PERSPECTIVE

Primary surgery for primary open angle glaucoma – justified or not?

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The goal of glaucoma treatment is to prevent (further) visual loss. It is assumed that this visual loss occurs because the intraocular pressure (IOP) is 'too high for the eye'.¹ Long term follow up of successfully treated glaucoma patients reveals that despite reducing IOP to 'normal' levels visual loss can still occur (see Palmberg² for review). Comparison of the percentage of each cohort studied that loses field and its IOP shows that the proportion of each group still 'progressing' after surgery diminishes the lower the mean IOP.² It seems that for most effective glaucoma control, 'target' IOPs must be set at the middle or low normal range.¹ (It should be emphasised that this is not a new concept, most writers on glaucoma have insisted that low IOPs should be sought in eyes with glaucomatous cupping, and the worse the disease the lower the 'target pressure'.) It can be difficult to achieve and maintain these target pressures with medical or laser treatment whereas surgery may be more likely to do so.

The current approach to a glaucoma patient is to initiate treatment with topical antiglaucoma drugs, resorting to laser or fistulising surgery only if the 'target pressure' is not reached. As it can be many months before such a decision is taken, and the glaucoma continues to progress, the question arises as to whether fistulising surgery should not just be an early option but the primary option – why fiddle while Rome burns? In this review I will discuss whether primary (initial) surgery has a role in the management of primary open angle glaucoma (POAG). For the purpose of the review primary surgery will refer to fistulising surgery given as the initial treatment to a newly diagnosed case of POAG.

I will cover the following areas: (a) Does primary surgery achieve the 'target IOP'? (b) Does primary surgery produce better results than 'delayed' surgery? (c) Are the side effects and complications of primary surgery acceptable? (d) Are the financial costs of primary surgery acceptable?

Does primary surgery produce the necessary target IOP?

Primary surgery for POAG has not been seriously considered in Western countries until recently. In the 1980s Cairns suggested this approach, concerned that the long term application of topical antiglaucoma medicines could have a detrimental effect upon the eye. Although his observations were based upon extensive personal experience they were not generally accepted. Smith conducted a long term trial comparing Scheie's operation with medical treatment. His results with analysis on the Lister perimeter showed benefit from surgical treatment, while those patients who fared worst initially received medical treatment and, only later, had surgery when medical treatment failed.³ It was not until the results of two recent long term studies comparing primary surgery with medical treatment that the concept of primary surgery for POAG began to be seriously considered.^{4,5} Both studies were conducted in the United Kingdom. Although

both studies began before the concept of a 'target IOP' was developed, the pressures obtained may be related to today's 'target' requirements.

The studies differed to a certain extent in their protocols. The earlier (Glasgow) study compared primary surgery with the conventional treatment given in west Scotland at the time. This conventional treatment involved medical treatment sufficient to control IOP at what was considered an adequate level. Should this level not be achieved or should there be optic disc or visual field change despite apparent intraocular pressure control then surgery was advised. There was no specific failure level for IOP control in this 'medical' group, but, in principle, it was agreed that an IOP of 20–22 mm Hg did not by itself constitute adequate pressure control except where it represented a marked reduction from pretreatment levels in an eye with mild field loss or cupping; in short, the indication for surgery was if the IOP was considered unsafe for the eye. It should be noted that the final management decision was left to the consultant in charge of an individual case. The mean IOPs achieved by those patients undergoing surgery whether or not they had had prior medical treatment was the same at 15 mm Hg.⁶

The second study also randomly assigned patients to primary treatment with medicine, laser, or surgery. However, the criterion for failure was rigidly defined as repeated IOPs exceeding 21 mm Hg.⁵

The IOP results from the second, Moorfields, study⁵ showed one failure within the surgical group (occurring within the first 3 months of surgery). This patient was rerandomised and given additional treatment. No other patient in this group required any antiglaucoma treatment. A mean IOP of 15 mm Hg for the whole group was achieved within the first 3 months after the operation and maintained for the duration of follow up. Annual daytime diurnal curves for this group confirmed the maintenance of 'success' by the criteria of the trial. For this cohort it appeared that a reasonable target pressure had been achieved.

In contrast, patients in the other two groups were more difficult to control and had a higher failure rate. A comparison of the mean IOPs for all the patients in the surgery group with all the patients in the other two groups (including those who 'failed' and were rerandomised to additional treatment) showed a consistent 5–6 mm Hg IOP difference throughout the duration of the trial.

From these two studies it would appear that primary surgery will produce an average IOP which would be adequate for most 'target pressures'. This is less certain although still possible with medical treatment.

Does primary surgery produce better results than 'delayed' surgery?

In this context the term 'results' can refer to IOP control, and/or visual field preservation.

INTRAOCULAR PRESSURE

The IOP results from primary surgery obtained in the trials quoted above^{4,5} do not differ markedly from those seen after fistulising surgery performed when medical treatment has been found inadequate.² However, to compare results from different patient groups operated on by different surgeons from different centres can be misleading. It is more instructive to look at the results from one centre. To date such a prospective trial has not been undertaken. Jay⁴ prospectively studied the results of patients cared for by nine consultant surgeons in five Glasgow hospitals and looked at the effect of medical treatment on the results of later, 'delayed' surgery.⁶ Eighty per cent in the primary trabeculectomy group did not require treatment as their IOP remained below 21 mm Hg; 8% were treated despite an IOP <21 mm Hg for potential or actual visual field deterioration; 6% had less than a 6 mm Hg IOP reduction ('unchanged'); and an additional 6% had 'mild residual raised pressure'. By contrast in his delayed surgery group 74% did not require further treatment; 19% did for potential or actual visual loss; and 7% for 'mild residual raised pressure'. He felt that 2–3 years of medical therapy did not make the operation less successful.

At Moorfields we conducted a retrospective review of patients with POAG who had received at least 1 year of medical treatment before undergoing surgery.⁷ The demographic data and postoperative course of the group were compared with patients undergoing primary surgery. The operations for both groups were carried out over the same period by the same surgeons using the same technique. The criterion for success was the same, an IOP <22 mm Hg without additional medical treatment. The demographic data were very similar for the two groups. The success rate in this 'delayed surgery' group after 1 year of follow up was only 75%, and all the failures occurred in the first 3 months and could be attributed to the initial wound repair. In addition, a higher mean IOP was seen in this group than in the primary surgery group. From this and one other study of glaucoma triple procedures⁸ we felt that prolonged medical treatment could be a 'risk factor' for the success of subsequent fistulising surgery.

Studies on the conjunctiva in eyes with glaucoma show that those treated medically have signs of chronic inflammation in the episclera and conjunctiva when compared with untreated control eyes.^{9,10} Long term follow up of the delayed surgery group⁷ has now been performed, and shows that the failure rate increases with time (De Vivero C, Stuermer J, Broadway D, Hitchings RA. Delayed glaucoma surgery, how successful is it? To be submitted). This suggests progressive long term fibrosis of the fistula site can and does occur. The Moorfields results suggest that lower IOPs for longer periods would be obtained from primary surgery than 'delayed' surgery, and that the cause of early and perhaps late failure is progressive fibrosis of the fistula site (remember, none of these eyes received treatment with an antimetabolite).

VISUAL FIELDS

The Glasgow study compared the visual field loss in its primary surgery group with that seen in its delayed surgery group and found that for 'mildest disease' (stage 1 on their classification) the visual field deterioration was less in the primary surgery group.⁴ It was noted that the median time to surgery was 4 months when poor response to medical treatment was the sole criterion for operation, and 11 months when high IOP plus visual field loss was identified. The most severe progressive loss in those with mild disease occurred with the most prolonged attempts (mean 23 months) at IOP control.⁶

In the Moorfields study visual fields were obtained using both suprathreshold perimetry (Friedmann) and for the last

3–4 years of the study, computer assisted perimetry (Humphrey). The Humphrey fields were obtained without the strict prestudy training requirements now considered necessary.¹¹ In consequence a learning curve was seen with these patients during the study period. Linear regression analysis of individual retinal locations¹² showed improvement in performance occurring in up to the first six visual fields. Deterioration 'set in' for many of these eyes after that but the period of follow up was too short to separate the three groups.¹³

The Friedmann field data were analysed for spots missing 0.4 log units below threshold and for absolute defects. Analysis of the data showed no difference between the starting scores for the three groups.¹⁴ By 27 months into the trial significant differences had appeared – the surgery group remaining unchanged, whereas the medical and laser groups were showing steady deterioration.¹⁴ A comparison of the starting vs final visual field scores for the three groups showed a continuation of that process with significant deteriorations in the laser ($p < 0.001$) and medical ($p < 0.001$) but not the surgery group (Wilcoxon paired test). Furthermore, stratification of patients from all three groups into IOP bands shows an inverse relationship between IOP and visual loss (Midgal CM, Gregory W, Hitchings RA. The primary treatment trial, visual field results. Presented at the UK College of Ophthalmologists' meeting, May 1993), a finding predicted by an earlier review.² It should be noted that these results included patients with all stages of visual loss at the outset, suggesting that all would be protected by a rapid control of IOP and not just those with early visual loss.

The results from the Glasgow and Moorfields studies show that for POAG the early establishment of an IOP of around 15 mm Hg offers greater protection against progressive visual loss than an IOP at the upper limit of normal. They also show that progressive visual field loss detectable by relatively unsophisticated perimetry is present at least by 2 years from the onset of treatment if the IOP is allowed to remain at the upper limit of normal. Sophisticated computer assisted perimetry could be expected to detect this progression more quickly.

Are the side effects and complications acceptable?

Every operation on the eye carries some risk. With modern anaesthesia and sutures the risk of modern fistulising operations has been minimised but not eliminated. All patients for whom surgery is recommended need to be informed of that risk. In the Moorfields trial 20% of the 'medical' group were rerandomised to one of the other two treatments during the 5 year follow up period. That 20% failure rate would have been higher if the 'target' pressure had been significantly below the 22 mm Hg which comprised failure in the study. A sizeable number of patients will require surgery despite initial medical treatment. Primary surgery means that every patient with POAG could be exposed to that risk.

While it can be accepted that better IOP control can be obtained with surgical treatment there remains abiding concern about the visual and other side effects. Postoperative visual fluctuations from hypotony or glare from lens opacities are perceived problems. These are subjective observations made by the patient and difficult to measure. Snellen acuity measured during the Moorfields study showed that after surgery correctable vision fell by an average of half a line by comparison with the fellow unoperated (and often non-glaucomatous) eye. There was no significant difference between the acuities of the surgical or medically treated groups, however, suggesting that visual changes occurred after medical treatment too. There seems little doubt that operating on a diseased eye will induce more intraocular

effects than operating on a healthy eye. Cataract formation will be one of those effects. It has to be said that visual change after both surgery and medical treatment, although small in terms of Snellen acuity, can be upsetting to the patient. For the surgery group it may not be reversible. It also has to be remembered that the visual change was principally that seen in eyes without significant lens opacities, eyes with them are likely to have rapid progression after surgery.

In addition to the visual effects a minority will suffer other complications, including delayed reformation of the anterior chamber, hypotony, and possible infection; all worrying for the surgeon as well as the patient.

Patients need to be told that if they need fistulising surgery they will lose a small amount of vision which may not be correctable.

A number of patients in the Moorfields trial suffered from bilateral glaucoma; one eye was entered into the study and operated upon. These patients had a uniform request, after instilling drops into one eye, that they be operated on in the second eye, if only to free them from the need to instil the drops.

Are the costs acceptable?

To equate the financial costs of primary surgery with those of medical treatment followed, perhaps, by surgery depends on many local factors. These include the cost of continued medical treatment, the cost of office visits, and the cost of surgery and postoperative visits. In the United Kingdom such costing exercises have been performed for both the Glasgow and the Moorfields trial (Ainsworth *et al*¹⁵ and Hitchings *et al*, unpublished data). In both trials the 5 year costs were analysed based on the known outcomes of the trials. Both showed that surgery was no more expensive than medical treatment and therefore, fiscally, an acceptable alternative.

Discussion

This paper has reviewed the results that could be obtained from primary fistulising surgery for POAG in the light of 'target pressures', gains in terms of visual preservation, risks, and costs. It has in general terms come down in favour of primary surgery as treatment for POAG. In Western countries additional questions need to be asked before the ophthalmologist can recommend this treatment to the next patient: (a) Would I get the same results? (b) Is this approach possible in every case? (c) Is primary surgery necessary in every case?

WOULD I GET THE SAME RESULTS?

It is an old maxim among glaucoma surgeons that 'I do the operation that does best in my hands'. The results noted above are for particular groups of surgeons with expertise varying from resident to consultant ophthalmologist operating on white patients with POAG who had a mean presenting IOP >30 mm Hg and who had not been treated before. The differences in IOP results between primary and 'delayed surgery' at Moorfields could be attributed to the presence of one risk factor, namely, previous medical treatment. Any significant risk factor for failure will reduce the chance of a 'target pressure' being achieved. The known and quantified risk factors which are assumed to enhance the wound healing response include: previous conjunctival surgery,¹⁶ aphakia,¹⁶ previous medical treatment,^{7,8} prior glaucoma surgery, and prior laser therapy.¹⁶ They may also include race,¹⁷ age,¹⁸ chronic blepharitis, and the starting IOP.¹⁶

To achieve the same IOP results in the presence of known risk factors which enhance wound healing it is necessary to restrict this healing response. A 1 month's course of topical

fluoromethalone combined with cessation of topical sympathomimetic therapy will reverse the conjunctival inflammatory changes.¹⁹

In the short term 5-fluorouracil has been shown to enhance the success rate of medium term IOP control in 'high risk' eyes.²⁰ However, long term follow up of eyes treated in this way suggests that after 2 years the success rate falls,²¹ presumably due to slowly replicating fibroblasts. Such eyes may well need long term 'top up' of antimetabolite to prevent this from occurring. It is of interest that the higher dose of 5-fluorouracil used in the Fluorouracil Filtering Surgery Study trial has not shown the late decay in success rate (Parrish RK, personal communication 1992) while preoperative mitomycin may also avoid the problem of late failure although at the increased risk of hypotony and infection. To obtain the same long term IOP results in the presence of these risks it is necessary to suppress both the initial wound healing response, and to be prepared to 'top up' the antimetabolite effect during follow up.

The fact that both the Glasgow and Moorfields results produced similar mean IOPs would suggest that, providing no serious risk factors for failure are present, between centre differences in operative technique will not seriously affect the outcome.

All surgical patients run a risk of major intraoperative complications; it has to be left to the individual surgeon to decide whether these risks are acceptable in his hands.

IS PRIMARY SURGERY POSSIBLE IN EVERY CASE OF POAG?

In Western countries primary surgery can be difficult to achieve because most cases of POAG referred for surgery have already received medical treatment. It is not clear which topically applied medicines and/or preservatives induce chronic episcleral inflammation. Recent studies suggest that sympathomimetics and miotics rather than β blockers are mostly to blame, and perhaps also the preservative benzalkonium chloride.^{22,23} Nor is it clear for how long they have to be applied, although the effect is likely to be cumulative⁸ and would only affect surgical results after years rather than months of treatment. The presence of this inflammation and any other of the risk factors noted above means that pharmacological manipulation of wound healing will be required to achieve long term target IOPs for these pretreated eyes. Such pharmacological manipulation of the wound healing response does mean, however, that target pressures can still be achieved.

IS PRIMARY SURGERY NECESSARY IN EVERY CASE OF POAG?

Many eyes will have their IOP kept around 15 mm Hg on medical treatment alone. For these eyes it is reasonable to assume that visual decay will be slow, if it occurs at all and that surgery would not be necessary. For these patients primary surgery means an extra and unnecessary risk. For others the same results will not be achieved, or control of IOP is lost after a prolonged period of successful treatment. For these eyes continued medical treatment while the IOP is not around 15 mm Hg could allow further visual loss to occur, as well as introduce an extra risk factor for failure of subsequent surgery.

The timing of fistulising surgery when IOP 'targets' are not achieved will depend on two actuarial analyses: firstly, will the patient treated medically and not reaching an 'ideal' target pressure suffer clinically significant visual loss in his or her lifetime? The second question follows the first; will I be able to measure the rate of visual loss in this patient? The need for surgery in an elderly patient with moderately elevated IOPs who is a good performer on computer assisted perimetry, must be minimal. In contrast the younger,

preoccupied businessman who has no patience for perimetry is likely to need it. The eye which has had the IOP lowered from 35 to 20 mm Hg rather than 15 mm Hg may be more likely to decline, but at a slower rate than if left without treatment. Conversely an eye which deteriorates at a pressure of 18 mm Hg is unlikely to slow its rate of decline if treatment only reduces the IOP to 16 mm Hg. The patient may lose IOP control during follow up, or target pressures may need downward revision if continued field loss occurs. It would need to be remembered that prolonged medical treatment would add another risk factor for failure although the use of antiproliferative agents should suppress this heightened wound healing response.

It would seem reasonable therefore that the 'new' POAG patient need *not* be subjected to primary surgery, but could be tried on medical treatment and evaluated over time. If it was not possible to achieve a target pressure (presumably around 15 mm Hg) the patient should be considered for 'early' surgery. A decision not to operate at this stage would be based on the actuarial analyses noted above although the treating surgeon would have to take responsibility for withholding surgery.

Conclusion

The results of the British studies comparing primary surgery with conventional treatment for POAG have demonstrated the importance for visual field preservation of reaching a target pressure of around 15 mm Hg. The studies showed that for the cohorts studied this IOP level could be achieved with primary surgery, without the use of antifibrotic agents. While medical treatment can also achieve these target pressures any delay in so doing may increase the risk of visual loss, while prolonged medical treatment adds a risk factor for failure of glaucoma surgery, and increases the need for antifibrotic agents. The decision to treat medically has to be taken with these considerations in mind.

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