

The Collaborative Initial Glaucoma Treatment Study—What We Have Learned so Far

BY JESS T. WHITSON, MD

What have we learned so far from the Collaborative Initial Glaucoma Treatment Study (CIGTS)? How does this landmark study help us better care for our glaucoma patients? Should we operate right away or prescribe eye drops for patients initially diagnosed with primary open-angle glaucoma? Are patients with advanced disease better off having surgery initially? Does smoking adversely affect trabeculectomy outcomes? Who is most likely to worry about blindness when diagnosed with glaucoma? What is the most important lesson from the CIGTS?

In this installment of “Landmark Studies,” Jess T. Whitson, MD, answers these questions and enlightens us about this important research. Dr Whitson carefully, thoughtfully, and wisely emphasizes the take-home messages from this landmark study.

—Section Editor Ronald L. Fellman, MD

WHAT QUESTION WAS THE CIGTS DESIGNED TO ANSWER?

Although medications have traditionally been used as first-line therapy for glaucoma, recent reports have favored early or even immediate surgery to prevent progressive visual field (VF) loss.^{1,2} The CIGTS was designed to determine whether patients with newly diagnosed open-angle glaucoma (primary, pigmentary, or pseudoexfoliative) are managed better by initial treatment with IOP-lowering medications or by immediate trabeculectomy. Outcome measures included clinician-assessed and patient-reported visual function and IOP control. Quality-of-life (QOL) measures were also used to evaluate how these therapies affect patients.

HOW WAS THE STUDY DESIGNED TO ANSWER THE QUESTION?

The CIGTS³ is a prospective, multicenter, randomized clinical trial that enrolled 607 patients with newly diagnosed open-angle glaucoma between October 1993 and April 1997 at one of 14 participating centers. Subjects were between 25 and 75 years of age with a visual acuity better than 20/40, had undergone 2 weeks or less of lifetime glaucoma treatment, and had an IOP of at least 20 mm Hg in either eye with definitive VF loss or an IOP of at least 27 mm Hg with normal VFs but obviously damaged optic discs. After two qualifying baseline visits, patients were randomized to receive either a stepped medical regimen or trabeculectomy (with or without 5-fluorouracil). Target IOP was determined from baseline IOP (average of six measurements) and a baseline VF score. Before randomization, patients participated in a baseline telephone QOL interview, which incorporated previously designed questionnaires such as the Visual Activities Questionnaire⁴ and the Sickness Impact Profile,⁵ along with several components made specifically for the CIGTS. Three months after treatment was initiated, patients were observed at the clinical centers and completed telephone QOL interviews every 6 months.

CONSIDERING THE PRIMARY OUTCOME VARIABLE, WHAT DID WE LEARN FROM THE CIGTS?

An early report revealed that, after 5 years of therapy, patients who underwent trabeculectomy maintained the same VF scores on average.⁶ Patients who received medical therapy had an initial improvement in VF scores,

but after 5 years, both groups converged toward similar scores. Although the surgery group achieved a lower mean IOP than the medication group (14-15 vs 17-18 mm Hg), both groups had similarly low rates of VF progression. Approximately 11% of medically treated patients and 14% of surgically treated patients had significant VF progression, which was defined as a 3-unit increase in VF score based on a 20-point scale. Longer-term follow-up is addressed later in this article.

WHAT FACTORS AFFECTED VF PROGRESSION IN THE CIGTS?

Through the first 5 years of follow-up, patients who underwent trabeculectomy were much more likely to develop a cataract, which affected their VF scores, than those treated medically. Also, patients with more advanced VF loss at baseline, older patients, nonwhite patients, and those with diabetes were more likely to experience progression.⁶ Greater IOP fluctuation also led to more VF progression, especially in patients treated with medications.⁷

DOES THE STUDY SUPPORT THE CONCEPT OF EARLIER SURGERY FOR CERTAIN CLINICAL CONDITIONS?

A recent report from the CIGTS⁸ revealed that, with longer-term follow-up (8 or more years), significant VF progression occurred in more than 21% and 25% of the surgery and medication groups, respectively. Patients with mild VF loss at baseline (mean deviation < -2 dB) did equally well with either initial surgical or medical therapy. In general, patients with more advanced baseline VF loss (mean deviation > -10 dB) had less VF progression if they underwent initial trabeculectomy than if they were treated with medications. Interestingly, diabetic patients actually had more VF progression if they were treated with surgery initially. African Americans also did less well with surgery first. Although the incidence of transient perioperative complications such as anterior chamber shallowing or serous choroidal detachment was high (approximately 50%), there were very few complications resulting in sustained vision loss.⁹ Results from the CIGTS thus far appear to support early surgical intervention for patients who present with more advanced disease, with the possible exception of diabetic patients and African Americans.

WHAT DID WE LEARN ABOUT DISC DAMAGE?

Baseline stereoscopic photographs of the optic disc were taken in both eyes of all participants in the CIGTS. At the 5-year follow-up visit, a subset of patients (348 eyes) had an additional set of photographs taken. These were assessed by

two independent readers in a masked fashion for evidence of change and then confirmed by an independent committee. The majority of eyes, about 87%, showed no change; 6.3% showed progression of cupping, while 6.6% showed a reversal of cupping. The incidence of progressive cupping was significantly higher in the medication group (10% vs 3%, $P = .007$), whereas a reversal of cupping occurred more often in the surgical group (13% vs 1%, $P < .001$). Subjects who demonstrated VF worsening typically experienced progressive optic disc cupping as well. Although a reversal of cupping was seen in subjects with lower postoperative IOP, it was not associated with an improvement of either visual acuity or central VFs.¹⁰

DID THE STUDY DEMONSTRATE THAT CERTAIN FACTORS SUCH AS SOCIOECONOMICS, SMOKING, AND OTHER ASPECTS PLAY A ROLE IN IOP CONTROL?

Through the first 9 years of follow-up, surgically treated subjects demonstrated consistently lower IOPs than those treated with medications (15 vs 17.2 mm Hg). A higher IOP during follow-up was associated with a higher baseline IOP ($P < .0001$), worse baseline VF ($P < .0001$), and lower level of education ($P = .0019$). Smokers who underwent trabeculectomy had significantly higher IOPs postoperatively than nonsmokers (16.7 vs 14.6 mm Hg, $P = .0013$).¹¹

WHAT ARE THE IMPORTANT FACTORS WE LEARNED ABOUT QOL FOR OUR PATIENTS?

The CIGTS provides a unique opportunity to study the impact of glaucoma and its treatment on individuals' QOL. Thus far, both medical and surgical therapy have very similar effects on QOL. Surgical patients reported more problems with activities related to vision and were more bothered by local eye symptoms.¹² Patients with a self-reported decline in visual function were more likely to experience depression and mood alteration.¹³

FEAR OF BLINDNESS WAS STUDIED IN THE CIGTS. WHAT DO YOU TEACH YOUR RESIDENTS TO SAY TO GLAUCOMA PATIENTS ABOUT THIS TOPIC?

Fear of blindness was common in the CIGTS, with 34% of patients expressing at least a moderate worry about blindness after being diagnosed with glaucoma. Younger patients, whites, and those with less education and a lower income were the most likely to express a fear of blindness. Although this percentage declined over time, 11% still had at least a moderate fear of blindness after 5 years. Initial treatment assignment (medications vs surgery) was not associated with fear of blindness.¹⁴

It is important for residents and all physicians who treat patients with glaucoma to know that many of our patients will be afraid of going blind when they are diagnosed with glaucoma. This provides a great opportunity to counsel patients on the nature of the disease, the importance of compliance with therapy and follow-up, and the low risk of blindness in most patients with proper treatment.

WHAT ARE THE MOST IMPORTANT CLINICAL TAKE-HOME POINTS FROM THE CIGTS?

Thus far, the CIGTS has demonstrated that both medications and surgical therapy can be used to safely and effectively treat most patients with glaucoma. Some patients, in particular those who present with more advanced disease, may benefit from earlier rather than later incisional surgery. Finally, fear of blindness and depression are common among glaucoma patients, especially those who perceive a decreased ability to perform visual tasks. In the years to come, the CIGTS should continue to provide valuable insights into the treatment of glaucoma and its impact on our patients. ■

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1. Migdal C, Hitchings R. Control of chronic simple glaucoma with primary medical, surgical and laser treatment. *Trans Ophthalmol Soc UK*. 1986;105 (pt 6):653-656.
2. Sherwood MB, Grierson I, Millar L, et al. Long-term morphologic effects of antiglaucoma drugs on the conjunctiva and Tenon's capsule in glaucomatous patients. *Ophthalmology*. 1989;96:327-335.
3. Musch DC, Lichter PR, Guire KE, et al; the CIGTS Study Group. The Collaborative Initial Glaucoma Treatment Study: study design, methods, and baseline characteristics of enrolled patients. *Ophthalmology*. 1999;106:653-662.
4. Sloane ME, Ball K, Owsley C, et al. The Visual Activities Questionnaire: developing an instrument for assessing problems in everyday visual tasks. *Tech Dig Noninvas Assess Vis Sys*. 1992;1:26-29.
5. Bergner M, Bobbitt RA, Carter WB, et al. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care*. 1981;19:787-805.
6. Lichter PR, Musch DC, Gillespie BW, et al; the CIGTS Study Group. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology*. 2001;108:1943-1953.
7. Musch DC, Gillespie BW, Niziol LM, et al; the CIGTS Study Group. Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*. 2011;118:1766-1773.
8. Musch DC, Gillespie BW, Lichter PR, et al; the CIGTS Study Group. Visual field progression in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*. 2009;116:200-207.
9. Jampel HD, Musch DC, Gillespie BW, et al; the CIGTS Study Group. Perioperative complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol*. 2005;140:16-22.
10. Parrish RK, Feuer WJ, Schiffman JC, et al; the CIGTS Optic Disc Study Group. Five-year follow-up optic disc findings of the Collaborative Initial Glaucoma Treatment Study. *Am J Ophthalmol*. 2009;147:717-724.
11. Musch DC, Gillespie BW, Niziol LM, et al; the CIGTS Study Group. Factors associated with intraocular pressure before and during 9 years of treatment in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*. 2008;115:927-933.
12. Janz NK, Wren PA, Lichter PR, et al; the CIGTS Study Group. The Collaborative Initial Glaucoma Treatment Study: interim quality of life findings after initial medical or surgical treatment of glaucoma. *Ophthalmology*. 2001;108:1954-1965.
13. Jampel HD, Frick KD, Janz NK, et al; the CIGTS Study Group. Depression and mood indicators in newly diagnosed glaucoma patients. *Am J Ophthalmol*. 2007;144:238-244.
14. Janz NK, Wren PA, Guire KE, et al; the CIGTS Study Group. Fear of blindness in the Collaborative Initial Glaucoma Treatment Study: patterns and correlates over time. *Ophthalmology*. 2007;114:2213-2220.