Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Prevalence of Herpes Zoster Ophthalmicus

March 2020

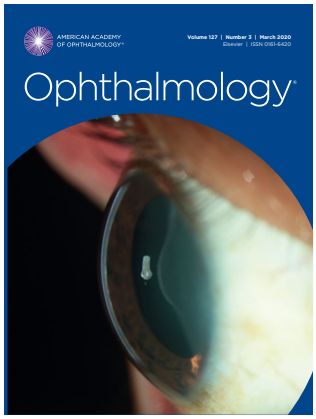
Kong et al. assessed the incidence of herpes zoster ophthalmicus (HZO) and explored potential relationships between HZO and age, sex, race, and geographic region. They found that the incidence of HZO climbed 3.6% annually from 1994-2018 in the United States and that female and white individuals were at greatest risk.

This claims-based and electronic health record dataset included patients with a new ICD-9 or ICD-10 code for herpes zoster and HZO in the OptumLabs Data Warehouse. The incidence rate of HZO was calculated by calendar year, 10-year age group, gender, race, and region. Main outcomes were differences in incidence rate throughout the 15-year study period.

Of the 633,474 reported cases of herpes zoster, there were 49,745 (7.9%) cases involving the eye. During this period, the annual incidence of HZO increased by approximately 1.1 case per 100,000 person-years ($p < .001$); the estimated relative increase was 3.6% annually. The incidence of HZO increased in all but the youngest age group until 2007 and then started declining for those under 21 and older than 60. The incidence rate stabilized in 21- to 30-year-olds and increased less dramatically in 31- to 60-year-olds.

Women had a higher incidence rate than men (44.5 vs. 33.1 cases per 100,000 person-years, respectively), and incidence rates by race were 43.1 for whites, 32.2 for blacks, 30 for Asians, and 27.5 for Hispanics. Individuals in northeastern states were most likely to be affected by HZO, while those in western states were least likely.

Given the possible shift in HZO burden toward middle-aged people, "it is crucial for clinicians to support vaccination efforts for individuals 50 years of age and older," the authors said.



Cataract Surgery: Volume and Complications

March 2020

Using 10-year data from the Swedish National Cataract Register, **Zetterberg et al.** evaluated cataract surgery volume and compared it with surgical outcomes. They found that the rate of complications dropped as surgeons' caseloads increased.

For this retrospective study, the change in operation volume over time was determined for individual surgeons. The annual incidence of capsule complications was compared with the operation volume of individual surgeons and clinical units. Outcomes of interest included the number of procedures performed, the proportion of capsule complications, and changes in surgical volume and complication rates.

The analysis showed that the number of surgeons who performed at least 500 procedures per year (defined as "high volume") rose from 15% to 34% during the study timeline. The proportion of cataract procedures performed by high-volume surgeons was 36.9% in 2007, which increased to 68.1% by 2016. The mean annual incidence of capsule complications decreased as the number of per-surgeon cases increased. In 2016, the rate of these complications was 2.15% for low-volume surgeons (10-99 extractions/ year), 1.32% for medium-volume surgeons (100-499 extractions/year), 0.59% for high-volume surgeons, and 0.48% for surgeons who performed at least 1,000 procedures annually. The incidence of capsule complications decreased gradually over time, from 1.5% in 2007 to 0.8% in 2016. No significant correlation was found between the rate of capsule complications and the surgical volume of clinical units.

The authors noted that while surgery for advanced cataracts presents a greater risk for capsule complications, the study was not adjusted for case mix, and higher-volume surgeons operated on patients with better best-corrected visual acuity (a surrogate for less advanced cataracts). Moreover, in addi-

tion to the potential effect of increased volume, the authors noted that other factors likely contribute to the lower complication rate, including advancements in technology and the fact that more patients are undergoing cataract surgery at an early stage of the disease.

Medical Errors and Surgical Confusion

March 2020

Parikh et al. evaluated medical errors in ophthalmic surgery as well as their incidence, root causes, and effects on patients and physicians. They found that episodes of surgical confusion often related to the use of incorrect IOLs in cataract surgery and that the most common cause of confusion was an inadequately performed or erroneous time-out assessment. Nearly two-thirds of errors were deemed preventable.

For this retrospective study, the researchers included 143 cases of ophthalmic surgical confusion identified during a 12-year period by the New York State Health Department or by closed-case files of the Ophthalmic Mutual Insurance Company. Main outcomes included error types, incidence rates, impact, causes, and preventability.

In two-thirds of the cases (95 of 143; 66.4%), the confusion involved implantation of the wrong IOL in cataract surgery. Thirty-three (34.7%) of these could not have been prevented by the Universal Protocol. Other errors were incorrect eye blocks or anesthesia (20 cases [14%]), wrong eye (10 cases [7%]), and inaccurate refractive surgery measurements (six cases [4.2%]).

The most common cause of confusion was an inadequately performed time out; this was responsible for nearly a third of the errors. The second most common cause—incorrect IOL order or calculation before surgery ("upstream" errors)—accounted for more than a fifth of cases. The average legal indemnity was greatest for incorrect medication ($284,000), followed by erroneous refractive surgery measurement ($123,125), wrong IOL choice ($57,514), and performing the wrong procedure ($50,000).

The authors noted that minor modifications of the Universal Protocol, particularly concerning upstream errors and poor communication during time outs, may help prevent future errors.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Macular Findings Point to Immunoproliferative Disorder

March 2020

Smith et al. evaluated four patients with neurosensory macular detachment and asymptomatic monoclonal gammopathy of undetermined significance (MGUS). They found that angiographically silent and treatment-resistant submacular fluid may point to an underlying immunoproliferative subset of MGUS, which they term *monoclonal gammopathy of macular significance.* In addition, they found that the condition developed into malignant disease in three of the four patients. Given this heightened risk of malignancy, they recommend that patients with neurosensory macular detachment not attributable to known causes should undergo serum protein analysis.

For this retrospective case series, the researchers gathered clinical, laboratory, and imaging findings for four patients with refractory serous macular detachment associated with MGUS. Two of the patients were diagnosed incidentally with MGUS by their primary care team while being followed up for chronic submacular fluid; the others were diagnosed after their retina specialist ordered specific laboratory tests for immunogammopathy.

Of eight eyes, seven demonstrated neurosensory macular detachment with treatment-resistant submacular fluid and vitelliform material. None of the involved eyes showed signs of significant hyperviscosity retinopathy, and no definite leakage was evident on fluorescein angiography. All four patients were resistant to treatments aimed at resolving the subretinal fluid, including anti-VEGF drugs, photodynamic therapy, and topical dorzolamide.

Three of the four patients underwent malignant transformation (two to multiple myeloma, and one to lymphoplasmacytic lymphoma). The fourth patient remained free of any malignancy eight years after diagnosis.

This case series illustrates that MGUS may rarely be associated with sub- and intraretinal fluid that is angiographically silent. The authors hypothesize that preexisting chorioretinal disease—and, in some patients, genetic factors—may predispose patients with MGUS to macular fluid accumulation, and they recommend lab evaluation for immunogammopathy in patients who have serous macular detachment that cannot be attributed to known causes.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish III, MD

Deep Learning Algorithm for Glaucoma Diagnosis

March 2020

Jammal et al. compared diagnostic performance of human graders to predictions generated by a machine-to-machine deep learning algorithm trained to quantify retinal nerve fiber layer (RNFL) damage.

The algorithm was trained with RNFL thickness parameters from spectral-domain optical coherence tomography. It was then applied to a subset of 490 fundus photos of 490 eyes (370 subjects) that had been graded by two glaucoma specialists for the probability of glaucomatous optic neuropathy (GON) and estimates of cup-to-disc (C/D) ratios. Spearman correlations with standard automated perimetry (SAP) global indices were compared between the human gradings and the RNFL thickness values predicted by the algorithm. The area under the receiver operating characteristic curves (AUC) and partial AUC for the region of clinically meaningful specificity (85%-100%) were used to compare the ability of each output to discriminate eyes with repeatable glaucomatous SAP defects versus eyes with normal fields.

The algorithm-predicted RNFL thickness had a significantly stronger absolute correlation with SAP mean

deviation (rho = 0.54) than the probability of GON given by human graders (rho = 0.48; p < .001). The partial AUC for the algorithm was significantly higher than that for the probability of GON by human graders (partial AUC = 0.529 vs. 0.411, respectively; p = .016).

The researchers concluded that the algorithm outperformed human graders in detecting signs of glaucomatous visual field loss on fundus photographs. They pointed out that the algorithm provides objective and quantitative assessment of neural damage that potentially could be used for glaucoma diagnosis and screening, thus avoiding the biases and labor of human subjective gradings. However, they advised that further refinement is desirable before the algorithm can be applied to either clinical or screening settings.

Periventricular Leukomalacia and Pseudoglaucomatous Cupping

March 2020

Groth et al. set out to describe two young patients with a history of prematurity who presented with enlarged cup-to-disc ratio, normal intraocular pressure, retinal nerve fiber layer thinning superiorly, and visual field (VF) defects inferiorly and homonymously. The authors explained that, as advances in perinatal care have improved survival for premature babies, many will later present to clinicians who may be unaware of the relationship of cupping, field defects, and prematurity —and who may diagnose manifest or suspected normal tension glaucoma (NTG). However, the correct diagnosis may be periventricular leukomalacia (PVL), a structural loss of white matter pathways that carry visual information from the lateral geniculate bodies to the visual cortex.

For this case series, the authors illustrated the pseudoglaucomatous cupping related to PVL with optic disc photographs. Coronal and sagittal magnetic resonance images of the PVL patients' brains, along with those from normal controls, were used to illustrate the loss of white matter. These periventricular white matter pathways are part of the optic radiations that are adjacent to the lateral ventricle and carry visual impulses to the visual cortex; a secondary trans-synaptic degeneration of the retinogeniculate axons produces cupping similar to that seen in glaucoma.

The authors emphasize that PVL should be added to the differential diagnosis of NTG when there is a history of prematurity. Similarly, when NTG is suspected, the clinician should be careful to obtain a birth history. Careful examination of the optic nerve will assist in differentiating the two conditions. Specifically, horizontal cupping with minimal or no nasal displacement of vessels and superior optic nerve thinning with inferior VF defects should raise suspicion of PVL.

—Summaries by Arthur Stone

JAMA Ophthalmology

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

Prevalence, Types, and Severity of OCTA Artifacts

February 2020

Artifacts on optical coherence tomographic angiography (OCTA) images can lead to misinterpretation of the scans in clinical trials and real-world settings. **Holmen et al.** evaluated the prevalence and types of these artifacts and assessed their impact on image reliability. They found that more than half the study images had an artifact affecting the reliability of quantitative output. The most common artifacts were shadow, defocus, and movement.

For this cross-sectional study, the authors acquired OCTA images from multiple multicenter clinical trials and submitted them to the Wisconsin Fundus Photograph Reading Center during a three-year period (2016-2018). The images had been captured with commercially available OCTA systems in accordance with the appropriate scan protocol (3 × 3 mm or 6 × 6 mm). The specific types of artifacts were assigned a severity grade, based on involvement of cross-sectional OCT and the area of OCT grid affected. Primary outcomes were the prevalence and severity of artifacts, as well as area under the receiver operating characteristic curve (AUC) of quality indices with image reliability.

Overall, 406 OCTA images (from 234 eyes) were included in this study. Of these, 221 (54.4%) were 6-mm scans, and 185 (45.6%) were 3-mm scans. At least one artifact was detected in 395 images (97.3%). An artifact severe enough to affect the reliability of quantitative output was present in 217 images (53.4%). The most common artifacts were shadow (26.9%), defocus (20.9%), and movement (16%). Although artifact prevalence did not vary by imaging system or scan protocol, the types of artifacts differed. The commercially recommended quality index thresholds had an AUC of 0.80 to 0.83, sensitivity of 97% to 99%, and specificity of 37% to 41% for reliable images.

The findings suggest that artifacts affecting quantitative output of OCTA devices are highly prevalent at this time. *(Also see related commentary by David Sarraf, MD, and SriniVas Sadda, MD, in the same issue.)*

Ocular Changes: Spaceflight Versus Bed Rest

February 2020

Optic disc edema is a risk for all astronauts and is most common in lengthy spaceflights. **Laurie et al.** looked at whether the ocular changes in individuals exposed to a ground-based analogue of weightlessness would be similar to those observed in astronauts. Since intracranial pressure (ICP) is higher when the head is tilted downward than when it is in a supine position, the authors hypothesized that the magnitude of optic disc edema and choroidal thickening may be greater during bed rest than in spaceflight. They found that peripapillary total retinal thickness became greater during bed rest than in spaceflight—and that choroidal thickening developed only during spaceflight.

For this cohort study, the researchers enrolled 11 healthy civilians and 20 astronauts. The civilian participants were examined before, during, and after 30 days of strict bed rest with the head tilted 6 degrees downward, while the astronauts were examined before and

during approximately 30 days of spaceflight. Main outcome measures were peripapillary total retinal thickness and peripapillary choroid thickness, determined from optical coherence tomography images.

Participants on bed rest had a greater increase in peripapillary total retinal thickness than did the astronauts (mean difference of 37 μm; p = .005). Conversely, choroidal thickness did not increase with bed rest but did in spaceflight (mean difference of 27 μm; p < .001). The authors posit that the mild long-term elevation in ICP that occurs with bed rest may explain the differences in optic disc edema between the study groups. Gravitational gradients that remain present during bed rest may prevent choroidal thickening; during spaceflight, there are no such gravitational gradients.

Despite the possibility that different mechanisms may underlie optic disc edema development in different conditions, use of the terrestrial model of spaceflight-associated neuro-ocular syndrome will help in developing effective countermeasures for protecting astronauts' eyes during space missions, said the authors. They emphasized that replication of their findings is needed and that identifying the factors underlying these differences should provide new insight into the mechanisms of optic disc edema in astronauts. Although both groups have long-term mild elevation of ICP, the authors surmise that small differences in ICP between the two settings may dictate the severity of optic disc edema. *(Also see related commentary by Ari Shinojima, MD, PhD, in the same issue.)*

Using AI to Characterize Central VF Loss in End-Stage Glaucoma

February 2020

Wang et al. used artificial intelligence (AI) to quantitatively identify and classify patterns of central visual field (VF) loss in chronic glaucoma. They found that the patterns in end-stage glaucoma may be subtype specific and that the initial sign of central VF deterioration is likely to be nasal loss. In most of the identified patterns, at least part of the inferotemporal region was preserved.

The authors collected retrospectived data from five U.S. glaucoma services for a 15-year period. Central VF patterns were determined by an unsupervised AI algorithm that the authors termed "archetypal analysis." An advantage of this form of AI is its ability to determine representative VF patterns lying at the corners of the data space. The identified VF patterns closely resemble those identified by physicians, and the findings are easy to interpret.

The researchers also performed longitudinal analyses to investigate whether central VF loss affects certain vulnerability zones. Their cutoff point for end-stage glaucoma was 24-2 VF mean deviation (MD) of –22 dB.

Altogether, there were 2,912 reliable 10-2 VFs (1,103 eyes of 1,010 patients), which were measured after end-stage 24-2 VFs. The mean (standard deviation) age of patients was 70.4 (14.3) years, and the 10-2 MD was –21.5 (5.6) dB. Fourteen central VF patterns were determined, including temporal-sparing patterns (27.5%), mostly nasal loss (25.4%), hemifield loss (15.3%), central island (10.9%), total VF loss (8.3%), nearly intact field (5.1%), and others that occurred less frequently.

Location-specific analyses demonstrated two major zones of involvement: superonasal (more vulnerable) and inferotemporal (less vulnerable). Follow-up at one and two years showed that new defects were more common in the superonasal zone and that initial encroachments on an intact central VF were more likely nasal related. One pattern of nasal loss had a high risk of shifting to total VF loss by two years.

The zone-related findings of this study corroborate those of the Hood model. The early-onset nasal loss is analogous to the known nasal step patterns in early glaucoma, as measured by the 24-2 VF test. The authors emphasized that learning more about nasal loss may shed light on the pathophysiologic mechanism responsible for the onset of central VF deficiency. *(Also see related commentary by Paolo Brusini, MD, in the same issue.)*

—Summaries by Lynda Seminara

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Smartphone Tonometer Effective in Measuring IOP

British Journal of Ophthalmology
Published online Dec. 23, 2019

Wu et al. evaluated the accuracy of a novel smartphone tonometer. They found that the intraocular pressure (IOP) measurements taken with their prototype were roughly equivalent to those obtained via other tonometers used in clinical practice, with the best correlation seen using Goldmann applanation tonometry (GAT).

The tonometer used in this study clamps onto an iPhone 6 that aligns with the camera and flash. It uses fixed force applanation in conjunction with a machine-learning computer algorithm to calculate IOP. For this proof of concept study, the researchers enrolled 81 patients (162 eyes) at a university glaucoma clinic. Topical fluorescein/benoxinate (Fluress) was applied to both eyes of each patient, and IOP was measured by trained ophthalmic technicians, first using GAT and then the smartphone device. A subset of 38 patients also were evaluated with other tonometers.

Of the 162 smartphone recordings obtained from the 162 eyes, the machine learning algorithm was successful in processing 92 (56.8%). Of these, 90 (97.8%) were within ±5 mm Hg of GAT, and 58 (63%) were within ±2 mm Hg of GAT. The mean difference for IOP measurements of the smartphone tonometer versus the other tonometers was +0.24 mm Hg for GAT, –1.30 for Tono-Pen, –1.39 mm Hg for iCare, and –3.71 mm Hg for pneumotonometry.

The authors noted that a smartphone-based tonometer such as theirs complements other smartphone attachments and applications to facilitate a portable ophthalmological examination, which may improve access to eye care in resource-poor regions.

—Summary by Arthur Stone

EXTRA **MORE ONLINE.** For an additional summary, see this article online at aao.org/eyenet.