

Effectiveness of Argon Laser Peripheral Iridoplasty in Plateau Iris Syndrome Patients after Laser Peripheral Iridotomy

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ABSTRACT

Objective: There is controversy surrounding the next best step in treating plateau iris syndrome (PIS) patients with persistent angle dysfunction despite a patent laser peripheral iridotomy (LPI). The aim of this study was to examine the effectiveness of argon laser peripheral iridoplasty (ALPI) in PIS patients with a patent LPI.

Methods: Retrospective review of medical records in consecutive patients that underwent ALPI to treat persistently narrow angles due to underlying PIS after a patent LPI. Patients in whom angle configuration could not be ascertained by review of medical records, those with less than 12 months follow-up at our institution, or those younger than 18 years of age were excluded. Kaplan-Meier survival analysis was used to determine treatment survival time. Paired t-tests were used to compare intraocular pressure (IOP), number of glaucoma medications, and best-corrected visual acuity (BCVA) 12 months post-ALPI and at the last follow-up visit.

Results: Fifty-one eyes of 51 patients were included in the analysis. The median survival time for a successful ALPI procedure was 1023 days (34.1 months). The majority of failure events were attributed to cataract extraction to open a persistently narrow angle, performed at approximately 934 (\pm 694) days (31.1 months) after ALPI. No changes in IOP, number of glaucoma medications, or BCVA from baseline were observed after 12 months or at last follow-up.

Conclusion: ALPI is a potentially effective treatment for PIS following LPI. While angle dysfunction may re-emerge over time, ALPI can potentially delay the need for lensectomy in patients without visually significant cataracts.

Keywords: Argon Laser Peripheral Iridoplasty (ALPI); Laser Peripheral Iridotomy (LPI); Glaucoma; Plateau Iris Syndrome (PIS); Angle Dysfunction; Lensectomy

INTRODUCTION

There is continued controversy surrounding the next best step in the treatment of a patient with persistently narrow angles after a patent laser peripheral iridotomy (LPI). Treatment options include argon laser peripheral iridoplasty (ALPI), cataract extraction, or observation, depending on the individual clinical scenario. Optimizing the treatment algorithm would be highly impactful as it is estimated that by 2021, 5.3 million people will suffer from blindness due to primary angle-closure glaucoma [1].

Relative pupillary block is often regarded as the most common mechanism of primary angle closure, in which LPI would both

open the angle and lower intraocular pressure (IOP) [2,3]. However, it has been reported that approximately one-third of patients present with persistent angle dysfunction despite a patent LPI [2,3]. This is often observed in cases of plateau iris syndrome (PIS), a mechanism of angle-closure that persists despite a patent LPI.

In 1977, Wand and colleagues differentiated plateau iris configuration (anteriorly positioned ciliary body resulting in angle closure prior to intervention) from plateau iris syndrome (PIS, plateau iris configuration that persists despite LPI) [4]. ALPI was first described by Ritch in 1982, and it has since been

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considered a potentially effective treatment for persistently narrow angles after a failed LPI [5]. ALPI delivers continuous wave laser energy to the peripheral iris causing the iris tissue to contract, thereby pulling it away from the TM and opening the angle. However, to date only a limited number of studies have investigated the efficacy of ALPI, with sample sizes of 22 to 48 eyes and variable follow up between 76 and 92 months [6-8]. Furthermore, factors affecting the survival of ALPI efficacy have not been previously reported. In this study, we performed a survival analysis on the effect of ALPI in order to elucidate factors associated with failure.

PATIENTS AND METHODS

Approval for this retrospective review was obtained from the Partners Healthcare Institutional Review Board. All research activities adhered to the tenets of the Declaration of Helsinki and was compliant with the Health Information Portability and Accountability Act. Consecutive patients who underwent ALPI were identified using financial claims data (Current Procedural Terminology code 66762) between 2013 and 2018. Patients were included in the analysis if they had documented PIS (defined below) and a patent LPI prior to ALPI, and at least 12 months of follow-up at our institution following ALPI. Patients were excluded from the analysis if they were not 18 years of age, or if angle configuration could not be ascertained by review of medical records. If both eyes were treated, only the right eye was selected for the analysis.

Study definitions

Plateau iris syndrome (PIS): inability to visualize posterior trabecular meshwork (PTM) in more than 2 quadrants on gonioscopy post-LPI, ultrasound biomicroscopy findings indicating PIS, post-dilation IOP spike ($\geq 10\%$), or as indicated by clinical diagnostic codes.

Baseline IOP: baseline IOP was calculated as the average of the values at the two most recent pre-ALPI visits.

Failure criteria: inability to visualize PTM in more than 2 quadrants on gonioscopy (gonioscopic failure), an acute-angle closure attack, lens surgery for the purpose of improving angle function, or an increase in IOP $\geq 20\%$ from pretreatment baseline at 2 consecutive visits.

Censor criteria: Reaching the end of the follow-up period, lens surgery for visually significant cataracts, or the addition of glaucoma medications from pretreatment baseline without first meeting the failure criteria for uncontrolled IOP. If failure and censoring criteria were reached on the same day, failure was declared.

Main outcome measures

The main outcome measure was Kaplan-Meier survival using the above defined failure criteria. Secondary outcomes included IOP, number of glaucoma medications, and best-corrected visual acuity (BCVA) assessed at 12 (± 4) months post-ALPI and at the last follow-up visit.

ALPI procedures

ALPI was performed by multiple glaucoma specialists with similar technique as described elsewhere [5].

Data analysis

Demographic and baseline clinical data were summarized by mean (\pm standard deviation) or frequency (percentage) for categorical variables. Snellen BCVA was converted to the logarithm of the minimum angle of resolution (logMAR) for analysis. Paired t-tests were used to compare changes in IOP, number of glaucoma medications, and logMAR visual acuity from baseline to 12 (± 4) months and last follow-up. Any patient that did not have a follow-up visit within 12 (± 4) months was excluded from the 12-month analysis. IOP and medication data for patients that underwent an IOP-lowering procedure prior to the 12-month visit or last follow-up were excluded from the IOP and medication analyses. Visual acuity data for patients that underwent phacoemulsification prior to the 12-month visit or last follow-up were excluded from the BCVA analyses.

A Kaplan-Meier curve was created based on the above defined failure criteria. A Cox Proportional-Hazards model was utilized to determine the effect of baseline characteristics on the likelihood of survival. All assumptions required for the Cox Proportional-Hazards model were met. Fifteen patients were selected at random to assess the frequency with which patients underwent gonioscopy throughout their follow-up. All statistical tests were conducted at a 5% level of significance. Analysis was performed using R statistical programming software (version 3.6.2).

RESULTS AND DISCUSSION

A total of 64 patients were screened, and 51 eyes from 51 patients were included in the analysis. Patient demographics are given in Table 1. The median age was 59 [IQR 15] years and the mean age was 57.3 (± 10) years. The median follow-up period was 1385 [IQR 1023] days (46.2 months) and the mean follow-up was 1328 (± 654) days (44.3 months). Average laser settings were as follows: spot size of 389 (± 160) microns, power of 256 (± 105) milliwatts, and a duration of 473 (± 160) milliseconds. An average of 30 (± 10) evenly spaced spots were placed over 360 degrees.

Baseline characteristics

Thirty-five percent of patients had a glaucoma diagnosis at the time of ALPI. The distribution of glaucoma diagnoses, as well as baseline IOP, number of glaucoma medications, and logMAR BCVA are given in Table 2. The mean baseline IOP was 16.5 (± 4.8) mmHg. The mean number of glaucoma medications was 0.82 (± 1.3). Twenty (39%) eyes used at least one glaucoma medication to control IOP. Seven (35%) of these 20 patients were using pilocarpine. The mean logMAR visual acuity was 0.08 (± 0.2). Ten (19.6%) patients had peripheral anterior synechiae (PAS) present preoperatively.

Table 1: Patient demographics.

Median Age [IQR] (years)	59 (15)
Sex % (n)	
Female	67 (34)
Male	33 (17)
Race % (n)	
White	72 (37)
Black or African American	6 (3)
Hispanic	14 (7)
Asian	4 (2)
Pacific Islander	2 (1)
Unknown	2 (1)
Median age [interquartile range] and distribution of sex and race amongst study participants.	

Table 2: Baseline characteristics.

PIS patients with glaucoma % (n)	
Glaucoma diagnoses % (n)	35 (18)
CACG	29 (15)
MMG	6 (3)
Baseline IOP (\pm sd) (mmHg)	16.5 (\pm 4.8)
Baseline medications (\pm sd)	0.82 (\pm 1.3)
Baseline logMAR BCVA	0.08 (\pm 0.2)
Note: PIS: Plateau Iris Syndrome; CACG: Chronic Angle-Closure; Glaucoma; MMG: Mixed-Mechanism Glaucoma; IOP: Intraocular Pressure; BCVA: Best Corrected Visual Acuity was converted to logMAR: Logarithm of the Minimum Angle of Resolution.	

Outcomes

Kaplan-Meier survival analysis: The Kaplan-Meier survival function is shown in Figure 1. The median survival time for a successful ALPI procedure was 1023 days, or approximately 34.1 months. The cumulative probability of success was 70% (95% CI 0.58-0.84) and 56% (95% CI 0.43-0.72) at 12 months and 24 months, respectively. There were 29 failure events in total. Cataract surgery to open the angle with or without additional IOP-lowering measures accounted for 13 failure events while gonioscopic failure accounted for 8. Elevated IOP \geq 20% from baseline accounted for 7 failure events and an acute angle closure attack for 1. Of those who failed for reasons other than surgical intervention, 8 would go on to have cataract surgery

with or without adjunctive IOP-lowering measures to treat progressive angle dysfunction.

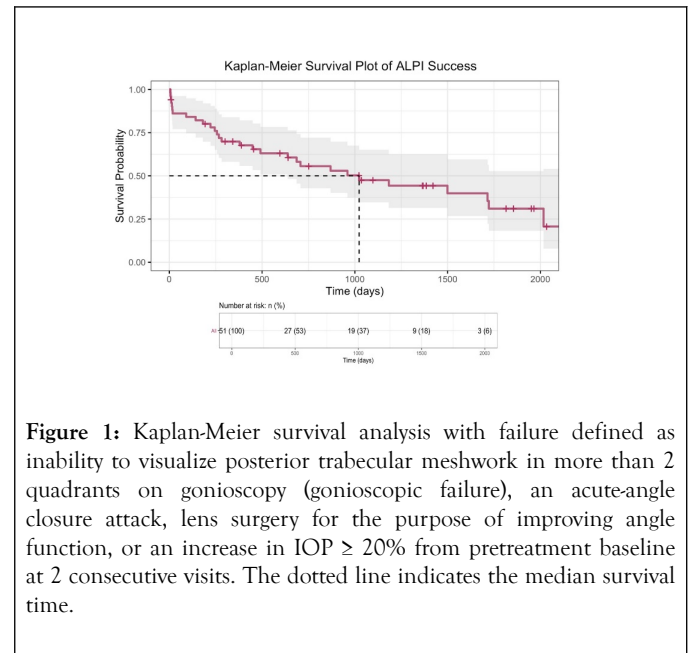


Figure 1: Kaplan-Meier survival analysis with failure defined as inability to visualize posterior trabecular meshwork in more than 2 quadrants on gonioscopy (gonioscopic failure), an acute-angle closure attack, lens surgery for the purpose of improving angle function, or an increase in IOP \geq 20% from pretreatment baseline at 2 consecutive visits. The dotted line indicates the median survival time.

As previously mentioned, the frequency at which patients had gonioscopy was assessed in a subset of 15 randomly selected patients. Gonioscopy was performed on all 15 patients at their first follow-up visit after ALPI. The median number of times gonioscopy was performed throughout these patients' follow-up was 4 [IQR 2.5], over a median of 1441 [IQR 888] days, or approximately 48 months.

A Cox Proportional-Hazards analysis was performed to investigate predictors of failure (Table 3). Neither sex, non-white race, nor age were significant predictors of failure ($p=0.7, 0.7, 0.2$, respectively). Pretreatment baseline IOP, medications, BCVA, and diagnosed glaucoma were also not significant predictors of failure ($p=0.2, 1, 0.3, 0.1$, respectively).

Table 3: Hazard ratios for ALPI failure risk factors.

Covariate	HR	95% CI	p value
Sex	1.18	0.54-2.56	0.7
Non-white race	1.18	0.53-2.58	0.7
Age	1.03	0.99-1.06	0.2
Baseline IOP	0.95	0.88-1.03	0.2
Baseline glaucoma medications	1.0	0.74-1.36	1.0
BCVA	2.11	0.52-8.52	0.3
Diagnosed glaucoma	0.52	0.23-1.14	0.1

HR: Hazard ratios for baseline covariates from the Cox Proportional-Hazards model reported with 95% CI: Confidence Intervals; IOP: Intraocular Pressure; BCVA: Best Corrected Visual Acuity.

Intraocular pressure, number of glaucoma medications, and visual acuity

Forty-three of 51 patients had a follow-up visit within 12 (\pm 4) months from their initial ALPI procedure with no additional IOP-lowering procedure and were therefore included in the analysis of IOP and medications. There were no differences

between baseline and 12-month IOP ($p=0.99$) or medications ($p=0.52$) (Table 4). Forty-two patients had a follow-up visit within 12 (\pm 4) months without prior phacoemulsification, and they were therefore included in the comparison of BCVA means. There was no significant difference in logMAR BCVA at 12 months compared to baseline ($p=0.05$) (Table 4).

Table 4: IOP, medications, and visual acuity at baseline, 12 months, and last follow-up.

	IOP (\pm sd) (mmHg)	Medications (\pm sd)	logMAR BCVA (\pm sd)
Baseline	17.1 (4.6)	0.67 (1.0)	0.08 (0.21)
12 months	17.2 (5.3)	0.74 (1.0)	0.18 (0.41)
n	43	43	42
p value	0.99	0.52	0.05
Baseline	16.7 (5.0)	0.56 (0.97)	0.03 (0.09)
Last follow-up	15.8 (3.2)	0.44 (0.84)	0.17 (0.44)
n	45	45	26
p value	0.22	0.32	0.07

Intraocular pressure (IOP), glaucoma medications, and logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) at baseline, 12 (\pm 4) months, and last follow-up. Mean time to last follow-up was 45 ± 22 months. Patients that had an additional IOP-lowering procedure prior to the 12-month mark or last follow-up were excluded from the IOP and medication comparison of means. Patients that had phacoemulsification prior to the 12-month mark or last follow-up were excluded from the BCVA comparison of means.

Forty-five of 51 patients were included in the comparison of baseline and last follow-up IOP and number of glaucoma medications. There were no differences between baseline and last follow-up IOP ($p=0.22$) or medications ($p=0.32$) (Table 4). Twenty-six patients that had not undergone phacoemulsification were included in the BCVA analysis. There was no significant difference in logMAR BCVA at last follow-up compared to baseline ($p=0.07$) (Table 4).

Postoperative complications and additional treatment

Two (3.9%) eyes experienced an acute angle-closure attack during follow-up. Angle-closure attacks occurred 222 and 510 days after ALPI, respectively. Both were treated pharmacologically and with repeat LPs, and one required eventual cataract extraction. Two (3.9%) eyes underwent a repeat ALPI (one of which required eventual cataract extraction as well), and 1 (1.9%) eye underwent Ahmed valve insertion. Phacoemulsification was not performed with the Ahmed procedure in this eye because the patient was young without a visually significant cataract and had poor visual potential.

A total of 25 phacoemulsification procedures with or without adjunctive IOP-lowering measures were performed. Four (8%) were to remove a worsening visually significant cataract. The vision in these patients at the last visit before

phacoemulsification was $0.34 (\pm 0.24)$ and the average IOP was $18 (\pm 4.5)$ mmHg. Twenty-one (41%) phacoemulsification procedures were performed to treat persistent angle dysfunction. The average vision of these patients at the last visit before phacoemulsification was $0.20 (\pm 0.33)$ and the average IOP was $17.8 (\pm 4.7)$ mmHg. Sixteen (31%) procedures were phacoemulsification alone, 2 (4%) had concomitant endoscopic cyclophotocoagulation (ECP), 2 (4%) had trabeculectomy, and 1 (2%) had ECP and goniotomy. The mean time to cataract surgery with or without adjunctive IOP-lowering measures after ALPI was $934 (\pm 694)$ days (approximately 31.1 months). One (1.9%) patient developed new PAS after ALPI. No other post-laser complications were observed.

DISCUSSION

Only a handful of studies have reported results of ALPI, and to the best of our knowledge the current study is the only to report survival data. Our results suggest that ALPI is a relatively safe and potentially effective treatment option for the management of PIS. Based on our clinical definition of procedure success the cumulative probability of success was 73% after 12 months and 58% after 24 months. Twenty-one patients required cataract extraction to treat a persistently narrow angle on average $934 (\pm 694)$ days (approximately 31.1 months) after ALPI. This suggests

that ALPI may delay the need for cataract surgery to treat the narrow angle in patients without visually significant cataracts up to more than 2 years post-ALPI. We did not find any baseline characteristics including sex, non-white race, age, baseline IOP, medications, BCVA, or glaucoma status to be significant predictors of ALPI failure.

In the Kaplan-Meier survival analysis, increases in IOP \geq 20% from baseline accounted for 7 (7/29, 24%) failure events. We did not observe any statistically significant changes in IOP at 12-months or last follow-up compared to baseline. This is similar to the findings reported by Romito et al. and Ritch et al., who did not observe any changes in IOP over the courses of their respective studies [6,7]. In contrast, Peterson et al. observed statistically significant reductions in IOP compared to baseline up to 4 years following ALPI [8]. However, the authors noted that at last follow-up or the last visit prior to additional treatment, the mean IOP gradually increased to the baseline level.

Different findings with regard to IOP reduction may be attributed to different patient populations, as the mean pre-ALPI IOP in Peterson's study was 21.3 mmHg, while that of our study was 16.1 mmHg. Interestingly, Peterson et al. also reported that 36% of eyes underwent filtration surgery over the course of 4 years of follow-up. In contrast, only 4% of patients in the current study underwent subsequent filtration surgery. This difference could in part be attributable to slight differences in follow-up time, and the fact that patients in the Peterson study underwent trabeculectomy if IOP > 21 mmHg and if they were intolerant to topical therapy or noncompliant. In our study the decision to proceed with glaucoma filtration surgery remained subjective according to each respective surgeon.

The majority of failure events (13/29, 45%) that occurred in the Kaplan-Meier survival analysis were attributed to phacoemulsification to treat persistent angle dysfunction. In their study of 22 eyes with PIS, Peterson et al. reported that 41% of eyes required phacoemulsification on average 49 months after ALPI to treat a persistently narrow angle [8]. Likewise, 41% of eyes in the current study underwent eventual phacoemulsification, approximately 31.1 months after ALPI. With regard to additional IOP-lowering surgery, only 2 (4%) of eyes in the current study required filtering surgery, while 2 (4%) had ECP and 1 (2%) had ECP with angle surgery. This finding aligns with those of Romito et al. and Ritch et al., who did not report any instances of filtration surgery post-ALPI [6,7].

A substantial proportion (41%) of patients in our study underwent eventual phacoemulsification to treat progressive angle dysfunction. A prospective, randomized study comparing ALPI versus phacoemulsification after LPI could help determine the best clinical management algorithm for PIS. However, it remains that most PIS patients are young and have yet to develop cataract symptoms [9]. As such, low rates of post-laser complications and its ability to maintain IOP and medication burden, may suggest a role for ALPI in postponing the need for cataract surgery in these often-young patients in need of angle-closure prevention.

There are several limitations to our retrospective study. Our sample size is modest and therefore caution must be taken when extrapolating these findings to the population at large. Additionally, we cannot discount the possibility of underestimating failures based on angle configuration because gonioscopy was not performed regularly after the first post-ALPI visit. However, this is unlikely because our randomly sampled subset of patients underwent gonioscopy a median number of 4 times over 48 months, or once a year. Moreover, a more in-depth analysis of angle configuration following ALPI based on angle depth was prohibited by variable physician reporting of gonioscopy exam, and while the gonioscopy findings were carefully described on a case-by-case basis, they remain subjective. The decision to perform further interventions (i.e., repeat ALPI, phacoemulsification, filtration surgery) was based on the clinical judgement of the acceptable IOP for each individual case and not by predetermined study criteria. Lastly, this study would benefit from a comparative arm of patients with persistently narrow angles who did not receive ALPI after LPI. This was unfortunately impossible to execute as the standard of care for most providers at our institution as of 2019 is to perform ALPI in the setting of persistent appositional angle closure after LPI.

CONCLUSION

In summary, our results suggest that ALPI is an effective treatment option for PIS eyes with persistently narrow angles post-LPI. This may be especially relevant to young PIS patients without visually significant cataracts. However, it must be noted that the effect of ALPI may wane overtime. A substantial proportion of patients in the current study required further surgical intervention, most commonly phacoemulsification, to control IOP due to persistent angle dysfunction approximately 31.1 months after ALPI.

AUTHOR CONTRIBUTORSHIP

D.S.V and E.K. contributed to the conception and design of this work. E.K., M.C., and A.N. contributed to the collection of the data. E.K. and N.H. were involved in the analysis and interpretation of the results. E.K. drafted the manuscript, and D.S.V and T.C. provided critical revision of the article. All authors gave explicit approval of the final version to be published.

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