

Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO*, AND *ARCHIVES*

Ophthalmology

Cost Analysis of Treatment Regimens for Diabetic Macular Edema

Ophthalmology

Published online Oct. 10, 2012

Smiddy examined the visual benefits and the costs of multiple treatment modalities for diabetic macular edema (DME). He found that substantial savings could be achieved without forgoing clinical benefit by employing specific treatment regimens in certain subgroups of patients.

In this study, the author reviewed published clinical trials of laser, intravitreal corticosteroids, intravitreal anti-VEGF agents, and vitrectomy for the treatment of DME. Main outcome measures included visual acuity saved, cost of therapy, cost per line of VA saved, cost per line-year saved, and costs per quality-adjusted life-year saved. Calculations were based on one year of treatment.

The author discovered that when the results of the various treatments were held equivalent, opting for a less-expensive treatment option could yield cost savings of 40 to 88 percent. He based this conclusion on several main findings that he derived from the index studies. First, most studies lumped together all eligible patients

when comparing results. For example, patients with particularly good or particularly bad vision, if studied at all, were only occasionally stratified. These fringe patients might have achieved better outcomes from a different (and less costly) therapy. Second, another subgroup, pseudophakic patients, did not experience as much VA benefit from anti-VEGF agents compared with phakic patients and, therefore, might be considered candidates for less costly intravitreal triamcinolone therapy. Third, when less frequent dosing could be accomplished without sacrificing VA, both the risks and costs of treatment were

reduced. And finally, the author found that use of related, but less expensive, anti-VEGF agents yielded substantial cost reductions without apparent loss of VA benefit.

10-Year Incidence of Glaucoma Linked to Retinal Vessel Caliber

Ophthalmology

Published online Oct. 10, 2012

In a population-based cohort study, **Kawasaki et al.** found that narrowed retinal arteriolar caliber is associated with an increased long-term risk of developing primary open-angle

glaucoma (POAG). This finding suggests the possibility of retinal microvascular changes in the early course or pathogenesis of POAG. However, the authors were not able to determine whether this observation is an early sign of vascular change prior to or concurrent with the clinical manifestation of POAG, or a secondary change due to progressive loss of the retinal nerve fiber layer.

This investigation included 2,417 adult Australian patients from the Blue Mountains Eye Study found to be at risk of POAG during the study's five- or 10-year examinations. The authors defined incident POAG as the development of typical glaucomatous visual field loss combined with corresponding optic disc rim thinning and either a cup-to-disc ratio of greater than 0.7 or cup-to-disc asymmetry between the two eyes.

The authors identified 82 patients (104 eyes) who developed incident POAG over the 10-year period. After adjustment for age, sex, family history of glaucoma, smoking, diabetes, hypertension, hypercholesterolemia, body mass index, spherical equivalent refraction, and cup-to-disc ratio, narrower central retinal artery equivalents were associated with a higher risk of incident POAG. This association remained significant when analyses were confined to eyes with IOP of less than 20 mmHg and cup-to-disc ratio of less than 0.6 at baseline. There were



no independent associations between central retinal vein equivalents and incident POAG.

Predictors of Visual Outcome One Year After AMD Treatment

Ophthalmology

Published online Oct. 8, 2012

In a cohort study, Ying et al. investigated baseline predictors of visual outcomes in patients with age-related macular degeneration (AMD) one year after treatment with ranibizumab or bevacizumab. In both treatment groups, predictors for less improvement in VA included older age, better baseline visual acuity, larger choroidal neovascularization area, predominantly or minimally classic lesion, absence of retinal angiomatous proliferans lesions, presence of geographic atrophy, greater foveal thickness, and elevation of the retinal pigment epithelium.

This study included 1,105 patients with AMD whose baseline VA ranged from 10/25 to 20/320. The authors randomly assigned participants to ranibizumab or bevacizumab on a monthly or as-needed basis. At one year, the mean VA score was 68 letters, mean improvement from baseline was seven letters, and 28 percent of participants gained three lines or more.

The authors identified several independent predictors of VA outcomes using regression techniques. Older age, larger area of choroidal neovascularization, and elevation of retinal pigment epithelium were associated with worse VA at one year, less gain in VA, and a lower proportion gaining three lines or more. Geographic atrophy and predominantly or minimally classic lesions were associated with worse VA at one year. Retinal angiomatous proliferans lesions were associated with greater gain in VA and a higher proportion of patients gaining three lines or more. Better baseline VA was associated with better VA at one year but also with less gain in VA and a lower proportion gaining three lines or more. Predictors did not vary by treatment group.

The investigators cautioned that

their study should not be used to justify a reduced interest in these anti-VEGF treatment approaches, since all of the subgroups experienced some benefit in VA.

Cost Differences Between IOLs and Contact Lenses in Congenital Cataract Surgery

Ophthalmology

Published online Oct. 8, 2012

Carrigan et al. described the differences in treatment costs for patients in the Infant Aphakia Treatment Study (IATS) randomized to either contact lens correction or IOL implantation after unilateral cataract surgery.

They found that for infants up to 12 months of age, cataract surgery combined with IOL implantation and spectacle correction was 37.5 percent (approximately \$4,000) more expensive than cataract surgery combined with contact lens correction. The use of spectacles in IATS patients undergoing IOL implantation was necessary to correct residual refractive error.

The IATS was a randomized, multicenter clinical trial that compared the costs of primary IOL versus contact lens for the treatment of aphakia in 114 infants with unilateral congenital cataract. The mean cost of treatment for a unilateral congenital cataract with primary IOL implantation was \$14,752 versus \$10,726 with contact lens correction. The initial cataract surgery accounted for approximately 50 percent of the treatment costs for both groups. Contact lens costs accounted for 15 percent (\$1,600 per patient) in the aphakic group, whereas glasses costs represented only 4 percent (\$535 per patient) in the IOL group.

The authors attributed the higher costs in the IOL group to cost differences of the initial surgical procedure and increased frequency of subsequent surgeries. When they looked at the minimum cost of IOL implantation without additional surgeries, they found that the difference was substantially reduced, with the IOL group costing only 9 percent more.

American Journal of Ophthalmology

Progression Rates of Visual Field Defects in Normal-Tension Glaucoma Patients

December's *AJO*

Cho and Kee investigated the progression rate of early hemifield defects in patients with normal-tension glaucoma. The authors found that the initial location of the retinal nerve fiber layer (RNFL) defect and the corresponding visual field defect were independent predictors for more rapid future visual field loss in the future, and that the location of the defect strongly affected the risk of disease progression.

In this retrospective, observational cohort study, 142 patients with normal-tension glaucoma who had more than five reliable visual field tests were divided into three groups. Group 1 consisted of patients showing superior RNFL defects with corresponding inferior hemifield defects; group 2 included patients showing inferior RNFL defects with corresponding superior hemifield defects, and group 3 comprised patients who showed both superior and inferior RNFL defects with corresponding bihemifield defects. The investigators inspected changes in the mean thresholds of the 10 zones of the glaucoma hemifield test and the entire hemifield.

The progression rate in group 2 was significantly faster than in group 1, especially in the central and nasal zones, and significantly faster than the rate in the superior hemifield of group 3. There were no significant differences in the progression rates between group 1 and the inferior hemifield of group 3, or between the superior and inferior hemifields of group 3.

Persistent Corneal Edema After Collagen Cross-Linking for Keratoconus

December's *AJO*

Collagen cross-linking (CXL) is a safe and effective procedure with few known side effects. In

this case series, however, Sharma et al. reported the possibility of corneal endothelial damage with visually significant corneal edema after CXL treatment. Based on the extent of damage, they found that patients might require penetrating keratoplasty.

The authors reviewed the charts of 520 patients with progressive keratoconus. Postoperative corneal edema was identified in 10 (2.9 percent) of the 350 patients who had received CXL. All CXL treatments followed the standard Dresden protocol.

Edema started on postoperative day 1 in all 10 affected patients and increased for three weeks. Additional findings included deep vascularization (two eyes), iris atrophy (six eyes), pigment dispersion (five eyes), persistent epithelial defect (three eyes), and infectious keratitis (one eye). Specular microscopy was attempted in all cases but was unsuccessful because of the degree of edema or residual stromal haze. All untreated fellow eyes had normal endothelial counts. IOP and lenticular evaluations were normal in all eyes. Corneal edema improved in four patients and resolved in one patient. In these five patients, logMAR BCVA was 0.5 ± 0.18 , and penetrating keratoplasty was offered when improvement reached a plateau at three months. However, only two patients underwent the procedure.

Topical Bevacizumab in the Treatment of Corneal Neovascularization

December's *AJO*

Conventional medical and surgical treatment options for corneal neovascularization are fraught with variable efficacy and numerous potential side effects. In this prospective, nonrandomized, interventional case series, Cheng et al. evaluated the safety and effectiveness of topical bevacizumab in the treatment of this condition. They found that short-term bevacizumab treatment could reduce the extent of corneal neovascularization as measured by neovascular area and vessel caliber.

The study included 20 eyes of 20

patients with stable corneal neovascularization. Patients were treated with topical 1 percent bevacizumab for three weeks and were monitored for a total of 24 weeks. Primary outcome measures included neovascular area, defined as the area of the corneal vessels themselves; vessel caliber, defined as the mean corneal vessel diameter; and invasion area, defined as the fraction of the total cornea into which the vessels extended.

Compared with baseline visits, patients exhibited a statistically significant improvement in neovascular area by week 6 and in vessel caliber by week 12. At the final visit, neovascular area, vessel caliber, and invasion area were reduced by 47 percent, 36 percent, and 20 percent, respectively. The decreases in neovascular area and vessel caliber were statistically significant; however, the reduction in invasion area did not reach statistical significance. The degree of treatment efficacy was also inversely proportional to the baseline invasion area. No significant adverse events were reported.

Minocycline in Moderate and Severe Meibomian Gland Dysfunction

December's *AJO*

Lee et al. assessed the differing clinical outcomes of patients with moderate and severe meibomian gland dysfunction (MGD) after treatment with either artificial tears or a combination of artificial tears and oral minocycline. The authors found that after two months of treatment, oral minocycline not only improved clinical signs and symptoms but also decreased cytokine levels.

This prospective, randomized clinical trial included 60 eyes of 60 patients with stage 3 or 4 MGD. All patients were randomized into two groups and evaluated before treatment and after one and two months of treatment. Group 1 took 50 mg of minocycline orally twice daily and used 0.1 percent sodium hyaluronate four times daily, and group 2 used 0.1 percent sodium hyaluronate four times daily for two months. The authors evaluated tear

film breakup times, Schirmer test results, corneal and conjunctival fluorescein staining scores, biomicroscopic examination of lid margins and meibomian glands, and tear cytokine levels.

Patients in group 1 demonstrated statistically significant improvement in all clinical signs and symptoms after one and two months of treatment and also had more significant improvement compared with patients in group 2. After two months of treatment, patients in group 1 also showed statistically significant reductions in IL-6, IL-1 β , IL-17 α , IL-12p70, and tumor necrosis factor- α .

Archives of Ophthalmology

CFH and *ARMS2* Genotypes, Macular Pigment Optical Density, and Neuroretinal Function in Persons Without AMD

November's *Archives*

Feigl et al. found that there is a difference in neuroretinal function and macular pigment optical density between persons with high- and low-risk gene variants for age-related macular degeneration (AMD) without ophthalmoscopic signs of the disease. Moreover, increased neuroretinal activity in persons with high-risk AMD genotypes might reflect genetically determined subclinical inflammatory or histological changes in the retina.

Of 32 total patients enrolled in the study, 22 showed no ophthalmoscopic signs of AMD, and 10 demonstrated early AMD. The 22 healthy patients had high- or low-risk genotypes for *CFH* and/or *ARMS2*. The authors assessed neuroretinal function using multifocal electroretinogram, and macular pigment optical densitometry by customized heterochromatic flicker photometry. They also analyzed first negative and first positive (N1P1) response densities and P1-implicit times in five concentric rings.

The data showed that healthy persons who had high-risk genotypes for AMD had, on average, significantly increased central neuroretinal responses compared with persons who had low-

risk genotypes and those with early AMD. N1P1 response densities for concentric rings 1 through 3 were significantly greater in participants who had high-risk genotypes compared with those who had low-risk genotypes and those with early AMD. P1-implicit times for ring 1 were delayed in the early AMD patients compared with participants who had high- and low-risk genotypes, although these differences were not significant. There was no correlation between macular pigment optical density and genotype in the healthy cohort.

Subjective Quality of Vision Before and After Cataract Surgery

November's Archives

Skiadaresi et al. found that cataract in one or both eyes caused a similar loss of subjective quality of vision (QOV), irrespective of the presence of ocular comorbidity. They also discovered that cataract surgery resulted in a large and comparable improvement in subjective QOV, regardless of ocular comorbidity and first- or second-eye surgery.

The authors recruited 212 patients (212 eyes) for the study and divided them into four groups: those having first-eye cataract surgery with or without ocular comorbidity and those having second-eye cataract surgery with or without ocular comorbidity. Prior to and three months after cataract surgery, all patients completed QOV questionnaires that measured frequency, severity, and nature of symptoms. Cataracts were graded and classified according to the Lens Opacities Classification System III. The authors calculated Rasch-scaled questionnaire scores before and after surgery.

All four groups reported improvement in QOV scores. There were no differences between groups in score improvement or in the pre- or postoperative QOV scores. The authors found that blurred vision was correlated with posterior subcapsular cataract. There were no statistically significant correlations between visual symptoms and either nuclear or cortical cataract.

BBS1 Mutations, Retinitis Pigmentosa, and Bardet-Biedl Syndrome

November's Archives

Bardet-Biedl syndrome (BBS) is a clinically and genetically heterogeneous disorder characterized by a wide spectrum of clinical features, including retinitis pigmentosa, polydactyly, and learning disabilities. Estrada-Cuzcano et al. investigated whether *BBS1* gene variants are specifically involved in the development of retinitis pigmentosa (RP). They found that, indeed, the *BBS1* p.Met390R allele is significantly associated with nonsyndromic autosomal recessive RP and mild forms of BBS. Because a homozygous p.Met390R variant was also identified in a control patient and in unaffected parents of BBS patients, the authors postulated that cis- or trans-acting modifiers might influence the disease phenotype.

This study involved restriction fragment length polymorphism analysis of the *BBS1* p.Met390R allele in 2,007 individuals affected by autosomal recessive RP and in 1,824 controls. Patients with two *BBS1* variants underwent extensive clinical and ophthalmologic assessment. The *BBS1* p.Met390R variant was detected homozygously in 11 RP patients and one control, compound heterozygously in three patients, and heterozygously in five patients and six controls. Fourteen patients with two *BBS1* variants exhibited a wide spectrum of disease characteristics, ranging from nonsyndromic RP to classical BBS. In eight of these patients, visual acuity was significantly reduced.

The authors concluded that an early diagnosis of mild BBS phenotypes is important in order to monitor for possible life-threatening conditions.

Profile of Women in Leadership Positions at Ophthalmic Publications

November's Archives

Mansour et al. examined how women's roles have changed over time at the editorial, reviewer, and author levels of three major oph-

thalmology journals. The authors found that female ophthalmologists are authoring publications in growing numbers that match or exceed their prevalence in the academic and overall workforce. The authors also noted that the relative proportion of female editors to female authors was less than the relative proportion of male editors to male authors. This discrepancy could be attributed to the relative youth of the female-ophthalmologist population, less desire among women to assume leadership roles, and/or the possibility of selection bias favoring men.

This cross-sectional study focused on the *American Journal of Ophthalmology*, *Archives of Ophthalmology*, and *Ophthalmology* for the years 1969, 1979, 1989, 1999, and 2009. Indices analyzed included first author, senior author, reprint request author, reviewer, editorial board, assistant editor, and editor. The researchers then compared this data with ophthalmologist-in-training and physician profiles in different areas of North America and Europe during the same period.

In the years studied, none of these journals had a woman as editor-in-chief. For all journals, the proportion of female editorial board members increased from 3.3 percent in 1969 to 18.8 percent in 2009. Across all journals and all years, women composed a higher proportion of first authors (29.2 percent in 2009) compared with senior authors (22.9 percent in 2009), reviewers (18.9 percent in 2009), and assistant editors (12.5 percent in 2009). For all journals, there was an abrupt shift in first authorship toward women between 1989 and 2009. This rise in authorship was closely paralleled by the increasing proportions of U.S. women entering ophthalmology training programs and finding employment as physicians over the same period of time.

Ophthalmology summaries are written by Lori Baker Schena, EdD, and edited by John Kerrison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. Archives of Ophthalmology summaries are written by the lead authors.

ROUNDUP OF OTHER JOURNALS

Grid Size and Effective Phaco Time in Femtosecond Cataract Surgery

Journal of Cataract and Refractive Surgery
Published online Sept. 14, 2012

Conrad-Hengerer et al. compared the effect of different fragmentation grids on reducing effective phacoemulsification time (EPT) during femtosecond laser–assisted cataract surgery. They found that the use of a 350- μ m grid resulted in a significantly lower EPT than a 500- μ m grid.

The study included 80 patients treated with 350- μ m fragmentation grids and 80 patients treated with 500- μ m grids. Mean preoperative Lens Opacities Classification System III grade was 3.7 ± 0.8 in the 350- μ m group and 3.5 ± 0.8 in the 500- μ m group. Mean absolute phaco time was significantly lower in the 350- μ m group (2.05 seconds) than in the 500- μ m group (5.85 seconds); mean overall EPT was statistically significantly lower in the 350- μ m group (0.03 seconds) than in the 500- μ m group (0.21 seconds); and mean phaco power was lower in the 350- μ m group (1.6 percent) than in the 500- μ m group (2.5 percent), though this difference was not statistically significant. The femtosecond laser creation of the capsulotomy and lens fragmentation lasted a mean of 66.4 seconds in the 350- μ m group and 52.8 seconds in the 500- μ m group. The capsulotomy took approximately four seconds in every case; however, the lens fragmentation time varied according to the volume treated.

Lid-Parallel Conjunctival Folds as Diagnostic Test for Dry Eye

British Journal of Ophthalmology
Published online Sept. 5, 2012

Németh et al. investigated whether the grading of lid-parallel conjunctival folds (LIPCOF) is a useful tool in the diagnosis of dry eye disease. They found that the LIPCOF test demonstrated medium sensitivity and specificity with a good posi-

tive predictive value—prompting the authors to recommend it as a clinical screening test.

This study included 272 eyes of 272 dry eye patients with a mean age of 53 years. The investigators graded LIPCOFs by means of slit-lamp examination. Each patient was asked to blink several times in the primary gaze position. The examiner looked for a horizontal conjunctival fold at the transition zone from the middle to the temporal third of the lower eyelid. Test grades were based on the height of the normal tear meniscus and on the number of individual folds contained in the LIPCOF. The investigators also measured tear film breakup time and performed fluorescein staining and Schirmer I tests. Subjective symptoms were evaluated by questionnaire.

The results showed significant positive correlations between the LIPCOF score and age, dry eye severity, and fluorescein staining, and negative correlations with tear film breakup time and results of the Schirmer I test. The LIPCOF score also exhibited a weak, but significant, correlation with overall subjective dry eye complaints.

Whole-Body Dehydration Linked to Dry Eye

Investigative Ophthalmology & Visual Science
2012;53(10):6622-6627

Walsh et al. found that compared with controls, individuals classified as having dry eye possess higher plasma osmolality (Posm), which indicates suboptimal whole-body hydration.

The authors measured both dry eye and hydration in 56 men and 55 women with a mean age of 77. Dry eye assessment included tear osmolarity (Tosm), the five-item dry eye questionnaire (DEQ-5), ratings of eye dryness using a visual analogue scale, and noninvasive tear film breakup time. Hydration was assessed by measuring plasma osmolality with freezing-point

depression osmometry. The authors found that Posm was higher in dry eye patients than controls when using multiple Tosm cutoffs for dry eye classification. Posm was also higher in dry eye patients than controls when they were assessed according to composite dry eye measures, including Tosm and DEQ-5; Tosm and noninvasive tear film breakup time; and the visual analogue scale and DEQ-5.

Ocular Neovascularization Associated With Central and Hemicentral Retinal Vein Occlusion

Retina
2012;32(8):1553-1565

Hayreh and Zimmerman looked at the incidence of ocular neovascularization (NV) after central (CRVO) and hemicentral (HCRVO) retinal vein occlusion. They found that in ischemic CRVO, anterior segment NV is much more common than posterior segment NV, and that the cumulative chance of developing anterior segment NV is at its highest during the first six months from onset of RVO. In ischemic HCRVO, however, posterior segment NV is much more common than anterior segment NV. The authors also discovered that development of anterior segment NV—but not disc or retinal NV—was significantly associated with peripheral retinal hemorrhages.

The study included 912 (673 non-ischemic and 239 ischemic) CRVO eyes and 190 (147 nonischemic and 43 ischemic) HCRVO eyes. In addition to the findings noted above, the investigators discovered that anterior chamber flare was associated with anterior segment NV—and may possibly precede development of NV. Further, patients who developed NV were significantly younger, and a greater prevalence of NV glaucoma was noted in patients with primary open-angle glaucoma.

Roundup of Other Journals is written by Lori Baker Schena, EdD, and edited by Deepak P. Edward, MD.