**Noncycloplegic Measurements in Students**

Measuring cycloplegic refraction in school settings can pose logistical and consent challenges, leading to suboptimal participation in school-based vision programs. Although noncycloplegic refraction in the same setting is less complicated, it's unclear if this parameter is a viable starting point for prescribing glasses. Guo et al. explored differences between autorefraction measurements, with and without cycloplegia, among predominantly Black and Hispanic students in Chicago. They found that spherical equivalents (SEs) for cycloplegic and noncycloplegic measurements varied by less than a diopter in three-fourths of their study group. Concordance was more likely in myopic and older participants.

This cross-sectional review included 11,119 participants (mean age, 10.8 ± 4 years). In addition to documenting differences between cycloplegic and noncycloplegic measurements for each participant, the authors explored factors linked to significant discrepancies between the two types of measurements. They collected demographic data during eye exams and performed autorefration before and after the cycloplegic state. Myopia, hyperopia, and astigmatism were established from cycloplegic and noncycloplegic measurements.

Slightly more than half (52.4%) of the participants were female, 62.9% were Black, and 32.3% were Hispanic. Noncycloplegic SE measurements were found to be .65 ± 1.04 D more myopic than cycloplegic SE measurements. After adjusting for demographics and refractive error, individuals with at least 1 D of more myopic SE refraction by noncycloplegic autorefraction (25.9%) tended to be younger than 5 years of age (odds ratio [OR], 1.45; 95% confidence interval [CI], 1.18-1.79) or between 5 and 10 years of age (OR, 1.32; 95% CI, 1.18-1.48). An SE difference of at least 1 D was more common in Hispanics (OR, 1.23; 95% CI, 1.10-1.36) and in those with hyperopia (OR range, 4.20-13.31). Factors linked to a cylindrical difference of at least .75 D (5.1%) between refractions were young age (<5 years); male sex; the presence of mild, moderate, or high myopia; and the presence of moderate to high hyperopia.

Understanding differences in the measurements used to assess refractive error may be helpful for future studies and school-based vision programs, said the authors. They cautioned that the generalizability of their findings may be limited by the racial/ethnic makeup of their study cohort.

**Tumor Staging: Conjunctival Melanoma Outcomes**

Although conjunctival melanoma (CM) is a rare cancer, it has grown in prevalence and has the potential to metastasize. Jia et al. studied the predictive value of the tumor staging system described in the AJCC Cancer Staging Manual (8th edition) and explored histologic features linked to outcomes and metastasis patterns in patients with CM. In their review, the staging system was effective prognostically. Most cases of CM presented in an advanced stage, and the rate of distant metastases was high.

The retrospective cohort included 83 patients with CM who were treated in China during the last two decades. The authors documented clinical and histologic findings for each patient and used Kaplan-Meier survival curves and Cox proportional-hazards models to analyze risk factors. Main outcome measures were disease-specific survival period, metastatic pattern and site, and time to nodal/distant metastasis.

At presentation, the tumors of five patients (6%) were staged as cT1 (clinical tumor 1), those of 34 patients (41%) were classified as cT2, and those of 44 patients (53%) were graded as cT3. Four patients (5%) had nodal metastas-
sis at presentation, and none had dis-
tant metastasis. During the follow-up
period, nodal metastasis was observed
in 12 patients (14%), distant metastasis
occurred in 29 (35%), and there were
26 (31%) disease-related deaths. Com-
mon sites of metastases were the brain,
Liver, and lungs. Patients with brain
involvement had a poor prognosis,
and their median survival time was
only five months.

A high cT category carried greater
risk of distant metastasis (p < .001)
and disease-specific death (p = .002).
A separate analysis that included pri-
mary and recurrent tumors showed that
metastatic risk was highest for cT3
tumors. Ulceration, thicker tumors,
and regression correlated with distant
metastasis. Among the 29 patients
who experienced distant metastasis,
11 (38%) had nodal metastasis before
distant metastasis, and 18 (62%) had
distant metastasis without previously
known nodal metastasis. Grade cT3
tumors generally followed the latter
pattern. Previously unreported mu-
tations were detected in the tumor
suppressor genes FAT4 and SYK.

These findings indicate that patients
who present with a cT3 tumor are more
likely than those with lower-grade tumors
to develop distant metastasis without
previous nodal metastasis. The authors
emphasized that histologic features such
as thickness and ulceration may help
to determine prognosis and optimal
treatment. The results of this study
will allow physicians to provide more
accurate prognostic information for
patients with CM.

Enduring Effects of Microstent
Use
July 2022

Randomized trials of the Hydrus Micro-
stent (HMS) have found that it signifi-
cantly reduces IOP and medication
burden through two years following
surgery for primary open-angle glau-
coma (POAG). By year 3, recipients
of the HMS were less likely to require
additional incisional surgery for glauco-
ma. Subsequently, Ahmed et al. looked
at five-year outcomes of the HORIZON
trial, in which cataract surgery alone
was compared with combined cataract/
glaucoma surgery with the HMS. They
found that the stent group had greater
reductions in IOP, lower medication
use, and less need for post-op incisional
glaucoma-filtration surgery. Long-term
presence of the implant did not ad-
versely affect corneal endothelial cells.

HORIZON was a prospective,
multicenter, randomized controlled
trial. Participants included those with
cataract and POAG who had received
at least one glaucoma medication and
had not undergone incisional surgery
for glaucoma. Washed-out diurnal IOP
ranged from 22 to 34 mm Hg. Eyes
were assigned randomly (2:1) to receive
either the HMS or no stent after suc-
cessful cataract surgery. Main outcomes
included IOP, use of glaucoma medica-
tion postoperatively, need for addition-
al glaucoma surgery, visual acuity and
visual field, procedure-related adverse
events, and endothelial cell counts.

Of the original HORIZON cohort,
five-year follow-up was complete for
83.5% of the HMS group and 71.7% of
those who underwent cataract surgery
alone. At five years, the HMS group had
a higher proportion of eyes with IOP
≤18 mm Hg (49.5% vs. 33.8%; p = .003) and greater likelihood of an
IOP reduction of at least 20% (54.2%
vs. 32.8%; p < .001). The number of
glaucoma medications used at the
five-year mark was 0.5 ± 0.9 in the
HMS group and 0.9 ± 0.9 in the cata-
ракt surgery–only group (p < .001);
no glaucoma medication was used in
66% of HMS eyes and 46% of cataract
surgery–only eyes (p < .001). Moreover,
the cumulative risk of further incisional
surgery was lower in the HMS group
(2.4% vs. 6.2%; p = .27). From three
to 60 months post-op, no clinically or
statistically significant differences were
noted in the rate of endothelial cell loss.

The authors emphasized that by
reducing medication burden and low-
ering risk of repeat glaucoma surgery,
the HMS would likely have durable and
meaningful effects on quality of life.
The results suggest that HMS place-
ment at time of cataract surgery offers
long-term benefit for management of
POAG.

—Summaries by Lynda Seminara

Ophthalmology Retina

PPV Versus PPV Plus Scleral
Buckle for RDs
July 2022

In an international study, Ong et al. set
out to determine surgeons’ preferences
for treating giant retinal tear–related
retinal detachments. They found that
pars plana vitrectomy (PPV) and PPV
plus scleral buckle (PPV+SB) are equally
common and have comparable anatom-
ic and visual outcomes among adults.
Among children younger than age 18
years, however, PPV+SB was superior
to PPV alone at the one-year mark.

For this retrospective cohort study,
the researchers reviewed electronic
medical records from seven medical
institutions around the world. A total
of 195 patients (200 eyes), 42 of whom
were children, were included in the
study. All told, 101 eyes underwent PPV
alone, and 99 underwent PPV+SB.
Baseline demographics and ocular
characteristics studied did not differ
between the two groups except
for those patients with a history of
developmental abnormalities or who
had prior intraocular surgery and were
phakic.

With regard to anatomic outcomes,
the overall success rates were similar
between the two groups at six and
12 months: 82.2% and 77.2% for
PPV alone, respectively, and 87.9%
and 85.7% for PPV+SB, respectively.
However, when stratified by age, the
12-month success rate was higher for
PPV+SB than for PPV alone for chil-
dren younger than age 18 (88.5% versus
56.3%; p = .03).

With regard to visual outcomes,
the mean best-corrected visual acuity
at baseline did not differ between PPV
and PPV+SB groups. Once again, how-
ever, when stratified by age, children
who underwent PPV+SB had better
outcomes at 12-month follow-up than
those who underwent PPV alone (p = .001). No such difference was found for
adults.

The mean time to first redetachment
was 7.9 months in the PPV group and
5.5 months in the PPV+SB group, with
proliferative vitreoretinopathy as the
most common cause of redetachment. Postoperative complications were similar between the two groups.

Overall, these results support the use of PPV+SB in children and PPV alone in adults as an option for treating giant retinal tear–related retinal detachments, the authors said.

—Summary by Jean Shaw

**American Journal of Ophthalmology**
Selected by Richard K. Parrish II, MD

**Thyroid Function and AMD Risk**
July 2022

Although a link between thyroid hormones and risk of age-related macular degeneration (AMD) has been reported for animal models, findings of subsequent observational studies have been inconsistent, suggesting that hidden confounding factors could affect results. To eliminate potential confounders, Li et al explored the relationship between thyroid hormone function and AMD using Mendelian randomization (MR). They found that genetic variants predisposing patients to free thyroxine (FT4) levels in the high-normal range were associated with greater AMD disease risk. However, there was no clear evidence of an independent causal relationship between AMD and levels of thyroid-stimulating hormone (TSH).

To enhance their study’s statistical power, the authors used two separate population samples. In one, the single-nucleotide polymorphisms associated with FT4 and TSH were extracted from a genome-wide association study (GWAS) of 72,167 people of European descent. In the other, summary-level data for AMD were obtained from an International Age-Related Macular Degeneration Genomics Consortium GWAS that included 16,144 patients with AMD and 17,832 control subjects, recruited from 26 studies.

The results showed that each standard deviation (SD) increase in genetically predicted FT4 levels was significantly associated with an 18.9% increase in overall AMD risk (p = .005). In the multivariable MR analysis that was controlled for TSH level, the causal effect of FT4 level on the risk of AMD also was strong (odds ratio, 1.207; p = .004). In contrast, a 1-SD increase in TSH levels coincided just nominally with a 10% reduction in overall AMD risk (p = .032). Subsequent multivariable MR analysis adjusted for FT4 level did not show a direct causal relationship between TSH level and AMD risk (p = .582).

Given the multiple sensitivity analyses for pleiotropic genes plus adequate statistical power to detect causal associations, the overall findings of this study suggest an intrinsic negative effect of thyroid hormone function on the development of AMD. The authors encourage investigation of the mechanism behind the apparent link between FT4 and AMD risk, which may be a basis for new risk-reduction strategies.

**COVID-19 Outcomes in Patients With AMD**
July 2022

COVID-19 and age-related macular degeneration (AMD) each are linked to inflamming, a term for human aging characterized by chronic low-grade systemic inflammation. Moreover, COVID-19 and AMD share an underlying mechanism—dysregulation of complement cascades—which may explain the observation that patients with AMD have a higher risk for severe COVID and poor outcomes. To further explore the relationship between AMD and SARS-CoV-2 susceptibility and outcomes, Yang et al stratified AMD subtypes and used propensity-score matching to reduce confounder bias in a large study of patients with SARS-CoV-2. They found that the presence of exudative AMD increases the likelihood of testing positive for COVID and is a harbinger of poor outcome after infection.

For this two-sample nationwide cohort study in South Korea, the authors gathered data from COVID-19 registries and a national claims-related database on patients ≥40 years of age who had a SARS-CoV-2 test during the first 4½ months of 2020. Self-referrals were excluded. Outcome measures were results of polymerase chain reaction testing for SARS-CoV-2 and related clinical outcomes. Confounders of interest included age, sex, and history of predesignated diseases (such as hypertension, diabetes, chronic kidney disease, and lung disease). Outcomes considered “severe” were ICU admission, mechanical ventilation, oxygen supplementation, and/or death.

The unmatched cohort comprised 135,435 patients who underwent SARS-CoV-2 testing. Of these, 4,531 (3.3%) had a positive COVID result, and 5,493 (4.1%) had AMD (mean age, 72.5 years). Patients with exudative AMD were older, more likely male, and more often had a history of comorbidity (all p < .001). Matched groups had no significant difference in baseline characteristics.

Of those who tested positive for COVID, 150 also had AMD. After propensity score matching, exudative AMD was associated with an increased likelihood of susceptibility to SARS-CoV-2 infection (adjusted odds ratio [OR], 1.50; 95% confidence interval [CI], 1.03–2.25). In addition, exudative AMD was associated with a greater risk of severe COVID outcomes (OR, 2.26; 95% CI, 1.02–5.26).

To validate findings of this study, the authors urge research in large national, international, and multiethnic populations. —Summaries by Lynda Seminara

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

**Association of Topical Prostaglandins With Miscarriages**
June 2022

Do topical prostaglandin analogues (PGAs) increase the risk of miscarriage in pregnant patients with glaucoma? Etmian et al examined this hypothesis and found no association between PGA use and spontaneous abortions.

For this case-series study, the researchers used the PharMetrics Plus database for health claims in the United States from 2006 to 2020. They quantified the percentage of spontaneous abortions among patients who took a
topical PGA and a control cohort of women in the database who did not take a PGA. All participants were between 15 and 45 years of age. The main outcome was billing codes for diagnosis and treatment of spontaneous abortion.

All told, the researchers identified 3,881 women of reproductive age who were prescribed a PGA. Of these, 261 were pregnant, and 26 had a spontaneous abortion code. In comparison, of the 3,881 women in the control group, 801 were pregnant, and 56 were identified as having experienced a spontaneous abortion. The researchers noted that both groups were comparable with respect to age, mood disorders, preeclampsia, and the use of drugs associated with spontaneous abortion (e.g., antiepileptics, selective serotonin reuptake inhibitors, and serotonin antagonists).

In their discussion, the authors noted that pharmacologic data indicate that oral PGAs may cause uterine contraction—and that systemic absorption has been reported with topical PGAs. In addition, they point out that topical PGAs are currently classified as pregnancy category C (teratogenic in animals), although the doses used in the relevant animal studies were up to 80 times higher than those used in humans.

Although the results of their study indicate no association between PGA use and the risk of spontaneous abortion, the authors recommend further exploration of the topic in epidemiologic studies that can better control for potential confounding variables. (Also see related commentary by Thasarat Sutabutr Jajaranant, MD, MHA, in the same issue.)

Missed Opportunities to Prevent Acute Angle-Closure

June 2022

How often do clinicians miss opportunities to diagnose and treat acute angle-closure crisis (AACC)? Wu et al. set out to identify Medicare patients who presented with AACC and assess factors that may have raised their risk of developing it. They found that there appear to have been multiple opportunities for interventions that may have averted AACC.

For this population-based retrospective cohort study, the researchers included a 20% nationwide sample of Medicare beneficiaries (n = 1,179). Patients aged 40 years or older with AACC were identified with billing codes. A two-year lookback period from the point of patients’ initial presentation with AACC was used to identify those who had at least one eye care visit, received a diagnosis of open-angle glaucoma (OAG), or received at least one medication associated with risk of developing AACC (e.g., selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, antihistamines, carbonic anhydrase inhibitors, and topiramate). In addition, among patients who had at least one eye care visit, the researchers identified those who either had undergone gonioscopy or were diagnosed with an anatomic narrow angle before developing AACC.

The mean age of those with AACC was 66.7 years (range, 40-96 years), and 766 (65%) were women. With regard to race, the majority (n = 791; 67.1%) were White. A total of 464 individuals (39.4%) had OAG or suspected OAG, and 414 (35.3%) had received a medication associated with increased risk of AACC before they developed the condition.

With regard to eye care, 796 of the 1,179 patients (67.5%) had consulted an ophthalmologist or optometrist during the two-year lookback period; the remainder had received no eye care during this time. Of those who were examined, 264 (33.2%) underwent gonioscopy in the two years preceding their diagnosis with AACC. Of those who had gonioscopy, 113 (42.8%) received a diagnosis of an anatomic narrow angle.

In their discussion, the authors noted that the results highlight multiple missed opportunities for interventions to prevent AACC. They recommend addressing risk factors associated with the underuse of eye care as well as additional emphasis on correct gonioscopy technique, greater use of gonioscopy to identify patients with eyes at risk, and prophylactic laser peripheral iridotomy when indicated. (Also see related commentary by Alexander C. Day, PhD, and Gus Gazzard, MA, MD, MBBS, in the same issue.)

Residency Program Websites: Signs of Diversity and Inclusion

June 2022

Ledesma Vicioso et al. evaluated U.S. ophthalmology program websites for information on diversity or inclusion. They found that this information is lacking on most program websites.

For this quality improvement study, the researchers included a cross-sectional review of ophthalmology program websites. The websites were reviewed for the presence of six predetermined diversity or inclusion information criteria, and the study was conducted in mid-2021.

The criteria, modeled after those implemented in previously published literature, were as follows: 1) evidence of commitment to, or value toward, diversity (i.e., in a message from the program director or department chair); 2) a separate diversity mission statement; 3) mention of rotations or fellowship opportunities for underrepresented minority medical students; 4) mention of diversity initiatives; 5) a web page or section on diversity; and 6) mention of diversity leadership positions.

Of the 121 U.S. program websites reviewed, 29 (24%) met at least one of the six criteria. Programs with more than 12 residents, as well as those programs ranked within the top 20 best hospitals for ophthalmology (as determined by the US News & World Report), were more likely to have at least one of the criteria on their website. Of note, 53 of the websites (44%) mentioned that their residency program offers trainees the opportunity to care for a diverse population.

In discussing the results, the authors noted that “these findings suggest that there is a gap in the information that prospective applicants can collect when evaluating ophthalmology residency program websites.” (Also see related commentary by Russell S. Gonnering, MD, MMM, in the same issue.)
Prompt Open Globe Repair Is Crucial
Clinical Ophthalmology
2022;16:1401-1411

Open globe injury from an intraocular foreign body (IOFB) can severely affect vision and lead to endophthalmitis. Although there is consensus on common risk factors and stratification schemes for these wounds, there is controversy about the type and timing of treatment. Keil et al. reviewed IOFB cases in an effort to define predictors of poor outcomes and explore management strategies. They found that poor visual acuity (VA) and severe injury at presentation were associated with poor visual outcomes. Prompt globe closure and antimicrobial prophylaxis were crucial to avoid infection.

For this study, the authors gathered details from medical records of 88 patients (88 eyes) who experienced IOFB-related injury and were seen at the University of Michigan Medical School from 2000 through 2019. Pertinent data were documented, including VA, injury characteristics, treatment modalities, and clinical outcomes. Multivariate logistic regression was employed to determine correlations between presenting factors and visual outcomes, which were classified as good (corrected VA of 20/40 or better) or poor (corrected VA of 20/200 or worse). Unpaired t tests and Fisher’s exact tests were used to compare continuous and categorical variables, respectively.

The analyses showed that delayed presentation (p = .016) and organic IOFB (p = .044) correlated strongly with endophthalmitis. Retinal detachment (p = .012), wound length >5 mm (p = .041), and reduced VA (p = .003) were linked to poor final visual outcomes. All patients were given antibiotic prophylaxis, but the choice of specific agent and route of delivery varied. More than 80% of patients received antibiotics systemically, and intravitreal administration was used in 50% of primary IOFB removals and in 86% of secondary removals. Endophthalmitis occurred in 4.9% of the eyes after initial management, and rates were similar for primary and secondary procedures.

Findings of this 20-year experience indicate that outcomes are optimized by prompt treatment, including globe closure and antimicrobial prophylaxis. The authors noted that if IOFB removal and globe closure cannot be done concurrently, aggressive antibiotic prophylaxis alone may be sufficient to prevent endophthalmitis.

Intereye Correlation in Patients With Glaucoma
Graefe’s Archive for Clinical and Experimental Ophthalmology
Published online May 2, 2022

About 50% of patients diagnosed with open-angle glaucoma will eventually develop it in both eyes. In some countries, patients can be hospitalized for 24-hour monitoring of IOP to capture elevations that may occur outside of office hours. Previously, Dakroub et al. developed an extraction tool for manually charted IOP curves (HIOP-Reader), analyzed data for right eyes, and found that 24-hour monitoring is a poor tool for detecting glaucoma progression. In a subsequent study, they looked at data for left eyes to compare intereye IOP, ocular perfusion pressure, and progression parameters. They hypothesized that even though 24-hour IOP data may be flawed, both eyes are affected similarly, and thus intereye measurements may help to predict glaucoma in contralateral eyes. As in their previous study, they found that measuring IOP in one eye inadequately predicted progression, but intereye correlations were meaningful for all parameters tested.

In this study, the authors gathered 24-hour data for left eyes using the HIOP-Reader software. They explored the relationship between mean ocular perfusion pressure (MOPP) and retinal nerve fiber layer (RNFL) thickness. They determined receiver operating characteristic (ROC) curves for peak IOP, average IOP, IOP variation, and historical IOP cutoff levels to assess glaucoma progression (i.e., rate of RNFL loss). They used bivariate analysis to look for intereye relationships.

The study included 217 eyes. Per the hospital’s standard protocol, IOP measurements were obtained at 10 a.m., 2 p.m., 5 p.m., 9 p.m., and midnight. During the monitoring period, the average IOP was 14.8 ± 3.5 mm Hg, and the mean variation was 5.2 ± 2.9 mm Hg. RNFL data indicated glaucoma progression in 52% of eyes. There were no significant differences in peak IOP, average IOP, or IOP variation between those who progressed and those who did not. Except for average IOP in relation to temporal RNFL, disease progression in any quadrant was not found to correlate with peak IOP, average IOP, or IOP variation. In- and outpatient IOP readings were not sensitive or specific for detecting progression.

Moreover, the correlation of intereye parameters was moderate, and the relationship to disease progression was weak.

This research and previous work suggest that IOP data are unreliable diagnostically but that intereye findings may be clinically relevant. For most patients in this study, IOP and MOPP were similar for left and right eyes. Therefore, when substantive RNFL loss is observed in one eye, it is likely occurring in the contralateral eye as well.

—Summaries by Lynda Seminara

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