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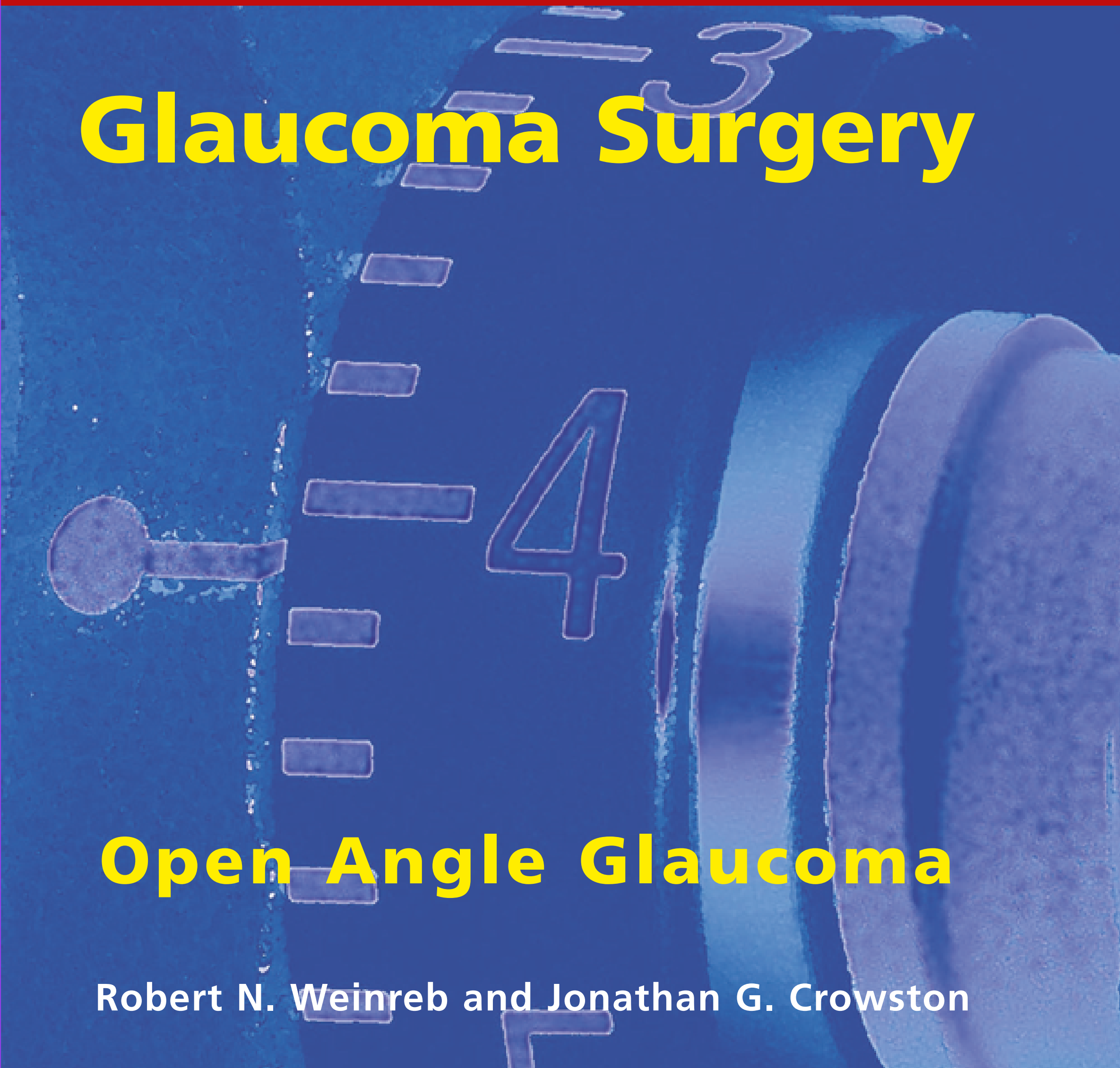

Glaucoma Surgery

Open Angle Glaucoma

Robert N. Weinreb and Jonathan G. Crowston

Consensus Series - 2

Association of International Glaucoma Societies

GLAUCOMA SURGERY

OPEN ANGLE GLAUCOMA

Everyone is entitled to their own opinion, but not their own facts.
David Patrick Moynihan

A genuine leader is not a searcher for consensus but a molder of consensus.
Martin Luther King, Jr.

GLAUCOMA SURGERY OPEN ANGLE GLAUCOMA

Reports and Consensus Statements of the 2nd Global AIGS Consensus Meeting on Glaucoma Surgery – Open Angle Glaucoma

Robert N. Weinreb and Jonathan G. Crowston

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Glaucoma Surgery for Open Angle Glaucoma Consensus Meeting Participants. Fort Lauderdale, April 30, 2005.

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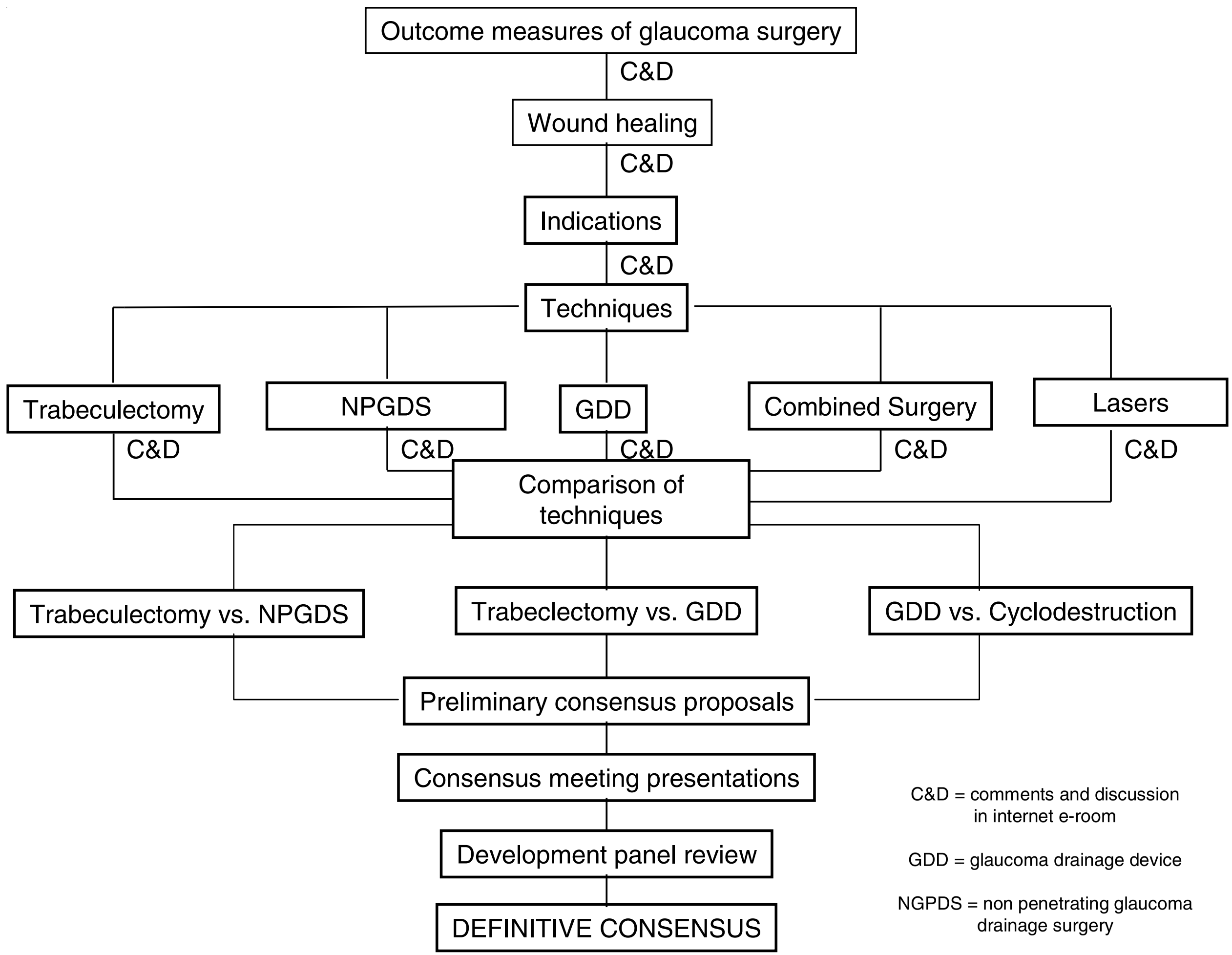

Outcome measures of glaucoma surgery
C&D
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DEFINITIVE CONSENSUS
C&D = comments and discussion in internet e-room
GDD = glaucoma drainage device
NGPDS = non penetrating glaucoma drainage surgery

CONTENTS

FOREWORD

This is the second Consensus Book published by the AIGS on: *Glaucoma Surgery – Open Angle Glaucoma.* A consensus meeting has great potential to impact patients, both individually and collectively. Reports for this consensus meeting have been prepared and discussed using an efficient internet based e-Room system. The Consensus Faculty consists of leading authorities in Glaucoma Surgery with representatives from six Continents. These 90 experts devoted their time, insight and energy to the preparation of the reports, over a period of three months. Each report was discussed extensively during the Consensus Meeting in Fort Lauderdale, April 30, 2005. Reports and Statements were revised following these discussions by each of the groups and the Consensus Development Panel.
A consensus is based on the published literature and expert experience. While one should strive to practice evidence-based medicine, it is clear that many aspects of surgical practice in ophthalmology have not been subject to, or are not amenable to long term prospective randomized controlled trials. Though consensus by experts is not a surrogate for rigorous scientific investigation, it has value, in particular where the appropriate evidence is lacking. Generating consensus in expert opinion for glaucoma surgery therefore aims to derive the most appropriate surgical management for our patients and will highlight areas where further research is required.

Robert N. Weinreb, President, AIGS
Erik L. Greve, Executive Vice President, AIGS

"But if you can assemble a diverse group of people who possess varying degrees of knowledge and insight, you're better off entrusting it with major decisions rather than leaving them in the hands of one or two people, no matter how smart those people are."

James Surowiecki. *The Wisdom of Crowds 2004*

OUTCOME MEASURES FOR STUDIES OF GLAUCOMA SURGERY

Paul Palmberg

Paul Palmberg

Intraocular pressure

The standard of intraocular pressure (IOP) control most widely used in assessing the success or failure of glaucoma surgery is based upon the normal distribution of intraocular pressures found in population-based studies. Those studies, conducted in England[1] and the United States,[2,3] reported that the mean pressure was 15 mmHg and the standard deviation about 3 mmHg. Thus, 21 mmHg (the mean plus two standard deviations) was considered the upper limit of the normal pressure distribution.

The categories of success and failure were further subdivided by the investigators in the 5-Fluorouracil in Filtering Surgery Study[4] to consider whether supplemental medication or re-operation had been required, and to consider devastating complications. The results were assessed yearly by life-table methods.

Complete success: IOP 21 mmHg or less, without medication, re-operation or devastating complication.

Qualified success: IOP 21 mmHg or less with supplemental medication, but without devastating complication.

Qualified failure: IOP > 25 mmHg, without medication or re-operation or devastating complication.

Failure: IOP > 21, even with supplemental medication, or re-operation or devastating complication.

Those standards of pressure control would now seem inadequate, given the results of such long-term clinical trials as the Advanced Glaucoma Intervention Study (AGIS),[5] The Comparison of Initial Glaucoma Treatments Study (CIGTS)[6] and the Early Manifest Glaucoma Trial (EMGT),[7] taken together suggest the desirability of reaching pressures lower than the statistical limit of the normal pressure range.

The results of the AGIS suggested that patients with advanced glaucoma (failure of medical therapy, actually moderate damage, MD averaging -10.5 dB) do well with an IOP that is always < 18 mmHg (average 12.3 mmHg), with no net visual field progression during eight years of follow up. Subjects in

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AGIS in whom the IOP failed to be below 18 mmHg at all visits had progressive visual field loss that was proportionate to the percentage of visits failing to meet that predetermined goal. The results of AGIS support the empirical observation of Chandler that patients with advanced disease (involving both poles of the disc) do best when the IOP is less than the population mean.[8]

The CIGTS demonstrated that adoption of an aggressive target pressure (minimum 35% reduction from baseline) achieved the desirable result of no net visual field progression over five years in newly diagnosed glaucoma with minimal damage (mean of MD -5 dB). Stability was achieved in both the group randomized to initial medical treatment (with supplemental LTP allowed, and crossover to surgery mandated for failure to achieve the target pressure), in which the IOP was reduced an average of 38% to 17.6 mmHg, and the group randomized to initial surgery, in which the IOP was reduced an average of 52% to 14 mmHg. The result suggests that a greater than 35% IOP reduction is not required to achieve stability at an early stage of disease, nor is it necessary to reduce the IOP to the low normal pressure range for an optimal result.

The EMGT, like CIGTS, was performed in newly diagnosed patients with, on average, early damage. Subjects were randomized to observation or to a treatment that was the same for all (betaxolol twice a day and laser trabeculoplasty), with no target pressure and treatment only adjusted for a rather high IOP or for progression. The risk of progression was quite high in the observation group (62% in five years), but also in the treated group (45% in five years). While the treatment strategy employed in the EMGT in retrospect was far less successful than that employed in the CIGTS, the EMGT generated a wide distribution of pressures, so that it provided a dose-response curve with a slope corresponding to a 13% reduction in risk for each mmHg average lower pressure during follow up (in the effective range).[9] The EMGT results have yet to be reanalyzed to see whether those subjects in whom the IOP was always reduced by 35% or more, as in CIGTS, would have done as well.

One might propose that new standards for IOP control be adopted that are based upon clinical trial results and serve therefore as a more appropriate surrogate for prevention of glaucoma progression. One could adopt either an absolute pressure goal, such as pressures below 15 mmHg for advanced cases and below 18 mmHg for early damage, or a percentage reduction, such as 30 or 35% for all cases (based upon CIGTS and the Collaborative Normal Tension Glaucoma Study).[10]

Indeed, as a good example, Carassa et al[11] have reported their results in a two-tier fashion, reporting results for a trial comparing viscocanalostomy to trabeculectomy as the percentage achieving an IOP of 6-21 mmHg and also those achieving 6-16 mmHg, so that one may judge the adequacy of each type of surgery to achieve results appropriate to patients with mild or advanced damage, respectively.

There is actually a long-standing historical precedent for this, going back to Chandler and Grant. Chandler[8] in 1960 and Burke and Grant[12] in 1982 reported the long-term visual field outcomes of glaucoma therapy for four classes of patients and gave their corresponding treatment goals: ocular hypertensives (do well under 30 mmHg), disc change without field loss (get to 20 mmHg), field loss in one hemi-field (get to mid-teens) and field loss in both hemi-fields (get to low teens).

Proposal

Report life-table results for annual pressures under 18 mmHg (and a 30% reduction from treated baseline), without and with supplemental medication and also report life-table results for annual pressures less than 15 mmHg, without and with supplemental medication.

One should also report the means and standard deviations of baseline and post-operative pressures, and exclude eyes from the success that have had devastating complications. The reduction in medications used should also be reported.

Visual function and structure

Visual function

The real goal of glaucoma surgery is to maintain function and structure. Results should include mean values for visual acuity (ETDRS)[13] and the percentage of subjects not suffering visual acuity loss, perhaps best presented as a life-table analysis of those not suffering a doubling of the visual angle, and those not reaching a standard definition of blindness. Visual field results should be presented for automated, threshold-related testing, and might use criteria developed by specific clinical trials (AGIS, CIGTS, CNTGS, even OHTS[14]), or new and probably better criteria that have a better satistical validity, such as the SITA-change program[15] or the Progresser Program.[16] This is an area under development and discussion, and so far we only know that there is fairly poor correspondence between the various criteria. Clearly, whatever level of change is accepted, be it a change of 3 dB of MD or PSD, or a cluster analysis, or Glaucoma Hemi-field, or SITA-change program, it is best if two to three baseline fields are obtained, and that change be sustained on two to three fields before diagnosing progression.

Structure

Changes in structure have now been documented to occur somewhat more frequently than changes in function in early damage cases, as in the prospective OHTS with stereoscopic disc photography[17] and the confocal scanning laser ophthalmoscopy of the ancillary OHTS.[18] In addition to stereo-photographs of the discs, quantitative imaging technologies, HRT,[19] GDX[20-21] and OCT,[22] may detect structural changes, which are not necessarily the same.[23] It is likely that future clinical trials of glaucoma surgery will receive greater credibility if they include a structural assessment of change, especially for surgery done in cases of pre-perimetric glaucoma (disc damage only) and in cases with mild damage. These technologies may also prove useful in even more advanced cases when emerging techniques with higher resolution can be implented.[24]

Quality of life

Ultimately, we are interested in how glaucoma surgery and the disease itself affect the quality of life of our patients, through loss of visual function, through the expenditure of time and money for treatment, or through complications and side effects of therapy that cause discomfort. In glaucoma surgery for early disease, quality of life considerations are often paramount since visual disability is quite unlikely to occur in the short term.

Ambitious attempts to study the effect of glaucoma interventions on the overall quality of life have generally failed, since only end-stage disease appears to have an impact. Even the Visual Function Questionnaire (VFQ), developed by the National Eye Institute of the United States, shows little change until fairly advanced functional change has occurred.[25] The most important cause of visual decrease after glaucoma surgery, cataract, generally has too transient an effect on vision to show up at study end. Change on the VFQ is more likely to be affected by advanced diabetic retinopathy or neovascular age-related macular degeneration than by the levels of glaucoma encountered in most clinical trials.

However, local eye symptoms are affected by medications and by filtering blebs, and changes were measured with linear symptom estimates (scale of one to ten) in the CIGTS,[26] and demonstrated a somewhat better tolerance of medication than of filtering surgery. Such measures are likely to be an important outcome in studies that compare trabeculectomy to non-penetrating glaucoma surgery, or to glaucoma drainage devices, or to new trabecular bypass shunts.

Complications

Complications of glaucoma surgery may cause only brief reductions in vision or may be devastating. Some, such as hyphema, low choroidal detachment or transient wound leaks soon pass and are of little consequence. Cataract, though it causes a symptomatic reduction in vision and requires important expenditures of time and money to alleviate, has little lasting effect (unless the patient is young and suffers a premature loss of accommodation). The important complications - late bleb leaks and infection, suprachoroidal hemorrhage, corneal decompensation, hypotony maculopathy and retinal detachment - often require intensive management and additional surgery, and not infrequently result in permanent loss of sight.

The purported advantages of non-penetrating glaucoma surgery usually relate to a reduction in complications - cataract, bleb-related pain or infection, or hypotony. However, recent advances is the application of mitomycin-C by Wells *et al.,*[27] have markedly reduced the long-term risk of late bleb leaks and infection and of painful blebs, and highly successful techniques for avoiding and for repairing hypotony maculopathy have been reported by Suner *et al.*[28] Furthermore, the more successful results of non-penetrating glaucoma surgery are now being obtained with methods that do create a filtering bleb, and that obtain a lower pressure when MMC is employed.[29] In other words, the techniques of trabeculectomy and some forms of non-penetrating glaucoma surgery are converging. Therefore, future comparisons of complications of different surgical techniques will have to be carefully qualified as to how the surgery was done, since it is difficult to compare evolving techniques.

Complications should be reported by incidence, but also by their visual consequence.

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Discussion on surgical outcomes: Ravi Thomas and Paul Palmberg (report author)

Erik Greve

Peng Khaw

Makoto Araie, Daniel Grigera and Paul Palmberg

INDICATIONS FOR GLAUCOMA SURGERY

Robert Fechtner and Roger Hitchings

Robert Fechtner
(Presenter)

Contributors: Makoto Araie, Keith Barton, Daniel Grigera, Kenji Kashiwagi, Gunter Krieglstein, Clive Migdal, Tony Realini and George Spaeth

Consensus points

- The decision for surgery should consider the risk/benefit ratio**.** Although a lower IOP is generally considered beneficial to the eye, the risk of vision loss without surgery must outweigh the risk of vision loss with surgery.
- Surgery for glaucoma is indicated when:
  a. Optimum medical therapy and/or laser surgery fails to sufficiently lower IOP.
  b. A patient does not have access to or cannot comply with medical therapy.
- Clinicians should generally measure IOP more than once and preferably at different times of day when establishing baseline IOP prior to surgery. When IOP is markedly elevated, a single determination may be sufficient.
- Progression of glaucoma, considering both the structural and functional integrity of the optic nerve, is clearly a threat to vision and strongly influences the threshold for surgery.
- Ongoing care of the patient with glaucoma requires careful periodic evaluation of structure and function.
- Efforts should be directed at estimating the rate or risk of progression. A greater rate or risk of progression may lower the threshold for surgery but must be balanced against the risk and benefits of surgery and the life expectancy of the patient.
  Comment: An elderly patient with slow progression may suffer no effect on quality of life during his/her lifetime.
  Comment: Advancing glaucomatous optic disc damage or retinal nerve fiber loss without detected visual loss is progression and can in certain circumstances be an indication for surgery.

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- Risk factors for progression of glaucoma are emerging from prospective studies. (AGIS-older age, lower education, male sex, diabetes; CNTGS-female sex, migraine; EMGT- high IOP, pseudoexfoliation, worsening visual fields during follow up, disc hemorrhage, advanced stage of disease.) Presence of these risk factors may alter target IOP or lower the threshold to surgery.
- *Comment:* Fellow eye vision loss from glaucoma may lower the threshold IOP for consideration of surgery. It is not clear that it is a risk factor for threat to vision.
  Comment: Family history of blindness from glaucoma is not a known risk factor for vision loss, but such patients warrant close observation.
- Primary surgery may be indicated on the basis of socioeconomic or logistic constraints.
  Comment: There is insufficient evidence to recommend primary surgery in all patients.
- Patients who are unable or unwilling to use their medical therapy as prescribed represent failures of treatment efficacy and may need surgery to achieve consistent IOP reduction, even when isolated IOP measurements appears normal at office visits.
- The extent and location of damage may alter the threshold for surgery. Patients with advanced damage or damage threatening central vision may require lower IOP than those with early disease.

Introduction

It is difficult to capture and articulate the indications for glaucoma surgery for the open angle glaucomas; every patient has a unique manifestation of disease and interaction between disease, treatment and quality of life. There are no clearly defined and accepted rules to dictate when surgery is the appropriate therapeutic choice, but there are principles that seem to guide this decision.

Assumptions

Several assumptions underlie the recommendation of surgery for the treatment of glaucoma. The most basic are supported by evidence:

- Surgical IOP lowering stops or slows progressive glaucoma damage.[1,2]
- Greater IOP lowering can be achieved with surgery than with medication in many patients.[2]
- Surgery has greater risk than medical treatment of glaucoma. Intraoperative risks such as suprachoroidal hemorrhage and post-operative risks such as bleb related endophthalmitis can result in rapid and profound loss of vision.[3]

Goals of glaucoma surgery

The treatments for glaucoma all have in common reduction of intraocular pressure (IOP). IOP is no longer part of the definition of glaucoma; glaucoma is defined by the damage that occurs. However, IOP is consistently identified as a risk factor for presence or progression of glaucoma.[1,4-7] Evidence exists from several large clinical trials that reduction of intraocular pressure by medication or by surgery is beneficial in preserving visual function or optic nerve structure.[5,6,8] We accept lowering of IOP as a surrogate indicator for successful treatment; it often takes years to determine if there is progression of disease. It is clear that the goal of care for the patient with glaucoma is not simply lowering IOP, but rather is preservation of sufficient vision so that the patient does not suffer a glaucoma-related reduction in quality of life.[9]

To state it differently, the goal of glaucoma care is to reduce or eliminate the pressure-related threat to vision. This goal is often approached by setting and then achieving a pressure range for 'target IOP'.[10] Target IOP is most honestly defined as that IOP level at which the clinician believes the threat to vision is sufficiently reduced that the patient will not suffer a decrease in quality of life due to glaucoma-related vision loss. The challenge is to know *a priori* what level of IOP will be adequate to substantially slow or halt progressive optic neuropathy, whether defined by structural or functional criteria. At present, there is no way to determine this for individuals.

Implied in threat to vision is that the patient has disease that is either severe or progressing at such a rate that visual function will be compromised during his or her lifetime. Available diagnostic techniques allow us to determine the stage of the glaucomatous damage based on structure, function, or both and monitor for progression. Actuarial tables can provide a population-based estimate of expected remaining life span.

The indication for treatment is best defined as an identified need to reduce threat to vision. At present, all approved and generally accepted treatments are aimed at reducing IOP-related threat to vision (TTV). As a general principle, the therapy likely to be effective with the least morbidity should be attempted first. This is rarely surgery. There are often many appropriate medical options.[11] In some cases where TTV is judged to be very high, primary surgery may be justified. Thus, the indication for surgery is to reduce TTV when other options are unavailable, inappropriate, or ineffective for a patient.

It is stressed that the decision for surgery always has an IOP component. No decision for glaucoma surgery can be made in the absence of consideration of IOP. But it is the expected TTV rather than the IOP itself that motivates surgery. Likewise, the only favorable result of surgery for glaucoma is the lowering of IOP without complication. In this respect, the short-term efficacy of surgery – reduction of TTV – cannot be determined unless the target IOP is established. The long term efficacy of surgery – preservation of vision – is only established in retrospect.

Fig. 1. There are multiple dimensions to the threat to vision from glaucoma (IOP). The surgeons must consider these in approaching the decision to operate.

The TTV cannot be quantified by any available data. Rather, there are factors that are considered for each patient that affect the clinicians estimate of TTV. These are commonly referred to as 'indications for surgery', but it should be appreciated that they are the factors that determine threat to vision. In the future, it may be possible to quantify the relative contributions of each of these factors to calculate the risk. At present this remains a qualitative evaluation by the surgeon in consultation with the patient.

The decision for surgery must consider the risk/benefit ratio: a lower IOP must be considered beneficial to the eye, and the risk of vision loss without surgery must outweigh the risk of vision loss from surgery.

IOP

It is tempting to equate IOP reduction with glaucoma treatment. IOP reduction is the surrogate for reduction of TTV. But for IOP to serve as an adequate surrogate, IOP measurement artifacts must be accounted for, and multiple measurements of this dynamic variable are required to fully characterize the need for – and likely success – of TTV reduction.

Central corneal thickness

Central corneal thickness (CCT) influences applanation tonometry; IOP measurements are lower than true IOP with a thinner cornea and higher with a thicker cornea. There is not a validated conversion scale although several have been suggested. Measured IOP must be interpreted in the context of CCT.[12,13]

Diurnal and nocturnal fluctuation

In practice, determination of IOP in the clinic is based on one (or only a few) isolated IOP measurements. A single IOP determination inadequately describes the variability of IOP for a patient. Diurnal and nocturnal fluctuations can encompass a wide range of IOP in an individual. It is desirable to have more fully characterized IOP profiles on all patients to guide therapy and indications for surgery, but in practice we have only a few IOP snapshots.[14]

High IOP

Extremely high IOP alone, particularly in an acute setting, can pose a sufficiently high risk of threat to vision (directly through IOP effect or by vascular occlusion) to be an indication for surgery. More commonly other factors will impact the decision for surgery in patients with moderately elevated IOP, or IOP at average or low levels.

Degree of damage

Since it is the damage to the optic nerve that results in loss of vision, the more advanced the nerve damage the greater the chance the patient will have a vision-related decrease in quality of life. It is not clear that the risk of progression increases based on the extent of nerve damage, but there is general agreement that the more advanced the damage, the lower the target IOP should be to minimize the risk of additional IOP-related vision loss. These very low IOPs can often only be achieved with surgery.[15]

While the degree of damage influences the estimate of TTV, it is not necessary for damage to be present for surgery to be indicated. When the TTV is sufficiently high (*e.g.*, IOP 50 mmHg on medications with a secondary glaucoma) surgery may be indicated prior to the development of glaucomatous damage.

Progression

Progression of damage is the hallmark of glaucoma. Glaucoma may progress following IOP reduction.[1,2,5,6] This implies either insufficient IOP reduction, or a non-IOP dependent component of the disease. When there is still believed to be a pressure-related component to the damage, additional IOP reduction is warranted.

Most clinicians monitor the visual field and make management decisions, including surgery, based on them. Recognizing that progressive visual field loss is both an outcome to be prevented as well as a risk factor for further loss of vision, we must consider progressive visual field loss as a strong risk factor for TTV. However, with careful clinical examination, the appearance of progressive damage of the optic disc or RNFL can be detected, even in the absence of visual field progression. Changes in optic nerve or nerve fiber layer structure are strong risk factors for TTV.

Age

The prevalence of glaucoma increases with age.[4,16] Age is a risk factor for progression of disease for both ocular hypertension and POAG.[2,5,6] However, one must consider the age in the context of progression of disease and likelihood of developing vision loss affecting QOL within the lifetime. It must be remembered that as other senses fail (such as hearing loss) patients may need to rely more upon vision. We often underestimate the projected lifespan of our elderly patients. Use of actuarial tables may assist the development of TTV models. For the present one should not deny glaucoma surgery based on age alone, but should consider the extent of damage, rate of progression and likely lifespan for older patients. Conversely, young patients with advanced disease have many years in which their useful vision must survive. This increases the lifetime TTV and would lower the threshold to surgery.

Non-surgical options are unavailable or unsuccessful

Medication may be inappropriate in some clinical settings

Extremely high IOP may be unlikely to be sufficiently reduced by medications. In this case medical treatment may be initiated briefly in order to operate at lower IOP.

Far advanced glaucoma damage at modest IOP threatening remaining vision may require very low IOP to reduce TTV.

Some patients have secondary conditions that interfere with the ability to administer medication such as dementia, mental illness, or arthritis.

In some secondary glaucomas, IOP is very high and unlikely to be lowered sufficiently with medication or may need definitive surgery (*e.g.*, iridectomy for pupillary block angle closure).

Pediatric or childhood glaucoma is a special case in which medical therapy is unlikely to be successful and primary surgery is usually indicated.

Medication is unavailable

Economic problems are challenges for patients in many locations. This may limit or effectively exclude access to medical treatment for glaucoma.

Limited access to medical resources may be based on other factors such as distance from medical care and limited availability of practitioners and medications.

In some settings, surgery will be indicated as primary intervention even though IOP might respond to medication.

Medication is not sufficiently effective

In the past, maximal medical therapy has been considered the last step before surgery. Although adverse effects may restrict medical therapy, nowadays the maximum amount of medication an eye can tolerate is often less than maximal available therapy. One eye may tolerate, say five different medications, but could have reached the maximal hypotensive effect with, for example, only three of them, or perhaps one. The era of maximum tolerated medical therapy (MTMT) is past.[17] Medical treatment of glaucoma should be viewed as 'optimal medical therapy' or 'rational medical therapy'.[11] This is not a minor or a merely semantic issue – it addresses important issues such as promptness of treatment advancement (and not dallying with additional medications that are unlikely to further lower IOP), avoiding unnecessary costs, and limiting exposure to chronic inflammation associated with long-term polypharmacy to provide the best chance for surgical success.

All medical therapy for glaucoma is aimed at reducing IOP to limit TTV. Target IOP remains a useful concept for assessing the efficacy of medical therapy. Clinical settings in which medical therapy is judged not sufficiently effective include: failure to achieve desired target IOP; IOP rise in a patient already under optimal medical therapy; damage progression in spite of target IOP achieved (provided that IOP variability has been assessed and reveals high-risk characteristics).[18]

Tolerability of other treatment

All medications have potential adverse effects. These can range from local ocular intolerabilities to life-threatening systemic effects. Adverse effects have a direct impact on quality of life and may influence later surgical results through ocular tissues changes.[19,20] This may influence the decision to proceed with surgery after an evaluation and discussion of the relative risks and benefits. Adverse effects may understandably lead to non-compliance (see below).

Compliance

Medical therapy for glaucoma can only reduce TTV if the patient is using the medications. Lack of compliance is a well recognized problem in all therapeutic areas including glaucoma. For IOP reduction, where most of the drugs have a relatively short onset to action, it is impossible to determine objectively if the patient is compliant or if drops were used only prior to the office visit. Discussions with patients or family can reveal lack of compliance. Lack of compliance implies insufficient IOP control and can be a substantial contribution to TTV.[21,22]

Fellow eye vision lost due to glaucoma

It is not clear that the loss of useful vision in one eye increases the risk of loss of vision in the fellow eye, but certainly it increases the impact of loss of vision in the remaining eye. The unacceptability of TTV in the one remaining eye may justify a lower target IOP.

Family history of blindness from glaucoma

Family history of blindness from glaucoma may be vague. There is a difference between going blind with glaucoma (possibly from another cause) and going blind from glaucoma. Confirmed glaucomatous vision loss in a first degree relative may suggest increased TTV, but data to support this are not available.

Special cases

Blind painful eye

The blind painful eye has no remaining useful vision to save and does not fit the model of needing additional therapy to reduce threat to vision to prevent decrease in quality of life. However, the impact on quality of life from a blind painful eye is substantial and surgery may be indicated for pain relief. In this situation, surgery can improve quality of life.

Pediatric or childhood glaucoma

These glaucomas are a special case of non-surgical therapy being ineffective. In most cases surgery is primary therapy for pediatric and childhood glaucoma unless other health issues make the administration of anesthesia too risky.

Summary

Articulating clearly the objective for surgical intevention in glaucoma is important to properly evaluate our current indications for surgery. While ‘achieving target IOP’ places emphasis on IOP, a major risk factor for glaucoma, it takes the focus away from the prevention of visual disability, the consequence of glaucoma. A better understanding of risk factor assessment in glaucoma will also improve our ability to identify individuals who are at particular risk of vision loss. Risk factor assessment may permit evaluation of surgical interventions not only in the context of IOP lowering, but more importantly, in the context of minimizing threat to vision.

The goal of glaucoma treatment is to prevent vision loss that negatively impacts quality of life. The only accepted therapeutic mechanism is reducing IOP. In theory, IOP should be reduced to a level at which the IOP-related threat to vision is minimized. Surgery is indicated when the IOP reduction cannot be achieved by non-surgical means.

Goals of glaucoma care

- The goal of care for the patient with glaucoma is preservation of sufficient vision that the patient does not develop a glaucoma-related reduction in quality of life.
- The means to achieve this goal are to reduce or eliminate the intraocular pressure (IOP)-related threat to vision.

Assumptions

- Every patient has a unique manifestation of disease and interaction between disease, treatment and quality of life.
- There are no clearly defined and accepted rules to dictate when surgery is the appropriate therapeutic choice, but there are principles that guide this decision.
- It is not possible to know *a priori* what level of IOP will be needed to substantially slow or halt glaucoma and preserve quality of life.
- IOP lowering should provide risk reduction for the development or progression of glaucoma and is not, by itself, the goal of therapy.

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ARGON LASER TRABECULOPLASTY

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Consensus points

- Laser trabeculoplasty (LTP) with diode, or frequency doubled Q-switched Nd:YAG are effective methods to lower IOP. (1, A)
- The principal indication for laser trabeculoplasty remains the failure of medical therapy to sustain acceptable IOP levels in adult eyes with POAG or intolerance of medical therapy. However, in appropriate cases LTP may be used as a primary therapy. (III, A)
- Although IOP lowering after LTP tends to wane with time, it may produce clinically significant IOP reduction in phakic eyes for up to several years (II, A)
  Comment: LTP often is effective in pseudophakic eyes for up to several years.
- Postoperative monitoring of IOP and follow up treatment of intraocular pressure spikes is appropriate. (III, A)
  Comment: IOP spikes tend to occur within the first few postoperative hours.
- Uveitis, ICE syndrome, congenital anomalies of the anterior chamber angle, and poor visualization of angle structures are contraindications for LTP, while age < 40 year, angle recession, traumatic glaucoma and high myopia are relative contraindications. (III, A)
- All commonly employed methods of LTP appear to be equivalent with respect to short-term side effects and IOP lowering. (III, A)
- There is longer follow-up data available for argon laser trabeculoplasty (ALT) than for selective laser trabeculoplasty (SLT). Randomized studies comparing these two modalities are not yet available. (III, A)
- Retreatment with ALT (applying additional laser spots to areas of the meshwork previously treated) is likely to be ineffective and perhaps detrimental.

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Although retreatment with SLT has a theoretical advantage, studies to prove this have not yet been reported. (III, A)

American Academy of Ophthalmologists

Ratings of strength of evidence (I-III)

- ***Level I*** provides strong evidence in support of the statement. The design of the study allowed the issue to be addressed, and the study was performed in the population of interest, executed in such a manner as to produce accurate and reliable data, and analyzed using appropriate statistical methods. The study produced either statistically significant results or showed no difference in results despite a design specified to have high statistical power and/or narrow confidence limits on the parameters of interest.
- ***Level II*** provides substantial evidence in support of the statement. Although the study has many of the attributes of one that provides Level I support, it lacks one or more of the components of Level I.
- ***Level III*** provides a consensus of expert opinion in the absence of evidence that meets Levels I and II.

Ratings of importance (A-C)

- ***Level A,*** defined as most important.
- ***Level B,*** defined as moderately important.
- ***Level C,*** defined as relevant but not critical.

Concept and indications

Laser trabeculoplasty (LTP) utilizing argon (ALT), krypton, diode, Nd:YAG (SLT), and krypton lasers has been reported to lower intraocular pressure (IOP) when applied to the trabecular meshwork. To date ALT has received the most attention in published literature. The general indication for LTP is open-angle glaucoma uncontrolled with tolerated topical and or systemic agents. ALT is more likely to succeed in phakic than aphakic eyes.[1,2] In eyes with both cataracts and uncontrolled glaucoma, it has been suggested that ALT should be performed before cataract surgery because of the possibility of obtaining a greater response in the phakic eye.[1,2] The indications for diode and SLT are similar to those for ALT but the relative advantages of each are still being elucidated. Krypton laser trabeculoplasty remains little studied.

ALT as initial therapy

The success of ALT in medically treated eyes motivated several studies of its use as primary treatment.[3-10] After two years of follow-up in the Glaucoma Laser Trial, 44% of patients receiving initial ALT for POAG had controlled IOP without topical medication, and 70% were controlled by ALT alone or ALT combined with timolol.[5] Odberg and Sandvik[11] found the probability of treatment success (no medication required) was 67% after 5 and 8 years for POAG and 54% and 36% respectively for exfoliative glaucoma. As of 1993, the majority of members of the American Glaucoma Society still initiated medical treatment for newly diagnosed glaucoma, only 2.3% indicating they performed ALT as initial therapy.[12]

180 vs 360 Degrees initially or sequentially

Wise and Witter initially applied 100 to 120 evenly spaced laser burns on and immediately posterior to the pigmented band of the trabecular meshwork over 360° of the circumference.[13] Many patients are controlled with treatment of just one half of the angle. In eyes that require further IOP lowering, the results of treating an additional 180° are comparable to those obtained in eyes treated over 360° in a single session. The success rate is similar in eyes treated in one session with 100 spots over 360° compared to those treated in two sessions of 50 spots over 180° each.[14] In the Glaucoma Laser Trial, 180° of angle was treated initially and the second 180° treated one month later. Grayson *et al.*[15] found no difference in IOP reduction whether the superior or inferior 180 degrees was treated initially. Application of 50 burns over 180° or 360° of the angle instead of 100 burns over 360° can reduce the magnitude and frequency of a post treatment IOP spike.[16-20] In a survey of members of the American Glaucoma Society, 19.4% always treated 180° initially and 37.1% usually treated 180°. While 50.4% never or rarely treated 360° in one sitting, 12.8% always treated 360° and an additional 22.4% usually treated 360° in one sitting.[12] Among those who used 360° treatment in one sitting more than half the time, 66% believed that it offered significantly greater and longer lasting pressure lowering than 180° treatment.

Retreatment

'Retreatment' is defined as adding laser marks to previously treated areas of the meshwork. Treating 180 degrees and, when the effect wears off, doing the other 180 degrees is not retreatment but rather sequential treatment of separate portions of meshwork. The literature is not always clear as to the extent of the initial ALT treatment and the term 'retreatment' has been used both for patients receiving 360 degrees initially and for patients initially treated with 180 degrees and then 'retreated' when the initial effect wore off.

A summary of the literature suggests that repeat ALT has a low rate of only transient success. Brown *et al.*[21] and Starita *et al.*[22] reported a decrease in IOP in 38% and 53%, respectively, of the eyes in which they repeated treatment. However, there was a risk of sustained IOP rise of 12% in each study, necessitating immediate surgical intervention in some eyes. In another study, repeat ALT was successful in only 25% of patients seven months after treatment.[23] In other small case series, repeat ALT was most effective for those patients who had shown a prolonged response to their initial treatment.[24-26]

ALT basic technique

Preoperative treatment

Both apraclonidine[27-30] and brimonidine[27,31] are effective at reducing both the magnitude and frequency of IOP spikes in patients already receiving medical therapy. In previously untreated eyes, timolol effectively prevents post-laser spikes.[32] Pilocarpine may open a narrow angle and enhance visibility of the trabecular meshwork. Topical anesthesia is routinely used, as is a bubble-free coupling agent.

Laser delivery lenses

The three-mirror Goldmann lens with antireflective coating including a dome-shaped mirror angled at 59° optimizes visualization of angle structures. The Ritch trabeculoplasty lens offers two basic mirrors, one inclined at an angle of 59°, which allows a face-on view of the inferior half of the angle, and one inclined at 64°, which allows a similar view of the superior half.[33, 34] The Latina lens has been designed to optimize delivery of SLT.

ALT laser parameters

The most commonly used treatment parameters for ALT are 50 μm spot size, 0.1 sec duration and approximately 800 mW power. The desired response is a blanching of the trabecular meshwork with or without minimal bubble formation. The variability of trabecular pigmentation requires that power settings be adjusted throughout the treatment session to achieve the desired response. Continuous refocusing of the aiming beam on the trabecular meshwork is essential. The beam spot should be circular, relatively central in the goniolens and the coagulation spot in the meshwork as small as possible in size. It is easiest to start with the goniolens at 12 o'clock to begin treatment in the inferior angle with clockwise rotation, treating the temporal portion of the right eye and the nasal portion of the left eye if only 180° is being photocoagulated. Approximately 50 applications should be placed with even separation in each 180° treated. The surgeon should use a consistent method of spot application and lens rotation to avoid inadvertent over treatment of an area.

Placement of burns with ALT

Anterior placement appears to minimize the early post-laser pressure rise and PAS formation.[16,35] Traverso *et al.*[36] found that PAS developed in 12% of eyes in which the anterior meshwork was treated and 43% of eyes in which the posterior meshwork (over Schlemm's canal) was treated. However, there was no difference in the pressure-lowering effect in eyes treated by either method. Schwartz *et al.*[35] also reported no difference in treatment effect between eyes treated in the anterior versus posterior meshwork.

Laser wavelength

Almost all reported studies have employed argon blue-green light with a major peak at 488 nm. There is no difference in postoperative IOP or complication rate with argon green.[37] As argon blue-green light is strongly absorbed by long and medium wavelength cones and may impair color discrimination, it is possible that argon green laser, compared with argon blue-green laser, may be less hazardous to the eyes of the surgeon.[38]

Postoperative ALT management

A post ALT IOP spike has been associated with visual loss in patients with severe glaucomatous damage.[17,19] The IOP should be monitored for 1 to 3 hours following treatment and follow-up determined accordingly. Patients are usually initially maintained on their regular regimen of anti-glaucoma medications after the procedure. Many surgeons prescribe prednisolone acetate 1% q.i.d. for four days, with or without a rapid taper.

Intraocular pressure is reassessed after 4 to 12 weeks. The second half of the trabecular meshwork may be treated as necessary if the initial treatment was limited to 180°. Once IOP is stabilized, the physician may attempt to sequentially discontinue some glaucoma medications, particularly systemic carbonic anhydrase inhibitors.

Results of ALT

POAG

The American Academy of Ophthalmology's Procedure Assessment (1996) estimated that ALT is initially effective in about 85% of treated eyes with a mean reduction in IOP of 6-9 mmHg (20-30%). The Advanced Glaucoma Intervention Study found ALT to be more effective than trabeculectomy for African-American patients who were on maximum medical therapy. While ALT is generally performed in patients on maximum medical therapy, the Glaucoma Laser

Trial found that patients initially treated with ALT had slightly lower IOPs than patients initially treated with timolol.

Most investigators report a five year success rate of about 50%, with an attrition rate of 6% to 10% per year.[39-43] Spaeth and Baez[44] found that ALT deferred filtration surgery for at least 5 years in 35% of progressive, uncontrolled, open-angle glaucoma patients. However, there is no uniform definition for success. In some studies, for example, a successful outcome is one in which IOP is less than a certain value; in others, success is functionally defined as a pressure reduction sufficient to prevent further optic nerve and visual field damage.

ALT is less successful in eyes with no pigmentation of the trabecular meshwork.[11,45,46] Patients over age 40 respond better to ALT than younger ones.[1,14,47,48] Schwartz *et al*.[49] found that, although short-term success was equivalent, only 32% of African-American patients were successful after 5 years versus 65% of white patients. Indian[50] and Japanese[51] patients respond similarly to ALT as white patients.

Aphakic and pseudophakic eyes respond less well to ALT than phakic ones[14] demonstrated glaucoma, although others demonstrated a pressure reduction not significantly different from that found in phakic eyes.[17] Good results also have been reported with ALT in aphakic and pseudophakic eyes with open-angle glaucoma after penetrating keratoplasty.[52]

Juvenile open-angle glaucoma

Characteristically, patients under 40 years of age have not responded well to ALT, perhaps due to the relative lack of angle pigmentation. Younger patients, particularly those with little or no pigment in the trabecular meshwork, may be worsened by ALT. The success rate is not only poor, but most patients soon require trabeculectomy, often within weeks.[12,17,53] Eyes of young individuals often have significant postoperative inflammation and a paradoxical and prolonged rise in IOP. Most treating ophthalmologists (67.5%) usually or always recommend filtration surgery before ALT in patients with juvenile glaucoma.[12]

Twenty-two percent of US glaucomatologists usually or always recommend filtration surgery before ALT in patients younger than 40 years.[12] In patients with pigmentary glaucoma, however, younger patients have a higher success rate.[54]

Normal-tension glaucoma

Schwartz *et al.*[55] described a 73% success rate with ALT at 12 months with a mean drop in IOP of 4.9 mmHg. The effect however was rapidly diminished. By 30 months the mean drop in IOP was 2 mmHg. In another report, a significant increase in outflow (means = 0.084 ± 0.031) and a reduction in IOP (means = -4.13 ± 1.25 mmHg) were observed.[56]

Exfoliative glaucoma

Patients with exfoliation respond well to ALT with a greater mean drop in IOP compared to POAG. As in POAG the effect is often lost with time. Some patients with exfoliation will experience a rebound of the IOP to levels higher than pretreatment IOPs. Success rates range from 68% at 12 months[57] to 55% at 5 years.[42] Ritch and Podos[58] noted a sudden, late elevation (at 1.5 to 2 years) of IOP in 4 of 15 patients followed for 6 months to 2 years after ALT and suggested that continued pigment liberation from the iris may overwhelm the trabecular meshwork following a period of time after successful initial treatment. They suggested that continued miotic treatment post laser might prevent this late failure. Pohjanpelto[59] also noted this phenomenon. Long term success appears lower in exfoliative glaucoma than in POAG.[10,11,60,61] Spaeth and Baez[44] reported a 50% (7 of 14 patients) failure rate one year following ALT in patients with progressive and uncontrolled exfoliative glaucoma, compared to a 19% rate in POAG patients.

Pigmentary glaucoma

ALT is not usually effective in young patients, but is effective in pigmentary glaucoma. Lunde[62] confirmed an initial decrease of IOP in 13 eyes of 10 patients, but five eyes had higher IOP at an average of 9 months post laser than pre-laser. This tended to occur in older patients and in persons who had glaucoma for longer periods of time. Life-table analysis indicated a cumulative success for all eyes of 80% at 1 year, 62% at 2 years, and 45% at 6 years. Younger patients had a significantly greater chance of long-term success at six years ($P < 0.05$), in marked contrast to success of ALT in other forms of open-angle glaucoma. The authors suggested that age-related response differences are due to the difference in pigment distribution - uveoscleral and corneoscleral meshwork in young versus the corneoscleral and external wall of Schlemm's canal in the older patients, the former being beneficial and the latter being detrimental to ALT. Harasymowycz *et al.*[63] reported 3 patients with pigmentary glaucoma who had intractable post-laser IOP spikes and suggested that using lower energy settings (0.4 mJ – 0.6 mJ), fewer applications, and/or treating a smaller amount of angle (90 degrees to 180 degrees)] may decrease this risk.

Angle recession

ALT is not effective in angle recession.[64,65]

Uveitis

ALT is basically ineffective for uveitis-associated glaucoma.[65-67] It is particularly inadvisable when there are extensive PAS or active inflammation. Most reports have not considered the type or severity of the uveitis. If there is minimal inflammation or structural damage to the trabecular meshwork, an eye may respond favorably to ALT. However, no improvement would be expected in eyes with an extensively blocked meshwork or when the ALT exacerbates the uveitis.[68]

Patients with prior filtering surgery

Successful lowering of IOP may be realized in patients having had failed trabeculectomy without previous ALT.[65,69]

Pathophysiology of ALT

Opening of Schlemm's canal

Decreased IOP following ALT is associated with increased outflow facility.[70-72] Wise and Witter[13] initially proposed that laser treatment caused shrinkage of the inner 'trabecular ring' with resultant separation of the trabecular sheets, reopening the spaces between the trabecular beams, and stretching open the lumen of Schlemm's canal, thus partially restoring aqueous outflow. Support for this mechanism can be inferred by the observation that pilocarpine which contracts the longitudinal muscle of the ciliary body pulling posteriorly and mechanically opening the trabecular meshwork[73-75] is not as effective following ALT.[76]

Morphologic changes in the trabecular meshwork immediately following ALT have been studied in non-glaucomatous cynomolgus monkeys. There is coagulative necrosis of the treated tissue and disruption of trabecular beams with fragmented cells and fibrocellular tissue noted in the juxtacanalicular trabecular meshwork.[6,77] Trabecular cells were absent from trabecular beams, and some cells were observed in different stages of leaving the beams as well as in the process of phagocytizing debris.

Rodrigues *et al.*[78] investigated the acute and long-term histopathologic effects of ALT in specimens obtained at trabeculectomy following laser therapy in human eyes. Early changes showed disruption of trabecular beams and accumulation of cellular and fibrinous debris. One week after treatment, shrinkage of treated uveal and corneoscleral trabecular meshwork was noted in a localized area (50 to 60 μm). Trabecular meshwork which was located away from the area of laser treatment appeared normal. Tissues that were excised at longer intervals after laser treatment (6 months to 1 year) demonstrated confluent areas of fibrosis and abnormally migrating corneal endothelial cells lining the uveal meshwork and occluding the trabecular spaces, possibly obstructing aqueous outflow.

Stimulation of cell proliferation

Thermal injury to the trabecular meshwork causes biological effects as well as mechanical ones. ALT activates trabecular cells, inducing abundant rough endoplasmic reticulum and a well-developed Golgi system.[79] Increased cell division has been observed with both argon and Nd:YAG lasers in monkey eyes.[80] In human corneoscleral explant organ culture, increased trabecular DNA replication is seen during the first 48 hours after ALT[81] and there is approximately a six-fold increase in division in a population of anterior trabecular cells.

The freshly replicated cells migrate to the burn sites and repopulate them.[82] Van Buskirk[83] proposed that cellular stimulation activates a biologic chain of events possibly in the trabecular extracellular matrix resulting in improved facility of outflow. There are increases in trabecular stromelysin and gelatinase B after ALT.[84] If diminished juxtacanalicular extracellular matrix turnover is responsible for the glaucomatous reduction in aqueous outflow, a stromelysin increase localized primarily to the juxtacanalicular region of the trabecular meshwork following ALT should degrade trabecular proteoglycans, thought to be a major source of outflow resistance in glaucoma. Another study supports this hypothesis.[85] ALT induces the expression and excretion of both IL-1beta and TNF-alpha within the first eight hours after treatment. Both cytokines mediate an increase in trabecular stromelysin expression which may effect a remodeling of the juxtacanalicular extracellular matrix and increasing outflow facility.[86]

The transient increase in trabecular cell division within the first two days after ALT in human corneoscleral explant organ cultures has been studied by cell culture methods and autoradiography.[81,84,87] Extracellular matrix turnover in the trabecular meshwork may play a role in regulating aqueous humor outflow and may be altered by laser trabeculoplasty.[85,86]

Complications of ALT

Elevated intraocular pressure

As many as 50% of eyes that undergo ALT without perioperative medication develop elevated IOP post-laser. IOP increase is usually transient and less than 10 mmHg in magnitude. However, in a small percentage of eyes the increase can be marked (greater than 20 mmHg) and may be associated with loss of visual field.[18,19] The incidence and magnitude of a post-laser IOP spike is significantly greater in eyes receiving 100 laser burns over 360° compared with 50 laser burns over 180°. At least one report indicated no correlation between trabecular pigmentation and IOP spikes.[88] In the Glaucoma Laser Trial, moderate or heavy pigmentation of the trabecular meshwork was the strongest risk factor for IOP rise following ALT in 271 eyes.[3] However, there was no association between the pressure spikes and either power level or burn effect. Patients with insignificant IOP spikes at one hour post laser may develop spikes later.[3,89]

Rarely, sustained IOP rises, occasionally requiring trabeculectomy, may be associated with uveitis[68,90] and PAS formation[53] and are more common in eyes of patients under age 40. Whether transient elevated IOP has an effect on long-term prognosis and treatment has produced conflicting reports.[1,14]

Iritis

Post ALT inflammation is usually mild and clears rapidly, but occasionally may persist for weeks or months. Inflammation peaks two days following ALT and is greater in pigmentary and exfoliative glaucoma than in POAG.[91] Topical diclofenac (0.1%) blocked the flare increase after ALT but the clinical significance of this is not known.[92]

Hemorrhage

Hemorrhage during or after ALT is rare and may result from inadvertent photocoagulation of blood vessels in the iris root or a circumferential ciliary vessel. Bleeding typically ceases with tamponade by the goniolens. Should it persist, it can be photocoagulated after adjusting the power and treatment interval (200 mW power, 200 μm spot size, and 0.2 sec duration).

Pain

Pain and a burning sensation are uncommon during ALT and may be due to inadvertent photocoagulation of the ciliary band. Postoperative pain and photophobia may occur if significant iritis results but can usually be rapidly ameliorated with anti-inflammatory treatment.

Peripheral anterior synechiae

PAS can occur in up to 43% of eyes that have undergone ALT.[36] Brown irides have greater than two-fold PAS formation rate (57%) compared to lighter ones (24%) following ALT.[3] PAS appear to occur more frequently when laser burns are placed on posterior trabecular meshwork. PAS are characteristically small and rarely reach beyond the scleral spur. Six months following ALT, Rouhiainen [et al.46] observed a significantly smaller IOP lowering effect in patients with post-ALT PAS (mean: 3.6 mmHg) than those without synechiae (mean: 6.0 mmHg). In contrast, the Glaucoma Laser Trial found IOP control in the ALT first group to be better in POAG patients with post-trabeculoplasty PAS than in those without synechiae.[5] Differences in these studies may be due to difference in length of follow-up or in patient populations. In the Rouhiainen study, patients were equally distributed between chronic open-angle and exfoliative glaucomas, whereas only POAG patients were enrolled in the Glaucoma Laser Trial. The long-term consequences of PAS are not known.

Corneal complications

Corneal abrasions may occur during ALT. Corneal epithelial burns during ALT usually disappear within hours of treatment. Endothelial burns have also been reported and may contribute to focal corneal edema. No change in the postoperative central corneal endothelial cell density has been found 1 to 4 months postoperatively.[93]

Contraindications to Argon ALT

- ICE syndrome
- Congenital glaucoma
- Goniodysgenesis
- Axenfeld-Rieger syndrome
- Elevated episcleral venous pressure*
- Complete angle-closure
- High myopia*
- Angle-closure above the level of the scleral spur
- Uveitic glaucoma*
- Juvenile glaucoma*
- Less than 35 years old*
- Inadequate visualization
- Hazy media
- Corneal edema

(*Relative contraindications.)

Comments on Selective Laser Trabeculoplasty

Pathophysiology and clinical comparisons to ALT

Selective laser trabeculoplasty (selective photothermolysis, SLT) selectively targets pigmented TM cells while sparing adjacent cells and tissues from collateral thermal damage.[94] SLT relies on selective absorption of a short laser pulse to generate and spatially confine heat to pigmented targets.[95] It is performed with a 532 nm frequency doubled, Q-switched Nd:YAG laser beam using low energy (0.4 mJ to 1.2 mJ), short pulse duration (approximately 3 ns), and a large spot size (400 μm), achieving selective targeting of pigmented cells and less dissipation of energy.

Unlike ALT, SLT does not produce scarring of the TM. Lysis of intracellular melanosomes kills pigmented cells while leaving cellular membranes and neighboring non-pigmented cells intact.[96,97] Cvenkel *et al.*[98] noted some disruption of the trabecular beams with SLT, but to a much smaller extent than

ALT. Kramer and Noecker[96] compared the histopathologic changes in the human trabecular meshwork after ALT and SLT in human autopsy eyes. Evaluation of the meshwork after ALT revealed crater formation in the uveal meshwork at the junction of the pigmented and the non-pigmented TM. Coagulative damage was evident at the base and along the edge of the craters, with disruption of the collagen beams, fibrinous exudates, lysis of endothelial cells, and nuclear and cytoplasmic debris. Evaluation of the TM after SLT revealed no evidence of coagulative damage or disruption of the corneoscleral or uveal trabecular beam structure. Minimal evidence of mechanical damage was present after SLT.[99]

Disruption or killing of pigmented TM cells alone appears to induce a response that results in a reduction of IOP after SLT. The biological effect rather than a mechanical process could account for the IOP-lowering effect of SLT reported in the eye contralateral to the one undergoing treatment.[100-102]

SLT treatment technique

A Goldmann 3 mirror goniolens, a Latina SLT lens, or a Ritch lens may all be utilized with SLT. The low power helium-neon aiming beam is focused on the pigmented TM and its spot size (400 um) encompasses the entire TM from Schwalbe's line to the ciliary body band. Standard therapy is to deliver fifty adjacent but non-overlapping laser spots over 180 degrees of TM. The power is adjustable from 0.2-1.7 mJ and the power is initially set at 0.8 mJ. More pigmented meshwork requires lower power. Unlike in ALT, blanching or cavitation bubbles within the TM are not desirable as end points with SLT. Bubble formation means that the energy is above the selective targeting range and the energy must be decreased by increments of 0.1 mJ until there are no visible bubbles.

Repeat treatments

Because of its non-destructive nature, multiple treatments with SLT are theoretically possible.

ALT vs SLT

SLT seems to be as effective as ALT in patients with open angle glaucoma on maximally tolerated treatment in short-term and some long-term success evaluations.[100,103-110,111-113] In a prospective randomized trial simultaneously treating one eye of a patient with SLT and another with ALT, both groups had an equivalent decrease in IOP at 4 weeks (ALT $n = 17$, SLT $n = 22$).[114] In another prospective, randomized trial, both treatment modalities at 6 months were equivalent ($p = 0.97$).[115]

SLT has been demonstrated to be as effective in both pseudophakic and phakic patients, unlike ALT which has been shown to be less effective in pseudophakic eyes. In eyes with baseline IOP $\geq$ 15 mmHg, 60% of phakic and 62% of pseudophakic eyes experienced a successful SLT outcome using the success criteria described above.[113]

Overall efficacy of SLT is less dependent than ALT on TM pigmentation. Because of the short pulse duration of SLT compared to ALT, only a few melanin granules within the TM cell are required to be an effective target for SLT, whereas the TM requires many more pigment particles to be effective targets with ALT. Substantial IOP reductions can be achieved with SLT in nonpigmented TM, where this is unlikely with ALT. However, for both SLT and ALT, overall greater IOP reductions are probably greater in more pigmented meshwork.

Suggested studies for LTP

- Steroids vs NSAIDS vs nothing after SLT.
- Pilocarpine peri-SLT.
- Ritch lens vs Latina lens in SLT.
- SLT after failed trabeculectomy.
- SLT after 360 degrees of failed ALT.
- Effect of pigmentation on success rate.
- Prospective study, initial ALT vs initial SLT in exfoliative and pigmentary glaucomas.
- SLT in normal-tension glaucoma.
- SLT vs medications as initial treatment of open-angle glaucoma. Who starts with ALT, who starts with SLT?
- SLT after failed trabeculectomy before going on to TCNR, revision.
- Resurvey AGS or even globally regarding practice patterns would be of interest and might reveal a substantial shift in practice habits regarding initial therapy, especially with increasing availability of SLT.

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WOUND HEALING

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Consensus points

- Excessive healing at the conjunctiva-Tenon's fascia-episcleral interface is the major cause of inadequate long term IOP lowering after trabeculectomy.
- Risk factors for scarring should be evaluated and documented in all patients prior to undergoing glaucoma filtration surgery (see appendix).
  Comment: Conjunctival inflammation should be minimized prior to surgery.
- The use of adjunctive antifibrosis agents should be considered in most patients undergoing trabeculectomy and should be titrated against the estimated risk of postoperative scar formation and estimated risk for postoperative complications.
  Comment: Although some patients may have a successful result without adjunctive antifibrosis use, there is no systematic method for identifying these patients.
  Comment: Different antifibrotic agents may be associated with different risks and benefits. MMC may be a more effective adjunct than 5-FU but is associated greater complications.
  Comment: A large antifibrotic treatment area is desirable to achieve diffuse non-cystic blebs with a lower risk of discomfort and leakage.
  Comment: Complications related to the use of antifibrosis agents are usually related to excessive inhibition of wound healing, which may result in or prolong early (wound leak, hypotony, shallow anterior chamber, choroidal detachment, etc.) and late (hyptonony maculopathy, wound leak, and bleb-related ocular infection, etc.) complications.
- Modern trabeculectomy techniques that include the use of lasered / releasable / adjustable sutures should be employed to minimize the complications of excessive filtration.

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- Early intervention (subconjunctival 5-FU and increased topical steroids) is recommended in eyes with evidence of active scar formation (conjunctival hyperemia and anterior chamber inflammation)
  Comment: Use of subconjunctival 5-FU in eyes with a wound leak, corneal defect or ocular hypotony should be cautioned.
  Comment: Postoperative IOP elevation typically occurs after significant scarring has already taken place. As the scarring process might be slowed with additional measures, but not likely reversed, it is advised to intervene prior to an actual IOP rise, based on signs indicating the likelihood of an active scarring process.
- Antifibrosis use is associated with enhanced bleb formation and lower intraocular pressure. However, they also have an increased long-term risk.
  Comment: It is essential to inform patients about the signs and symptoms of ocular infection and advise them that they should seek ophthalmological advice urgently, should they occur. Long term follow up of these eyes is advisable.

Physiology and Pathophysiology

The wound healing response

The wound healing process is the most important determinant of the final intraocular pressure after trabeculectomy and drainage implant surgery. The fibroblast is the effector cell responsible for subconjunctival scar formation. Histological evidence from animal models of filtration surgery demonstrated that fibroblasts proliferate and migrate to the wound site to produce and contract extracellular matrix.[1] Fibroblast activity is modulated by aqueous humor constituents[2,3] and interaction with other inflammatory cells, in particular lymphocytes and tissue macrophages.[4] Concomitant angiogenesis leads to formation of fibrovascular granulation tissue.[5] Following a prolonged remodeling phase, fibroblast and inflammatory cell numbers decrease towards previous levels through apoptotic cell death.[6]

Sites of outflow resistance

Three potential sites of outflow resistance include:
1. Internal sclerostomy if occluded with iris or vitreous or imperforate;
2. External sclerostomy;
3. Episcleral Tenon's capsule.

The major site of outflow resistance after trabeculectomy in the human is at the episcleral level or at the level of the subconjunctival Tenon's capsule.[7] Scar formation at the level of the sclerostomy may have a less important role in humans.

Resistance to outflow in the immediate postoperative period is determined by scleral sutures. In a mature bleb, Tenon's capsule usually provides the major resistance to outflow. Bleb wall thickness and surface area are important in determining fluid resistance (hydraulic conductivity).

Pathophysiology of scar formation

Scarring increases the resistance to aqueous ouflow and elevates intraocular pressure. The pathophysiology responsible for bleb fibrosis is not completely understood, but may result from increased fibroblast number and/or increased or prolonged fibroblast activity. Histopathological studies are largely restricted to a small numbers of blebs that have failed due to subconjunctival scarring or required bleb revision for hypotony.[8] Scarred blebs had dense collagenous connective tissue in their walls whereas functioning blebs had loosely arranged connective tissue with microcystic spaces in the subepithelial connective tissue.[7]

Inflammatory cells and growth factors may promote fibroblast activity. Transforming growth factor-beta, and Connective Tissue Growth Factor in particular, increased fibroblast activity in cell culture and animal filtration models.[9-11] Blood-aqueous barrier breakdown alters the constituents of aqueous humor and chronic conjunctival inflammation at the time of surgery may also lead to a more aggressive healing response.

Clinical evaluation of post operative healing

Regular clinical evaluation of the drainage bleb and the anterior chamber for inflammation in the post operative period is critical to determine the degree of active scar formation. Active fibrosis may be associated with increased bleb vascularity, corkscrew conjunctival vessels, anterior chamber white cells and flare.[12] Poor bleb function is associated with absence of conjunctival epithelial microcysts, thick bleb walls and immobile conjunctiva. Thin walled blebs with large avascular zones are more prone to bleb leak[13] and therefore more susceptible to endophthalmitis.[14]

Bleb classification and clinical evaluation

Bleb classification systems may help establish decision criteria for postoperative interventions.[15] A number of standardized bleb classification systems have been used in research studies,[15-18] but have not been widely adopted into routine clinical practice. A recent interobserver agreement study revealed good levels of agreement for bleb vascularity and wall thickness with moderate agreement for bleb leak (although the number of leaks was small), and poor agreement for bleb height and the presence or absence of microcysts.[18]

Risk factors for excess scar formation

A careful preoperative assessment of risk factors associated with postoperative scar formation should be performed in all patients prior to trabeculectomy. A small number of adequately powered studies with sufficient follow-up periods have identified risk factors associated with poor outcome. In the Advanced Glaucoma Intervention Study (AGIS), surgical failure was associated with higher pre-op IOP, diabetes, any postoperative complication as well as postoperative inflammation. Black race was of borderline significance.[19] In the Fluorouracil Filtering Surgery Study, high intraocular pressure, a short time interval after the last procedure involving a conjunctival incision, the number of prior procedures with conjunctival incisions, and Hispanic ethnicity were associated with failure.[20] Additional risk factors have been identified in smaller studies and these can be categorized as patient or surgical risk factors (see appendix).

Patient factors

Known risk factors for filtration failure due to scar formation include: iris neovascularization, aphakia, active uveitis, disrupted blood-aqueous barrier, conjunctival inflammation, previous failed trabeculectomy, previous cataract extraction, conjunctival incisional surgery, iridocorneal endothelial syndrome and developmental glaucoma with anterior segment dysgenesis.

The following patient factors *may* be associated with increased risk of scar formation: Black race, youth (< 40 years), male gender, previous trabeculoplasty, previous long-term topical glaucoma medication (particularly those that are associated with conjunctival inflammation), and poor compliance with topical postoperative anti-inflammatory agents.

Surgical factors

Reduced success is associated with: combined surgery, incomplete sclerostomy, iris incarceration and vitreous prolapse into the sclerostomy and possibly early postoperative bleb leaks.

Current approaches to inhibiting wound healing

Anti-scarring agents in current use were developed on the basis that they reduced fibroblast number at the wound site. In the 1970s, Molteno and co-workers recommended a systemic (prednisolone, flufenamic acid and colchicines) and topical (steroid, atropine and adrenaline) regime to decrease scarring responses after drainage tube implant or filtration surgery.[21] Cell culture studies have since demonstrated that single short applications of mitomycin-C and 5-fluorouracil inhibit Tenon's fibroblast proliferation,[22] migration, extracellular matrix production[23] and contraction.[24] Mitomycin-C also induces fibroblast death by apoptosis, and this is likely to contribute to the long-term inhibition of scarring.[25,26] and risk of late bleb infection.

Mitomycin-C

Mitomycin-C (MMC) was first isolated from Streptomyces caespitosus. Chen first described the single peri-operative application of mitomycin-C to inhibit scarring following trabeculectomy in 1981.

Mode of action

Once taken up by the fibroblast, intracellular mitomycin-C is reduced by an NADH-dependent reductase to an active form. Mitomycin-C is a cytotoxic agent that disrupts DNA by forming DNA-DNA cross-links and free radicals. MMC inhibits both transcription and translation.

5-Fluorouracil

5-Fluorouracil (5-FU), a pyrimidine analogue, was first used to inhibit subconjunctival scarring by Parrish and co-workers, in the form of multiple post operative subconjunctival injections.[27,28] Subsequent laboratory studies revealed that single, short applications of 5-FU induced a prolonged dose-dependent antiproliferative effect on cultured Tenon's fibroblasts[22] and prolonged bleb survival in animal models of filtration surgery.[29,30] This opened the door for more convenient single intraoperative applications of 5-FU.

Mode of action

5-Fluorouracil inhibits DNA synthesis by competitively inhibiting thymidilate synthetase and therefore mainly inhibits proliferating cells in S phase of the cell cycle. However, 5-fluorouracil is also incorporated into RNA and inhibits the activity of a number of intracellular enzymes.

Complications

The benefits derived from the potent and persistent anti-scarring activity of mitomycin-C has been tempered by a reported increase in the incidence of postoperative hypotony maculopathy, late bleb leaks and endophthalmitis. This increase in complication rates may be associated with the presence of large avascular hypocellular blebs.[13]

Corneal toxicity leading to punctate epitheliopathy, filamentary keratopathy and epithelial defects can occur in up to two-third of patients subject to a large number of multiple subconjunctival injections of 5-FU (21 injections in two weeks), but this number of injections is rarely used. Titrating the number of postoperative injections to the clinical response rather than using a fixed number of injections reduced the incidence of epitheliopathy compared to previous published studies and did not reduce filtration success.[31]

Beta-radiation

Beta-radiation delivered via a Strontium-90 (^{90}SR) source is less widely used compared to 5-FU and MMC. Single short applications of beta radiation induce long-term dose-dependant proliferation arrest in cultured human Tenon's capsule fibroblasts.[32] Unlike 5-FU and MMC, beta-radiation had no effect on other fibroblast activities including collagen contraction and fibroblast migration.[33]

There is limited clinical data regarding its efficacy and safety. A retrospective 7-year follow up in a non-comparative study of Chinese patients revealed a success rate (IOP $<$ 21 mmHg no drops) of 61%.[34] A small prospective randomized trial using 750 rads demonstrated no significant advantage in a low-risk population.[35] A retrospective observational study of 66 eyes with congenital glaucoma demonstrated increased IOP lowering up to three years in the beta radiation treated eyes.[36] However, results from a large prospective masked study from South Africa and Moorfields Eye Hospital are awaited.[37]

Future approaches

Initial Phase I and Phase II clinical trials of human monoclonal antibody to TGF-β_2 showed initial promise,[38] however, two larger phase III randomized studies recently failed to confirm the superiority in efficacy over placebo. It is possible that the dose was not adequate[39] and a more prolonged dosing regimen was required.[40]

Future approaches to inhibiting the wound healing response include gene therapy,[41,42] antisense oligonucleotides,[43] growth factor inhibition,[38,44] inhibition of matrix metalloproteinases,[45] photodynamic therapy[46] and novel nanomolecules with anti-inflammatory effects.[47]

Clinical indications

Antifibrotic agents should be considered in all patients where postoperative subconjunctival scar formation is considered likely to lead to inadequate postoperative IOP control or in patients with advanced disease or where a low (< 12 mmHg) post- operative IOP is required. Careful assessment of the risk factors that predispose to aggressive postoperative scarring is critical to selection of antifibrotics agent and dosing regime. In addition, selection criteria should consider patient characteristics including age and ethnicity.

Antifibrotics can be indicated for primary and secondary trabeculectomy, needle revision, but there is no convincing evidence that they are helpful in glaucoma drainage implant surgery. Two non-randomized and one small prospective randomized control study did not elicit a significant improvement in outcome with adjunctive mitomycin-C in glaucoma implant surgery.[48-50]

What antifibrotic?

In spite of clear differences in the potency of MMC and 5-FU in cell culture studies, there is less convincing data regarding comparison of surgical outcomes between these two agents, in particular in first-time trabeculectomy.[51-53] This may in part be due to limitations in study design. A detailed review of the clinical studies using MMC and 5-FU is provided elsewhere.[54] It is clear that the clinical response to a given treatment may vary between patient populations and is likely influenced by differences in surgical technique including post operative manipulations including suture release and needling with injections of 5-FU.

Mitomycin-C has more potent and long-lasting antiscarring activity and is recommended for patients at high risk of scarring and in patients with long-term stimuli for active scarring. The risk of hypotony is increased in young myopic patients in whom MMC should be used judiciously.

5-Fluorouracil is less potent than MMC, does not induce widespread cell death and exerts temporary antiscarring activity. Single applications of 5-FU in high risk patients may not provide sufficient anti-scarring activity.[55]

Handling antifibrotics

Mitomycin-C and 5-fluorouracil are cytotoxic agents and should be handled appropriately and in line with Occupational Safety and local institutional guidelines. Tissues not intended for treatment should be protected and irrigated immediately in the event of contamination. Following treatment of the subconjunctival tissues and sponge removal, the treatment area should be irrigated thoroughly with balanced saline solution.

5-Fluorouracil is available in 25mg/ml and 50mg/ml concentrations, but the 50mg/ml concentration is now most commonly used. Drug application times commonly vary from 1 to 5 minutes.

Mitomycin-C is reconstituted from powder form and commonly used at concentrations of 0.1 mg/ml to 0.5 mg/ml (usually 0.2 mg/ml to 0.4 mg/ml). Treatment times have varied from 1 to 5 minutes.

Drug application

Mitomycin-C is routinely applied intraoperatively during trabeculectomy using drug-soaked sponges. Post operative subconjunctival injections and transconjunctival application have also been reported,[56] but are not common.

Initial postoperative administration of 5-fluorouracil was performed with repeat subconjunctival injections. This has been largely replaced by intraoperative delivery with 5-FU soaked sponges. Additional postoperative subconjunctival injections are still used routinely in blebs with signs of active scarring.

The precise dose administered to tissues using sponge applications is not known. Wilkins and colleagues applied radiolabelled 5-FU to cadaver pig eyes and demonstrated that subconjunctival uptake rises sharply after application but plateaus at 3 minutes. Uptake was also dependent on 5-FU concentration and sponge type.[57]

Modification of surgical technique including the use of fornix-based flaps and larger dissection/antifibrotic application areas appears to generate diffuse blebs with reduced or no avascular zones. Large MMC treatment areas in the rabbit filtration model produced more diffuse blebs compared to small treatment areas that resulted in focal cystic avascular blebs.[58] A retrospective nonrandomized study of trabeculectomies in children and young adults recently demonstrated a reduced incidence of cystic blebs and related complications with fornix (and large MMC treatment area) compared to limbus-based flaps (and small MMC treatment area).[59]

Perioperative management

Preoperative

Preoperative intraocular inflammation and conjunctival hyperemia where possible should be minimized prior to surgery. Discontinuation of topical medications and the application of topical steroids may reduce conjunctival inflammation.[60] The effect of these actions on long-term surgical outcome still needs to be established.

Post operative

Topical steroids inhibit inflammation and wound healing after trabeculectomy and are frequently required for prolonged periods after trabeculectomy. Frequent (up to hourly) application of topical steroid, commonly dexamethasone 0.1% or prednisalone acetate 1%, is recommended for the immediate post operative period. The frequency of application is then reduced according to clinical signs of active inflammation. The role of systemic steroids, topical nonsteroidal anti-inflammatory agents and mydriatic agents is less clear.

Recommended postoperative care

Careful evaluation and documentation of the bleb appearance should be performed in all eyes with previous trabeculectomy. Intraocular pressure may be a poor indicator of the level of scarring activity. Early intervention is recommended in blebs with signs of active scarring. These include: increased bleb vascularity, bleb wall thickening, bleb contraction and anterior chamber flare and cells.

Bleb failure intervention options

Laser suture lysis, use of releasable or adjustable sutures can increase flow under the scleral flap and lower IOP in the early postoperative period.

Subconjunctival 5-FU and increased frequency of topical steroids are further measures commonly used to inhibit active scarring in the postoperative period.

Bleb needling

Needle revision of failed blebs provides an alternative to repeat trabeculectomy. This may be performed at the slit lamp or in the operating room. This procedure is usually performed under topical anesthesia with a bent needle (25G to 30G).

Adjunctive 5-FU or MMC is administered. Data regarding the outcome of needle revisions is largely limited to retrospective or observational non-comparative studies.

Appendix

Risk factors for failure due to scarring after glaucoma filtration surgery

Risk Factors 1) OCULAR	Risk (+ to +++)	Comment
Neovascular glaucoma (active)	+ + +	Good evidence[61]
Previous failed filtration surgery	+ + (+)	Good evidence[20]
Previous conjunctival surgery	+ +	Moderate[62]
Chronic conjunctival inflammation	+ + (+)	Good evidence[63]
Previous cataract extraction (conjunctival incision)	+ + (+)	Good evidence[20]
Aphakia (intracapsular extraction)	+ + +	Good evidence[64]
Previous intraocular surgery	+ +	Depends on type of surgery
Uveitis (active, persistent)	+ +	Depends on type of uveitis[65,66]
A red, hyperemic eye	+ +	Anecdotal[63]
Previous topical medications		Good evidence,
(beta-blockers + pilocarpine)	+ (+)	particularly, if they cause
(beta-blockers + pilocarpine + epinephrine)	+ + +	a red eye[63]
Other new topical medications	+ (+)	
High preoperative intraocular pressure(higher with each 10 mmHg rise)	+ (+)	Moderate evidence[20]
Time since last surgery (especially if within 30 days of last surgery)	+ + (+)	Moderate evidence[20]
Inferiorly located trabeculectomy	+	Some evidence[67]
2) PATIENT		
African origin	+ +	Good evidence
May vary, *e.g.,*		A prospective trial of
West African origin	++ (+)	intraoperative
East African origin	+	fluorouracil during trabeculectomy in a black population.[68,69]
Indian subcontinent origin	+	Moderate evidence[70]
Hispanic origin	(+)	Moderate evidence[20]
Japanese origin	(+)	Moderate evidence[71]
Elderly (+) vs Young + (+)		
(particularly children) + +		Poor evidence[72]

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Section participants: Eytan Blumenthal, Gregory Skuta, David Greenfield, Doug Rhee

Discussing wound healing: Peng Khaw (co-Chair), Jonathan Crowston and Neeru Gupta

Mark Sherwood (co-Chair)

Participants vote

TRABECULECTOMY

Jeffrey M. Liebmann and Joshua Kim

Contributors: D. Broadway, S. Gandolfi, R. Gross, R. Parrish II, S. Seah, T. Shaarawy, R. Susanna, R. Thomas and T. Wang


Jeffrey M. Liebmann
(Presenter)

Consensus points

- Incisional surgery for glaucoma is indicated when medical therapy and/or laser fail to sufficiently lower IOP or the patient does not have access to, or cannot comply with, other forms of therapy.
  Comment: Primary surgery may also be indicated on the basis of socioeconomic or logistical constraints.
- Trabeculectomy is the incisional procedure of choice in previously unoperated eyes.
- Postoperative hypotony should be avoided and sequential IOP adjustment should be performed with suture modification.
- Trabeculectomy provides better and more sustained IOP lowering than non-penetrating procedures.
- Although adjunctive antifibrosis agents enhance the success of trabeculectomy, their risk/benefit ratio should be assessed for each individual patient prior to use. This applies to initial and repeat surgeries.
- Preoperative conjunctival inflammation and postoperative conjunctival and intraocular inflammation should be suppressed vigorously with glucocorticoids.
- Trabeculectomy success is highly dependent on postoperative care and management.
  Comment: Early recognition of postoperative complications and timely, appropriate intervention enhances the success rate of surgery and minimizes patient morbidity.
- Patients that have had trabeculectomy should be warned of the signs and symptoms of late bleb-related ocular infection and should be counseled to seek immediate attention should these occur.

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Indications

Trabeculectomy is indicated for eyes with open angle glaucoma that have an intraocular pressure (IOP) that is inadequate despite maximum tolerated medical therapy and appropriate use of laser trabeculoplasty. Indications include progressive (or the high likelihood of progressive) functional or structural glaucomatous injury. Patients without access to medical treatment or laser surgery may require trabeculectomy as an option to these therapies. Primary surgery may also be indicated on the basis of socioeconomic or logistical constraints. Individual patient factors, such as an inability to comply with the prescribed medical therapy, inability to instill eye medications, and low target IOP may also influence the decision to proceed to surgery.

Trabeculectomy has been, and remains, the most widely performed incisional surgical procedure for glaucoma worldwide. This is a result of its high success rate, efficacy at IOP lowering, and technical advances over the past thirty years designed to enhance surgical success and minimize complications.

Many factors may affect the success rate of trabeculectomy. These include type of glaucoma, race,[1,2] age,[3,4] prior history of failed trabeculectomy,[1] aphakia or pseudophakia, intraocular inflammation,[3] the use of antifibrotic agents,[1,5,6] and co-morbidities requiring combination surgeries such as cataract,[1,7] retinal disease, and corneal disease. In general, individuals with risk factors that may lead to excessive scarring, such as African ancestry, prior incisional surgery or glaucomas associated with intraocular inflammation, are at increased risk for filtration failure.

Preoperative evaluation and risk assessment

The risks of trabeculectomy can be categorized as intraoperative, early postoperative, and late postoperative. Intraoperative complications include hyphema, suprachoroidal hemorrhage and effusion, iridodialysis, cyclodialysis, conjunctival injury, scleral flap or conjunctival dehiscence, vitreous hemorrhage, and vitreous loss. Early postoperative complications include wound leak, shallow/flat chamber, endophthalmitis, hypotony maculopathy, corneal abrasions, suprachoroidal effusion and hemorrhage, malignant glaucoma, and over- and underfiltration. Late complications include, cataract, bleb related ocular infection, bleb leak, bleb dysesthesia, and filtration failure (including Tenon's cyst, and scarring at the conjunctiva-Tenon's fascia-episcleral interface).

One can use topical, local infiltration, peribulbar, retrobulbar (used with caution in those with advanced field loss), or general anesthesia. These methods can be augmented with a lid block. The choice depends on the patient and the surgeon's comfort level. Topical anesthesia with local infiltrative supplementation offers an excellent approach for cooperative patients. Surgical exposure can be enhanced by instructing the patient to look in a position of gaze and does not require the use of corneal or superior rectus traction sutures. While topical anesthesia is useful for the experienced surgeon, the surgeon who performs glaucoma surgery on a less regular basis may find the use of regional anesthesia more comfortable. Poorly cooperative or uncooperative patients are better candidates for regional anesthesia than topical anesthesia.

Preoperative assessment includes considering the discontinuation of anticoagulants (aspirin, warfarin, etc.) prior to surgery whenever possible to minimize the risk of intraocular hemorrhage. Medications known to increase conjunctival hyperemia also may be discontinued provided that IOP remains satisfactorily controlled.[8] One may choose to start preoperative antibiotics and/or steroids (for inflamed eyes) prior to surgery. This might include a topical antibiotic administered four times daily to both eyes commencing three days prior to surgery and topical prednisolone acetate 1% to the operative eye beginning one week preoperatively. The latter causes a decrease in conjunctival hyperemia and may help reverse glaucoma drug-induced changes in conjunctival morphology.

Procedure

Trabeculectomy reduces IOP by bypassing the outflow tract[9] and allowing aqueous humor to exit through the internal ostium, beneath the scleral flap and under the conjunctiva where it forms a filtering bleb.[10] This fluid is then absorbed into the periocular tissues.

After the correct eye is identified and confirmed with the patient, the patient is prepped and draped in the usual fashion for intraocular surgery. A single drop of Betadine 5% should be administered in the operating room for bacterial prophylaxis. A superior corneal traction or superior rectus bridle suture may be placed if required for adequate exposure[11] or the patient should be instructed to infraduct the globe if topical anesthesia is used. Depending on the choice of a limbus- or fornix-based flap, the conjunctiva is incised approximately 10 mm behind the limbus or at the limbus, respectively.[12,13] A fornix-based conjunctival flap offers the theoretical advantage of a more diffuse, posterior bleb. A limbus-based conjunctival flap is technically more difficult, may limit the posterior extent of filtration due to scarring at the suture line, and requires more operating room time, but often provides for an easier watertight closure. Creation of the conjunctival flap should be performed with blunt dissection to create a plane in the episcleral space. Toothed forceps should be avoided or used with caution when handling conjunctiva to minimize trauma and prevent creation of an inadvertent buttonhole. Hemostasis is controlled with focal light cautery to minimize bleeding.

Antifibrotic agents such as mitomycin C or 5-flurouracil on a sponge may be placed at this time or after the dissection of the partial thickness scleral flap. The antifibrosis agent is best placed between Tenon's fascia and episclera and should cover a wide area to reduce the risk of creating a small, focal bleb.

Although adjunctive antifibrosis agents enhance the success of trabeculectomy, their risk/benefit ratio should be assessed for each individual patient prior to use. This applies to initial and repeat surgeries.

Eyes undergoing trabeculectomy should have a paracentesis to allow reformation of the anterior chamber and to test the security of the scleral flap and conjunctival closure. It is important to avoid lens touch when forming the paracentesis.

Following dissection of the partial thickness lamellar scleral flap into clear cornea, the anterior chamber is entered at the base of the scleral flap with sharp blade, diamond knife or similar instrument. A punch or other instrumentation is used excise a section of cornea and trabecular meshwork. An iridectomy is performed. To close the flap, 10-0 nylon sutures, which can be preplaced are used. The anterior chamber is reinflated, flow through the flap is adjusted to allow egress of aqueous while maintaining adequate pressure, and the sutures are tied. The conjunctiva is brought back to the limbus in a fornix-based flap and sutured. A limbus-based flap requires a running closure. A fluorescein strip can be used to test for leaks. Cycloplegia is placed in phakic patients to help maintain the depth of the anterior chamber. Subconjunctival injection or topical steroids and antibiotics may be given.

Although operating time may vary depending on experience of the surgeon and the technique used, the surgical technique is within the ability of most ophthalmic surgeons. Identification and management of postoperative complications requires significant experience, and may be more important than even the surgery to obtain a successful outcome.

Postoperative management

Postoperative medications are begun on the day of surgery. These include postoperative antibiotics qid for one week, long-acting cycloplegia, when indicated, to maintain anterior chamber depth and frequent dosing of topical prednisolone acetate 1% for several weeks after surgery. Cycloplegics help maintain anterior chamber depth by relaxing the ciliary muscle, tightening the zonular apparatus, and pulling the lens posteriorly.

Suppression of inflammation is critical to success.[3] Topical steroids are tapered based upon the anterior chamber response initially, but later based upon conjunctival hyperemia. The duration of topical steroid therapy varies widely, and some patients require continuation for four or more months. Supplemental 5-fluorouracil may be used as necessary to limit scarring[14] and is typically given in 5.0 to 7.5 mg doses several times per week as required. Minimizing aqueous suppressant use may enhance bleb formation.

Laser suture lysis or removal of releasable sutures, if necessary, is often performed within several weeks of surgery to enhance aqueous drainage. With planned sequential suture release, initial postoperative hypotony and excessive filtration can be avoided. Suture release should be performed within one week in eyes not receiving antifibrosis agents, but may be postponed for a few weeks after 5-fluorouracil surgeries and for even longer after mitomycin-C.

Interventions are needed as complications arise. Early recognition of post-operative complications and timely, appropriate intervention enhances the success rate of surgery and minimizes patient morbidity. The surgeon must be prepared and equipped to manage post-filtration surgery complications such as hypotony, anterior chamber shallowing, and malignant glaucoma, among others. Adjunctive techniques to limit excessive filtration include patching, large diameter contact lenses, and symblepharon rings. Anterior chamber shallowing may require reformation. Choroidal effusion typically resolves with elevation of IOP, but may upon occasion necessitate drainage.

Late complications of filtering surgery include prolonged hypotony associated with hyptony maculopathy and bleb-related ocular infection. Loss of vision due to hyptony maculopathy is more common in younger, myopic patients and may require surgery to repair the hypotony and restore normal IOP. Thin-walled blebs, often associated with focal leakage, are more prone to late bleb-related ocular infection. Conjunctivitis in the presence of a filtering bleb or bleb infection should be treated as a medical emergency as it may lead to infectious endopthalmitis and loss of vision or the eye. Patients that have had trabeculectomy should be warned of the signs and symptoms of late bleb-related ocular infection and should be counseled to seek immediate attention should these occur.

Research considerations

The IOP measurement for research studies should include a mean pressure at different time points after the surgery. A successful surgery should be defined as one that achieves a target IOP that prevents, or will likely prevent, further damage to the visual field or optic nerve/ganglion cells. One can include success rates exclusive and inclusive of additional medical therapy. The progression of glaucoma can also be followed by assessing the RNFL/ONH. No study of surgery should include results that are less than 12 months for an initial report and should preferably be longer than 2 years. Long-term success (greater than 5 years) should be reported whenever possible.

The quality of life can be measured by detailed questionnaires,[15] that can be internet based in the future. Complications can be measured by considering separately intraoperative, immediate postoperative, and late complications.

Levels of evidence

There is no evidence on the relationship between the size/shape of the scleral flap and the success of the operation. There is a higher chance of success with antifibrotics; however, the incidence of postoperative complications is greater than without antifibrotics.[1,5,16] In general, lower pressure measurements with less IOP fluctuation can be achieved with filtering surgery than with medical therapy.[17-21]

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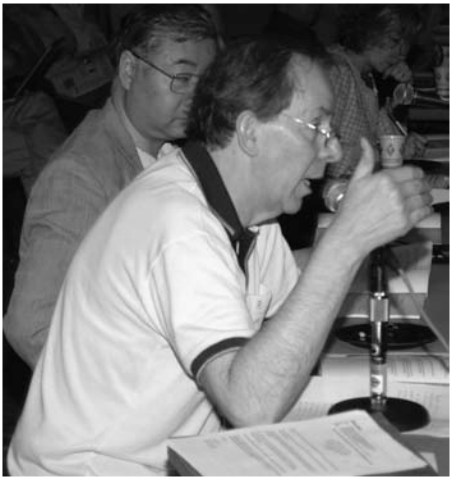
Discussion on trabeculectomy: Clive Migdal and Stefano Gandolfi

Ravi Thomas, Ron Gross (middle) and Eytan Blumenthal



Roger Hitchings

Eric Greve and Ivan Goldberg

Robert Weinreb, Franz Grehn, Jeff Liebmann (speaker)

COMBINED CATARACT/ TRABECULECTOMY

George A. Cioffi, David S. Friedman and Norbert Pfeiffer

George A. Cioffi
(Presenter)

Contributors: M. Aihara, J. Caprioli, A. Crandall, J. Ge, D. Kim, F. Lerner, R. Lewis, G. Manni, F. Medeiros, J. Nordmann and P. RojanaPongpun

Consensus points

- A combined procedure is usually indicated when surgery for intraocular pressure (IOP) lowering is appropriate and a visually significant cataract is also present.
  Comment: Patients with glaucoma who are undergoing cataract do not necessarily require combined surgery. To avoid the complications associated with increased postoperative IOP, however, combined procedures should be considered in those patients on multiple medications or with advanced glaucomatous optic neuropathy.
- The indication for combined surgery in an individual patient should take into account the level of desired IOP control after surgery, the severity of glaucoma and the anticipated benefit in quality of vision after cataract extraction.
  Comment: Visual rehabilitation may take longer following combined surgery compared to cataract surgery alone.
- There is limited evidence to differentiate a one-site *vs.* a two-site approach for combined surgery. Therefore, surgeon preference and experience will dictate the choice.
- There is limited evidence to differentiate a limbal *vs.* a fornix-based conjunctival incision for combined surgery. Therefore, surgeon preference and experience will dictate the choice.
- Mitomycin-C should be considered in all combined procedures to improve the chance of successful IOP control, unless there is a clear contraindication for its use.
  Comment: Evidence for the use of adjunctive 5-fluorouracil data is limited and the bulk of the evidence suggests that it does not work well or at all.

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- Combined procedures are less successful for IOP reduction than trabeculectomy alone.
  Comment: Subsequent cataract surgery may compromise the success of earlier trabeculectomy surgery.
- In patients with cataract and stable glaucoma, a clear corneal approach is preferable in patients who may require subsequent trabeculectomy.

Introduction

When considering surgical intervention in a patient with both glaucoma and cataracts, a number of important, and at times conflicting, findings complicate the decision making process. Should the cataract be removed and a trabeculectomy performed at a later time? Should a trabeculectomy be performed followed by cataract extraction? When is it appropriate to perform both surgeries in the same setting? It has become obvious that most, if not all, of the participants in this discussion perform combined cataract surgery and trabeculectomy for some patients with concurrent disease. This review will attempt to outline the important points to be considered and the important questions that should be answered in this setting. For the purpose of this discussion, only chronic open angle glaucoma (OAG) will be considered. This is not to discount the importance of the angle closure glaucomas, but is to allow a focused and finite discussion on the topic. The inclusion of angle close was considered at length in the planning for this meeting and consensus document, however, due to the large number of topics needing to be covered, it was felt that only OAG should be considered and that angle closure merits its own consensus discussion.

The following is a list of questions that were asked of each of the participants in the consensus group and are addressed by this consensus statement:

1. What are the indications for combined surgery?
2. How should combined surgery be performed? (One site *vs.* two sites, limbal *vs.* fornix-based.)
3. Should intraoperative antimetabolites be used routinely in combined surgery?
4. What type of anesthesia is most appropriate?
5. How do the long-term results compare to other surgeries for glaucoma?
6. Is there a preferable type of IOL? (Silicone, acrylic, PMMA.)
7. What type of scleral flap closure should be used? (Suture lysis, releasable, etc.)
8. Is there a role of viscoelastics? (Remove at the end of surgery, leave in the eye.)
9. What postoperative medications should be used? (Hypotensive agents, others.)

In addition, there are other important points that should be considered prior to attempting to answer these questions. It is widely reported in many large case series that cataract extraction alone in OAG lowers intraocular pressure (IOP) by approximately 2 mmHg at one year.[1-9] While the reason for this has been debated ever since the time of intracapsular cataract surgery, it remains a mystery, but it is consistent in the literature. It also appears that the IOP lowering following cataract surgery alone in OAG, is usually a transient benefit. This point is important because it may confuse the interpretation of data comparing combined surgery versus cataract extraction alone. Another point to be considered is that there is likely a slightly increased risk of an acute IOP rise in the immediate post-operative period in OAG patients undergoing phacoemulsification cataract surgery.[10,11] This is important as it may encourage combined surgery, even in the medically controlled OAG patient, to eliminate the potential damage caused by a pressure rise. However, most clinicians do not consider blebs desirable unless completely necessary. In addition, the literature supports the fact that combined surgery results in poorer IOP control than trabeculectomy alone.[12-16] Even with the advent of antimetabolite therapies, surgical results are not as favorable with combined surgery. Therefore, two separate surgeries (cataract extraction first, followed by trabeculectomy later) may be preferable in some patients. As well, the literature supports the use of mitomyicin-C for combined cases, but the strength of support is moderate.[17-22] This is not the case for trabeculectomy alone, where the routine use of mitomycin-C is not uniformly accepted. Finally, it is felt that any surgical intervention, including phacoemulsification cataract extraction, performed months or even years after trabeculectomy causes some decrease in bleb function. While the literature on this point is not over whelming, the general clinical consensus is. Surgery in an eye that has a functioning bleb results in failure of the bleb in some eyes and partial loss of IOP control in others. Case series show a decline in bleb function, but controlled studies examining this issue have been conflicting.[23-26] These points are described to illustrate the complexity of the co-management of cataracts and glaucoma.

What are the indications for combined surgery?

This is perhaps the most important question. Included in this question is the consideration of indications for subsequent surgery (*i.e.*, trabeculectomy followed by cataract surgery, or cataract surgery followed by trabeculectomy). The consensus group attempted setting strict criteria for IOP level or visual acuity level at which combined surgery should always be employed, however, we soon realized that such simple criteria are not practical. The consensus panel concluded that the only honest answer on the indications for combined procedures is that we simply do not have a single uniform recommendation for all cases. In fact, for many of the surgical decisions that are made regarding combined surgery, there are not adequately powered studies available to answer our questions. Many participants felt that the literature supports the statement that: combined glaucoma and cataract procedures are indicated when surgery for IOP control is indicated and visually significant cataract is also present. Less clear indications are cataract surgery planned in a patient with glaucoma in whom a post-operative IOP spike could lead to substantial loss of function. And a third, less well-supported indication is planned glaucoma surgery with co-existing cataract in which cataract surgery would not be performed at present. The reason for this is the well-documented likelihood that cataract will progress after glaucoma surgery.

The discussion focused on the adequacy of the pre-operative IOP control in an eye with a visually significant cataract. Cataract extraction alone is considered in a patient when the glaucoma is easily being controlled (for example with a single medication) and the patient has mild damage. In a patient with either more advanced disease or more difficult to control glaucoma (greater than one medication needed), combined surgery is considered. This obviously allows for a zone of uncertainty, such as a patient with mild to moderate damage and IOP controlled with a combined medication.

To summarize, cataract surgery alone is used if there is no indication for filtration surgery, but the cataract is visually significant. The cataract extraction will improve the therapeutic situation, both from a visual standpoint and possibly by lowering the IOP (even if it is transient). In this situation, there is a small, but acceptable, risk of transient IOP elevation in the immediate post-operative period. If there is an indication for surgery (*i.e.*, inadequate IOP control, progressive disease, intolerance to medication, etc.) and a concurrent cataract, it is unlikely that cataract extraction alone will reduce IOP sufficiently. While subsequent two-stage surgery may be considered (cataract extraction first and filtration surgery later), combined surgery offers many potential benefits. This accepts that filtering surgery following a cataract extraction performed with modern techniques (clear corneal phacoemulsification) works very well. Also it is realized that cataract extraction following a filtration surgery is less attractive, as the cataract extraction may compromise the result of the filtering surgery. In a combined procedure, the benefit for the patient of a single surgical event can not be denied. In addition, in the eye with significant and uncontrolled glaucoma, the benefit of IOP control immediately following surgery and avoidance of postoperative IOP spikes is attractive. If the indication for filtering surgery is present and there is a visually significant cataract (or a cataract that is likely to become visually significant in the near future), a combined procedure is advisable. If IOP control is essential, a trabeculectomy alone is the most likely to succeed. Therefore glaucoma filtration surgery is used alone, in patients with very advanced damage.

How should combined surgery be performed? (One site *vs.* two sites, limbal *vs.* fornix-based)

While there are many articles published about surgical procedures, direct comparisons between various technical nuances are difficult to study. Overall, the literature offers little insight, but there is a pattern of slightly better IOP control with two-site procedures.[27-32] As for conjunctival flap techniques, there is very little information in the literature and no consensus, but both approaches appear to offer similar success rates.

Should intraoperative antimetabolites be used routinely in combined surgery?

Antimetabolite use is much more common in combined surgery. Many surgeons use mitomycin-C in practically 100% of combined phaco-trabs, others use intraoperative 5-FU, but all use some form of antimetabolite. Review of the literature indicates that there is modest evidence in favor of better outcomes with mitomycin-C in combined surgeries.

What anesthesia is most appropriate?

There is almost no literature on this, and therefore the method of anesthesia depends on surgeon and patient comfort. Topical with or without sub-Tenon's or sub-conjunctival supplementation is typical.

How do the long-term results compare to other surgeries for glaucoma?

Combined procedures are less successful at IOP reduction than trabeculectomy alone.[33-37]

Is there a preferable type of IOL? (Silicone, acrylic, PMMA)

Very little is published on this topic and there probably is very little difference.

What type of scleral flap closure should be used? (Suture lysis, releasable, etc.)

No literature supporting one approach over another.

Is there a role of viscoelastics? (Remove at the end of surgery, leave in the eye)

There is no published data on this issue.

What postoperative medications should be used? (Hypotensive, others)

There is no literature that compares different post-operative regimens. Long-term (two to three months) topical steroids are used by most. Perhaps, post-operative depot steroids could be studied. Hypotensive medications are at times used in patients with moderate to severe damage at the end of procedure.

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Section participants: Gianluca Manni, Makoto Aihara, Felipe Medeiros, David Friedman

Discussing combined surgery: Norbert Pfeiffer, Robert Weinreb, Franz Grehn and George Cioffi (speaker)

James Brandt

AQUEOUS SHUNTING PROCEDURES WITH GLAUCOMA DRAINAGE DEVICES

Anne L. Coleman and Kuldev Singh

Anne L. Coleman
(Presenter)

Contributors: G. Baerveldt, P. Healey, D. Heuer, T. Krupin, R. Sihota, C. Traverso and J. Tsai

Consensus points

- Glaucoma drainage devices (GGD) are indicated when trabeculectomy is unlikely to be successful or because of socioeconomic or logistical issues.
  Comment: In some patients, GDDs should be considered for socioeconomic or logistical issues relating to safety, follow-up care, etc.
- The restriction of flow of aqueous humor from the eye is important in the prevention of immediate postoperative hypotony.
  Comment: GDDs that do not have mechanisms to restrict aqueous flow require a suture ligature or internal stent or other flow restricting mechanism.
- In general, larger surface areas of the plate are associated with **lower** IOP.
- Scar formation around the plate is the main cause of long-term device failure.
  Comment: Antifibrotic agents have not been shown to improve long-term success when used intraoperatively or postoperatively.
- Pars plana positioning of a GDD should be considered in a patient with a prior pars plana vitrectomy or in patient in whom a tube cannot be safely inserted into the anterior chamber.
- The preponderance of evidence addresses GDDs that drain to a posterior reservoir.
  Comment: Anterior drainage devices are under study. One should not extrapolate data from posterior drainage to anterior drainage devices.

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Introduction

Glaucoma drainage devices are designed to lower intraocular pressure by draining aqueous humor from the interior of the eye to a reservoir.[1-6] Potential indications for aqueous shunting procedures with glaucoma drainage devices implantation are listed in Table 1. There may be additional circumstances not listed where the presumed risk-benefit ratio with glaucoma drainage device implantation will make this the preferred procedure relative not only to trabeculectomy, but also to other treatment modalities including cyclophotocoagulation, laser trabeculoplasty and in rare circumstances, medical therapy.

Table 1. Potential indications for glaucoma drainage device implantation

A. Eyes in which trabeculectomy, even with adjunctive antifibrotic use, has a high risk of failure:
- Previous failed mitomycin-C trabeculectomy;
- Active neovascularization of the iris where IOP is too high to wait for regression of neovascularization;
- Sufficient retinal photocoagulation necessary for regression of iris neovascularization cannot be performed;
- Active or recurring, moderate to severe uveitis;
- Aphakic or pseudophakic bullous keratopathy where penetrating keratoplasty is contemplated;
- Advanced epithelial ingrowth;
- Coexistent vitreoretinal pathology for which vitrectomy is contemplated;
- Prior silicone oil injection for complicated retinal detachment repair;
- Chronic conjunctival inflammation, allergy and/or scarring;
- Developmental glaucomas associated with corneal opacification and/or severe anterior segment anomalies;
- Eyes with peripheral anterior synechiae.

B. Eyes in which trabeculectomy is technically not possible or with high risk of intraoperative complications:
- Extensive conjunctival scarring of the perilimbal conjunctiva/Tenon’s capsule superiorly;
- Marked limbal thinning superiorly.

C. Patients in whom trabeculectomy with mitomycin-C has a high risk of postoperative complications:
- Contact lens wearers;
- Severe lid margin and/or periocular disease;
- Patients who live and play in dirty and/or dusty environments which includes most children;
- History of blebitis or bleb-related endophthalmitis in operative or fellow eye;
- Moderate to high risk of suprachoroidal hemorrhage.

Types of drainage devices

There are several type of devices; however, they can be divided into two categories: anterior drainage devices and posterior drainage devices. The preponderance of evidence addresses posterior drainage devices which consist of one or more posterior plates or reservoirs connected to a tube; the tube not only serves as the means of egress of aqueous from the eye but also prevents the opening into the eye from closing and bypasses the anterior conjunctiva. Currently anterior drainage devices without plates or with small plates placed anteriorly near the limbus are under study. The data from posterior drainage devices cannot be extrapolated to anterior drainage devices.

Posterior drainage devices

Most posterior drainage devices are composed of a silicone or Silastic tube that is placed into the eye (through the limbus or pars plana) and through which aqueous humor passes into the episcleral-subconjunctival space near the globe's equator. In this area there is an episcleral plate that is designed to help form and maintain an aqueous reservoir. There are three key design features which distinguish different implants: 1. The presence of a valve or mechanism to restrict the flow of aqueous humor from the eye; 2. The surface area and configuration of the episcleral plate; and 3. The material used. The restriction of flow of aqueous humor from the eye is important in the prevention of immediate postoperative hypotony and its attendant complications. Drainage devices without a built in flow restriction mechanism, such as the Molteno, Baerveldt, and Schocket band implants,[7-23] may be inserted in either a two-stage procedure, where encapsulation of the bleb is allowed to occur before the tube is inserted into the eye at a second surgery, or in a one-stage procedure, where the flow of aqueous is restricted by a suture ligature around the tube or an internal stent. [evidence is case series] As methods to restrict flow in a more predictable manner following the implantation of devices without built in flow restriction mechanisms have evolved, there has been greater use of the one-stage rather than the two-stage procedure but there is no consensus opinion on this matter. Decisions regarding staging may be patient specific, based upon the potential benefits and risks of early filtration and overfiltration, respectively. A two-stage approach may be optimal for eyes that are at high risk for postoperative suprachoroidal hemorrhage as is the case, for example, in patients with Sturge-Weber Syndrome. Several contemporary posterior drainage devices, specifically the Krupin Valve implant[24-25] and Ahmed Glaucoma Valve implant,[26-29] have pressure-sensitive valves or mechanisms which restrict the flow of aqueous from the eye. Equally important is the mechanism or surgical technique that results in regulation of flow around the tube after it is placed in the eye.[30-31]

The surface area of the episcleral plate may influence the amount of intraocular pressure reduction because of its effect on the size of the bleb. Since the main resistance to aqueous flow and pressure reduction is the capsular wall surrounding the episcleral plate,[32] a potential advantage of a larger filtration bleb is a larger surface area for diffusion. [evidence is randomized clinical trials] Heuer and co-authors[11] have reported that there is a greater reduction in intraocular pressure in eyes with the double-plate Molteno implant compared to the single-plate Molteno implant, and Mills and co-authors[10] found two-year success rates of 67% and 85% for single and double-plate Molteno implants, respectively. Larger surface area implants result in lower postoperative intraocular pressures but there may be a threshold surface area above which a larger sized implant does not result in any further IOP lowering. There is no consensus opinion on the additional risks, beyond the greater potential for overfiltration, with larger rather than smaller drainage devices. Heuer and co-authors[11] reported that double-plate Molteno implants are associated with more complications than single-plate implants, while Lloyd and co-authors[16] did not find a statistically significant difference in the number of complications between 350 mm^2 and 500 mm^2 Baerveldt implants.

Even though the episcleral plates of drainage devices are made of relatively non-reactive substances such as polypropylene, silicone, Silastic (a soft, pliable plastic), and polymethylmethacrylate, they are associated with the formation of a collagenous and fibrovascular capsule around the plate. Histopathologically, this capsular wall has been described as a collagenous meshwork that progressively becomes denser from inside to out.[32] The thickness of this capsule is important in the resistance of aqueous flow from the episcleral plate to the surrounding vasculature. Excessive fibrous reaction around the bleb appears to be a major cause of long-term drainage device failure. In a rabbit model, Ayyala and colleagues[33] have shown that polypropylene end-plates are more inflammatory than silicone ones, and that the rigidity and shape of the end-plate may promote inflammation. Anti-fibrotic agents such as mitomycin-C and 5-fluorouracil have been tried at the time of surgery to decrease fibrous reaction. Several studies have shown no advantage of these anti-fibrotic agents compared to controls, whereas the incidence of complications such as late hypotony, flat anterior chamber, and conjunctival melts causing tube and plate erosions were higher.[34-37] [evidence is case series and randomized clinical trials] There is no consensus opinion regarding whether or not antifibrotic agents should have any role as adjuncts to drainage device implantation. The possibility exists based upon anecdotal reports that these agents may be helpful adjuncts when used with some devices but not with others. There is little evidence at this time to support the use of either 5-FU or Mitomycin C adjunctively with drainage device implantation. There is also insufficient data to support needling of encapsulated drainage devices with adjunctive antifibrotic use.

To date, there are no prospective, double-masked, adequately powered randomized clinical trials comparing the different drainage devices. Wilson and colleagues[38] recently reported similar success rates with primary Ahmed implants versus trabeculectomies in a prospective, randomized clinical trial, although the postoperative mean IOP was lower in the trabeculectomy group relative to the Ahmed group. Despite this study, there is consensus opinion that posterior drainage devices are not usually done as primary surgery. Primary drainage device implantation, at present, is generally reserved for eyes considered at high risk of failure with an antifibrotic augmented trabeculectomy as is the case, for example, in some eyes with neovascular glaucoma, particularly when iris neovascularization does not adequately regress following panretinal photocoagulation. Cyclophotocoagulation is generally preferred over drainage device implantation in eyes that have poor visual potential, unhealthy conjunctiva or cannot undergo a surgical procedure for health reasons. [consensus opinion]

Intraocular tube implantation may or may not be performed beneath a scleral flap. Donor sclera, irradiated pericardium and irradiated sclera are the tissues most commonly used to cover the tube externally. There is no consensus opinion regarding which approach is best and choices may be patient specific. Excessive flow of aqueous humor around the implanted drainage tube can result in complications due to overfiltration. The size of the needle used to create an opening through which a tube will pass vary from 23 to 25 gauge when inserting the tube in the anterior segment of the eye and 22 to 23 gauge when the entry is via the pars plana. There is no consensus opinion regarding the optimal method for tube occlusion following the implantation of devices that do not restrict flow.[39-45] The two most popular methods are internal occlusion via a suture that can be removed postoperatively and external occlusion with a dissolvable suture, with or without fenestration of the tube proximal to this ligature. Viscoelastic use is common with the insertion of devices, which have flow-restriction mechanisms such as the Ahmed implant. In contrast, tube occlusion or ligation with the ‘non-valved’ implants makes viscoelastic use hazardous in that it may be associated with early postoperative pressure spikes.

Postoperative topical antibiotic and steroid use is routine following drainage device implantation. While the use of oral agents including steroids or other antiproliferative agents in the perioperative period have been proposed, these agents are generally not used primarily because of associated systemic side effects. IOP lowering medications are used postoperatively as needed. If IOP lowering is inadequate after drainage device implantation, even with the adjunctive use of medications, the choices include revision of the existing implant, placement of a second device or cyclophotocoagulation. There is no consensus or clinical trials regarding the number of posterior drainage devices that can be placed in one eye.

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Kuldev Singh (co-Chair) and Robert Weinreb

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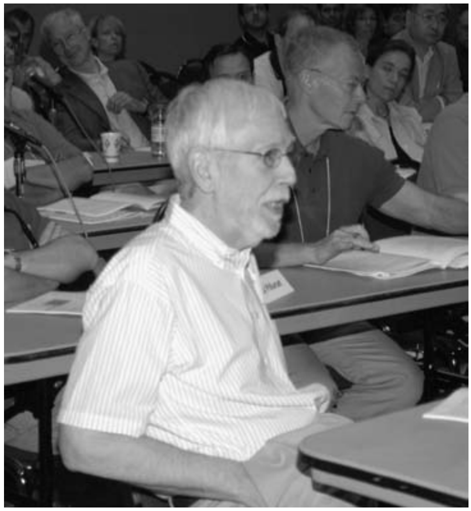
Discussion of glaucoma drainage devices: Robert Fechtner



Theodore Krupin

Anne Coleman (Speaker)

COMPARISON OF PROCEDURES: TRABECULECTOMY VERSUS AQUEOUS SHUNTING PROCEDURES WITH GLAUCOMA DRAINAGE DEVICES

Dale K. Heuer
(Presenter)

Felipe A. Medeiros and Dale K. Heuer

Consensus points

- Trabeculectomy with MMC is less expensive and requires less conjunctival dissection than aqueous shunting procedures.
  Comment: Cost of GDDs vary significantly throughout the world.
- With increased conjunctival scarring, the success of MMC trabeculectomy is reduced. Aqueous shunting procedures should be considered in patients with failed MMC trabeculectomy.
- In general, lower IOP can be achieved with MMC trabeculectomy compared with aqueous shunting procedures, but good clinical studies are lacking.
  Comment: There are currently limited data from prospective randomized comparisons between MMC trabeculectomy and aqueous shunting procedures. To adequately compare MMC trabeculectomy with aqueous shunting procedures, comparable patient populations are required.
- Bleb related complications are less prevalent after aqueous shunting procedures. However, aqueous shunting procedures introduce a distinct set of complications including tube erosion or plate erosion, endothelial decompensation and strabismus.
- Aqueous shunting procedures (ASPs) should be considered in patients at high risk of MMC-related postoperative complications. These include severe lid margin disease, chronic contact lens wear, and a history of blebitis or bleb-related endophthalmitis.

Aqueous shunting procedures have been traditionally regarded as an alternative to standard filtering surgery or cyclodestructive procedures in eyes with complicated glaucomas at high risk of failure. However, few studies have adequately compared success rates and complications of trabeculectomy and ASPs.

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A direct comparison between these two procedures using the published literature is limited, because the majority of studies are largely restricted to non-randomized, retrospective case series with different definitions of success, different follow-up times and lack of homogeneity in the cases included. In the present report, we review the evidence regarding the success rates and complications of trabeculectomy and ASPs in patients with open-angle glaucoma, emphasizing randomized studies that have compared the two procedures.

Success rate

A recent review of the literature by Hong *et al.*,[1] encompassing 54 articles on ASPs, reported a success rate ranging from 72% to 79% among 5 different glaucoma drainage devices (Molteno, modified Molteno, Baerveldt, Ahmed and Krupin), with no statistically significant difference among the devices at the last follow-up time. Mean follow-up times for the different studies ranged from 18.6 to 27.1 months and patients with different types of glaucoma were included.

Reported long-term success rates for trabeculectomy have varied considerably in the literature. It is generally believed that lower IOP can be achieved with a trabeculectomy with antimetabolites compared with an ASP; however, this has not been convincingly demonstrated in clinical trials. Lower success rates reported for ASPs compared to trabeculectomy may be just a reflection of a higher rate of patients with a poor prognosis for filtration surgery being selected to undergo ASPs.

Molteno *et al.*[2] described the results obtained in a series of 130 eyes of 103 patients with primary open-angle glaucoma or pseudo-exfoliative glaucoma that underwent Molteno implantation as their initial filtering surgery. In 40 eyes, Molteno implant insertion was combined with cataract extraction. All patients had additional risk factors deemed to be associated with a poor prognosis for standard filtering procedure, such as aphakia, pseudophakia or history of bleb failure after trabeculectomy in the fellow eye. Interestingly, several patients were selected for primary ASP based on the existence of general 'risk factors' that limited the ability to cope with postoperative care and possible complications of trabeculectomy, such as severe cardiovascular disease and dementia. After two years of follow-up, they reported successful IOP control (defined as IOP $<$ 21 mmHg) in 110 of 111 eyes, with an average number of ocular hypotensive medications of 0.63. Although the authors have also reported successful results with long-term follow-up, the drop-out rate in the study was very high, with only 55 eyes followed for 5 years and 9 eyes followed for 10 years.

El Sayyad *et al.*[3] performed a non-randomized, case-control study, comparing the outcomes of 43 patients who underwent trabeculectomy with mitomycin-C (MMC) with 43 patients who underwent Molteno implantation (38 single-plate and 5 double-plate). The patients were matched by age, glaucoma diagnosis and number of previous filtering procedures. They reported a 12-month success rate (defined as IOP ≤ 21 mmHg) of 81% for trabeculectomy and 61% for Molteno surgery, a difference that was statistically significant. Patients who underwent Molteno surgery also were more likely to require hypotensive medications during follow-up.

Only two randomized clinical trials have compared the success rates of ASPs and trabeculectomy.[4, 5] Both studies were performed by the same group and compared trabeculectomy with Ahmed valve implantation. In one study,[5] 177 patients were included, 62 randomized to trabeculectomy (92% with MMC) and 55 to Ahmed implantation. Patients were followed for an average period of 9.7 months. Primary glaucoma accounted for 83 of the 117 eyes (71%) whereas 34 (29%) eyes had secondary glaucoma (neovascular, uveitic or traumatic glaucoma). After approximately 1 year of follow-up, the trabeculectomy group had significantly lower IOP than the Ahmed group (11.4 mmHg vs. 17.2 mmHg, respectively). However, the success rate (IOP < 21 mmHg and at least 15% IOP reduction from preoperative level) was similar in the two groups (83.6% for trabeculectomy and 88.1% for Ahmed implant), although patients that underwent Ahmed implantation required more post-operative medications to control IOP. On the last visit, 10 (16%) of the trabeculectomy eyes and 19 (35%) of the Ahmed implant eyes required at least one topical glaucoma medication. In a subsequent study, Wilson *et al.*[4] randomized Asian patients with primary glaucoma to receive either a trabeculectomy with or without MMC (at the discretion of the surgeon) or a single-plate Ahmed implant. Thirty-one of the 123 (25%) patients included in the study were diagnosed as having primary angle-closure glaucoma, whereas the remaining subjects had a diagnosis of primary open-angle glaucoma. Patients with other diagnoses or with previous history of intraocular surgery were excluded. Sixty-four patients underwent trabeculectomy (91% with MMC at the dosage of 3 mg/ml for 3 minutes) and 59 patients underwent Ahmed valve implantation. The mean follow-up time of the study was 31 months with approximately 45% of the patients being followed for at least 3 years. Success was defined as IOP less than 21 mmHg and at least a 15% reduction from preoperative IOP, no need for glaucoma surgery and no loss of light perception visual acuity. The trabeculectomy group tended to show lower IOP values and a higher success rate than the Ahmed group during the early post-operative period, with cumulative probabilities of success of 93% vs. 88% and 90% vs. 80% after approximately 1 and 2 years of follow-up, respectively. However, at approximately 3 and 4 years of follow-up, the cumulative probabilities of success for the trabeculectomy and Ahmed groups were similar, 72% vs. 70% and 68% vs. 70%, respectively, with no significant difference between the two groups. The average number of medications at last examination was also similar in the two groups (0.93 ± 0.11 vs. 1.13 ± 0.14, respectively). Therefore, although lower IOP was observed in the short-term postoperative period with trabeculectomy, the success rate of the two procedures was comparable with longer follow-up.

The Trabeculectomy versus Tube (TVT) Study, a multicenter randomized clinical trial to determine the safety and efficacy of trabeculectomy with MMC compared to ASPs in pseudophakic eyes and eyes after failed trabeculectomy,[3b] has recently completed the enrollment process. Eligible patients were randomized to receive either a trabeculectomy with MMC (0.4 mg/ml for 4 minutes) or a Baerveldt implant. When available, the results of this study will provide further insight on the success rate and complications of these two procedures.

Post-operative complications

As with success rate, the comparison of the incidence of post-operative complications following ASPs or trabeculectomy is limited by the paucity of studies adequately comparing the two procedures. In the randomized study by Wilson *et al.*,[4] described above, the number and severity of complications experienced by both groups were comparable. Although previous studies have reported a higher incident rate of post-operative complications following ASPs, these studies generally included eyes with poorer prognosis for filtration surgery in which complications would be more likely to occur.

ASPs are generally regarded to be associated with a lower incidence of endophthalmitis than trabeculectomy. However, the exact incidence of endophthalmitis following ASPs is unknown. Several retrospective studies have included a single case or a few cases of endophthalmitis resulting in rates ranging from 0.8% to 6.3%.[6-10] The main risk factor for endophthalmitis following ASPs seems to be tube exposure following conjunctival erosion.[7, 11]

The reported incidence of late postoperative bleb-related endophthalmitis after trabeculectomy ranges from 0.9% to 6.9% in several studies over the past decade.[12] However, it is believed that this incidence has been increasing with the increased use of antifibrotic agents. In fact, after trabeculectomy with MMC, it is estimated that the incidence of endophthalmitis ranges from 0.8% to 1.3% per year.[13, 14] DeBry *et al.*[13] reported a 5-year incidence of developing a bleb leak, blebitis or endophthalmitis of up to 23% after trabeculectomy with MMC. The very high risk of endophthalmitis associated with inferiorly located trabeculectomies strongly supports the selection of ASPs or cyclodestructive procedures in eyes with extensive corneolimbal scarring precluding trabeculectomy in the superior quadrants. Greenfield *et al.*[15] reported an incident rate of endophthalmitis as high as 7.8% per patient-year with trabeculectomies performed at inferior location. Inferiorly located blebs are more exposed to bacteria-rich tear film and to mechanical irritation from the lower eyelid, being afforded less protection by the superior eyelid. The presence of blepharitis or contact lens wear has also been reported as increasing the risk of bleb-related infections following trabeculectomy. In a case-control study, Jampel *et al.*[16] reported relative risks of 1.92 and 4.86 for the association between development of late-onset infection after trabeculectomy and presence of blepharitis and contact lens wear, respectively. However, the number of patients wearing contact lenses in that study was very low and chart documentation regarding blepharitis might have been incomplete.

The lower rate of late-onset complications after ASPs is probably explained by the nature and location of the filtering bleb that develops around the explant portion of the device. After trabeculectomy, the anteriorly located bleb commonly evolves into a thin-walled avascular area, especially when antimetabolites are used. These thin blebs are at a much greater risk of developing leakage and endophthalmitis.[17] On the other hand, the lower risk of endophthalmitis after ASPs is probably related to the thicker subconjunctival tissue and fibroblastic response overlying the plate, located posteriorly. In fact, avascular blebs are rarely, if ever, seen overlying drainage implants, even when high concentrations of mitomycin-C are used.[18] Therefore, ASPs may be a preferred procedure for patients with severe eyelid margin disease, contact lens wearers or patients with a history of blebitis or bleb-related endophthalmitis.

Although bleb-related complications are less prevalent post ASPs, a distinct set of complications may develop related to the presence of an implanted foreign body such as diplopia, strabismus, tube or plate erosion and corneal decompensation.

Endothelial decompensation has been reported in up to 30% of patients with long-term follow-up after ASPs.[19] The higher incidence of endothelial decompensation after ASPs compared to trabeculectomy may be related to a mechanical loss of corneal endothelium cells by tube-endothelium contact. Alternatively, the higher incidence of corneal decompensation after ASPs may be related to the state of the endothelial cells prior to surgery. As ASPs are usually reserved for eyes with worse prognosis which commonly have undergone multiple surgical procedures or had previous episodes of inflammation, the postoperative corneal decompensation may be just a reflection of the natural course of the disease, rather than a direct damage caused by the aqueous shunt device. In fact, Molteno *et al.*[2] reported only 2 cases (1.5%) of corneal endothelial decompensation in 130 eyes with primary open-angle glaucoma or pseudoexfoliative glaucoma that underwent Molteno implantation as primary filtering surgery. Only one study provided data on corneal endothelium cell counts after ASPs. McDermott *et al.*[20] reported no clinically significant endothelial cell loss in 19 patients undergoing uncomplicated Molteno implants during follow-up periods ranging from 5.4 to 25.7 months. It is likely, therefore, that the etiology of corneal decompensation following ASPs is multifactorial.

Other considerations

Several other factors need to be taken into account when deciding the procedure of choice for filtration surgery in a particular patient. Trabeculectomy is generally a shorter procedure, requiring less operating room time and is less expensive than a drainage device implantation. However, the post-operative care in trabeculectomized eyes is usually more labor intensive, requiring a higher degree of patient cooperation and an increased number of post-operative visits than after ASPs. Further, although the primary purpose of a filtering procedure is to reduce the IOP, the degree of necessary IOP reduction will vary according to patient characteristics, such as severity of disease, target intraocular pressure, life expectancy, etc.

In conclusion, the ultimate demonstration of which procedure is safer and more effective awaits further additional clinical trials. At the beginning of this chapter, we summarize the final consensus points regarding the comparison of trabeculectomy versus ASPs for open angle glaucoma reached at the Second Association of International Glaucoma Societies Consensus Meeting held in Fort Lauderdale, USA, 2005. It should be noted that the consensus points are dynamic and as more evidence accumulates, changes are likely to occur.

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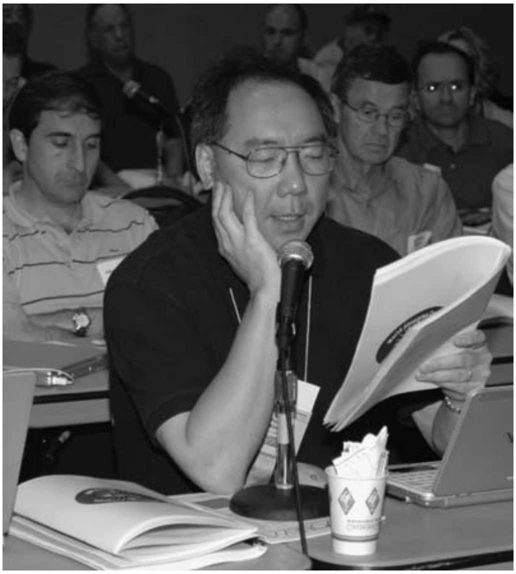
Discussing the pros and cons of trabeculectomy: Franz Grehn

Carlo Traverso and Kuldev Singh



Peng Khaw

Ivan Goldberg

NON PENETRATING GLAUCOMA DRAINAGE SURGERY (NPGDS)

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Consensus points

- NPGDS provides an alternative surgical approach to trabeculectomy for moderate lowering of IOP in glaucoma patients.
- Post-operative Nd:YAG laser goniopuncture may be an integral part of the procedure.
  Comment: Laser goniopuncture is akin to flap suture manipulations following trabeculectomy.
- Unlike viscocanalostomy, external filtration with deep sclerectomy may enhance the success of the procedure.
- Deep sclerectomy may provide a lower IOP than viscocanalostomy, although the evidence for this is limited.
- Failed NPGDS may compromise the success of subsequent trabeculectomy.

Indications

Open-angle glaucomas:
  Primary open-angle glaucoma
    Early damage when medical therapy difficult (non-compliance, dyscompliance) or impossible (intolerant to multiple drugs or preservatives)
    When target intraocular pressure > 15 mmHg
  Secondary open-angle glaucomas*
    Pseudoexfoliative glaucoma
    Pigmentary glaucoma
    Uveitic glaucoma

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(*The primary condition may rarely reduce post-operative aqueous flow through the Descemet's trabecular membrane, increasing the need for Yag laser goniopuncture.)

Contraindications

Prior damage to physiological outflow pathways (Schlemm's canal or downstream) – *e.g.*, from failed surgery / trauma

Open-angle glaucoma
- With narrow angles
- When a low target IOP is required

Closed-angle glaucoma
- With peripheral anterior synechiae
- With appositional closure that cannot be eliminated

Secondary glaucomas with covered trabecular meshwork
- Irido-corneal endothelial syndrome
- Neovascular glaucoma

Congenital glaucomas
- Angle anomalies
- Scleral thinning (*e.g.*, buphthalmia)

Juvenile glaucomas
- Angle anomalies

Indications: deep sclerectomy (DS) versus viscocanalostomy (VC)*

Deep sclerectomy
- Open-angle glaucoma
- Target IOP mid-high teens mmHg
- High myopia
- Aphakia

Viscocanalostomy
- Open-angle glaucoma
- Target IOP mid-high teens mmHg
- High myopia
- Aphakia
- No prior limbal surgery
- Increased risk of infections (*e.g.*, blepharitis, contact lens wear)

(*There is little evidence to guide choice between these two procedures. Currently individual surgeons decide between them on the basis of individual anecdotal experience. Study design (surgical method, criteria for success and postoperative manipulations) differs greatly between published papers, making it difficult to develop evidence-based indications that separate or facilitate a choice between NPGDS and trabeculectomy, as well between different sorts of NPGDS.)

Preoperative care

Surgical risk factor assessment

This is similar to that for trabeculectomy, with the suggestion that NPGDS may be more effective in aphakic glaucoma:

- Young age
- Previous conjunctival / limbal surgery
- Chronic inflammation (*e.g.*, chronic topical medication use / effect of preservatives)
- Active uveitis
- Angle synechiae in the surgical quadrant
- Neovascularisation of the angle
- ICE syndrome
- Scleral thinning (*e.g.*, buphthalmos)

Method of anaesthesia

Usually this is recommended to the patient by the surgeon, as it is for penetrating drainage surgery:

- Topical
- Sub-Tenon's capsule
- Peri-bulbar block
- Retro-bulbar block
- General anaesthesia

Preoperative medical treatment and/or discontinuation of treatment

This is similar to penetrating drainage surgery:

- Limit conjunctival scarring (virgin conjunctiva best - especially for deep sclerectomy)
  - Limit / discontinue chronic use of anti-glaucoma medications
  - Treat chronic blepharo-conjunctivitis and dry eye syndrome
- Manipulate immune system to lessen stimulus for fibrosis
  - Pre-treat with topical cortisone directly preoperatively
- Discontinue/change medications affecting clotting and bleeding time

Aspirin and other anti-platelet medications
Warfarin

Procedures

Description of technique

Viscocanalostomy and deep sclerectomy: similarities

- For good exposure of the surgical area, both procedures require a traction suture, which can be placed in the cornea or under the superior rectus.
- A conjunctival flap is raised either limbus- or fornix-based.
- Fashion a rectangular or parabolic 5 x 5 mm, one-third thickness limbal-based scleral flap extended 1.5 mm into clear cornea.
- Remove a second, deep scleral flap in a parabolic or equilateral triangle form at a depth allowing visualisation of the darker colour of the ciliary body below the scleral fibres.
- Remove the deep scleral flap to form an empty space: 'scleral lake', 'sub-scleral lake' or 'aqueous decompression space' where aqueous humour collects before its drainage. This dissection is in the plane of the scleral spur and Schlemm's canal (SC).
- SC is externalised and its external wall removed.
- Dissect anteriorly by gently pulling the internal scleral flap with forceps with counter traction on the bed of the canal with a triangular cellulose-sponge. Cleavage should occur between the corneal stroma and Descemet's membrane.
- Advance this dissection 1-1.5 mm anteriorly until only a thin layer of Descemet's membrane separates the surgical plane from the anterior chamber. This provides outflow resistance.[15] Evidence of aqueous outflow through the trabecular-Descemet's membrane is mandatory.
- To increase aqueous outflow across this membrane, remove the inner wall of SC either by gentle peeling with forceps or by careful scraping of its bed.[2,18,21]

Viscocanalostomy and deep sclerectomy: differences

- In VC,[9,11] a high-molecular-weight viscoelastic substance (Healon GV) is injected into the exposed ostia of the SC to enlarge the canal. Use the specific blunt 150-micron cannula to inject Healon GV into the SC: position the cannula tip just in front of Schlemm's canal ostia; after the ostia have been dilated with viscoelastic, insert the tip less than 1 mm into the canal; repeat these gentle injections 6-7 times per side.
- In VC, paracentesis removes aqueous from both anterior and posterior

chambers. The first scleral flap is then sutured in a watertight manner and viscoelastic is injected into the 'scleral lake' at the end of the procedure in order to prevent fibrin cross-linking. The conjunctival flap is then sutured.

In non-penetrating deep sclerectomy with external trabeculectomy there is no need for injection of viscoelastic. The crucial part of this procedure is the external trabeculectomy; this involves the selective removal of the external part the trabecular meshwork (TM) which is mainly involved in aqueous outflow resistance (the inner wall of SC and the adjacent TM layers), while leaving intact the innermost TM layers.[2,18,21] The procedure requires careful scraping of the bed of SC with a forceps. This leads to the removal of a homogenous external trabecular membrane in one coherent plane that allows aqueous humour to egress through the remaining inner trabecular layers.[6,7,18] Alternatively the external trabecular tissues can be removed by trabecular aspiration.[17] The first scleral flap may be loosely sutured followed by closure of the conjunctival flap.

Non-penetrating deep sclerectomy: surgical adjuvants

To keep the scleral lake open, different implant devices have been used. First was the Aquaflow implant (STAAR, Collagen Glaucoma Drainage Device), a highly purified porcine collagen dehydrated into a cylinder (2.5 x 1 x 0.5 mm).[6,7] Placed radially in the centre of the deep sclerectomy dissection, as far anteriorly as possible to be in contact with the trabecular-Descemet's membrane it is secured with a single 10/O nylon suture. The superficial scleral flap is sutured loosely over this implant with two 10/O nylon sutures. The device swells rapidly from its dehydrated form once exposed to aqueous fluid. It is resorbed within 6 to 9 months after surgery;[5] it is claimed to inhibit bleb fibrosis.[6]

A similar device is the reticulated hyaluronic implant (SKGEL, Corneal, 3.5 mm long, 450 μm thick). Its biocompatible material is composed of cross-linked sodium hyaluronate derived biosynthetically (bacterial fermentation of a natural wild strain Streptococcus) and hydrated with phosphate buffer. Sutured to the floor of the deep sclerectomy with two buried 10/O nylon, the device is covered by the superficial scleral flap. Absorption time is unknown in humans,[27] but the surgical space appears to be visible at 4 months by using UBM.[8]

The recently developed the T Flux implant (Ioltech Lab) has a 4 mm arm length, 2.75 mm body height and is 0.1-0.3 mm thick. This creates a draining canal along each arm, which is inserted into the openings of SC. The drain is secured onto the scleral bed with a 10/O nylon suture passed through a hole in its arm. It is made of Poly Megma, a highly hydrophilic acrylic, and is designed to provide active drainage by means of capillarity and osmosis.

In order to maintain the decompression space, some surgeons use a sponge soaked in 5-fluorouracil (5-FU)(50 mg /ml)[7,16] or mitomycin-C (MMC)[36] directly applied to the bed of the deep sclerectomy to inhibit fibrosis at the level of the superficial scleral flap.

Non-penetrating deep sclerectomy: surgical adjuvants to maintain intra-scleral space

- Collagen Glaucoma Drainage Device (STAAR).
- Reticulated hyaluronic implant (SKGEL).
- T Flux implant (Ioltech Lab).
- 5-fluoro-uracil or MMC soaked sponge to bed of deep sclerectomy.

Mechanisms of action

Deep sclerectomy: aqueous percolates through the trabecular / Descemet's membrane to reach the scleral lake and then the subconjunctival space. Probably aqueous outflow facility is increased by damage to the inner wall of SC and adjacent trabeculum. While filtering blebs are common in DS, they are usually more diffuse or smaller than trabeculectomy blebs.

A supraciliary hypoechoic area suggesting aqueous drainage into the subchoroidal space has been reported in 60% of DS eyes with external trabeculectomy.[8,27]

Viscocanalostomy: SC enlargement with viscoelastic aims to enhance aqueous egress through the cut ends and previously non-functional sectors of SC to collector channels. Injection of viscoelastic into SC not only dilates the canal and associated collectors, but also disrupts the walls of SC and adjacent trabecular layers.[46] The procedure may act as a trabeculotomy. As in deep-sclerectomy, external filtration and uveoscleral absorption also may be involved in lowering IOP.[32]

Duration of surgery

NPGDS is a more complex procedure than trabeculectomy and takes longer (25-45 minutes).

Learning curve / surgeon dependence

NPGDS is difficult, demanding and more complex than trabeculectomy. It requires knowledge of angle anatomy, good surgical skill, and a long learning curve. Microscopic analysis of the deep scleral flap has shown that even if the surgeon was trained in NPGDS, the procedure was wrongly made in 64% of operated eyes: the dissection level was too deep in 29% of cases (with trabecular tissue excised) and too superficial in 35% of the eyes (with no signs of SC).[22] An example of this learning curve is a series of studies from the same clinic, showing success rates rising from 0% in 2001, through 30% in 2002, to a final 40% in 2003.[26,30,34]

Postoperative management

Topical medications

For at least six weeks post-operatively:

- Topical antibiotic.
- Topical corticosteroid.
- Mydriatics are unnecessary (lack of intraocular inflammation) and relatively contraindicated as they increase the risk of iris incarceration.
- Miotics can be used for 3-4 weeks to minimise iris incarceration, especially if trabecular perforation has occurred.

Postoperative IOP is frequently low for the first 7-14 days (5-10 mmHg); with no AC shallowing or choroidal effusion, no intervention is required.

Anti-scarring treatments / interventions

Increased IOP in the early postoperative period can be from steroids, iris incarceration in the filtration site or to insufficient permeability of the trabecular-Descemet's membrane. Gonioscopy and ultrasound biomicroscopy (UBM) examination are helpful. Iris incarceration often leads to pupillary distortion: suspect if the IOP is high and the bleb flat; treat with Argon laser iridoplasty (100-500 micron spot size, 0.1 to 0.2 second duration, 300-400 mW).

With an open angle and high IOP despite steroid discontinuation, suspect insufficient permeability of the trabecular-Descemet's membrane. This is most frequent 6-8 months post-operatively. An Nd:YAG goniopuncture is required. With a gonioscopy contact lens the aiming beam is focused on the semi-transparent trabecular-Descemet's membrane, which often has a concave appearance. In the free running Q-switched mode with a power of 4-8 mJ, 4 to 15 shots are applied. An uncommon but most relevant complication from this is iris incarceration, especially if the IOP is not lowered with medications before treatment and if digital massage is performed afterwards. It can be treated by Argon laser iridoplasty.

As in trabeculectomy, complications from conjunctival scarring are managed with supplemental 5-flurouracil injections.

In late failure, when needling and/or goniopuncture have proven to be ineffective, the choice of a second procedure depends on the surgeon's preferences and the reason(s) for failure of the original procedure. Some surgeons opt for trabeculectomy with mitomycin-C and others for repeat NPDS with mitomycin-C.

Levels of evidence

Deep sclerectomy (DS)

Table 1 summarizes results with DS[7,10,12,14-16,19,23,35,37,38,43,44] and Table 2 summarizes results from studies comparing DS with trabeculectomy.[12,20,24,28,29,45]

Retrospective studies

These studies are not easy to compare because criteria for success differ, length of follow-up varies, surgical techniques are different and patient composition is not uniform.

DS lowers IOP usually to the mid - high teens. While IOP control may be better when a device is implanted compared with no device, intra-operative 5-FU achieves a similar IOP level.

Goniopuncture effectively lowered IOP over 24 months. Various goniopuncture rates after sclerectomy have been reported, and that rate increases with longer follow up. Lachkar[38] reported a rate of almost 50% by six years. Ablation of the inner part of SC during surgery seems to decreases this rate. Laser goniopuncture is a minor post-operative procedure, equivalent to laser suture lysis post-trabeculectomy; it is not a 'complication' of NPGDS. Goniopuncture effectively converts the technique from non-penetrating to 'perforating', producing a staged penetrating procedure.

Unroofing SC (*i.e.*, removing its outer wall) can damage the inner wall as well; resulting micro-perforations may well allow aqueous to percolate through the thin Descemet's / trabecular membrane with the anterior chamber remaining deep. While the term 'non- penetrating' surgery may not be accurate, it suggests overall integrity of the innermost trabecular meshwork layers so that the anterior chamber is not open macroscopically, the AC remains deep and sudden decompression of the eye is avoided.

'Perforation' is used when surgery creates an inadvertent hole with direct visualization of iris, and AC shallowing. Bas *et al.*[10] described an increased number of complications during a surgeon's learning period with perforation of anterior chamber as the main complication.

Useful comparison of these retrospective studies with those published about conventional trabeculectomy is difficult. Nouri Mahdavi *et al.*[4] reported an IOP control for trabeculectomy of 48% and 40 % at 3 and 5 years respectively, based on criteria of IOP = < 20 mmHg AND a minimal IOP reduction of 20%. If the criterion for success was an IOP of 20 mmHg or less, the probability of IOP control was 91% and 81%, 3 and 5 years after surgery. Migdal *et al.*[3] reported a higher success rate, possibly because their patient cohort had not had long-term medical treatment.

Table 1. Summary of outcomes for deep sclerectomy.

N	FU	IMPLANTS/ ANTFIBROTICS	IOP (PRE)	IOP (POST)	SUCCESS <21MMHG	GP	5FU	AUTHOR	JOURNAL
148	13,3±5,8	ci			68%	no		Demailly 1997	Int Ophthalmology
55	7,2±3,5	no			69%	no		Demailly 1997	Int Ophthalmology
15	8	ci	22,6±6,9	16,2±3,9	66%	yes		Hamard,1999	J Fr Ophthalmol
50	14.3	no			81%	no		Massy 1999	J Fr Ophthalmol
44	24	ci	26,7±7,3	11±4,4	69%	no		Mermoud 1999	J Cataract Refract Surg
100	36	ci	27.8	13±3,8	45%	no		Karlen,1999	Br j Ophthalmol
34	5.3			15,3±3,5				Bas, 1999	Bull Soc Belge Ophthalmol
86	46	no	30.4	15.35	44%	no		Dahan, 2000	J Cataract Refract Surg
105	60	ci	26,8±7	11,8±3	62%	no	Yes, 23,8%	Shaarawy ,2001	J Cataract Refract Surg
105	60			16,7±5,7	77%	no		Whishart,2003	Acta Opthalmol Scand
52	48	ci	23,3±7,2	12.7	63%	no	no	Shaarawy ,2003	Br J Ophthalmol
52	48	no	25,6±4,9	14	34%	no	no	Shaarawy, 2003	Br J Ophthalmol
13	24	ci		17,8±2,8		no		Neudorfer, 2004	Ophtalmic Surg Lasers Imaging
13	24	ci+MMC 3'		15,8±5,6		no			
258	60	157ci,90 5FU	24,47±5,92	15,8±3,79		Yes(47,3%)	Yes, 7%	Lachkar,2004	Eur J Ophthalmol
105	96	ci	26,8±7,7	12±3	57%	Yes 51 pt	Yes, 23.8%	Shaarawy,2004	J Cataract Refract Surg

ci= collagen implant, MMC= mitomycin C, 5FU= fluorouracil, GP=goniopuncture

Table 2. Summary of studies that compared deep sclerectomy with trabeculectomy.

		N	FU	IMPLANTS/ ANTFIBROTICS	IOP PRE-OP	IOP POST-OP	SUCCESS		%5FU POST-OP	GP	AUTHOR	JOURNAL
DS		44	24	CI	26,7-7,3	13,8-3,7	69%	<21	9 Pt	10 Pt	Mermoud, 1999	J Cataract Refract Surg
TR		44	24		25,4-7,3	11,9-4,4	57%	<21	10 Pt			
DS		39	12	NO	27,9-5,9	15,6-4,2	93.20%	<21		Yes , 10,3%	EL Sayyad, 2000	Ophtalmology
TR		39	12	NO	28,2-4,7	14,1-4,6	94.20%	<21	5FU(43,6%)	Slide		
DS		17	18					<21			Chiselita, 2001	Eye
TR		17	18					<21				
DS		20	24	CI	22.9	13,9-4,5	40%	<21	7	9 Pt (45%)	Ambresin 2002	J Glaucoma
TR		20	24	NO	29.3	12,9-4,8	45%	<21	2			
DS		11	12	Hyaluronate, MMC 0,02%		11.5					Schwenn, 2004	Ophthalmologe
TR		11	12	MMC 0,02%		11						
DS		45	36	NO	25,84-3,66	18,71-2,9	42.50%	<22	17(37,77%)	NO	Kozobolis, 2002	J Glaucoma
DS	MMC	45	36	MMC 0,2 mg/ml	27,64-4,53	15,96-1,71	50%	<22	13(28,88%)	NO		

ci= collagen implant, MMC= mitomycin C, 5FU= 5-fluorouracil, GP= goniopuncture

Prospective studies

A few studies have compared penetrating and non-penetrating filtering surgery. Once again, the wide variety of surgical procedures makes valid comparison difficult.

In trabeculectomy, ‘on the table’ assessment of the rate of filtration by anterior chamber irrigation plus adjustment of scleral flap suture tension reduces early complication rates. Laser suture lysis and/or release of sutures can yield hypotony.

Similarly, in non-penetrating surgery, the intra-operative peeling of the inner wall of SC and/or the post-operative use of Nd:YAG goniopuncture enhances chances of achieving lower IOP levels. Such goniopunctures do not decompress the eye acutely. In one study comparing NPGDS with and without adjunctive intra-operative MMC (0.2 mg/ml for 2.5 min), a significant increase in pressure reduction (42.2% versus 27.6%) and complete success rate (72.5% versus 42.5%) was found in the antifibrosis group.[29]

Two prospective, randomised studies, which compared trabeculectomy with DS combined with external trabeculectomy showed equivalent results.

El Sayad[20] included 78 eyes of 39 patients with bilateral primary open angle glaucoma. At 12 months, mean IOP reduction was 12.3 ± 4.2 mmHg with combined surgery versus 14.1 ± 6.4 mmHg for trabeculectomy alone, while an IOP < 21 mmHg was achieved in 92.3% in the combined group and 94.9% in the trabeculectomy eyes.

One study compared results of DS without external trabeculectomy with trabeculectomy[24] for 34 eyes of 17 patients with medically uncontrolled glaucoma. Statistically significant differences in post-operative IOP levels between the two groups were reported at 1, 2, 3, 6, 12 and 18 months: trabeculectomy yielded a lower IOP. At 18 months, IOP was 17.3 ± 1.2 mmHg following trabeculectomy and 20.9 ± 4.0 mmHg after NPDS. In this study the non-penetrating technique was different from the papers cited above: only the external wall of SC was removed without peeling its inner part and the adjacent trabeculum. YAG laser goniopuncture was not considered in the follow up.

Ambresin compared the efficacy of DS with collagen implant in one eye versus trabeculectomy in the fellow eye on 20 patients.[28] Trabeculectomy was studied retrospectively while DS prospectively. The mean pressure at 24 months was 13.9 ± 4.5 mmHg for DS and 12.9 ± 4.8 for trabeculectomy. Intraocular pressure below 21 mmHg without treatment was achieved in 40% in the DS group and in 45% in the trabeculectomy group. The DS group showed 50% less hyphema and choroidal detachment than the trabeculectomy group.

Viscocanalostomy (VC)

Table 3 summarizes results with viscocanalostomy[9,11,25,34,35,37] and Table 4 summarizes results from studies comparing viscocanalostomy with trabeculectomy.[26,30,31,33,36,39,40]

Table 3. Summary of outcomes for viscocanalostomy.

N	FU	fu mean	ADJUNC-TIVE	IOP PRE-OP	IOP POST-OP	SUCCESS	CRITERIA	5FU POST-OP	GP	AUTHOR	JOURNAL
33	10		no	27,7-9,5	12±3	86.20%	<21	no	no	Carassa,1998	Eur J Ophthalmol
214	64	35	no	47,4±13	16,85±8	82.70%	<22	no	no	Stegmann,1999	J Cataract Refract Surg
67	36		no	24,2±6,56	14,7±2,8	59%	<21	no	no	Sunaric-Megevand, 2001	Am J Ophthalmol
57	60		no	24.6	13.9	60%	<21	no	21 Pt (37%)	Shaarawy,2003	Br J Ophthalmolol
40	12		no	26,5±6,1	16,5±5,8	40%	<22	no	no	Luke,2003	Br J Ophthalmolol
105(27)	36		no	26,1±8,5	16,8±3	92.60%	<22	no	no	Wishart,2003	Acta Ophthalmol Scand.

Table 4. Summary of studies that compared viscocanalostomy with trabeculectomy.

	n	fu	ANTI-FIBROTICS	IOP PRE	IOP POST	SUCCESS	CRITERIA	5FU POST-OP	GP	AUTHOR	JOURNAL
VS	10	6	no	31,2±6,96	18,3±5,03	0.00%	<20	no	no	Jonescu-Cuipers,2001	Ophthalmology
TR	10	6	no	28,1±5,84	15,6±3,17	50.00%	<20	no			
VS	25	12	Healon-GV	24		64.00%	<21	8 Pt, 35%	12%	O'Brart, 2002	Br J Ophthalmol
TR MMC/5FU	25	12	MMC/FU	24.2		100.00%	<21	11 Pt 44%			
VS	30	12	no	27,2±6,9	17,1±5,4	30.00%	<22	no	no	Luke,2002	J Glaucoma
TR	30	12	no	26,9±6,4	15±3,5	56.70%	<22	no	36.70%		
VS	25	12		25±2,2	17,1±1,5	64.00%	<21	no		Kobayashi,2003	Graef Arch
TR MMC	25	12	MMC	24,8±2,6	12,6±4,3	88.00%	<21	no			
VS	25	24	no	24,75±6,73	16,29±5,10	76.00%	<21	no	no	Carassa,2003	Ophthalmology
TR	25	24	no	22,8±7,18	14,04±4,64	80.00%	<21	Yes			
VS MMC	25	12	MMC	25.7		60.00%	<21	no	13%	O'Brart,2004	Br J Ophthalmol
TR	25	12	No	27.9		91.00%	<21		Needling		
VS	25	36	no	36±8	17,8±4,6	35.30%	<21	no	no	Yalvac,2004	J Cataract Refract Surg
TR	25	36	no	37,7±9	16±7,07	55.10%	<21	no			

As for DS, a direct comparison between different studies is difficult, because criteria for success, length of follow-up and techniques are different. Nevertheless, VC seems effective in lowering IOP with a good safety profile.

When compared with trabeculectomy many of the studies lacked sufficient power to find significant differences between the procedures; nevertheless final IOPs seem higher after VC when compared with trabeculectomy.

Retrospective studies

Stegmann[11] reported results of VC in 214 eyes of 157 African patients with open-angle glaucoma and a mean pre-operative IOP of 47.4 ± 13.0 mmHg. After an average follow-up of 35 months, mean IOP was 16.9 ± 8.0 mmHg; 83% of eyes achieved an IOP less than 22 mmHg off all glaucoma medications.

Two recent studies showed viscocanalostomy a successful procedure in glaucoma secondary to uveitis. Miserocchi et al. found a complete and qualified success rate of 54.5% and 90.9% respectively, after 46 months of follow-up. Final IOP was 18.1 ± 11.6 mmHg.[41] Auer *et al*. performed NPGDS (including viscocanalostomy) on 14 eyes: complete and qualified success rates were 45.4% and 90.4% at 12 months. Final IOP was 12.1 ± 4.0.[42]

Prospective studies

Carassa *et al*.[9] reported a series of 23 VCs performed in 23 patients. In four eyes, the procedure was converted to trabeculectomy. Of the 16 eyes with IOP less than 21 mm Hg, mean IOP was 11.6 ± 4.4 mmHg.

Sunaric-Mégevand *et al.*[25] evaluated VC in 67 eyes of 67 consecutive patients with chronic open angle glaucoma (patients with angle closure, post traumatic, uveitic, neovascular and congenital glaucoma were excluded). Complete success was an IOP = < 20 mmHg with 30% or greater IOP reduction without ongoing medical or additional surgical treatment. Qualified success was an IOP = < 20 mmHg with further treatment or an IOP reduction less than 30% from preoperative level. The overall success rate was 88% at 1 year, 90% at 2 years and 88% at 3 years. The complete success rate was 68% at 1 year, 60% at 2 years and 59% at 3 years. No serious complications were reported in this series.

Luke *et al*., when comparing VC with and without a SKGel implant, showed a success rate (IOP < 22 mmHg without medications) of 40% in both groups at 12 months, with a very low complication rate.[34]

Shaarawy *et al*., in a 5-year follow up study, showed a final IOP of 13.9 mmHg and a complete success rate with IOP < 21 mmHg in 60% of the eyes. Goniopuncture was performed in 37% of the cases.[35]

Randomized controlled studies

Jonescu-Cuipers *et al.* in 2001, showed at 6 months, a complete success rate (IOP < 20 mmHg) of 0% after VC and 50% after trabeculectomy on 20 eyes.[26] The same group in 2002, showed an IOP < 22 mmHg without medications in 30% with VC and 56.7 after trabeculectomy group at 1 year on 60 patients. VC showed significantly less complications compared with trabeculectomy.[30] O'Brart showed a 1-year success rate (IOP < 21 mmHg on no medications) of 60% after viscocanalostomy and of 91% after trabeculectomy.[31]

In a 24-month controlled randomized trial comparing VC with trabeculectomy, Carassa *et al.*, reported similar final IOP levels of 14.1 ± 4.7 mmHg after viscocanalostomy and 16.3 ± 5.1 mmHg after trabeculectomy. No significant difference was found between the 2 procedure as for IOP < 21 mmHg (76% versus 80%) or < 16 (56% versus 72%) on no medications.[33]

A recent study by Yalvac *et al.* on 50 eyes followed for 36 months found similar results.[40] At 3 years, the mean IOP was 17.8 ± 4.6 mmHg in the VC group and 16.0 mmHg ± 7.07 in the trabeculectomy group ($P = .694$). Complete success (IOP 6 to 21 mmHg without medication) was achieved in 35.3% after VC and 55.1% after trabeculectomy ($P > .05$). Postoperative hypotony and cataract formation occurred more frequently in the trabeculectomy than in the VC group ($P = .002$).

O'Brart *et al.*, in a 20-month RCT comparing VC with trabeculectomy with adjunctive use of antimetabolites on 50 eyes, found a significantly lower complete success rate (IOP < 21 mmHg) after VC (34%) than after trabeculectomy (68%). Early transient complications such as anterior chamber shallowing and encysted blebs were more common in the trabeculectomy group ($p < 0.05$). Late postoperative cataract formation was similar between the two groups.[39]

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COMPARISON OF TRABECULECTOMY WITH NON-PENETRATING DRAINAGE GLAUCOMA SURGERY IN OPEN-ANGLE GLAUCOMA

Franz Grehn
(Presenter)

Franz Grehn

Consensus points

- Lower IOP can be achieved with trabeculectomy than with NPGDS.
- Short-term complications associated with NPGDS may be fewer and less severe.
- NPGDS is technically more challenging, with a longer operative time.
  Comment: Both procedures may require postoperative intervention.

Introduction

The main goal in glaucoma surgery is to achieve a constantly low intraocular pressure (IOP) with a low immediate and long-term complication rate. However, procedures that are more effective at lowering IOP may be associated with a higher incidence of complications. A balance between the complication profile and the need of an individual target IOP is to be considered when selecting a procedure for glaucoma surgery.

Deep sclerectomy and viscocanalostomy are two newly developed techniques that have been introduced for surgery in primary open-angle glaucoma. Both methods have been extensively studied in case series and in prospective randomized controlled trials and compared to trabeculectomy.

Indications

From the data available to date, the indications for non-penetrating glaucoma drainage surgery (NPGDS) include cases where the target IOP is set > 15 mmHg. This condition applies mainly for patients with early glaucoma who are at low risk of progression. Results from the Advanced Glaucoma Intervention Study

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(AGIS),[1] indicated that visual field progression on average was halted in patients where the IOP was below 18 mmHg at all postoperative office visits. This group of patients had a mean IOP of 12.4 mmHg. NPGDS has also been indicated in secondary glaucoma such as pseudoexfoliative, pigmentary, uveitic and traumatic glaucoma, but prospective randomized clinical trials are not yet available for these indications. Viscocanalostomy has also been largely used in the black population of South Africa.[2]

Surgical techniques

The similarities and differences between deep sclerectomy and viscocanalostomy, and their mechanism of action are described in more detail elsewhere in this volume. Postoperative management is essential in all types of glaucoma surgery to improve long-term outflow and to overcome problems of the wound healing process. For both deep sclerectomy and viscocanalostomy, goniopuncture with the Nd:YAG laser has been advocated when IOP increases beyond target IOP. As deep sclerectomy includes the concept of filtration, both needling and postoperative 5-FU injections have been used to improve outcome. In contrast, the mechanism of outflow in viscocanalostomy is assumed to take place through improvement of natural outflow routes (widening of Schlemm's canal and collector channels). In trabeculectomy, postoperative management with needling and antimetabolites are current adjuncts to obtain low target IOPs.

Evaluation of studies

Only randomized prospective studies are selected in this overview. Success in terms of IOP control is evaluated only without medication. Although additional medication after surgery may be helpful for the patient, from a scientific point of view the resulting IOP without medication allows a better comparison of various surgical glaucoma procedures. In addition, complication rates are taken into consideration and should be regarded as a counterbalance for interpretation of the results.

Randomized studies: Viscocanalostomy

Lücke *et al.*[3] reported a prospective trial comprising 60 patients (60 eyes) randomized to either trabeculectomy or viscocanalostomy. With the IOP criterion of ≤ 21 mmHg, after 1 year the success rate of trabeculectomy was 56.7% and the success rate of viscosanalostomy was 30.0%. In the viscocanalostomy group, choroidal detachment, shallow anterior chamber and cataract progression did not occur, and hyphema and hypotony were less frequent than in the trabeculectomy group. However, 17 of 30 eyes (56.7%) of viscosanalostomies developed a visible filtering bleb and in 10.8% a rupture of the trabeculodescemetic membrane was desribed. No Nd:YAG laser goniopuncture was applied in any of the viscocanalostomy patients.

O´Brart *et al.*[4] found similar success rates in their prospective study of 50 eyes randomized to viscocanalostomy and trabeculectomy. Follow-up varied between 12 and 24 months (except one case = 6 mo). Intraoperative 5-FU or MMC was allowed for the trabeculectomy group. Postoperative interventions such as needling and postoperative 5-FU injections were allowed in both groups. Without medication, the IOP success rate defined as ≤ 15 mmHg was 76% in the trabeculectomy group and 26% in the viscocanalostomy group. In a recent paper by O´Brart *et al.*,[5] the success rate defined as IOP < 21 mmHg without medication was 68% in the trabeculectomy group and 34% in the viscocanalostomy group after average follow-up of 20 months.

Carassa *et al.*[6] compared eyes of 50 patients randomly assigned to trabeculectomy or viscocanalostomy without intraoperative antifibrotics in either group. The trabeculectomy group could receive 5-FU injections or suturelysis but Nd:YAG laser goniopuncture was not allowed in the viscocanalostomy group. After 24 months of follow-up, IOPs ≤ 21 mmHg or a drop in IOP of > 6 mmHg, without additional topical IOP lowering medication, was achieved in 80% of trabeculectomy eyes and in 76% of viscocanalostomy eyes. IOPs of ≤ 16 mmHg (> 6 mmHg) were achieved in 72% of trabeculectomy eyes and in 56% of viscocanalostomy eyes, respectively. Mean IOP was 2-3 mmHg lower in the trabeculectomy group over the whole observation period.

A 3-year follow-up study with 50 eyes (patients) was presented by Yalvac *et al.*[7] An IOP of 6-21 mmHg without medication was found in 55.1% of the eyes with trabeculectomy and in 35.3% of the eyes with viscocanalostomy. The mean difference between the groups in final IOPs was 1.7 mmHg.

Adjunctive Mitomycin C was used in the trabeculectomy arm of a randomised paired eye study by Kabayashi *et al.* comparing trabeculectomy to viscocanalostomy in 50 eyes of 25 patients.[8] After 12 months of follow-up, 88% of trabeculectomy eyes and 64% of viscocanalostomy eyes achieved an IOP ≤ 20 mmHg. The mean final IOP differed by 4.5 mmHg between procedures.

Randomized studies: Deep sclerectomy

El Sayyad *et al.*[9] randomized 78 eyes of 39 patients to either trabeculectomy or deep sclerectomy. After 12 months, IOP ≤ 21 mmHg without medication was found in 85% of the trabeculectomy eyes and 79% of the deep sclerectomy eyes. Laser suturelysis and goniopuncture were permitted in the follow up period if required. Such intervention was performed in 43.6% of the trabeculectomy eyes and in 10.3% of the deep sclerectomy eyes, respectively. The difference in mean IOP between both procedures was 1.5 mmHg.

In a similar study, Chiselita[10] compared trabeculectomy to deep sclerectomy in 34 eyes of 17 patients. With a 30% IOP reduction as the primary endpoint, survival was 85.2% in the trabeculectomy and 40.8% in the deep sclerectomy group. The mean postoperative IOP difference between the two procedures was 3.6 mmHg after 18 months of follow-up. No data are given regarding the untreated postoperative success rates. The number of medications was significantly lower in the trabeculectomy group as compared to the deep sclerectomy group (0.29 and 0.88, respectively).

Deep sclerectomy with collagen implant in one eye (prospective) was compared to previously performed trabeculectomy (retrospective) in the other eye of the same patient in 20 cases by Ambresin *et al.*[11] Without additional medication, an IOP < 21 mmHg was achieved in 45% of the trabeculectomy eyes and in 40% of the deep sclecectomy eyes. The mean follow up was 24 months, but follow up time was highly variable. In addition, the follow up was retrospective in the trabeculectomy eye and prospective in the deep sclerectomy eye. A similar series was published by Mermoud[12] with a detailed evaluation of complications with both procedures.

Complication rate

Immediate postoperative complications including hypotony, choroidal effusions, shallow or flat anterior chambers are lower for NPGDS compared to trabeculectomy. These are, however, related to surgical technique. Long-term complications after trabeculectomy include cataract formation, iris prolapse or incarceration, and bleb encapsulation.

Cataract is usually considered an easily treatable condition, as clear cornea phacoemulsification gives favourable results. However, cataract surgery performed even late after successful filtering surgery may result in loss of IOP control in half of the cases and hence may significantly influence the long term success rate.[13]

Table 1 summarizes some of the main complications according to the randomized studies reported.

Interpretation of the results

In the randomized studies comparing trabeculectomy to viscocanalostomy, as well as those comparing trabeculectomy to deep sclerectomy, trabeculectomy always achieved a higher success rate whatever cut off limit or percentage reduction of IOP was set. However, the absolute success rates differed significantly between studies. The quotient of sucess rates within a individual study, defined as: (Percentage success trabeculectomy / Percentage success NPGDS) and the corresponding individual success criteria is given in Table 2 for the above mentioned studies.

Table 1. Main complications after trabeculectomy

Procedure	flat ch/hypot.	choroidals	encapsulation.	cataract	iris incarc.
Trabeculectomy/Viscocanalostomy					
Lücke *et al.*[3]	37% / 20 %	20% / 0%	¢	7% / 0%	¢
O´Brart *et al.*[4]	20% / 4%	¢	16% / 13%	20% / 0%	4% / 4%
Carassa *et al.*[6]	20% / 0%	4% / 0%	¢	¢	0% / 13%
Yalvac *et al.*[7]	28% / 4%	¢	12% / 4%	28% / 8%	¢
Kobayashi *et al.*[8]	20% / 0%	¢	¢	8% / 0%	¢
Trabeculectomy/Deep sclerectomy					
Procedure	flat ch/hypot.	choroidals	encapsulation.	cataract	iris incarc.
El Sayyad *et al.*[9]	8% / 0%	¢	¢	3% / 0%	0% / 5%
Chiselita[10]	18% / 0%	¢	6% / 6%	24% / 0%	¢
Ambresin *et al.*[11]	20% / 0%	30% / 0%	¢	25% / 10%	¢
Mermoud *et al.*[12]	18% / 0%	20% / 5%	29% / 34%	25% / 9%	¢
Gandolfi *et al.*[13]	¢	¢	¢	50% / 12%	¢

Table 2.

Author	Quotient TE/NPGDS	IOP criterion
Viscocanalostomy		
Lücke *et al.*[3]	1.87	≤ 21 mmHg
O´Brart *et al.*[4]	2.92	≤ 15 mmHg
O´Brart *et al.*[5]	2.00	< 21 mmHg
Carassa *et al.*[6]	1.05	> 6 mmHg d•21 mmHg
	1.29	> 6 mmHg d•16 mmHg
Yalvac *et al.*[7]	1.56	> 6 mmHg < 21 mmHg
Kobayashi *et al.*[8]	1.38	≤ 20 mmHg
Deep sclerectomy		
El Sayyad *et al.*[9]	1.08	≤ 21 mmHg
Chiselita[10]	2.09	30% IOP reduction
Ambresin *et al.*[11]	1.13	< 21 mmHg
Gandolfi *et al.*[13]	1.11 (1.58)	< 21 mmHg (no gp)
	1.28 (2.83)	< 18 mmHg (no gp)
	1.96 (15.00)	< 16 mmHg (no gp)

Conclusions

NPGDS has a lower immediate and long term complication rate compared to trabeculectomy, particularly when cataract formation is considered. Cataract formation due to glaucoma surgery with subsequent need of cataract surgery is currently underestimated as a source of later bleb failure in trabeculectomy. Even clear cornea phacoemulsification may considerably interfere with bleb function in previously well filtering trabeculectomies. According to most of the randomized controlled clinical trials NPGDS is considerably less effective in lowering the intraocular pressure in an intermediate time period, such as 3-7 years. With the need for target IOPs in the low teens for advanced glaucoma damage, NPGDS may not be adequate to halt progression.

There is still need to improve details of the technique and evaluate modifications such as stripping of the inner trabecular sheath, separating devices to keep the scleral lake open and the use of stents into Schlemm's canal. The necessity to improve the long-term efficacy of IOP control of NPGDS has also prompted the use of antifibrotics although a filtering bleb is not the primary goal in NPGDS. Filtration is also the mechanism of action when Nd:YAG laser goniopuncture is added to routine postoperative interventions as advocated by most of the surgeons using deep sclerectomy and even viscocanalostomy.

Although the general value of NPGDS has become more clear during the last years through a number of randomized prospective studies that compared NPGDS to trabeculectomy, there is still need for further detailed evaluation of the technical details and standardization of the technique to improve the learning curve and the efficacy of these procedures.

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CYCLODESTRUCTION

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Consensus points

- Of the cyclodestructive procedures, laser diode cyclophotocoagulation with the G-probe is the procedure of choice for refractory glaucoma when trabeculectomy and drainage implants have a high probability for failure or have high risk of surgical complications.
- Transscleral cyclophotocoagulation may be considered when maximal medical therapy, trabeculectomy or drainage implant surgery is not possible due to resource limitations.
- Prior to transscleral cyclophotocoagulation treatment, transillumination of the globe to reveal the location of the ciliary body may be useful, especially in morphologically abnormal eyes.
- Post-operative treatment consisting of topical steroids and cycloplegics is suggested to minimize post-operative complications and discomfort.
  Comment: The effectiveness of treatment should be assessed after 3-4 weeks, at which time re-treatment may be considered.
  Comment: Less intense laser therapy on a repeated basis rather than a single high dose treatment is suggested to minimize complications of treatment.

Cyclodestructive procedures aim to decrease aqueous humor secretion by damaging the ciliary processes, thereby reducing intraocular pressure (IOP). Modalities for cyclodestruction include cyclocryotherapy, and cyclophotocoagulation, using the Nd:YAG or diode laser. Endoscopic, non-contact and contact modes of cyclophotocoagulation are available, with the contact diode mode most widely used.

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Cyclocryotherapy

Mechanism of action

Cyclocryotherapy[1] refers to ciliary body damage by freezing. The damage is produced by transscleral application of temperatures of -80° C directed at the ciliary processes.[2] Rapid cooling results in the formation of intracellular ice crystals, which upon thawing leads to larger crystals which are highly destructive to cells. Hemorrhagic infarction results from obliteration of micro-circulation within the frozen tissue. Studies of cyclocryotherapy in human and primate eyes show destruction of epithelial and capillary components of ciliary processes with scar replacement, as well as blood-aqueous barrier breakdown.[3]

Indications

Cyclocryotherapy is rarely used today, except in the absence of an available laser for cyclophotocoagulation, or in conjunction with retinal cryotherapy. It is generally reserved for eyes with severely limited visual potential.

Surgical technique

Retrobulbar anesthesia is required. The anterior edge of a cryoprobe 2.5 mm in diameter, attached to a nitrous oxide or carbon dioxide cryosurgical unit, is placed 1 mm posterior to the limbus. Firm pressure is applied to the globe to reduce the insulative properties of the sclera. Once the probe temperature has been lowered to -60 to -80° C it is left in place for 60 seconds. The ice ball that forms is allowed to thaw until the probe detaches from the globe. Five to seven applications are applied to 180 degrees of the eye, avoiding, if possible, the 3 o'clock and 9 o'clock meridians. Post-operative care consists of topical and possible subconjunctival steroids to reduce inflammation. If the IOP is not sufficiently lowered, the treatment can be repeated a month later. Generally a repeat treatment consists of 90° in an already treated area and 90° in a previously untreated area.

Cyclophotocoagulation

Background

Cyclophotocoagulation refers to ciliary body damage by laser energy.[4] The transscleral application of the Nd:YAG laser in the free running mode or with the diode laser causes thermal tissue injury to the ciliary body.[5] The diode wavelength of 810 nm has greater melanin absorption compared to the Nd:YAG laser at 532 nm. Histological studies in cadaveric eyes confirm ciliary process destruction with the Nd:YAG laser.[6-8] Transscleral lesions produced by the diode laser are similar to those produced by the Nd:YAG continuous mode, with blanching at the gross level, and coagulative necrosis microscopically.[9-11] Under direct visualization, *endoscopic* diode laser applications produce an active whitening and shrinkage of the ciliary processes.[12]

Mechanisms of action

Decreased Aqueous Production

Ciliary body disruption, ciliary epithelium loss, and inflammatory effects[13] result in decreased aqueous production.

Increased Aqueous Outflow

Some of the IOP lowering effect of cyclophotocoagulation procedures may be due to increased outflow. In an *in vitro* perfusion model, laser lesions placed 6 mm posterior to the limbus (well away from the ciliary processes) had an equivalent effect on outflow to that of laser lesions directed towards the ciliary processes.[14]

Comparative studies

Few controlled clinical trials evaluating the differences between these techniques have been done. Youn *et al.* prospectively compared diode transscleral cyclophotocoagulation (TSCP) to Nd:YAG transscleral cyclophotocoagulation and found them equivalent in efficacy and complications.[15] To our knowledge, there are no prospective studies comparing TCP vs. endocyclophotocoagulation (ECP).

Indications for Transscleral Cyclophotocoagulation (TSCP)

There is no clear consensus on the indications for transscleral cyclophotocoagulation. While some suggest that it be reserved exclusively for refractory or endstage glaucoma, others suggest that any indication for drainage device surgery is a potential indication for cyclophotocoagulation. A recent prospective randomized clinical trial in which drainage implant was compared to endoscopic cyclophotocoagulation showed equivalent success rates.[16] Cyclophotocoagulation may also be a temporizing measure in high risk eyes such as those with buphthalmos, or with active neovascular glaucoma, in preparation for other glaucoma surgery.

Available resources in a particular region or country for the treatment of glaucoma may also affect when cyclophotocoagulation is used. In a region with good access to health care, cyclodestruction may be reserved for those eyes that cannot undergo glaucoma drainage implant surgery. In countries with less access or in non-compliant patients, the procedure could appear earlier in the regimen. In areas without ready access to medications or other forms of surgery, cyclophotocoagulation has been suggested as potentially useful as primary treatment (before medications), or as the primary surgical treatment (after medications), for glaucoma. Preliminary results from one small study in Ghana, however, showed modest IOP-lowering with short follow-up, and a worrisome incidence of vision loss.[17] The risks of loss of vision, loss of light perception and hypotony from cyclophotocoagulation must be weighed against the risk of endophthalmitis and suprachoroidal hemorrhage from filtration surgery and drainage device surgery. Longer and larger trials are indicated to determine if there is a role for cyclodestruction in certain settings as primary treatment.[18,19]

The indications proposed by the Ophthalmic Technology Assessment Committee of the American Academy of Ophthalmology are listed below.[19]

1. Eyes in which trabeculectomy and/or drainage implants, even with antibrotic agents, have high probability of failure:
   1.1. Eyes in which trabeculectomies with MMC and/or drainage implants have previously failed.[20-22]
   1.2. Eyes with silicone oil injection for complicated retinal detachment repair.[23,24]
2. Eyes with poor visual potential at risk of progression, pain, or complications (*e.g.,* corneal) of raised IOP, where medical treatment is ineffective or inappropriate.
3. Patients whose general medical condition precludes invasive surgery.
4. Patients who refuse to undergo more aggressive surgery (*i.e.,* filtration surgery or drainage implants).
5. Emergent situations (*i.e.,* acute onset of neovascular glaucoma).

Indications for endocyclophotocoagulation

Indications for endocyclophotocoagulation differ from the transscleral approach, because it is an intraocular procedure requiring an operating room, sterile technique, increased instrumentation, and is more technically demanding. It carries risks inherent to any intraocular surgery, such as intraocular hemorrhage and endophthalmitis.

Candidates include patients with uncontrolled glaucoma in an eye undergoing pars plana vitrectomy for vitreoretinal disease[25] or penetrating keratoplasty.[26,27] It may be considered after repeated failure of transscleral diode-laser[28] or when drainage implant is being considered,[16] or at the time of cataract surgery instead of performing a filtration procedure.[53]

Surgery

Transscleral cyclophotocoagulation (TSCP)

Pre-operative assessment

There is no specific preparation for TSCP. Glaucoma medications are taken up to and including the day of surgery and in high risk cases are often continued until an IOP response to treatment is observed. TSCP is an extra-ocular procedure, with virtually no risk of postoperative infection unless burns are sustained to the ocular surface. Because of the mild transient uveitis quite common following TSCP, some practitioners use preoperative topical corticosteroids or non-steroidal anti-inflammatory medications. Systemic medications that predispose to bleeding (such as antiplatelet agents or anticoagulants) are not usually discontinued prior to treatment, but use of these drugs can be associated with peri- or post-operative intraocular bleeding due to tissue disruption.

Anesthesia

TSCP requires effective peri-ocular infiltration of local anaesthesia (LA). Most practitioners use a peri-bulbar block or even a retro-bulbar block to provide adequate LA. Sub-Tenons' LA may also provide a good combination of regional and truly local anaesthesia. Some claim that sub-conjunctival anaesthesia is adequate, presumably by a truly local effect on ciliary body innervation. A potential disadvantage of both sub-Tenons' and sub-conjunctival anesthesia is the chemosis and/or sub-conjunctival bleeding that can occur with these techniques. Such bleeding may make it difficult to achieve the conjunctival and scleral compression required for effective passage of laser energy through the ocular surface. General anaesthesia (GA) is preferred by some practitioners especially for bilateral treatments, treatment in children, and for treatment in patients who for whatever reason are unsuitable for local anesthesia.

Surgical Technique

Diode CPC

Technological advantages of the diode CPC include portability and low maintenance of the laser unit and use of a standard power outlet. The procedure may be done in an office, a minor procedure room, or in the operating room. The patient may be seated, reclining, or supine. Sedation may be used to augment the local anesthetic. An 810 nm diode laser with the G-probe is placed 1.2 mm behind the limbus perpendicular to the sclera.

Standard laser settings are 2 seconds duration and 2000 mW, although longer (4 seconds) applications of lower (1250 mW) are sometimes used. The energy is adjusted to just avoid audible 'pops'. Six to eight applications are applied per quadrant for 180 to 360 degrees, with the applications spaced approximately one half width of the probe tip apart. Some surgeons skip the 3 and 9 o'clock position to avoid the long posterior ciliary nerves. Excessive ocular surface pigmentation (including conjunctival and scleral pigmentation) is associated with increased risk of surface laser absorption; such uptake of laser energy has the potential to cause partial or full thickness burns to the ocular surface and also reduces laser transmission to the ciliary body. It is best to avoid TSCP in areas of ocular surface pigmentation. Burns that are placed too anteriorly, may cause more inflammation.

As shown by the Bristol-Norwich study[29] high-number/high-energy/long-duration treatments are best avoided, particularly in eyes with neovascular glaucoma, to reduce the chance of hypotony. Less laser therapy more often rather than a single high dose treatment may be preferable.

The effectiveness and risks of damaging the ciliary body region seem to be variable and may relate to how much tissue is devitalized or how precisely the localized damage is applied. Thus, transillumination using a bright focal light source from the opposite limbal area can reveal the location of the ciliary body with reasonable accuracy and avoid misplaced burns. This can be very useful in morphologically abnormal eyes such as those with microphthalmos, sclerocornea or buphthalmos and is recommended as a standard approach to burn localization.

Postoperative management

Use of postoperative medications after cyclophotocoagulation is directed to the prevention and treatment of discomfort and of the postoperative complications of inflammation, cystoid macular edema, hyphema, and in the case of endoscopic cyclophotocoagulation, intraocular infection. Classes of medications that have been used include cycloplegics and corticosteroids.[30-35] The most common cycloplegic used postoperatively is atropine 1% [30,34] usually twice daily for approximately 2 weeks. Sometimes, atropine ointment is applied immediately after cyclophotocoagulation. Topical steroids have included prednisolone and dexamethasone ranging from four times a day to hourly (initially) in the postoperative period, for a period of 2-4 weeks.[30-35] Routine use of topical antibiotics has been limited to endoscopic cyclophotocoagulation.[35]

Typically, pre-operative glaucoma medications, including oral carbonic anhydrase inhibitors, are continued in the short-term postoperative period, and tapered according to the IOP response. Miotics are often discontinued to prevent augmentation of the inflammatory response and synechiae formation. Consideration may also be given to discontinuation of prostaglandin agents, given their potential pro-inflammatory effects. Patients should be evaluated within one week of the procedure to measure the IOP, assess the degree of inflammation, and adjust IOP lowering medications and anti-inflammatory medications. The effectiveness of the treatment should be assessed at 3-4 weeks.[30-35]

Retreatment and further post-operative care

Retreatment rates after contact transscleral cyclophotocoagulation have ranged from 7% to as high as 55%,[31-35] with variable periods of follow-up. As most of the published series are retrospective, no specific criteria for retreatment have been defined. However, generally retreatment was undertaken when the IOP had once again increased to a clinically unacceptable level on maximal tolerated medications.

Retreatment after ECP was relatively infrequent (5 of 68 eyes) in the series by Chen *et al.*[26] The mean extent of initial ECP treatment (268 degrees of ciliary processes) in those eyes was not significantly different from those not requiring retreatment. In the pediatric series by Neely and Plager,[36] the retreatment rate was higher at 25% (9/36) and one-third of those eyes (3/9) had a favorable IOP response.

Other interventions that may be necessary after cyclophotocoagulation, but not necessarily a result of the cyclophotocoagulation, include cataract surgery, filtering surgery (trabeculectomy, drainage device surgery), and other surgical procedures needed to manage complications, such as hypotony.[31-35] The series of contact Nd:YAG transscleral cyclophotocoagulation cases by Lin *et al.*[37] has long-term follow-up (mean of 5.85 years), and it was found that 22% of patients required retreatment and 30% required an additional intervention other than cyclophotocoagulation. The interventions included drainage device surgery (8.8%), enucleation (7.3%), and cyclocryotherapy (16.2%), and trabeculectomy (4.4%).

Outcomes

Many eyes undergoing cyclodestruction already have vision loss to a level at which monitoring the visual field is impossible, and the optic nerve is damaged to the point where further morphological changes can not be detected or the optic nerve cannot be visualized well. Evaluation of outcome is further compromised because many of these eyes have ocular comorbidities that cause vision loss apart from glaucoma. The outcomes of greatest interest are intraocular pressure control, preservation of visual acuity and visual field, optimization of vision related quality of life, and absence of complications.

Diode TSCP appears to reduce intraocular pressure in two-thirds of patients with severe, medically uncontrolled glaucoma in the short, medium, and long-term,[22,30,32,33] with a frequent need for re-treatment. Success rates in children are lower.[44-46] Long-term data with Nd:YAG TSCP shows approximately 50%

success rate for IOP control at 10 years.[35] Vision is retained in at least two-thirds of patients.

Complications

The most common complication of diode TSCP is transient mild inflammation. Less common complications include mild to moderate discomfort, conjunctival hyperemia, conjunctival burns, hyphema, and uveitis, corneal decompensation and graft failure, decreased visual acuity, chronic hypotony, and phthisis. Rare complications include malignant glaucoma, retinal detachment, chronic severe uveitis, vitreous hemorrhage and severe pain. There is a single recent report of sympathetic ophthalmia.[52]

One of the major concerns about TSCP and other methods of CP is the 'unexplained' visual loss that is said to occur. It is a clinical impression that this visual loss occurs less frequently with diode laser TSCP than with cyclocryotherapy and Nd:YAG TSCP. When vision loss does occurs it is probably due to cystoid macular edema (CME), and this may be considered to be analogous to the way in which CME occurs with pharmaceutical agents such as adrenergic agents or PG analogues; presumably increased uveo-scleral outflow has an effect on RPE function and macular physiology such that it promotes CME.

Hypotony is another serious side effect of cyclodestruction. Particularly in eyes with high degrees of outflow obstruction, such as neovascular glaucoma, or complete angle closure, substantial portions of the nonpigmented ciliary body epithelium must be permanently ablated to achieve lower IOP. However, there is frequently a brittle relationship between outflow and inflow in these eyes, predisposing to hypotony if too much of the ciliary body is damaged. Treating in multiple sessions and never treating the entire circumference of the ciliary body may mitigate the long-recognized risk of excessive hypotony.

Future research needs

1. Laboratory – based

Further work on mechanisms of IOP lowering of cyclophotocoagulation, and a determination of the relative contribution of effects on outflow vs inflow.

2. Clinic -based

We need high quality data to address the questions of:

a. The role of cyclodestruction as a primary procedure for glaucoma;
b. The relative value of the different modes of cyclodestruction;

c. The role of endocyclophotocoagulation in eyes undergoing cataract surgery, and the relative roles of cyclodestruction and drainage devices in the management of glaucoma.

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COMPARISON OF CYCLOPHOTOCOAGULATION AND GLAUCOMA DRAINAGE DEVICE IMPLANTATION

Kuldev Singh

Kuldev Singh
(Presenter)

Consensus points

- Mechanism of action:
  a. Glaucoma drainage devices (GDD) increase aqueous humor outflow.
  b. Cyclodestructive procedures reduce aqueous production.
- GDD implantation requires greater surgical training and is a more extensive procedure than cyclodestruction.
- GDD implantation requires greater postoperative care than cyclodestruction.
- GDD implantation should be performed in an operating room while cyclodestruction can be performed in the office, minor surgery area or in the operating room.
- The marginal cost of GDD implantation is more expensive than cyclodestruction. The initial cost of cyclodestruction related to the purchase of the device used for the procedure may be greater than that with GDD implantation.
- Preoperative visual acuity may impact which of these two treatment modalities are preferred. All other things being equal, GDD are more commonly used for patients with better visual acuity and/or visual potential relative to cyclodestructive procedures. Strong evidence in support of this practice is not currently available.

Both glaucoma drainage device implantation and cyclophotocoagulation are generally reserved for eyes with refractory glaucoma that have failed one or more conventional surgical procedures: trabeculectomy in adults and in some cases, goniotomy or trabeculotomy in children. The mechanism of action between these two procedures differs fundamentally in that cyclodestructive procedures are considered to reduce aqueous humor inflow whereas aqueous shunting procedures with glaucoma drainage devices increase aqueous humor outflow. There is no convincing evidence or consensus opinion to guide one in choosing between these two procedures in most clinical situations.

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There are, however, some consensus opinions regarding the relative merits of these two treatment modalities. While glaucoma drainage device implantation is performed, almost exclusively, in the operating theatre, cyclophotocoagulation can be performed both in the office as well as in an operating room. There may be cost savings associated with performing a procedure in the office relative to in the operating room. In addition, diode laser cyclophotocoagulation is a more rapid procedure and requires considerably less operator skill.

The perioperative care associated with drainage device implantation is far greater than that needed with cyclophotocoagulation, especially when the latter is performed in an office or clinic setting. The cost associated with this perioperative care, including the extra time taken by the physician, would make cyclophotocoagulation more attractive if all other things were equal. The minimal postoperative care required with cyclodestruction makes it particularly attractive for patients who have difficulty making frequent visits to the ophthalmologist.

While the ability to titrate postoperative IOP following glaucoma drainage device implantation is not as precise as that seen with modern trabeculectomy, consensus opinion suggests that it is more predictable than IOP lowering following cyclophotocoagulation. Thus in eyes that have advanced glaucomatous optic nerve damage but have not lost fixation, drainage device implantation is more likely to be associated with IOP lowering to a predetermined target IOP range than a single cyclophotocoagulation treatment. With repeat cyclophotocoagulation treatment, the ability to titrate IOP to a safe level increases although this benefit must be weighed against the added risks of repeat therapy. The mean postoperative IOP may or may not differ substantially between eyes undergoing drainage device implantation and those receiving cyclophotocoagulation. The range of postoperative IOP is likely to be greater in eyes receiving cyclophotocoagulation. While there is consensus opinion on the differences in postoperative IOP predictability between cyclophotocoagulation and drainage device implantation there is no adequately powered head to head prospective randomized study to confirm this hypothesis.

The general aim of glaucoma therapy in patients who have remaining useful vision is to predictably lower IOP into a range where the likelihood of further progressive optic nerve damage is minimized. This approach may also be used in patients who subjectively state that they do not have useful vision in the eye being treated. In this latter group of patients, however, IOP lowering to a precise target may not be as critical as lowering IOP to a range where there will be no ocular discomfort and the eye will not require enucleation, either for comfort or cosmetic reasons. One would generally not argue against choosing the more precise IOP lowering therapy for all patients, regardless of the visual potential, if all other things were equal. But when it comes to comparing cyclophotocoagulation and drainage device implantation, all other things are not equal. Cyclophotocoagulation is generally cheaper, easier to perform and is associated with less postoperative management.

Many of the postoperative complications associated with drainage device implantation are different than those seen with cyclophotocoagulation. Drainage device implantation, by virtue of being a filtration procedure, is associated with a significantly greater risk of postoperative ocular infection relative to procedures that work primarily by decreasing aqueous humor production such as cyclophotocoagulation. This risk of infection becomes very high if any portion of the drainage device is exposed due to insufficient conjunctival closure at the time of surgery or postoperative wound leakage. Other postoperative complications that are associated with drainage device implantation but generally not seen following cyclophotocoagulation include ocular motility disturbances, flat anterior chamber, hyphema, vitreous hemorrhage, suprachoroidal hemorrhage, choroidal detachment, fibrous or epithelial downgrowth, tube related corneal decompensation and dellen. Complications that may be seen in eyes that receive either cyclophotocoagulation or drainage device implantation include persistent ocular inflammation, cataract and hypotony. It is generally accepted that there is a greater incidence of phthisis in eyes undergoing cyclophotocoagulation, especially when repeated, than in eyes receiving drainage device implantation. There has been no adequately powered, head to head prospective study to confirm this opinion. The possibility exists that clinical impressions regarding differential rates of phthisis following these two procedures may be related to patient selection. For the reasons outlined earlier, there is a tendency to perform drainage device implantation in eyes that have relatively better visual acuity and cyclophotocoagulation in eyes with less visual potential. There is consensus regarding this practice pattern which limits the validity of retrospective comparisons between these two procedures given the selection bias introduced by non random allocation to treatment groups.

The decision to perform drainage device implantation or cyclophotocoagulation in eyes that have failed trabeculectomy depends upon many of the factors listed above. One factor that has not been discussed, which may be the most important determinant of the treatment that is ultimately chosen, is the patient's view regarding what is most appropriate. There is consensus agreement that the decision to choose drainage device implantation or cyclophotocoagulation in eyes that may benefit from these procedures is amongst the most influenced by patient preferences in the surgical management of glaucoma. Factors such as the usefulness of existing vision, the likelihood of success, the inconvenience of perioperative care and the potential complications of the intervention are given varying degrees of importance by different patients based upon their own subjective views of what is and what isn't important. The manner in which this information is presented to the patient by the practitioner may also influence how patients perceive the risks and benefits of these interventions.

In summary, the lack of available scientific information regarding the relative merits of cyclophotocoagulation and glaucoma drainage device implantation make it difficult to reach consensus on several issues pertaining to these procedures. The few areas where consensus can be reached should be tempered by the great patient variability in perceiving the relative merits of these procedures which ultimately determines what therapy is chosen.

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CONCLUDING REMARKS

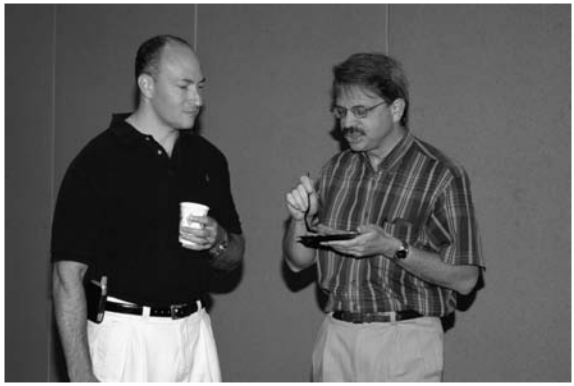
No single surgical procedure for open angle glaucoma is uniformly safe and effective. The surgical approach therefore has to be individualized and is highly dependant on patient characteristics, the stage of the disease as well as the availability of health care resources. Improvements in surgical outcome are derived not only from optimizing surgical technique but also from improvements in our ability to modulate the ocular response to surgery.

Recently, there has been considerable interest in new surgical treatments for open angle glaucoma and some have rapidly gained acceptance in clinical practice. Although some of these new modalities are promising, one should always keep in mind that it is essential to appraise all new surgical treatments with similar rigor to that demanded of new medical treatments.

This consensus in glaucoma surgery for open angle glaucoma provides valuable guidelines for surgical management and has highlighted areas where scientific evidence at present is lacking. The availability of data from well-designed and carefully conducted surgical studies in glaucoma will further shape our practice.

J.G. Crowston and R.N. Weinreb

Development Panel discussion



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