

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Comparison of Repair Strategies for Moderately Complex RRD

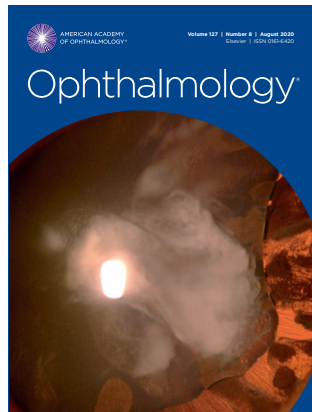
August 2020

Which surgical strategy is best for repairing moderately complex rhegmatogenous retinal detachments (RRDs)? Ryan et al. compared the visual and anatomic outcomes for patients with moderately complex RRD who were treated by scleral buckle (SB), pars plana vitrectomy (PPV), or the combination of PPV and SB. All three methods delivered good clinical outcomes. SB was superior to PPV in anatomic and visual outcomes, and the best anatomic results were achieved with the combination procedure.

For this retrospective study, data were derived from the phakic patient subset of the Primary Retinal Detachment Outcomes Study, gathered in 2015 from five large health care centers with strong expertise in all three retinal attachment procedures. The primary outcome was single-surgery anatomic success (SSAS), defined as attainment of retinal attachment without need for a follow-up procedure within 90 days. Another outcome of interest was final visual acuity (VA) following each procedure.

The final analysis set included 715 phakic patients. Among them, SSAS

was achieved in 155 of 169 (91.7%) SB cases, 207 of 249 (83.1%) PPV cases, and 271 of 297 (91.2%) PPV/SB cases. SB and PPV/SB were superior to PPV for achieving SSAS ($p = .0041$). SB produced better final VA outcomes ($p = .0089$) than did PPV or PPV/SB, even in patients whose cataract grade was 3+ or higher. SB also showed superior visual outcomes in macula-on and macula-split cases.



confounding variables, said the authors. Regardless, their data show the continued value of SB in the treatment of moderately complex phakic RRD and, as a result, the need for this technique to be an essential component of fellowship training.

Cataract Outcomes: FLACS Versus Phacoemulsification

August 2020

Day et al. set out to prospectively compare the effectiveness and safety of femtosecond laser-assisted cataract surgery (FLACS) with that of phacoemul-

sification. They found that the newer procedure, which remains costly, was similar to phacoemulsification in terms of vision outcomes, safety, and patient-reported quality of life.

This study included 785 patients and randomization by surgery type, surgeon, and facility (one of three participating hospitals). Only ophthalmologists who had performed at least 10 FLACS surgeries and were certified by the device manufacturers were allowed to participate. Standard phaco surgeries, as well as post-op care for both approaches, were conducted according to the practice standard of each hospital. The primary outcome was uncorrected distance visual acuity (UDVA) three months after surgery. Secondary outcomes included complications, the quantity of corneal endothelial cell loss, and the presence of unintended refractive errors. In addition, participants in both study arms completed post-op self-assessment questionnaires (at six weeks and three months)—one for quality of life, the other for vision health.

FLACS was performed on 392 patients, while 393 had standard phacoemulsification. Three months after surgery, the mean UDVA difference between treatments was -0.01 logMAR. Refractive outcomes were within 0.5 D of target values for 71% of each group and within 1.0 D in 93% of FLACS and 92% of phaco cases. Two posterior capsule tears occurred in the phaco arm and none in the FLACS arm. There were no significant between-group differences in any secondary outcome.

According to the authors, their sample size (determined by power analysis) was sufficient to distinguish major differences in vision between the two types of surgery. They concluded that FLACS is as good as standard phaco at three months in regard to vision, patient-centered outcomes, and safety. They acknowledged that larger randomized trials and meta-analyses are needed to analyze differences in complication rates and assess longer-term outcomes, including cost-effectiveness.

Changes in GCC Thickness and Microvasculature in POAG

August 2020

Research has shown that ocular blood flow impairment and decreased perfusion lead to neuronal damage, causing thinning of the circumpapillary retinal nerve fiber layer and ganglion cell complex (GCC). Moreover, reduced ocular perfusion has been detected in glaucomatous eyes. In a prospective longitudinal study, **Hou et al.** used optical coherence tomography angiography (OCTA) to detect and compare structural thinning and microvascular density changes over time in healthy, preperimetric, and glaucomatous eyes. Decreases in GCC and macular vessel density were detected in all groups. In eyes with primary open-angle glaucoma (POAG), the decline in macular vessel density occurred more quickly than the GCC thinning.

The authors recruited participants from the Diagnostic Innovations in Glaucoma Study, and categorized the eyes as healthy (no evidence of glaucomatous damage), preperimetric (suspicious signs of glaucoma, no repeatable measured visual field damage), or POAG (repeated verifiable visual field damage). POAG severity was graded at study start and reflected the extent of visual field damage. All patients had full ophthalmologic exams at baseline and six-month intervals, for a mean of at least two years. Using predefined protocols, OCTA and spectral-domain OCT scans were performed to measure GCC thinning and macular vascular density. Poor quality images were excluded.

The final analysis included 139

eyes (23 healthy, 36 preperimetric, 80 POAG). Throughout follow-up, all groups exhibited significant ($p < .05$) GCC thinning and decreased macular vascular density. The decrease in vascular density was greatest in POAG eyes, and the rate of decrease outpaced that of GCC thinning in these eyes. The rate of macular vascular density decline correlated strongly with glaucoma severity at baseline. Relative rates of GCC thinning and macular vascular density decline coincided with the range of glaucoma severity; quick rates of vascular density loss were common in severe disease. Intraocular pressure (IOP) during follow-up significantly influenced the rate of GCC thinning in all groups (higher IOP = faster thinning) but did not seem related to vessel density decline. These results are consistent with others showing no strong link between IOP and vascular density decline.

The authors suggest that OCTA may be useful to monitor glaucoma progression and identify factors other than IOP that may contribute to glaucoma. OCTA measurement of macular vessel density may be especially helpful to monitor progression of advanced disease. Further research with larger samples is warranted. (*Also see related commentary by Ji Eun Lee, MD, in the same issue.*)

—Summaries by Lynda Seminara

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MHS

Deep Learning Can Predict Glaucoma Before Its Onset

July/August 2020

Deep learning (DL) has shown promise for automated assessment of glaucoma from fundus photographs after disease onset. **Thakur et al.** tackled a more challenging question: Does the integration of DL models into portable fundus cameras help identify glaucoma before its onset? They found that these models consistently predicted the disease several years before clinical manifestations were apparent.

This prospective longitudinal study

included 66,721 fundus photographs of 1,636 participants (3,272 eyes) of the prospective multicenter Ocular Hypertension Treatment Study (OHTS). At baseline, patients had a normal-appearing optic disc and normal visual field. Ocular measurements and fundus photographs were collected annually for 16 years during the OHTS and were examined by two independent readers. Any observed abnormalities prompted retesting and confirmation by an endpoint committee.

Using these photographs, the authors generated datasets to develop three DL models. The first classified the images as glaucomatous or nonglaucomatous according to gradient-weighted class activation maps. The other two models were trained via transfer learning to predict glaucoma in two time periods before disease onset. The models were validated using 85% of the fundus photographs and were retested on the remaining 15%. Primary outcome measures were accuracy and area under the receiver-operating characteristic curve (AUC).

At study end, the AUC of the DL model for diagnosing glaucoma was 0.95. The AUC for predicting glaucoma development one to three years prior to onset was 0.88; that for predicting it four to seven years beforehand was 0.77.

These findings suggest that DL models are sensitive enough to identify pre-clinical signs of glaucoma from baseline fundus photographs, thus offering a simple, inexpensive, portable screening method to complement routine assessments. The authors cautioned that the models were less accurate for eyes without apparent glaucomatous optic neuropathy.

—Summary by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

SD-OCT Assessment of the Vitreomacular Interface in Adults

August 2020

Quinn et al. evaluated the ability of spectral-domain optical coherence tomography (SD-OCT) to assess the prevalence of vitreomacular interface

(VMI) features and risk factors in a representative sample of adults from Northern Ireland. In addition to observing a link between VMI interactions and age, they found a greater reduction in vitreous separation in the horizontal than in the vertical meridians, which differs from findings in other ethnic groups.

Geographically stratified participants aged 40 years and older were enrolled in the authors' multidisciplinary cross-sectional Northern Ireland Cohort for the Longitudinal Study of Ageing. For the study, which was conducted from December 2013 to April 2018, patients underwent multimodal testing, including SD-OCT for vitreomacular traction (VMT), macular hole (MH), and epiretinal membrane (ERM). All were graded according to International Vitreomacular Traction Study Group definitions. A subset of participants was evaluated further to estimate the prevalence, size, and location of vitreomacular adhesion (VMA).

Descriptive analysis and risk factors were determined for each VMI feature, and results were standardized to the 2011 Northern Ireland census population. The primary outcomes were cohort profile, standardized prevalence, and risk factor associations for each VMI feature, all weighted by age and gender.

In all, 3,351 participants (mean age, 62 years) had gradable SD-OCT images for at least one eye. VMT was found in 30 eyes, MH in 23 eyes, and ERM in 503 eyes. The subgroup analysis showed a weighted VMA prevalence of 22.6%, with VMA area ranging from 0.25 to 42.7 mm² (mean, 12.53 mm²). In multivariate analyses, older age was linked to higher odds of VMT, MH, and ERM; larger VMA area correlated with younger age and normal blood pressure. ERM and MH also were associated with worse myopia and elevated lipid and triglyceride levels.

These findings indicate that VMI interactions throughout life are age dependent. The authors recommend further longitudinal study of VMI changes to track and understand their evolution.

—Summary by Lynda Seminara

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Simple Scleral IOL Fixation Without Glue or Sutures

August 2020

Although ideal placement for an IOL is within the capsular bag, this may not be possible in difficult cataract cases. Scleral-fixated IOLs (SFIOLs) are an alternative in such situations, and their risk of corneal endothelial damage, adhesions, and glaucoma are lower than for anterior chamber or iris-claw lenses. Boral and Agarwal assessed the effectiveness of a modified SFIOL in cataract surgery. The SFIOL significantly improved patients' vision and did not require any complicated instruments or scleral-fixation tools.

This retrospective study included 81 eyes (73 patients) with post-op follow-up of at least six months. The procedures were performed by a single surgeon during a four-year period and involved the following steps:

- Two diagonally opposed paralimbal curved self-sealing pockets were created 3 mm from the limbus. During surgery, patients underwent sutureless vitrectomy and sclerotomy.
- An acrylic multipiece foldable IOL was used for scleral fixation. The external haptics were placed inside a linear scleral tunnel that was created under the superficial scleral flap of the scleral pockets.
- Forceps were used to place the haptics in this tunnel, and the IOL was positioned properly. The haptics stayed in place without suture or glue because the scleral fibers held them in the linear scleral tunnel. Cautery was used to replace the conjunctival flap.
- All patients received topical steroids postoperatively. Haptic positioning and optic tilt were assessed by optical coherence tomography of the anterior segment and ultrasound biomicroscopy.

This simplified SFIOL approach significantly improved best-corrected visual acuity from pre-op values, without any major complications. (Two cases of haptic slippage into the vitreous cavity occurred; these were fixed

in a new scleral tunnel.) Moreover, the lenses maintained stability and optimal placement. These findings echo those of previous SFIOL investigations, and the authors encourage multicenter prospective studies to evaluate long-term outcomes.

Tube Shunts and Long-Term VF Outcomes

August 2020

Until recently, glaucoma drainage devices were reserved for patients with refractory glaucoma and poor vision. Now, however, these devices are popular for reducing intraocular pressure (IOP), even in patients with good vision. Previous studies of tube shunts focused on outcomes such as visual acuity, IOP, and overall surgical success. In a retrospective case series, Liu et al. looked at the visual field (VF) changes associated with these types of implants, with emphasis on global and regional VFs. During three years of follow-up, they noted that surgery and shunt implantation appeared to stabilize IOP and VF progression.

Study participants had been fitted with one of three tube shunts (Ahmed, Baerveldt, or Molteno) during a five-year period. All patients had visual acuity that was correctable to 20/20 and evidence of worsening glaucoma or IOP that would likely start contributing to further visual damage. VF testing was performed before surgery. Shunt placement was followed by a post-op regimen of antibiotic and prednisolone eye drops.

Data were collected for 95 patients (106 eyes) and included demographics, comorbidities, and results of glaucoma exams before surgery and annually thereafter for three years. Collaborative Initial Glaucoma Treatment Study (CIGTS) scores were applied to assess changes in VFs following the surgery. Regression analysis was used to determine risk factors that may affect VF changes after implantation.

Data analysis showed that shunt implantation led to decreases in IOP; the mean value dropped from 23.1 mm Hg to 12.7 mm Hg. The number of glaucoma medications needed by pa-

tients three years post-op also declined markedly. Global VF metrics (including mean deviation, pattern deviation, and CIGTS pattern deviation probability) remained stable, whereas global CIGTS total deviation probability increased mildly. The greatest risk factors for CIGTS changes were older age and higher number of pre-op glaucoma medications.

The authors suggest that the shunts offer safe and effective IOP control but may not be as good as traditional trabeculectomy. In their study, the Ahmed device was used more often than the others, so further work is needed to compare outcomes for the various implants.

—Summaries by Lynda Seminara

JAMA Ophthalmology

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

Impact of Dementia and Visual Impairment on Daily Functioning

July 2020

Patel et al. looked at a national sample of senior citizens and found that those with dementia plus visual impairment (VI) had greater limitations in self-care, mobility, and other daily activities than would be expected for either condition alone.

For this research, the authors gathered data from the National Health and Aging Trends Study, an annual sampling of U.S. adults 65 years and older. Participants of the 2015 survey who had complete data on outcomes, associated factors, and covariates were included. Main outcome measures were independent associations and interactions of dementia and self-reported VI status on three functional activity scales: self-care, mobility, and household activities. Marginal predicted proportions were calculated, and findings were adjusted for sociodemographic and medical factors.

The final analysis included 7,124 participants, 8.6% of whom reported VI. Probable dementia was present in 6.3% and possible dementia in 8.3%. Self-reported VI was associated with expected score decreases of 14.7% for

mobility, 9.5% for self-care, and 15.2% for household activities. For probable dementia, the expected declines were 27.8%, 22.9%, and 34.7%, respectively. Individuals with both VI and probable dementia had the greatest limitations, with score decreases of 50.1% in mobility, 42.4% in self-care, and 52.4% in household activity. This suggests that co-occurring VI and dementia yield poorer functional ability than either of these disabilities alone.

The severe limitations of concurrent VI and dementia show the need for strategies to address this burden. Such efforts should maximize vision, preserve or enhance cognition, and promote functional independence. (Also see related commentary by David S. Friedman, MD, PhD, and Pradeep Y. Ramulu, MD, PhD, in the same issue.)

Does IOP Variability Help Predict POAG?

July 2020

Whether and how the long-term variability of intraocular pressure (IOP) may contribute to the occurrence of primary open-angle glaucoma (POAG) is not well understood. In a post hoc secondary analysis of two randomized trials, Gordon et al. examined this issue. They found that, for people with untreated ocular hypertension, taking into account the variable long-term IOP data did not seem to improve the ability to predict POAG.

For this study, the researchers used data from the Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS). The model used in these two studies to predict POAG development included baseline values for age, IOP, central corneal thickness, vertical cup-disc ratio, and pattern standard deviation (SD). In this analysis, the authors tested whether predictions could be improved by replacing baseline IOP data with mean follow-up IOP, SD of IOP, maximum IOP, range of IOP, or coefficient of variation IOP. They used the C statistic to compare the predictive accuracy of multivariable landmark Cox proportional hazards regression models for the development of POAG.

The OHTS data consisted of 97 POAG end points from 709 of 819 participants (58.7% women, 25% African American, 69.1% white). Mean age was 55.7 years, and the median follow-up period was 6.9 years. EGPS data included 44 POAG end points from 397 of 500 participants in the placebo group (50.1% women, 100% white). The mean age was 57.8 years, and the median follow-up time was 4.9 years. The C statistic for the original prediction model was 0.741.

When the other IOP values were substituted for baseline IOP in the OHTS prediction model, the C statistic was 0.784 for mean follow-up IOP, 0.781 for maximum IOP, 0.745 for SD of IOP, 0.741 for range of IOP, and 0.729 for coefficient of variation IOP. EGPS findings were similar. No measure of IOP variability, when added to the complete prediction model, increased the C statistic by more than 0.007 in either cohort.

These findings suggest that factoring in long-term IOP variability does not strengthen POAG prediction models. Even so, given that IOP is the only known modifiable risk factor for glaucoma, understanding how its dynamic variation is linked to the onset and progression of POAG could play a crucial role in management, the authors said.

Need to Check for Uncorrected Refractive Errors

July 2020

Guo et al. measured the degree of visual acuity (VA) improvement attained in adults with previously uncorrected refractive error who also had glaucoma or retinal disease. Nearly 28% of patients in their study (mean VA, 20/100) had improvement of at least 2 lines, and more than half improved by 1 or more lines. Overall, African Americans and middle-aged working adults experienced the greatest visual benefits.

This study was a retrospective review of patients who were new to low vision rehabilitation (defined as no visit to address VA in the preceding three years) and were receiving care for glaucoma or a retina-related condition. Uncorrected refractive error was defined as

absent, inaccurate, or outdated correction of refractive error. Habitual VA of the 2,923 patients ranged from 20/40 to counting fingers. Patients younger than 20 years of age were excluded from the analysis, as were those with habitual VA of 20/40 or better or counting fingers or worse.

The mean habitual VA of included patients ($n = 1,773$) was 20/100. Refraction showed improvement of at least 2 lines in 27.8% and at least 1 line in 57.7%. Improvement of 2 or more lines was more common in the older subset (40–64 vs. 20–39 years; odds ratio [OR], 1.57), in African American than in white patients (OR, 1.41), and with moderate versus mild visual impairment (OR, 1.36). Patients with corneal disease had greater refractive benefit than those with other conditions, despite having poorer habitual VA. Improvement of 6 or more lines occurred in 1.2%, and VA of at least 20/40 was attained for a third of the study group.

These findings show that uncorrected refractive error is prevalent among patients with ocular disease. The authors encourage routine refractive checks to maximize social, psychological, and occupational functioning. Moreover, optimally corrected VA can reduce the need for magnification and enhance quality of life. Understanding how patients become connected to low vision care would help in designing outreach programs that improve delivery of refractive care, the authors said. They also suggested that future work include assessing the effects of refractive correction on patient-centered outcomes in those with ocular disease.

—Summaries by Lynda Seminara

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Real-World Assessment of BRVO Treatment

British Journal of Ophthalmology

Published online June 12, 2020

Evidence from clinical trials suggests that anti-VEGF drugs are more effective than dexamethasone implants for the treatment of macular edema

secondary to branch retinal vein occlusion (BRVO). However, it can be difficult to translate clinical trial results to daily practice. Therefore, Gale et al. set out to evaluate this conclusion in a real-world setting with data from a large and diverse population, and they included macular laser outcomes for additional comparison. They found that visual acuity (VA) improved more with anti-VEGF treatment than with the other strategies. In addition, although anti-VEGF injections conferred a higher treatment burden, some of the impact of that burden decreased over time.

For this study, the researchers used data collected at 27 U.K. National Health Service centers between February 2002 and September 2017 from patients who received treatment for BRVO. Of an initial dataset of 19,141 eyes, 5,251 met the inclusion criteria of being treatment-naïve at the start of therapy and having both baseline and follow-up VA measurements. The mean age of the study population was 72.1 years, and 52.6% were female. Outcomes of interest were changes in VA and mean number of treatments over a 36-month period.

Mean baseline VA was 57.1 ETDRS letters in those treated with anti-VEGF injections ($n = 3,939$), 53.1 in those who received the dexamethasone implant ($n = 676$), and 62.3 for those treated with laser ($n = 636$). Following treatment, VA changed as follows:

- At 12 months, mean VA was 66.72 letters in the anti-VEGF group, 57.6 in the dexamethasone group, and 63.2 in the laser group.
- At 18 months, mean VA was 66.6, 56.1, and 60.8 letters, respectively.
- Only the anti-VEGF group had adequate 36-month data; mean VA in this group at that point was 68 letters.

With regard to treatment burden, the anti-VEGF group received a mean of 5.1 treatments during the first 12 months, while the dexamethasone and laser groups received 1.5 and 1.2, respectively. During the first 18 months, the mean number of treatments were 5.9, 1.7, and 1.2, respectively. Again, 36-month data were available for only those in the anti-VEGF group, who received a mean of 6.9 treatments

during this time period. The authors suggest that, despite the treatment burden, visual outcomes were better with anti-VEGF therapy.

Medication Burden After Combined CyPass/Cataract Surgery

Journal of Glaucoma

Published online May 26, 2020

Law et al. set out to assess how well combined cataract surgery and implantation of the CyPass Micro-Stent controlled intraocular pressure (IOP). They found that the combined surgery reduced the glaucoma medication burden at one year by 28% to 42%, depending on different target IOP levels.

For this retrospective study, the authors reviewed all cases of combined surgery performed at two U.S. eye institutes between February 2017 and July 2018. The primary outcome was qualified success with IOP targets as follows: 1) final IOP of ≤ 18 mm Hg and reduction of 20%; 2) final IOP of ≤ 15 mm Hg and reduction of 25%; and 3) final IOP of ≤ 12 mm Hg and reduction of 30%. Secondary outcomes included post-op IOP and number of medications, complications, additional glaucoma surgery, and postoperative refractive error.

All told, 141 eyes (107 patients) were included in the analysis. Mean pre-op IOP was 15.4 ± 3.4 mm Hg on an average of 2.2 ± 1.1 medications. At 12 months postoperatively, IOP was 13.8 ± 4.2 mm Hg, and medication use was 1.3 ± 1.3 . Cumulative success rates based on the three IOP targets were 42%, 33%, and 28%.

Fifteen eyes experienced a post-op IOP spike (defined as a postoperative IOP of ≥ 30 mm Hg or an increase of more than 10 mm Hg over preoperative IOP). Additionally, 13 eyes experienced 17 complications, and additional glaucoma surgery was performed in three eyes of two patients. Factors associated with failure included lower pre-op IOP, greater number of pre-op medications, and the occurrence of a post-op IOP spike. Further study is needed to determine the amount of long-term IOP control gained by combined surgeries.

—Summaries by Jean Shaw