity. Delayed rod-mediated dark adaptation was more likely to occur in eyes with more HRF and HRS.

In their discussion of the findings, the researchers said that HRS may represent lipofuscin translocating inwardly within cone photoreceptors. They also noted that because HRF and HRS are visible and quantifiable on OCT, they may be useful structural end points in clinical trials targeting the early stages of AMD.

—*Summary by Jean Shaw*

JAMA Ophthalmology

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

Ocular Symptoms and Outcomes in Children With COVID-19

October 2020

Little is known about the symptoms and clinical course of COVID-19 in pediatric patients. In a study at Wuhan Children's Hospital, Ma et al. evaluated children with laboratory-confirmed COVID-19. They found that cough and systemic clinical symptoms were commonly linked to conjunctival discharge and eye rubbing. The ocular issues resolved or improved over time.

The study included 216 hospitalized children (mean age, 7.25 years; range, 2.6–11.6 years). Main outcome measures

were the onset and duration of clinical symptoms (including ocular signs) and the need for medication. Among symptomatic children, the most common symptoms were fever (37.5%) and cough (36.6%). No systemic or respiratory symptom was observed in 43.1% of the study population. Recovery occurred in all children whose symptoms were mild (46.8%) or moderate (53.2%).

Ocular symptoms were noted in 49 children (22.7%) and were the first signs of COVID in nine. The most common ocular issues were conjunctival discharge (55.1%), eye rubbing (38.8%), and conjunctival congestion (10.2%), and they were more likely to occur in children with cough or systemic symptoms.

Management of the 49 patients with ocular symptoms included observation without treatment or eyedrops. Forty-one of these patients recovered fully; the other eight had persistent eye rubbing. The median duration of ocular symptoms was seven days.

Mobile App Improves Eye Care for Military Personnel

October 2020

Gensheimer et al. conducted a beta test of a secure telehealth mobile app at military treatment facilities in Afghanistan. They found that app-based ophthalmology consults prevented some aeromedical evacuations and allowed many patients to continue duty.

This study was a prospective case series of consults placed in 16 military treatment centers, 15 of which are forward operating bases within Afghanistan. Thirty point-of-care medics and medical professionals participated in the care. Patients requested teleophthalmology consults via their cell phones using the app, and an expeditionary ophthalmologist at a military hospital in Afghanistan responded. The app, known as Foxtrot (Forward Operating Base Expert Telemedicine Resource Utilizing Mobile Application for Trauma), has security and reliability features that make it suitable for environments with low or no connectivity.

The patient-users graded the app on

a scale of 1 (very dissatisfied) to 5 (very satisfied). Other outcome measures were response times, concordance of the teleophthalmology diagnosis and final diagnosis, appropriateness of treatment (per clinical practice guidelines of the Joint Trauma System), avoidance of aeromedical evacuation, and security. The latter included HIPAA compliance.

Overall, 28 consults (by 18 patients) occurred in the six-week study period. Patients' mean age was 30.3 years, and most were male (93%) and in active duty (78%). The median overall satisfaction score was 5. The mean initial response time from the ophthalmologist was just under four minutes. In 24 consults (86%), the teleophthalmology diagnosis was the same as the final diagnosis. In all cases, treatment and management adhered to the Joint Trauma System guidelines. The app consults prevented aeromedical evacuation of four patients. In 54% of consults, patients were able to return to duty. All 28 consults proved to be secure and HIPAA compliant. (*Also see related commentary by Kimberly M. Winges, MD, Allison R. Loh, MD, and Michael F. Chiang, MD, in the same issue.*)

Stargardt Disease More Likely in Women

October 2020

Autosomal-recessive Stargardt disease (STGD1) is the most common inherited macular dystrophy, but the mechanisms underlying phenotypic variability and disease penetrance are poorly understood. Identifying patient factors that contribute to this often-blinding disease would improve counseling for patients and family members and provide valuable management guidance. Runhart et al. studied genetic data for hundreds of patients with clinically suspected STGD1 and found a female preponderance among patients who carried a mild *ABCA4* genotype.

The main objective of the study was to explore the relationship between sex and incompletely penetrant *ABCA4* alleles in STGD1. The authors collected data from two multicenter genetic studies and calculated the penetrance of reported mild *ABCA4* variants by

comparing allele frequencies between patients and the general population. Sex ratios were determined for patients with and without an *ABCA4* allele who had incomplete penetrance.

Altogether, 550 patients (mean age, 45.7 years) were evaluated. Of these, 311 (57%) were women. All five mild *ABCA4* alleles, including c.5603A>T and c.5882G>A, were found to have incomplete penetrance. The female-to-male ratio in the subset with c.5603A>T was 1.7:1. The proportion of women was higher in this subset than in those without a mild allele (difference of 13%; $p = .02$). The female-to-male ratio in the c.5882G>A subgroup was 2.1:1; again, the female preponderance was greater than for those without a mild allele (difference of 18%; $p = .005$).

This study showed a sex imbalance among patients who carry a mild *ABCA4* allele, which involves about 25% of all patients with STGD1. In light of this, STGD1 should be considered a polygenic or multifactorial disease, said the authors, rather than a disease caused by *ABCA4* gene mutations alone. This research augments the evidence of reduced penetrance for some common *ABCA4* genotypes and emphasizes the potentially crucial role of sex in human health. Although the authors hypothesized that the factors

INFLUENZA ALERT

Winter is coming. In a typical year, fewer than 50% of all Americans get a flu vaccine, and the rate is even lower in minority communities.¹ This year, the threat of a "twindemic" (influenza plus COVID-19) has the CDC and the American Medical Association looking for ways to boost flu vaccination rates to 65%. As part of this, physicians are being asked to encourage their patients to get a flu shot—and to be vaccinated themselves. For information, see www.cdc.gov/flu/professionals/index.htm.

1 Grohskopf LA et al. *JAMA*. 2020;324(11):1029-1030.

linked to female preponderance could portend greater severity or earlier onset of the disease in women, this study did not indicate such consequences. Rather, the authors suspect that specific disease modifiers may play roles at certain stages of life, which may differ for men and women.

—Summaries by Lynda Seminara

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Multicenter Clinicopathologic Review of Lacrimal Gland Lymphoma

November 2020

The most common malignant tumor of the lacrimal gland is non-Hodgkin lymphoma (NHL), but little is known about the clinicopathology of lacrimal gland lymphomas. Vest et al. reviewed features of subtype-specific lacrimal gland lymphomas and their prognoses. They found that the most common subtypes of NHL resembled those in the ocular adnexa (OA). Although they observed a strong relationship between lymphoma subtype and disease-specific survival (DSS), prognosis was relatively good overall.

For this study, the authors analyzed biopsy and clinical data for patients with histologically verified primary or secondary lymphoma of the lacrimal gland. The main outcomes were overall survival (OS) and DSS.

Among the 260 patients identified at six international eye cancer centers, the NHL pathology was B-cell in 258 (99%) and T-cell in two (1%). Extranodal marginal zone B-cell lymphoma (EMZL) was the most common subtype ($n = 177$; 68%), followed by follicular lymphoma (FL; $n = 26$; 10%), diffuse large B-cell lymphoma (DLBCL; $n = 25$; 10%), and mantle cell lymphoma (MCL; $n = 17$; 7%).

With regard to location, the percentage of patients with EMZL was higher in India, and the preponderance of MCL was greater in Denmark. Low-grade lymphomas (including EMZL and FL) were often managed with external beam radiotherapy (EBRT), whereas high-

grade lymphomas (such as DLBCL and MCL) generally received chemotherapy plus rituximab and/or EBRT.

The five-year OS and DSS rates were 73.8% and 87.5%, respectively, which support the findings of previous studies. Both rates varied greatly between subtypes ($p < .001$). EMZL had the highest five-year DSS rate (93.4%), and DLBCL had the lowest (52.6%). The difference in subtype-specific DDS between the treatment centers was not significant.

The favorable survival rate for patients with EMZL supports earlier studies of the OA. However, the lymphoma subtype distribution in the current study resembles that of the orbit and OA, rather than that of the salivary gland, as assumed previously.

MIRM: Ocular Course and Management Suggestions

November 2020

Mycoplasma pneumoniae-induced rash and mucositis (MIRM) is a mild respiratory infection among a disease spectrum that includes erythema multiforme, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis. Although the incidence of MIRM is growing, little is known about the ocular and visual sequelae of this infection. To better understand how MIRM affects the eye and how ophthalmologists can best manage it, Gise et al. reviewed the medical records of patients with MIRM. Although they noted excellent visual outcomes, they stressed that careful monitoring and a low threshold for intervention are vital to avoid permanent ophthalmic damage.

For this study, the authors gathered data for patients with primary MIRM treated at Boston Children's Hospital, including treatments and visual outcomes. Primary end points were best-corrected visual acuity, long-term ocular sequelae, and duration and type of ophthalmic intervention.

Fifteen patients were included in the study (10 males; median age at diagnosis, 10.9 years). Four patients had more than one episode of MIRM, and ophthalmic involvement occurred in 13 (87%). Treatment varied according to the clinical course. A topical steroid was

prescribed for all 15 patients, and the 13 with eye involvement also received an antibiotic. The follow-up time for patients whose eyes were affected ranged from two weeks to 50 months.

Despite the steroid treatment, conjunctival involvement worsened, and permanent sequelae were a concern for several patients. Ultimately, three bilateral amniotic membrane transplantations were performed, and one bilateral sutureless amniotic membrane device (Prokera) was placed. No patient experienced visual loss. One patient who received less aggressive treatment had mild symblephara near the lateral canthus in each eye. Two others, both of whom had amniotic membrane transplantation, exhibited scarring/thickening of the eyelid margins and blepharitis.

To the authors' knowledge, this is the largest study of the ocular course for patients with formally diagnosed MIRM. Although the findings suggest that morbidity is much lower in MIRM than in related syndromes, the authors cautioned that lid margin scarring and symblephara may increase the risk of cicatricial conjunctivitis and ocular surface damage. Moreover, symblephara in patients who do not undergo amniotic membrane grafting emphasizes the importance of attentive follow-up and aggressive treatment when warranted.

—Summaries by Lynda Seminara

OTHER JOURNALS

Selected by Prem S. Subramanian, MD, PhD

Morphologic Differences Between NAION and NTG Eyes

Investigative Ophthalmology & Visual Science
2020;61(8):21.

Nonarteritic anterior ischemic optic neuropathy (NAION) can often mimic normal tension glaucoma (NTG) in terms of retinal nerve fiber defects and damage to the visual field (VF). However, morphologic changes in the lamina cribrosa (LC) of the optic nerve head result from glaucomatous damage and may help to distinguish the two conditions. In a study of Korean patients,

Kim et al. compared the LC of eyes with NAION to that of eyes with untreated NTG and found that LC depth (LCD) and curvature index (LCCI) were much greater in the NTG eyes.

The study included 48 NAION eyes, 48 NTG eyes, and 48 healthy eyes matched for age, intraocular pressure, axial length, and optic disc area. NAION eyes had undergone sudden painless loss of visual acuity but had no evidence of glaucoma or other retinal diseases. NTG eyes had glaucomatous optic nerve damage along with visual field loss. Control eyes had no history of ocular symptoms or surgical intervention other than simple cataract removal. The LCD and LCCI of each eye were scanned across seven horizontal planes of the LC using optical coherence tomography. These values were averaged and then compared for the three groups of eyes.

Findings of the analyses showed that average LC values were greater for NTG eyes than for NAION or healthy eyes ($p < .001$), even though intraocular pressure, axial length, retinal nerve fiber layer thickness, and visual field index were similar for the three groups. No meaningful difference was detected between NAION and control eyes. LCCI findings were more pronounced in the areas affected by NTG ($p = .010$ vs. unaffected areas) yet were consistent in all regions of NAION eyes. LCD did not differ between affected and unaffected areas of NTG or NAION eyes.

According to the authors, these findings offer further evidence of the pathophysiologic differences between NAION and NTG. They noted that the LCCI parameter seems more useful than LCD for evaluating affected and unaffected areas of NTG eyes, and therefore may be the more valuable biomarker for glaucoma diagnosis.

Use of Widefield OCTA in Proliferative DR

Graefe's Archive for Clinical and Experimental Ophthalmology 2020;258(9):1901-1909.

Pichi et al. compared the ability of widefield optical coherence tomography angiography (WF-OCTA), ultra-

widefield fluorescein angiography (UWF-FA), and ultra-widefield color fundus photography (UWF-CP) to detect retinal neovascularization in eyes with proliferative diabetic retinopathy (PDR). They found that WF-OCTA was superior to UWF-CP and noninferior to UWF-FA.

For this cross-sectional study, the authors evaluated treatment-naïve patients with active PDR. All patients were imaged with the three widefield modalities. Retina specialists examined the imaging results for neovascularization, which was defined on OCTA as extra-retinal proliferation of vessels in the vitreoretinal interface slab and was subcategorized by location as neovascularization “of the disc” (NVD) or “elsewhere” (NVE). Statistical analysis was performed to estimate the diagnostic accuracy of each modality, and B-scan OCT with flow overlay was applied as the reference standard.

Overall, 82 eyes (48 patients) were evaluated. NVD was detected in 13 eyes by UWF-CP, in 35 eyes by UWF-FA, and in 37 eyes by WF-OCTA. NVD was confirmed in the same 37 eyes by the reference standard, indicating 100% sensitivity and 100% specificity for WF-OCTA, 94.6% sensitivity and 100% specificity for UWF-FA, and 35.1% sensitivity and 97.8% specificity for UWF-CP. For NVE, 196 foci in 62 of the 82 eyes were identified by the reference standard. UWF-CP enabled detection of 62 of these foci and misclassified 11 others, corresponding to a detection rate of 31.6% and a false-positive rate of 15.1%. The detection rate for UWF-FA was 91.3%. WF-OCTA identified all 196 foci (100% detection rate). False-positive rates for UWF-FA and WF-OCTA were below 2%.

Although FA is the gold standard for detecting subtle signs of neovascularization in PDR, it is invasive and is accompanied by safety concerns. WF-OCTA is safer and faster, said the authors, and the diagnostic accuracy in their hands was similar to that of UWF-FA (and significantly better than that of UWF-CP). They concluded that WF-OCTA may have clinical utility for routine monitoring of PDR.

—Summaries by Lynda Seminara

Coming in the next EyeNet®

Feature

A Look Ahead Experts talk about developments from 2020 that may shape the field over the next five years. See what they say about their subspecialties: cataract surgery, pediatric ophthalmology, and technology.

Clinical Update

Glaucoma Bimatoprost implant: What role will it play in glaucoma management?

Neuro-Ophthalmology

Giant cell arteritis, Part 2: Case studies and malpractice cautions.

Pearls

Presumed Ocular Histoplasmosis Syndrome

Diagnosis and management of this presumed fungal infection.

Savvy Coder

ICD-10 Updates Catch up with the latest round of code changes.

Blink

Take a guess at the next issue's mystery image.

For Your Convenience

These stories also will be available online at aao.org/eyenet.

FOR ADVERTISING INFORMATION

Mark Mrvica or Kelly Miller
M. J. Mrvica Associates Inc.
856-768-9360
mjmrvica@mrvica.com