Results of a 25-year review of the complication rate in a well-defined population of patients with glaucoma treated with trabeculectomy at Mayo Clinic and Olmsted Medical Center suggest that the rate of trabeculectomy-related complications does not appear to be associated with mitomycin use. The long-term study shows more favorable outcomes than do studies that report higher complication risks during shorter study periods.

Cheryl L. Khanna, M.D., and a research team from Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota, used data from the Rochester Epidemiology Project (Sidebar) to determine the rate of trabeculectomy-related complications during the 25 years studied. Review results were published in *JAMA Ophthalmology* in 2015.

“Historically, trabeculectomy has been the surgical standard of care for patients with medically refractory glaucoma,” says Dr. Khanna. “The introduction of adjunctive antimetabolite agents such as fluorouracil and mitomycin increased the success rate of trabeculectomy by reducing scarring at the filtration site, but these agents also have been reported to increase the rate of post-trabeculectomy complications. This 25-year review, however, did not show a linear trend in complications with mitomycin.”

334 study participants, 460 eyes treated

Dr. Khanna and the research team identified 348 patients 18 years or older at the time of analysis who underwent trabeculectomy from Jan. 1, 1985, through Dec. 31, 2010. The average age at first trabeculectomy was 71 years. The average follow-up was 7.7 years. Follow-up visits were included through 2013.

In the 334 patients included in the study, 460 eyes underwent trabeculectomy. Among them, 159 eyes had complications, including:

- 100 eyes with early complications (less than three months)
- 59 eyes with late complications (three months or more) during the follow-up
- 10 eyes with both early and late complications

“The team recorded the concentration of mitomycin applied during surgery, intraoperative complications, and all postoperative complications and the occurrence of complications as they related to the mitomycin concentration administered during the operation,” says Dr. Khanna. Complications included bleb leak, hypotony, hyphema, choroidal effusion, choroidal hemorrhage, blebitis and endophthalmitis.

Mitomycin and complications

The team completed comparisons among various concentrations of mitomycin through the Cox proportional hazards regression model, which used robust sandwich estimates to account for the potential correlations among the eyes for patients with both eyes in the study. Cumulative probabilities of short- and long-term complications were determined using the Kaplan-Meier method, and the relation to mitomycin concentration applied during trabeculectomy. Results indicate:

- The 20-year cumulative probability of early, late or any complication was 20 percent (95 percent confidence interval, or CI, 16 to 24 percent), 26 percent (95 percent CI, 15 to 36 percent), and 45 percent (95 percent CI, 38 to 52 percent), respectively.
- The cumulative probabilities of vision-threatening complications during 20 years were 2 percent (95 percent CI, [0, 10]) and 15 percent (95 percent CI, 9 to 21 percent), respectively. The probabilities of vision-threatening complications were 0.002 percent (95 percent CI, 0.0001 to 0.01 percent) and 0.25 percent (95 percent CI, 0.15 to 0.4 percent), respectively.
Cheryl L. Khanna, M.D.

0 to 4 percent) for blebitis and 5 percent (95 percent CI, 1 to 9 percent) for endophthalmitis.

• There was no association between the rate of trabeculectomy complications and mitomycin dose.

“This study shows an overall lower rate of trabeculectomy-related complications than previous reports with shorter follow-ups published in *Eye* in 2002 and *American Journal of Ophthalmology* in 2012,” says Dr. Khanna. “The 20-year cumulative probability of early complications, at 20 percent, is lower than the probability in other published reports, in which it ranged from 37 to 47 percent in the short term.

“At Mayo, the initial surgical intervention for uncontrolled open-angle glaucoma is trabeculectomy. In 2007, the concentration of mitomycin used was decreased from 0.4 to 0.2 mg/mL in an attempt to decrease the number of complications and, unless contraindicated by other risk factors, the use of mitomycin was standardized at 0.2 mg/mL. In this study, the complication rate was unchanged during the 25-year study period regardless of changes in mitomycin administration before and after 2007. An increase in mitomycin concentration applied in patients only with increased risk of trabeculectomy failure, the surgical technique used, the limited duration of mitomycin administration, and a conservative approach to mitomycin C application at Mayo may contribute to the lack of association between mitomycin C and complications.”

For more information


**Adults With Nonparalytic Forms of Strabismus Face Increased Risk of Mental Illness**

A case-controlled, retrospective study indicates that adults with some forms of strabismus — divergence insufficiency (DI) and small-angle hypertropia (HT) — may be at increased risk of mental illness and its comorbidities.

“In studies published in 2008 in *Pediatrics* and 2012 in *Ophthalmology*, children diagnosed with some forms of strabismus, such as intermittent exotropia, convergence insufficiency (CI) and congenital esotropia, were found to have a threefold increased incidence of developing mental illness by early adulthood, compared with controls,” says Brian G. Mohney, M.D., with Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota.

“There was no research that indicated whether adults with nonparalytic forms of strabismus were similarly at risk.”

Using data from the Rochester Epidemiology Project (Sidebar, page 1), Dr. Mohney and a research team reviewed medical records of the 118 adults (19 years or older) diagnosed with CI, 80 adults diagnosed with DI and 99 adults diagnosed with small-angle HT in Olmsted County, Minnesota, between Jan. 1, 1985, and Dec. 31, 2008. Mental health disorders were diagnosed in:

• 65 (55 percent) adults with CI compared with 34 (46 percent) controls
• 51 (64 percent) adults with DI compared with 42 (53 percent) controls
• 63 (64 percent) adults with small-angle HT compared with 57 (58 percent) controls

The research team identified the timing of the initial mental health diagnosis among the adults — before or after their strabismus diagnosis. The majority of adults with CI (63 percent) and DI (59 percent) were diagnosed with a mental health disorder before they were diagnosed with strabismus, while the majority of adults with small-angle HT (57 percent) were diagnosed with a mental health disorder after their strabismus diagnosis.

Each case was then compared with a sex- and birth date-matched nonstrabismic control. The medical records of the adults with strabismus and the matched controls were reviewed for a diagnosis of mental illness using codes from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, text revision, use of psychotropic medication, mental health emergency department visits or hospitalizations, suicide attempts, and suicidal or homicidal ideation.

Study results, published in *Strabismus* in 2015, indicate:

• Adults with DI were significantly more likely to have psychiatric-related hospitalizations and psychotropic medication use than controls.
• Adults with small-angle HT had a mild increase in specific mental health disorders compared with controls.
• Adults with CI did not have an increased risk of mental health illness when compared with controls.
Adults with DI were found to have a higher number of psychiatric-related hospitalizations and psychotropic medication use (both number and length of time), and were also diagnosed with unspecified anxiety disorder more than their controls in this population-based study. Adults with small-angle HT had a higher rate of generalized anxiety disorder, while adults with CI had no increased risk of mental health illnesses compared to controls.

**Hypothesis-generating research**

“Although degenerative changes associated with aging are potential causes for the development of DI and small-angle HT, they may also be due to microvascular disease or other causes currently unknown. Mental illness and these two types of strabismus could both be a result of these vascular insults to the brain over time,” says Dr. Mohney. “Alternatively, CI is thought to be linked with the decline in the ability to accommodate with aging. The degenerative etiology for adult-onset CI could explain why those who have the condition are not at an increased risk of developing mental illness.

“Additionally, a link between constant exotropia and schizophrenia was found to be associated with polymorphisms in a gene encoding a transcription factor. Although the genetic and molecular basis of adult-onset nonparalytic strabismus is not yet known, it is possible that mutations could be responsible for the development and progression of both mental illness and strabismus. This study should be viewed as hypothesis-generating research. It is possible that some of the significant associations need to be confirmed by reproducing this study in a different population.”

**For more information**


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**Onset of Corneal Abnormalities in Fuchs’ Dystrophy Begins Early in the Course of the Disease**

Fuchs’ dystrophy is a bilateral, progressive, inherited disease of the corneal endothelium characterized by cornea guttata and corneal edema and resulting in decreased vision. Advanced and untreated cases result in corneal scarring and vascularization.

Due to advances in corneal transplantation techniques that enable earlier surgical intervention and the potential of nonsurgical treatments, staging Fuchs’ dystrophy based on the presence or absence of clinical edema may no longer be adequate. “The ideal is to identify patients who will benefit from intervention before any changes in the host tissue that affect outcomes become irreversible,” says Sanjay V. Patel, M.D., with Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota. “Improving our understanding of the onset of corneal changes that affect outcomes may help to determine the optimal time for intervention.”

Dr. Patel and a research team at Mayo Clinic in Rochester, Minnesota, conducted a cross-sectional study to determine when corneal abnormalities become evident in the course of Fuchs’ dystrophy. “Specifically, we examined corneas with a range of severity of Fuchs’ dystrophy by using confocal microscopy in vivo to measure corneal backscatter, stromal cell populations, and the presence of abnormal subepithelial cells,” says Dr. Patel.

The research team recruited 39 subjects (63 eyes) with a range of severity of Fuchs’ dystrophy and 13 subjects (25 eyes) with normal corneas from patients at Mayo Clinic in Rochester, Minnesota. All corneas were examined using slit-lamp biomicroscopy, ultrasonic pachymetry and confocal microscopy. The clinical grade of Fuchs’ dystrophy was assessed according to the presence and extent of guttae and clinically evident edema and was categorized as mild (grades 1 and 2), moderate (grades 3 and 4) or advanced (grades 5 and 6). Normal corneas were devoid of any central guttae (grade 0).

Corneal backscatter (haze) was measured from the confocal image light intensity profile. Stromal cell density and number and the presence of abnormal subepithelial cells were determined from confocal images. Comparisons between groups were made by using generalized estimating equation models.

**Anterior corneal backscatter**

“The primary outcome of this study was anterior corneal backscatter,” says Dr. Patel. The research team assessed differences in corneal backscatter between severities of disease using generalized esti-
In the News

AAO Best Poster Award
Lauren A. Dalvin, M.D., an Ophthalmology resident at Mayo Clinic’s campus in Rochester, Minnesota, was awarded a best poster award for Retinal Pathology More Likely in Complement-Mediated Than Immune Complex-Mediated Glomerulopathy at the American Academy of Ophthalmology’s 2015 annual meeting.

Education Opportunities

Mayo Clinic Anterior Segment Symposium — Frontiers in Glaucoma and Cataract 2016 — General Session
April 15-16, 2016, in Rochester, Minn.

For more information or to register, visit https://ce.mayo.edu/ophthalmology, call 800-323-2688 (toll-free) or email cme@mayo.edu.

In the News