Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Physical Activity Slows VF Loss in Patients With Glaucoma
July 2019

Growing evidence suggests that physical activity may protect against visual field (VF) damage. **Lee et al.** looked at the relationship between glaucoma-related VF loss and various levels of physical activity. They found that greater physical activity correlated with slower loss of vision.

This longitudinal observation study included 141 adults (mean age, 65 years) with confirmed or suspected glaucoma. Participants wore an accelerometer for one week to determine steps per day and the time spent being active. To measure the rates of VF loss, the authors analyzed all available VF data. The main outcome measure was the pointwise change in VF sensitivity associated with the various measures of physical activity.

Among the study group, eye mean deviation (MD) at the time of assessment was -6.6 dB, and the average number of steps per day was 5,613 ± 3,158. The unadjusted average rate of VF loss, measured by pointwise VF sensitivity, was 0.36 dB per year. Multivariable models showed slower VF loss for patients who took more steps (+0.007 dB/year/1,000 daily steps; $p < .001$), who had a higher level of moderate-to-vigorous activity (+0.003 dB/year/10 more minutes of moderate-to-vigorous activity per day;

$p < .001$), and who engaged in more nonsedentary activity (+0.007 dB/year/30 more minutes of nonsedentary time per day; $p = .005$). Factors linked to quicker VF loss included older age, nonwhite race, history of glaucoma surgery or cataract surgery, and moderate VF damage at baseline. Similar relationships between baseline accelerometer-measured physical activity and rates of VF loss were noted for extended time periods (i.e., within one, three, and five years of the activity assessment).

This study showed that taking an extra 5,000 steps per day (2.6 hours of nonsedentary physical activity) decreased the average rate of VF loss by about 10%. Further research is needed to confirm this association. If proven true, it would mean that physical activity is a novel modifiable risk factor for preventing glaucoma-related ocular damage.

EHR Use and Incentives Among Ophthalmologists: 2011-2016
July 2019

Boland et al. studied ophthalmologists' rate of meaningful use of electronic health records (EHR) in the Medicare
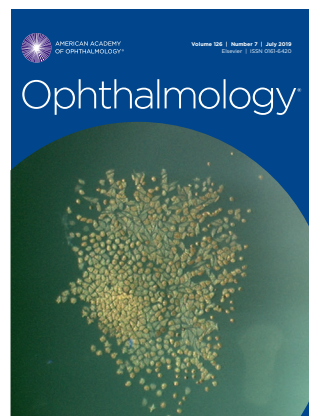
Incentive Program, as well as the compensation received. The authors compared these data with those of four other Medicare-billing specialties and found that ophthalmology had better results than optometry and dermatology but was outperformed by otolaryngology and urology. In addition, ophthalmologists were more likely to stay in the program after their first year of attestation than were all eligible providers from four other selected specialties.

The study included providers who participated in the Medicare EHR Incentive Program during program years 2011 through 2016. Publicly available sources were consulted to determine attestation and payment data, which were gathered for ophthalmology, optometry, dermatology, otolaryngology, and urology. Attestation data for each year and stage of the program were used to determine the number of participating professionals. Also calculated was the proportion of attestations for each EHR vendor. Outcomes of interest were the number of attesting ophthalmologists (by year and stage of the program), the number of attestations per EHR vendor, and the amount of incentive payments. Data were compared for the various specialties.

The authors found that, in the peak year of participation for each specialty, 51.6% of ophthalmologists attested to meaningful use of EHR systems (2016),

versus 37.1% of optometrists (2013), 50.2% of dermatologists (2016), 54.5% of otolaryngologists (2013), and 64.4% of urologists (2016). During the six-year period, the average incentive payments were $17,942 for ophthalmologists, $11,105 for optometrists, $16,617 for dermatologists, $20,203 for otolaryngologists, and $23,821 for urologists. The EHR systems used most often by ophthalmologists were Epic and NextGen.

Even though ophthalmology fared relatively well in meaningful EHR use, many ophthalmologists have not participated in the incentive program or stopped participating; 2015 data indicated that 25% were not engaged in the program. Top reasons for nonparticipation by ophthalmologists were high costs and complex reporting.

Systemic Safety Profile of Anti-VEGF Therapy for DME
July 2019

Although intravitreal anti-VEGF therapy is the standard of care for diabetic macular edema (DME), the systemic safety of this treatment has not been established. **Maloney et al.** used a large claims database to ascertain the risk of serious systemic events among patients with DME who received intravitreal injections of anti-VEGF drugs. Their analysis showed that, compared with patients treated by corticosteroids or macular laser, those who received intravitreal injections did not have a higher risk of cerebrovascular disease, myocardial infarction, or major bleeding.

For this retrospective cohort study, the researchers included adults treated with intravitreal anti-VEGF therapy from 2006 to 2015. Patients were identified from a large U.S. insurance database. Eligible participants had private insurance or were members of a Medicare Advantage plan; all had medical coverage for at least one year before starting DME treatment. Using the same database, the authors also identified patients who were treated with macular laser or intravitreal corticosteroids; these patients served as controls.

Main outcome measures were
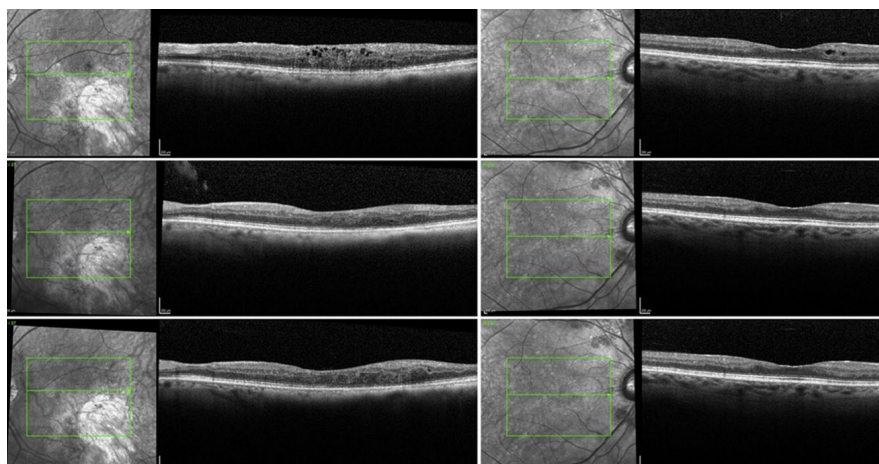
COMPARISON. *A patient in the treat-and-extend arm (left) and the fixed-schedule arm (right), during the initial visit (top), the fifth visit (center), and the final visit (bottom). Adapted from* Ophthalmology Retina.

associations between the treatments and predefined systemic outcomes, using Cox proportional hazards regression, and they included the risk of cerebrovascular disease, myocardial infarction (MI), major bleeding, and all-cause hospitalization occurring within six months of initial DME treatment.

For the comparison between anti-VEGF and macular laser therapy, inverse propensity score weighting was used to account for treatment selection bias. Because relatively few patients received corticosteroids, the comparison with anti-VEGF treatment required 2:1 propensity score matching for demographics, study year, and baseline comorbidities. Results were expressed as hazard ratios (HRs) and 95% confidence intervals (CIs).

Altogether, 23,348 patients met the inclusion criteria. Of these, 13,365 were initially treated with macular laser, 9,219 with anti-VEGF therapy, and 764 with intravitreal corticosteroids. The analysis showed no link between anti-VEGF therapy and elevated risk of cerebrovascular disease (HR, 0.96; CI, 0.65-1.41; p = .83), major bleeding (HR, 1.23; CI, 0.76-1.99; p = .41), or MI (HR, 1.03; CI, 0.73-1.44; p = .88), as compared to macular laser treatment. Rates of primary systemic serious event were similar for anti-VEGF and corticosteroid treatment (all p > .05). The risk of all-cause hospital admission after treatment was higher with anti-VEGF therapy than with macular laser (HR,

1.17; CI, 1.05-1.30; p = .01). This finding may warrant further study.
—*Summaries by Lynda Seminara*

Ophthalmology Retina
Selected by Andrew P. Schachat, MD

Aflibercept Effective for Radiation Maculopathy
July 2019

Murray et al. set out to evaluate whether intravitreal aflibercept could help maintain vision in patients who received radiation for uveal melanoma. They found that the anti-VEGF treatment appears to limit vision loss associated with radiation maculopathy.

For this prospective study, the researchers enrolled 40 patients with uveal melanoma and documented tumor control. All patients had visually compromising radiation maculopathy, which was documented by spectral-domain optical coherence tomography (SD-OCT) and confirmed by a decline in best-corrected visual acuity (BCVA).

The patients were randomly assigned to receive injections of aflibercept 2.0 mg/0.05 mL either on a fixed six-week schedule or under a treat-and-extend protocol. For those in the treat-and-extend arm, improvement in maculopathy, as seen on SD-OCT, allowed for a one-week increase in the follow-up interval; conversely, a worsening in maculopathy mandated a one-week decrease. Main outcome measures were

BCVA and SD-OCT measurements of central retinal thickness.

Thirty-nine of the 40 patients completed the study with 60 weeks of follow-up. Mean BCVA at baseline was 20/63; this was maintained at 20/62 at the study's conclusion. Mean SD-OCT central retinal thickness was 423 μm at baseline; this improved to 294 μm at 60 weeks.

Visual acuity improved by 3 or more lines in five patients, decreased by 3 or more lines in six patients, and held stable in the remainder. One patient experienced a single episode of an inflammatory response after receiving an intravitreal injection. No other adverse side effects were noted.

With regard to the two treatment approaches, the authors noted that they initially hoped that the treat-and-extend arm would allow for fewer intravitreal injections during the course of the study. However, this did not prove to be the case, as virtually all patients required treatment every six weeks.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Use of Confocal Microscopy to Diagnose Corneal Graft Rejection
July 2019

Chirapapaisan et al. investigated whether laser in vivo confocal microscopy can help support the diagnosis of corneal graft rejection. They found that it could, as immune cell density was significantly higher in rejected grafts than in those that were not rejected.

For this prospective case-control study, the researchers enrolled 38 patients who had undergone penetrating keratoplasty (15 with graft rejection; 23 without) and nine age-matched healthy controls. Full-thickness confocal microscopy scans were performed in the central cornea of all eyes with grafts and in one eye of each of the nine control subjects. In addition, multiple scans were taken of the epithelial, sub-basal, stromal, and endothelial layers, and five representative images of each layer were selected for analysis of immune cell density by a masked observer. The main outcome was the immune cell density in the corneal layers and its associations with any clinical signs and symptoms of graft rejection.

Significant differences in immune cell densities were found among normal control patients, nonrejected grafts, and rejected grafts: Total immune cell density was 48.60 ± 10.67 cells/mm^2 in controls, 187.70 ± 22.80 cells/mm^2 in nonrejected grafts, and 285.32 ± 53.23 cells/mm^2 in rejected grafts. When immune cell densities were compared layer by layer, higher densities were seen only in the sub-basal and endothelial layers of the rejected grafts than in the nonrejected ones.

With regard to clinical signs and symptoms of graft rejection, all of the 15 patients who had experienced graft rejection experienced decreased vision, 10 had ocular irritation, nine complained of light sensitivity, and seven reported ocular pain. Those with pain, ocular irritation, and light sensitivity were more likely to have increased immune cell density in the sub-basal layer, and those with pain were also more likely to have a higher density in the epithelial layer.

In addition, all patients with rejected grafts had one or more typical clinical signs of rejection, with specific signs associated with increased density in particular corneal layers. Patients with anterior chamber cells and the Khodadoust line were more likely to have elevated immune cell density in every corneal layer.

The results suggest that confocal microscopy may be useful as an adjunct tool for diagnosing corneal graft rejection during the early stages of immunologic reaction, particularly in questionable or subtle cases, the authors said.

Timolol and Aqueous Humor Outflow in Healthy Eyes
June 2019

Kazemi et al. assessed the effect of timolol on outflow facility in healthy human eyes. They found that the drug reduces outflow facility—and that this effect is greater in eyes with higher outflow facility at baseline.

For this prospective study, the researchers evaluated 113 participants who were 40 to 81 years old. At baseline, intraocular pressure (IOP) was measured in both eyes of each participant in both a sitting and supine position. Outflow facility was measured while participants were in a supine position. The participants were instructed to instill timolol 0.5%, one drop every 12 hours in both eyes, for one week. At that point, IOP and outflow facility measurements were repeated.

The mean IOP at baseline was 15.1 ± 3.0 mm Hg; this decreased to 12.4 ± 2.4 mm Hg after one week of timolol. Mean outflow facility at baseline was 0.23 ± 0.08 μL/min per mm Hg; this decreased to 0.18 ± 0.08 μL/min per mm Hg after the treatment week. In addition, higher baseline outflow facility was associated with greater decrease in outflow facility after timolol treatment.

This reduction in outflow facility may partially negate the overall IOP-lowering effect of timolol, the authors noted. Although the precise mechanism behind this phenomenon remains to be determined, one possible explanation may involve the blockade of beta-receptors in the trabecular outflow pathway. Alternatively, compensatory physiologic changes may be involved.

—Summaries by Jean Shaw

JAMA Ophthalmology

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

Impact of Vision Loss on Hospitalization Costs
June 2019

Patients with vision loss who are hospitalized for common illnesses may not be identified as needing special attention for their vision deficits. **Morse et al.** compared health care utilization for older adults with and without vision loss who were hospitalized for similar conditions. They found that those with severe visual impairment had longer hospital stays, higher readmission rates, and greater costs during and after hospitalization.

For this study, the authors looked at claims data from Medicare and the Clinformatics Data Mart. Individuals with vision loss were matched (1:1) to those with no visual impairment based on age, years since initial hospitalization, and other demographics. All patients were members of Medicare or a commercial health plan, and all had been hospitalized for a common illness such as congestive heart failure, major joint replacement, or pneumonia. Vision loss was categorized as either partial or severe. ICD-9-CM billing codes (369.xx) were used to classify those patients with severe vision loss (≥1 record of codes 369.0x to 369.4x), partial vision loss (≥1 record of 369.6x to 369.9x and no SVL code), or no vision loss (no record of any 369.xx code).

Main outcomes were lengths of stay, readmission rates, and hospital costs (during hospitalization and within 90 days after discharge). Multivariable logistic and linear-regression models were used to identify factors associated with these outcomes in each study arm. Data were analyzed for 2015 to 2018.

There were 6,165 Medicare beneficiaries with no vision loss (mean age, 82.0 years), 3,401 with partial vision loss (mean age, 80.4 years), and 2,764 with severe vision loss (mean age, 83.9). In the Clinformatics database, the number of patients in those categories were 5,929 individuals (mean age, 73.7 years), 3,515 (mean age, 71.8), and 2,414 (mean age, 76.6), respectively.

Hospital stays were longer, readmission rates were higher, and hospitalization costs (through 90 days following discharge) were greater for Medicare members with severe vision loss versus those with no visual impairment (mean stay, 6.48 vs. 5.26 days; mean readmission rate, 23.1% vs. 18.7%; mean costs, $64,711 vs. $61,060).

In addition, those with severe vision loss stayed 4% longer in the hospital (estimated ratio, 1.04; p = .02), had 22% higher readmission rates (odds ratio, 1.22; p = .007), and incurred 12% higher costs (estimated cost ratio, 1.12; p < .001). Results were similar for patients with commercial health plans.

In extrapolating their findings to nationwide hospitalization, the authors estimated that the additional cost of caring for patients with vision loss exceeds $500 million annually. In addition, they noted that addressing the vision deficits of hospitalized patients could result in substantial cost savings and better health outcomes. *(Also see related commentary by David W. Parke II, MD, and Anne L. Coleman, MD, PhD, in the same issue.)*

Advantages of the DUCK Scoring System for Determining Keratoconus Progression
June 2019

Defining keratoconus progression is crucial for treatment decisions, but consensus is lacking as to which parameters are best suited for this purpose. **Wisse et al.** compared two methods for determining keratoconus progression and found that the Dutch Crosslinking for Keratoconus (DUCK) score was superior to conventional methodology (e.g., change in maximum keratometry).

The comparative prospective study was conducted at two academic treatment centers (one for discovery and the other for validation). The discovery and validation cohorts were comparable with respect to demographics and maximum keratometry. Eligible patients had keratoconus and were referred from January 2010 through June 2014. The study goal was to assess whether the DUCK scoring system could identify patients who require corneal cross-linking (CXL).

The DUCK system includes five parameters that are assessed routinely: age, visual acuity, refraction error, keratometry, and the patient's subjective experience. Each item is scored on a three-point scale (0-2). For instance, patient-reported quality of vision is scored as 0 (no complaints), 1 (complaints mildly affecting quality of life), or 2 (complaints severely affecting quality of life). The overall DUCK score range is 0 to 10 points, with 10 indicating the highest rate of disease progression. In addition, a score ≥6 indicates the need for CXL.

The authors compared DUCK scoring with the conventional criterion of 1.0-D increase in maximum keratometry during the preceding 12 months and conducted sensitivity analyses. Main outcomes were the overall rate of treatment reduction and the rate of duly withheld treatment.

Among the 504 eyes (388 patients) that qualified for analysis, the DUCK score proved superior to maximum keratometry for recognizing progressive keratoconus. The overall treatment rate was reduced by 23% without increasing the risk of disease progression. The DUCK score also was more sensitive in identifying eyes for which treatment was correctly withheld.

Improving patient selection for CXL would avoid unnecessary treatment risks for patients who don't require this procedure, the authors said.

Accuracy of the WebMD Symptom Checker for Ophthalmic Diagnoses
June 2019

As the accessibility of internet-based resources continues to grow, more patients are conducting self-guided research of symptoms, making it important to determine the accuracy of online symptom checkers. In a cross-sectional study using validated ophthalmic clinical vignettes, **Shen et al.** looked at the accuracy of the popular WebMD symptom checker. They found that the primary diagnosis generated by the symptom checker was correct for only 26% of the clinical scenarios. Moreover, the correct diagnosis was not on the list of possibilities for nearly half of the vignettes.

This cross-sectional descriptive study involved generating 42 validated clinical vignettes of ophthalmic symptoms and distilling them to their core presenting signs. The "cases" were entered into the WebMD symptom checker by two people who were masked to the diagnoses (one of whom was medically trained).

Output from the symptom checker was documented, including triage urgency and the list of diagnoses ranked from most to least likely. The main outcome was diagnostic accuracy of the symptom checker.

The mean number of symptoms entered for each case was 3.6 (range, 1-8). The median number of generated diagnoses per case was 26.8 (range, 1-99). The checker's primary diagnosis was correct for only 11 (26%) of the 42 vignettes. The correct diagnosis was among the top three entries in 16 (38%) of cases. However, for 18 cases (43%), the correct diagnosis was not on the list.

The triage urgency for the top-listed diagnosis was appropriate in seven (39%) of 18 emergency cases and in 21 (88%) of 24 nonurgent cases. Inter-user variability for the correct diagnosis being among the top three was at least moderate.

The clinical vignettes generally were devoid of comorbid and distractor symptoms, which may indicate that the checker's accuracy was overestimated. However, the vignettes devised for this study resemble those used for training physicians in pattern recognition.

The authors emphasized that although the WebMD symptom checker may pinpoint an ophthalmic diagnosis, its overall accuracy is low. As a result, patients should exercise caution when using such online resources and should understand that symptom-checker output "is not a substitute for professional medical advice, diagnosis, or treatment," as stated on the main page of the WebMD tool.

After this study was completed, the WebMD interface and output scheme were revised. *(Also see related commentary by Rahul N. Khurana, MD, in the same issue.)*

—Summaries by Lynda Seminara

Other Journals

Selected by Deepak P. Edward, MD

Vision Screening of Disadvantaged Children
Journal of AAPOS
Published online April 24, 2019

Barugel et al. compared the specificity and sensitivity of the Spot Vision Screener, a handheld automatic photoscreener, with gold standard cycloplegic measurements in a population of underprivileged children and teenagers with limited access to medical care. They found that although the handheld screener detected most refractive errors, it fell short in accurately identifying cases of hyperopia.

For this study, 41 children 4 years and older with poor access to medical care were recruited by social workers and referred to a single hospital in Paris for refractive error screening during a full-day dedicated session. The children had a mean age of 126 months (range, 48-246 months).

The same orthoptist performed noncycloplegic refraction measurements using the Spot Vision Screener in all patients. In the absence of contraindications, cycloplegic autorefraction using the Retinomax K-Plus 3 autorefractometer (Righton) was performed and independently evaluated by an ophthalmologist. Slit-lamp and fundus examinations were performed in all cases. Glasses were prescribed as necessary.

The sensitivity of the Spot Vision Screener to detect myopia was high (>80%), at 84.61%. However, its sensitivity for the detection of hyperopia, astigmatism, and anisometropia was lower (<80%), at 27.27%, 78.57%, and 66.67%, respectively. The specificity for hyperopia, myopia, astigmatism, and anisometropia was high, at 100%, 98.55%, 89.71%, and 94.29%, respectively. The referral rate was 39.02%.

The Spot Vision Screener's low sensitivity with regard to hyperopia seems to remain a limitation of the device, the researchers said, and they recommended cycloplegic refraction be considered in public health initiatives. Even with this limitation, they noted that the study offered a real-world example of a dedicated day of screening in disadvantaged children.

Retinal Emergencies: Ultrasonography in the ER
JAMA Network Open
2019;2(4):e192162

Lahham et al. set out to determine whether ocular point-of-care ultrasonography (POCUS) could be effectively used to screen ER patients for retinal detachment, vitreous hemorrhage, and vitreous detachment. They found that emergency medicine practitioners can use POCUS to accurately detect these three conditions, thus allowing ER staff to confer needed information to the ophthalmologist.

This prospective study was conducted at four ERs in Southern California (two academic and two county hospital locations). All four sites support an emergency medicine residency, ophthalmology residency, and emergency ultrasonography fellowship.

The researchers enrolled 225 patients age 18 years and older who presented to the ER with symptoms suggestive of retinal detachment (RD), vitreous hemorrhage (VH), or vitreous detachment (VD).

Chief concerns included blurry vision, flashers and floaters, and vision loss. Patients who had ocular trauma or a suspected globe rupture were excluded from the study.

A total of 75 ER personnel (20 emergency medicine attendings, 50 emergency medicine residents, and five supervised physician assistants) evaluated the patients with POCUS. This was performed before the patients' ophthalmic consultations, and the ophthalmologists who examined the patients were masked as to the POCUS results.

All told, as diagnosed by an ophthalmologist, 47 of the patients (20.8%) had an RD, 54 (24%) had a VH, and 34 (15.1%) had a VD. The ER staff correctly identified RDs in 46 of the 47 patients, for a sensitivity of 96.9%. With regard to VH, they identified 46 of the 54 cases, for a sensitivity of 81.9%. Finally, the ER practitioners identified 19 of the 34 cases of VDs, for a sensitivity of 42.5%. Specificity results were as follows: 88.1% for RD, 82.3% for VH, and 96% for VD.

These results suggest that POCUS may be an effective adjunct technology in the ER, helping ER staff detect ophthalmic emergencies and provide needed information to ophthalmologists. In particular, the researchers noted, POCUS may be of particular benefit to ERs in areas where around-the-clock ophthalmologic consultation is not available.

—Summaries by Jean Shaw