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Factors influencing cataract formation after Nd: YAG laser peripheral iridotomy

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FACTORS INFLUENCING CATARACT FORMATION AFTER ND:YAG LASER PERIPHERAL IRIDOTOMY

BY **James C. Bobrow MD***

ABSTRACT

Purpose: The benign nature of Nd:YAG laser peripheral iridotomy (LPI) has recently been questioned because of increased cataract formation and other complications. This retrospective study includes 522 consecutive eyes of 275 individuals (group 1) on whom LPI was performed between January 1, 1991, and December 31, 2000, for which at least 5 years of complete follow-up was available.

Methods: Patients were all operated on by a single surgeon using a Zeiss Meditec Nd:YAG laser for all procedures. Total energy delivered, degree of cataract at time of LPI and at last visit, interval to cataract surgery if needed, intraocular pressure (IOP), use of ocular and systemic medications, and associated medical and ocular conditions were recorded. One hundred-fifty eyes of 75 individuals without evidence of glaucoma were used for comparison of outcomes (group 2).

Results: Group 1A consisted of 146 eyes (27.9%) that underwent cataract surgery 5.9 (95% CI, 5.6-6.3) years after LPI. The remaining 376 eyes composed group 1B. Groups 1A and 1B differed significantly in patient age, grade of cataract at time of LPI, and length of follow-up. Groups 1 and 2 differed significantly in patient age and frequency of use of topical medication to control IOP, but not in frequency of cataract surgery.

Conclusions: LPI does not increase the incidence of cataract surgery, and cataract surgery should not be used as primary therapy for angle-closure glaucoma. Patients who have LPI are at greater risk of requiring therapy to control IOP, even if they have a successful procedure.

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INTRODUCTION

The ophthalmologic practice of Robert Drews, MD, has had a long association with the performance of peripheral iridectomy (PI) and laser peripheral iridotomy (LPI). In the era of surgical iridectomy, Drews[1] followed the clinical course of 58 eyes of 32 patients for an average of 8.9 years following the procedure. He noted that 59% had cataract preoperatively, 48% progressed, and 26% ultimately needed surgery. He also summarized the results from 14 additional studies.

Bobrow[2] then reported on the change in the frequency of PI after the advent of YAG laser procedures. Analyzing data taken from Drews' patients, he found that the number of cases of acute angle closure declined precipitously in the 15 years following the acquisition of a Nd:YAG laser, but that the number of procedures climbed exponentially from 58 to 748 because of the new equipment and its lack of side effects. In addition, the indications for LPI changed from acute attacks and positive provocative tests to anatomically narrow angles with gonioscopic evidence of apposition.

A review of the effect of Nd:YAG laser on cataract formation prompted Lim and associates[3] to publish their finding that cataract progressed after LPI and created a second type of blindness. They suggested that in patients with angle closure and incipient cataract, cataract surgery might be the better initial procedure to deepen the chamber angle and to clear the visual axis permanently.

Yip and colleagues[4] commented in a subsequent volume that creating a situation in which correction of the second most frequent cause of blindness (ie, glaucoma) with a procedure that is likely to increase the frequency of the leading cause of blindness (ie, cataract) has serious implications, especially given that approximately one-half of glaucoma blindness comes from angle closure, with its highest frequency in East Asia. They also pointed out that the frequency of cataract in the population used as a control group may not have been comparable to the patients who had laser procedures.

To address these concerns in a primarily Caucasian population, a study was undertaken of patients who had LPI performed by a single surgeon over a 10-year period.

METHODS

A retrospective analysis was made of a consecutive series of 522 eyes of 275 patients who underwent LPI between January 1, 1991, and December 31, 2000 (group 1). All procedures were performed by a single surgeon using a Zeiss Meditec Nd:YAG OPL-3 laser, the third one to enter the United States after US Food and Drug Administration approval in 1981. All patients had either anatomically narrow angles, positive provocative testing, acute angle-closure glaucoma (AACG), fellow eye of an eye with acute angle closure, or evidence of chronic angle-closure glaucoma (CACG). The patients in group 1 were first evaluated with a slit-lamp biomicroscope using a Zeiss 4-mirror goniolens. The angles were considered capable of closure if the anterior trabeculum was not visible in at least 3 of 4 mirrors. Provocative testing consisted of measuring intraocular pressure (IOP) before and 20 minutes after instilling tropicamide 1% ophthalmic drops in Caucasians and tropicamide 1% and phenylephrine 2.5% ophthalmic drops in African Americans, Asian Americans, and Hispanics. After 20 minutes, if the IOP increased by more than 6 mm Hg, the test was considered positive after

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*Presenter.
Bold type indicates AOS member.

confirmation of angle apposition by gonioscopy. Following the dicta of Chandler and Grant [5] and Becker and Shaffer,[6] if one eye had a positive test and the eyes appeared symmetric, LPIs were performed bilaterally. Both eyes were included in the study. AACG was diagnosed when markedly elevated IOP, pain, congestion, fixed pupil, and reduced acuity were noted. The patients included in this study were those whose attacks were treated with pressure-lowering agents, both topically and orally. Prophylactic LPI was performed immediately on the fellow eye and on the eye with the acute attack as soon as possible. CACG was diagnosed when the angles appeared closed on gonioscopy, the pressure was normal either without or with medication, and prominent iris bombé was present. In situations in which pressure was uncontrolled, the eyes were excluded from this study because they underwent primary filtering surgery.

During the same period (January 1, 1991, through December 31, 2000), a group of 150 eyes of 75 patients (group 2) was chosen as a comparison group. These patients were taken consecutively from new patients whose first examination in this office occurred starting in January 1991 and who had no evidence of angle-closure glaucoma problems.

Group 1 was then divided into group 1A, consisting of eyes that had subsequent cataract surgery during the follow-up period, and group 1B, consisting of the remainder of eyes that did not have surgery.

Each patient had a complete ophthalmologic examination, and the initial best-corrected visual acuities, IOP, degree of cataract, refractive error, and presence of other systemic or ocular diseases were tabulated. For the laser patients, the diagnosis, method of determining the need for laser surgery, total amount of laser energy, intraoperative or postoperative complications, medications (ocular and systemic), and additional diagnoses were recorded when available. All patients in both groups then had the same information taken from the record at their most recent examination.

The degree of cataract was recorded at each examination using an additive scale. The examiner has always routinely evaluated each portion of the lens on a scale of 1 to 4: anterior cortex, nucleus, posterior cortex, and posterior subcapsular. The grades were added and used as a scale from 1 to 16 to indicate the degree of cataract. If a group 1 eye came to cataract surgery, the interval from the time of LPI was calculated. In group 2, the time to cataract surgery was measured from first visit.

Approval was obtained from the Human Studies Committee of Washington University School of Medicine for the review of the deidentified data, obtained by having the study coordinator extract the information from the record onto an Excel spreadsheet (Microsoft, Redmond, Washington), removing the patients' names and record numbers, and replacing them with study numbers. The data were analyzed using Stata 8.0 SE (College Station, Texas). Statistical significance was achieved if $P < .05$.

RESULTS

Table 1 displays the demographic characteristics of the eyes that underwent LPI (group 1), and Table 2 shows similar data for the comparison group 2. Table 3 demonstrates the comparison of groups 1A and 1B.

TABLE 1. DEMOGRAPHIC DATA FOR EYES (n=522) OF PATIENTS WHO HAD PERIPHERAL IRIDOTOMIES (GROUP 1)

Right:left	262:260
Caucasian:non-Caucasian	478:44
Male:female	120:402
Average age	69.2 yr
Cataract surgery	146 (28.0%)
Diabetes	99 (19%)
Anatomically narrow angles	380 (73%)
Positive provocative test	59 (11%)
Acute angle closure	22 (4%)
Fellow eyes	22(4%)
Chronic angle closure	39 (8%)
Medications for ↑IOP at last visit	192 (37%)

IOP, intraocular pressure.

The patients in group 1A had significantly greater cataract on presentation. Their refractive error (spherical equivalent) was less hyperopic, indicating that increased nuclear sclerosis had begun to occur. The patients were slightly older than those who did not have surgery, and they were followed up for a longer period of time, presumably because of their secondary procedures. Of importance,

they did not receive a higher level of laser energy to penetrate their irides, nor did either group experience significant complications from bleeding, nonpenetration, need for secondary laser treatment, or postoperative uveitis. They also did not require additional medication to control IOP more frequently than eyes in group 1B. No significant differences were found in frequency of other systemic or ocular diagnoses or IOPs before or after LPI. The frequency, however, with which eyes were treated for elevated IOP was significantly different (Table 4).

TABLE 2. DEMOGRAPHIC DATA FOR COMPARISON GROUP (GROUP 2)

Total patients	75
Total eyes	150
Male:female	74:76
Caucasian:non-Caucasian	138:12
Average age	79.0 yr
Diabetes	21 (14%)
Cataract at first visit	1.54
Cataract surgery	32 (22%)
Medications for ↑IOP at last visit	22 (15%)
Years of follow-up	6.7

IOP, intraocular pressure.

In group 1B (Table 3), the male:female distribution and the ratio of Caucasians to non-Caucasians were similar to group 1A, but the patients were older in group 1A. Table 5 demonstrates that the frequency of cataract surgery did not differ significantly between groups.

TABLE 3. COMPARISON OF EYES IN GROUP 1A WITH GROUP 1B

	CATARACT SURGERY (n = 146)	NO CATARACT SURGERY (n = 376)	*P* VALUE
Cataract at first visit*	1.55	1.30	.024
Refractive error†	+1.73 D	+2.07 D	.124
Diabetes	23 (15.6%)	76 (20.1%)	
Laser energy (mJ)	389	420	.64
Age (yr)	71.3	69.6	.006
Male:female	31:115	89:287	
Caucasian:non-Caucasian	134:12	344:32	
Years of follow-up	5.9	8.7	.001
Medications for ↑IOP at last visit	50 (34%)	142 (38%)	.23

IOP, intraocular pressure
*Cataract grading scale taken from patient record.
†Spherical equivalent in diopters.

In the subset of patients who had AACG (n = 22), LPI was performed on all fellow eyes in the immediate period after angle closure had occurred in the first eye. None of the fellow eyes required additional treatment for elevated IOP. Of the AACG eyes, 13 required no additional therapy, 9 were treated topically, and 3 had subsequent surgical procedures.

TABLE 4. FREQUENCY OF USE OF MEDICATIONS TO LOWER IOP IN GROUPS 1 AND 2

	GROUP 1	GROUP 2
Medication to lower IOP	192 (37%)	22 (15%)
No medication	330	128
	$P < .005$	

IOP, intraocular pressure.

TABLE 5. FREQUENCY OF CATARACT SURGERY IN PATIENTS WITHOUT VS WITH PREVIOUS PERIPHERAL IRIDOTOMIES

	CATARACT SURGERY	NO CATARACT SURGERY
No previous LPI	32 (22%)	118
Previous LPI	146 (28%)	376
	$P = .11$	

LPI, laser peripheral iridotomy.

DISCUSSION

The difficulty inherent in deciding which patients are at risk for developing angle closure has been thoroughly documented. From the advent of laser procedures, first with the ruby, then the argon, and most recently the Nd:YAG laser, the degree of risk has been thought to be low enough that the frequency of the procedure has increased by a factor of 13 from the era of surgical iridectomy.[2] The technique of provocative testing with multiple combinations of drugs has yielded no uniformity acceptable to all, and estimations of chamber angle depth, occlusion, and synechial closure have engendered numerous charts, photographic atlases, and descriptions.[7,8] Anterior segment scanning laser equipment may lay some of this controversy to rest.[9]

It is estimated that by 2010, 60.5 million people will have visual loss from glaucoma; of these, bilateral blindness will occur in 8.4 million, of whom 3.9 million will have angle-closure glaucoma of all types.[10] This disease is more frequent in East Asians, amounting to 2.4 % of Chinese citizens over the age of 50.

This study has been conducted in an almost exclusively Caucasian population. The findings, however, have been taken from a subset of the Caucasian population that has anatomic structures similar to those at risk for angle closure, no matter what their racial background.[11] Given the limited resources for other remedies (ie, cataract surgery) in the developing world, it may be preferable to perform laser iridotomy on 80% of the affected population and cataract surgery on 20% as the cataracts (that might have developed in any case) mature, rather than remove cataracts as a primary procedure in all cases.

In this study, patients who required LPI differed significantly from the comparison group in their tendency to develop elevated IOP postoperatively. The IOP post-LPI increased significantly, and 37% of patients required additional therapy to control IOP, in contrast to 15% of the comparison group. Nonaka and associates[12] have suggested that 13 of 70 eyes treated with LPI for angle closure had residual angle closure, which they chose to treat with cataract surgery. One may need to distinguish these eyes separately and consider primary cataract surgery in this smaller group.

In this study, 39 eyes had CACG, and of these only 5 eyes underwent filtering surgery for intractably elevated IOP after LPI, added to the 3 eyes that underwent filtering surgery after AACG. Indeed, Thomas and colleagues[13] indicated that 73% of their eyes with CACG were controlled with LPI alone; 11% were controlled with topical medication, and the remainder required primary trabeculectomy.

Although no attempt is being made to derive an economic analysis from this study, the 13-fold excess of LPIs over the prelaser era may be justified on the basis that the devastation of angle-closure glaucoma and the consequent loss of vision is so great that the 2008 Medicare-allowable charge of $361.73 per eye for each of 13 patients, or $9404.98, is far less than the economic cost of losing vision totally in one eye for any one person. In the subset of patients with AACG, our results mirror those of Ang and associates,[14] who noted that the fellow eyes of 80 patients with AACG in one eye needed only LPI to prevent angle closure, although IOP did increase after laser therapy. They caution that close monitoring of IOP after LPI is essential.

Although the group chosen at random without angle closure (group 2) is not a true "control" population, it does serve as an indication of the relative risk of developing cataract in comparison to the treated group. Although the average age of the patients in group 2 is 9.8 years older than the patients in group 1, the degree of cataract at initial presentation is approximately equal in both

groups (see Table 3). That the patients without LPIs developed cataracts at about the same interval as those who experienced the "trauma" of laser iridotomy suggests that the excess risk is minimal. The definitive study would occur if one eye in each patient served as the "control" for the treated eye. Given the risk of blindness from untreated angle-closure glaucoma, such a study would be difficult to justify.

CONCLUSION

The combination of the excess risk of intraocular surgery for cataract and the relatively benign nature of LPI makes the recommendation that cataract surgery be performed as the primary procedure for angle-closure glaucoma seem unnecessary. This report demonstrates that eyes with potential or actual angle closure are better served with primary LPI followed by surgery for cataract when the continuing aging process within the lens necessitates intervention. Advancement of lens opacity sufficient to require surgery occurred with statistically similar frequency, whether or not LPI was needed.

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PEER DISCUSSION

DR. JOHN C. MORRISON: In 2005, Lim and associates reported that prophylactic YAG laser iridotomy in fellow eyes of Asian patients with unilateral acute angle closure glaucoma was associated with a significant rate of cataract progression.[1] Noting that these asymptomatic eyes did not develop progressive angle closure or systemic factors to explain this increase in cataracts, they attributed it to release of inflammatory mediators by the laser itself. They conclude that these findings have implications for the use of prophylactic iridotomy in eyes at risk for angle closure.

This study reminds us that all procedures carry risks. However, findings that might discourage laser iridotomy in patients at risk of developing acute angle closure may lead some to conclude that cataract extraction is preferable to laser iridotomy need careful scrutiny and confirmation.

In the current paper, Dr. Bobrow reports that the frequency of patients undergoing laser iridotomy who later required cataract surgery is not significantly greater than in a control group that did not receive laser. He concludes that eyes at risk of acute angle closure are best served by iridotomy, with cataract extraction performed at a later date, if needed.

The difference between the results of the current study and that of Lim is due in part to the use of a control group, which, as

pointed out in a subsequent letter to the editor by Yip, et al,[2] is lacking in the Lim study. In their letter, this group also reports their own finding that the rate of visual acuity loss due to cataract after laser iridotomy is equal to that in a group of untreated controls from the same population, supporting the current study.

Another difference between these two studies is that Dr. Bobrow uses the percentage of eyes that require cataract surgery as his endpoint, whereas Lim relied on a statistical increase in cataract density as determined by a grading scale. Cataract surgery risks, while uncommon, can be severe and must be factored in to the decision of whether or not to do surgery. In this sense, Dr. Bobrow's assessment provides a real-world view of the actual impact of laser iridotomy on visually significant cataract development.

Dr. Bobrow also finds that iridotomy, even when successful, is associated with a greater need for glaucoma therapy. This suggests that these eyes, even those without angle closure attacks, are prone to develop subclinical episodes of angle closure, subtle inflammation and eventual dysfunction of the trabecular meshwork. The Lim study, in which asymptomatic, fellow eyes had an average of nearly 2 clock hours of anterior synechiae even before laser treatment, supports that such a process is indeed occurring and may itself contribute to cataract development in these patients.

I congratulate Dr. Bobrow on providing an important, real-world assessment of the potential role of laser iridotomy in creating visually significant cataracts.

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DR. ROBERT RITCH: No financial interest. I was very happy to see a negative study because that has been my impression over the last 30 years. There has been a lot of discussion about this topic in the past couple of years, and a lot of it on the Internet and in the glaucoma groups. I would like to suggest that any connection between cataract and iridotomy is not cause and effect, but an upstream phenomenon. In my thesis for the AOS in 1994, we found that 28% of our patients with occludable angles or angle closure had exfoliation syndrome. Exfoliation syndrome is vastly under-diagnosed. Exfoliation syndrome is a direct etiologic cause of both angle closure and cataract, and therefore any cataract after iridotomy could be in an eye with exfoliation syndrome. Similarly, exfoliation syndrome causes both open-angle and angle-closure glaucoma, and therefore could explain a rise in intraocular pressure even years after an iridotomy in eyes that had previous angle closure, because now they are developing elevated IOP with an open-angle on the basis of exfoliation syndrome. The Lim paper came from Hong Kong, and exfoliation is very rare in Hong Kong; however, 30% of the angle closure in Hong Kong is lens-induced. It is much more common there and is a different kind of angle closure. It is not just pupillary block, and these eyes are more prone to require cataract extraction after iridotomy because the cataract is more prominently involved in triggering the angle closure. Thank you.

DR. ALLAN J. FLACH: No conflict of interest. I would like to congratulate Dr. Bobrow on a wonderfully honest paper. During his presentation, he hesitated to call Group 2 a control group, and this is the basis for my question. A control group is the basis for comparison. Is the control group different in any other way from the treatment group? The question is very important to determine if laser peripheral iridectomy does increase cataract formation. I would like to know a more about Group 2. Additionally, since you do not include this in the abstract, was Group 2 added as an afterthought? If so, how do you handle that with an IRB approval?

DR. DON MINCKLER: I have no relevant conflict of interest. I have a general comment related to laser peripheral iridotomy in my region where, in my opinion, LPI is easily the most abused therapeutic intervention in glaucoma. I am not sure everybody feels that way, but we see patients all the time who have undergone bilateral LPIs who never had the need for it. I am also curious, since you looked at a number of patients who had PIs and then underwent cataract surgery, whether any of them had had the occasional symptoms of diplopia or lines or visual blur you noted that sometimes occur after LPIs. Presumably these are associated with placement of the PI at the lid margin that creates a base up prism effect. Do such post-laser problems disappear after cataract extraction? I am also curious to learn about your choice of a YAG-only technique. Many of us, including me, have long used a two-laser (Argon or diode then YAG) technique and believe it causes less inflammation and iris bleeding.

DR. JAMES C. BOBROW: Thank you all for your comments. Let me try and go back over what may be a difficult series of questions. Dr. Morrison, I appreciate your comments, and I also appreciate the fact that Dr. Morrison and I were able to correspond before the meeting. He helped me to make my presentation better, and I hope that it made it easier for all of you to understand. I appreciate that he liked the fact that this study did not support the need for cataract surgery as primary therapy. I must admit that I would have to re-examine my patients to determine if I could present data regarding how many of them had exfoliation syndrome. I suspect that I would, as many ophthalmologists, under-diagnose the condition, because I have only a visual means for finding exfoliation material. We know that there are certainly places where exfoliation material exists that may not be clinical apparent. The fact that the exfoliation syndrome is uncommon in the eastern Asian population may mean that some of the mechanisms are slightly different in different populations, as Dr Ritch suggests. We, of course, have a blunt instrument, so we simply use the Nd:YAG laser to

try to improve aqueous humor distribution between the anterior and posterior chambers for this type of glaucoma. I do not know if the Caucasian population has a lower chance of developing cataract because the mechanisms of angle closure are slightly different.

Regarding Dr. Flach's question, I amended the IRB when I decided to add the comparison group, and the revised study was accepted by the Human Studies Committee. This was submitted after the accumulation of data for groups 1A and 1B. As far as my hesitation about it being called a control group, I tried to define a group with a similar degree of cataracts. I believed that selecting this criterion was a reasonable initial decision. After assembling the data for these 75 patients, I determined that they were a slightly older group. Aside from that, their systemic diagnoses, ocular diagnoses, and other conditions were similar.

In respect to Dr. Minckler's question, perhaps LPI is an overused procedure. I believe that many of us err on the side of performing iridotomies for patients when we judge that they are at risk to develop angle closure. We regard this as a simple and safe procedure that can be performed in patients with borderline findings, rather than waiting for them to present with angle closure or secondary complications related to an acutely elevated intraocular pressure.

Relating to the question of using a one laser versus the two laser technique, I have had access to both lasers in my office and stopped performing argon followed by YAG laser PIs about 20 years ago. I found that I can very easily perform YAG laser iridotomy and not encounter enough bleeding or other problems to require that two-step procedure. Thank you very much