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Trabeculectomy Can Improve Long-Term Visual Function in Glaucoma

Joseph Caprioli, MD,[1] John Mark de Leon, MD,[1] Parham Azarbod, MD,[1] Andrew Chen, BS, MD,[1] Esteban Morales, MS,[1] Kouros Nouri-Mahdavi, MD,[1] Anne Coleman, MD, PhD,[1] Fei Yu, PhD,[1,2] Abdelmonem Afifi, PhD[2]

Purpose: To measure the magnitude and direction of visual field (VF) rates of change in glaucoma patients after intraocular pressure (IOP) reduction with trabeculectomy.

Design: Retrospective, comparative, longitudinal cohort study.

Participants: Patients with open-angle glaucoma.

Methods: Patients who underwent trabeculectomy (Trab) with mitomycin-C (74 eyes of 64 patients) with ≥4 reliable VF measurements before and after trabeculectomy and at least 4 years of follow-up before and after surgery were included. Decay or improvement exponential models were used to calculate pointwise rates of perimetric change before and after surgery. A separate comparison (Comp) group with unoperated glaucoma (71 eyes of 65 patients) with similar baseline damage, number of VF tests, and follow-up was used to address possible regression to the mean. Proportions of VF locations decaying or improving before and after surgery in the Trab group, and during the first and second halves of follow-up in the Comp group, were calculated. A multivariate analysis was used to explore variables associated with VF improvement.

Main Outcome Measures: The rate of pointwise VF change before and after surgery in the Trab group and Comp group.

Results: Patients in the Trab group were followed for 5.1±2.1 years (mean ± standard deviation) before and 5.4±2.3 years after surgery, with 8.9±4.7 VF tests before and 9.0±4.4 VF tests after surgery. The mean rate of change for all VF locations slowed from −2.5±9.3%/year before surgery to −0.10±13.1%/year after surgery ($P < 0.001$). In the Trab group, 70% of locations decayed and 30% improved preoperatively; postoperatively, 56% decayed and 44% improved. The differences between the Trab and Comp groups were significant ($P < 0.0001$, chi-square test). The magnitude of IOP reduction correlated with the excess number of VF locations that exhibited long-term improvement postoperatively ($P = 0.009$). In the Trab group, 57% of eyes had ≥10 improving VF locations postoperatively.

Conclusions: The results show that trabeculectomy slows the rate of perimetric decay and provides evidence of sustained, long-term improvement of visual function in glaucoma. These findings suggest the possibility of reversal of glaucomatous dysfunction of retinal ganglion cells and their central projections. *Ophthalmology 2015;■:1–12 © 2015 by the American Academy of Ophthalmology.*

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The importance of measuring the rate of visual field (VF) decay in glaucoma is well established.[1,2] Studies have documented reduction (13%–83%) in the rates of glaucoma VF decay after trabeculectomy.[3–15] Actual improvement of VF threshold sensitivity, however, has long and widely been thought not to occur. Conventional wisdom has dictated that vision loss from glaucoma is irreversible and that treatment can only preserve remaining vision, at best. Spaeth et al[16,17] previously presented the possibility of establishing new criteria for judging the benefit of reduced intraocular pressure (IOP) in glaucoma with improvements in visual function rather than its stability. Some studies examining VF threshold sensitivity changes after trabeculectomy show no significant change,[18–25] whereas others show some improvement.[26–31]

There are reports of VF improvement after trabeculectomy with "reversal" of structural damage.[23,32–34] A recent study showed evidence of VF improvement over a 5-year period after initial glaucoma treatment (both surgical and medical).[35] Wright et al[36] recently reported short-term improvement of central and peripheral VF sensitivity after surgical reduction of IOP in glaucomatous eyes. Psychofunctional tests with contrast sensitivity,[37,38] electroretinography,[20,39–41] and color vision testing[42] have also demonstrated short-term improvement after glaucoma treatment, which supports the possibility of revitalization of retinal ganglion cell (RGC) function. No improvement of visual sensitivity was found in normal eyes, suggesting that the presence of glaucomatous damage is required for the enhancement of visual sensitivity.[25]

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Although the slowing of VF damage as a consequence of IOP reduction has been established by landmark glaucoma randomized clinical trials,[43–48] the measurement and quantification of real and sustained VF improvement have been investigated little, and at that, not beyond the global VF indices. The objective of this study is to investigate the frequency and distribution of VF improvement by analyzing the magnitude and direction of the rates of change after the IOP reduction afforded by trabeculectomy.

Methods

Patient Selection

This is a retrospective review of consecutive patients with open-angle glaucoma who underwent trabeculectomy at the Glaucoma Division of the Jules Stein Eye Institute, University of California, Los Angeles (UCLA), between December 2, 1993, and January 13, 2014, and who satisfied all inclusion and exclusion criteria for this study. Trabeculectomy was performed if (1) the patient showed convincing evidence of progressive structural or functional glaucomatous optic nerve damage that could not be adequately treated with more conservative measures or if (2) in the opinion of the surgeon, the IOP was at a level that would probably cause additional damage. Three experienced glaucoma specialists performed a previously described standardized trabeculectomy with intraoperative adjunctive mitomycin-C.[49] A separate comparison group of patients with glaucoma who did not have surgery but, with a similar amount of baseline VF damage, similar numbers of VF measurements, and similar durations of follow-up, were used to help address possible regression to the mean effects. This study was approved by the UCLA Human Research Protection Program, was performed in accordance with the tenets set forth in the Declaration of Helsinki, and complied with Health Insurance Portability and Accountability Act regulations.

Visual Field Inclusion Criteria

All VF examinations were performed with a Humphrey VF analyzer (Carl Zeiss Ophthalmic Systems, Inc., Dublin, CA) with a 24-2 test pattern, size III white stimulus, and with full threshold or Swedish Interactive Threshold Algorithm (SITA) standard strategies. Each eye's VF series contained all SITA or all full-threshold examinations; examinations were never mixed for any eye in the series. The VF tests with less than 30% fixation losses, false-positive rates, and false-negative rates were considered reliable, and all VFs belonging to each series that fulfilled these criteria were included in the study. The last preoperative and first postoperative VFs were required to be within 1 year of surgery. The VF tests performed <3 months after surgery were excluded. Eyes with ≥ 4 VF tests both before and after trabeculectomy that fulfilled these criteria were included. The minimum required VF follow-up both before and after surgery was 4 years. Eyes that had cataract surgery within the required follow-up period were excluded. Pseudophakic eyes were included if cataract surgery preceded enrollment. Eyes that had other major ocular surgeries or medical events within the follow-up period that may have affected visual function were excluded. Visual field locations were eliminated from the analysis if they were part of the physiologic blind spot or the initial 3 measurements at those locations before or after trabeculectomy had threshold sensitivities of 0 decibels (dBs). For test locations that included a threshold sensitivity of 0 dB, the 0 dB value was converted to 1 dB to allow for logarithmic transformation.

Determination of Improvement or Decay

The slope of a linear regression fit was first measured at each test location to determine whether that location had an improving or decaying trend. If the regression coefficient was positive, the series was tagged as "improving," and if negative, the series was tagged as "decaying."

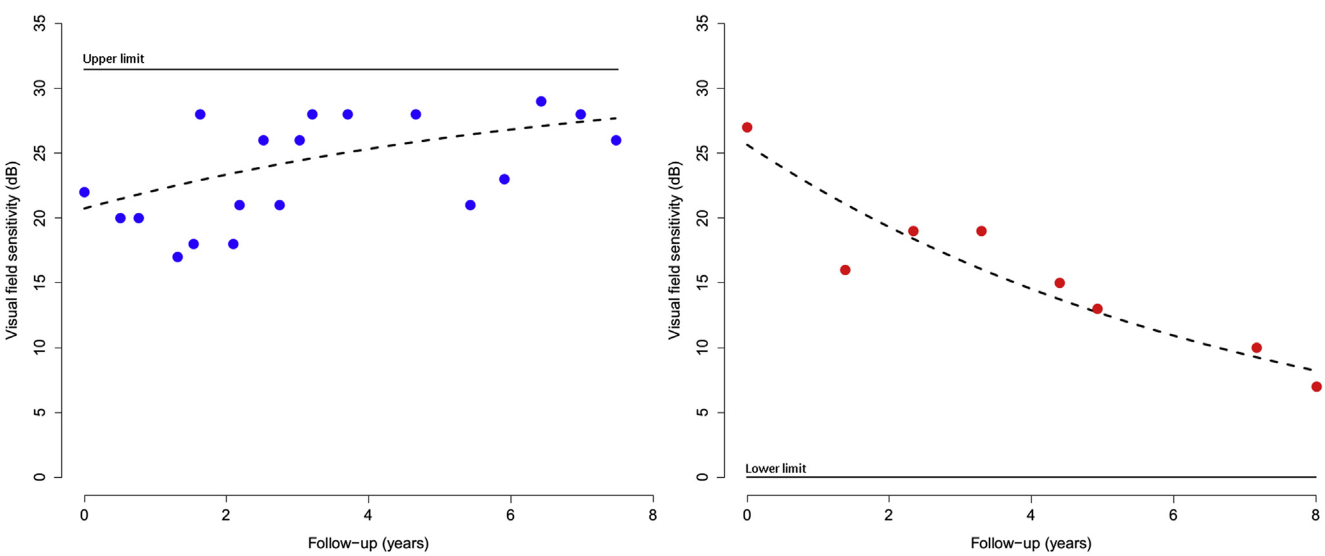

Figure 1. Observed decibel (dB) values and the improvement model fit based on the exponential decay curve bounded by an upper limit based on the age- and location-matched normal sensitivity (*left*). Observed dB values and the decay model fit based on the exponential decay curve bounded by a perimetric lower limit of 0 dB (*right*).