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Self-identified Black Race as a Risk Factor for Intraocular Pressure Elevation and Iritis Following Prophylactic Laser Peripheral Iridotomy

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Précis: In primary angle closure suspects (PACS), self-identified Black race was a risk factor for intraocular pressure (IOP) elevation and iritis following laser peripheral iridotomy (LPI). Laser type was not associated with either immediate post-LPI IOP elevation or iritis in multivariate analysis.

Purpose: The aim was to determine the impact of laser type and patient characteristics on the incidence of IOP elevation and iritis after LPI in PACS.

Materials and Methods: The electronic medical records of 1485 PACS (2407 eyes) who underwent either neodymium-doped yttrium-aluminum-garnet or sequential argon and neodymium-doped yttrium-aluminum-garnet LPI at the University of Pennsylvania between 2010 and 2018 were retrospectively reviewed. Average IOP within 30 days before LPI (baseline IOP), post-LPI IOP within 1 hour, laser type, laser energy, and the incidence of new iritis within 30 days following the procedure were collected. Multivariate logistic regression accounting for intereye correlation was used to assess factors associated with incidence of post-LPI IOP elevation and iritis, adjusted by age, sex, surgeon, and histories of autoimmune disease, diabetes, and hypertension.

Results: The incidence of post-LPI IOP elevation and iritis were 9.3% (95% confidence interval: 8.1%-10.5%) and 2.6% (95% CI: 1.9%-3.2%), respectively. In multivariate analysis, self-identified Black race was a risk factor for both IOP elevation [odds ratio (OR): 2.08 compared with White; $P = 0.002$] and iritis (OR: 5.07; $P < 0.001$). Higher baseline IOP was associated with increased risk for post-LPI IOP elevation (OR: 1.19; $P < 0.001$). Laser type and energy were not associated with either post-LPI IOP elevation or iritis ($P > 0.11$ for all).

Conclusions: The incidence of immediate IOP elevation and iritis following prophylactic LPI was higher in Black patients independent of laser type and energy. Heightened vigilance and increased medication management before and after the procedure are suggested to help mitigate these risks.

Key Words: laser peripheral iridotomy, intraocular pressure, primary angle closure suspect, anterior chamber inflammation, iritis

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Angle closure glaucoma is a major cause of irreversible blindness worldwide.[1] In 2013, an estimated 20 million people globally were affected by primary angle closure glaucoma (PACG), and this number is predicted to increase to 32 million by 2040.[2] Laser peripheral iridotomy (LPI) is the most often performed in-office procedure for reducing the risk of PACG in primary angle closure suspects (PACS).[3] Although LPI is generally considered safe, short-term complications are well-documented. The most common transient LPI complication is immediate intraocular pressure (IOP) elevation, occurring most often within the first 3 hours following the procedure.[4] As even transient IOP elevation can be detrimental in susceptible patients at risk for glaucoma or disease progression, eye care providers often spend a significant amount of time monitoring and managing IOP elevations after LPIs.[4] Laser iridotomies can also result in anterior chamber inflammation,[5,6] which can cause significant patient discomfort, as well as persistent or recurrent iritis.[7–9] Persistent iritis may then lead to peripheral anterior synechiae formation, IOP elevation, and chronic angle closure.[9,10]

Two different types of lasers are routinely used for LPI in the United States, consisting of neodymium-doped yttrium-aluminum-garnet (Nd:YAG) and argon. A combination of argon and Nd:YAG is most often used in patients with dark iris pigmentation, including those self-identified as Black. Nd:YAG alone often requires higher laser energy expenditure to achieve patency in highly pigmented irides, and has been associated with higher rates of iris hemorrhage.[6,11–14] Several benefits of sequential argon-Nd:

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YAG LPI over either Nd:YAG or argon alone have been reported for dark irides, including reduced rates of hemorrhage, reduced total Nd:YAG energy, and higher rates of patency after initial treatment.[13,15,16]

Despite the widespread use of LPI as a routine procedure for many eye care providers, the determinants of short-term complications following prophylactic LPI for PACS are not well known. Existing studies that investigated post-LPI complications either did not directly compared Nd:YAG and sequential argon-Nd:YAG lasers,[13,17–21] included mixed cohorts of PACG and primary angle closure (PAC) patients,[13,17,19,21] or were limited to only Asian populations.[13,18–20,22] In addition, while 3 studies examining LPI complications did include Black patients, they were limited by small sample sizes and the inclusion of Nd:YAG laser procedures only.[17,21,23] This study evaluated the determinants of short-term LPI complications in patients with anatomical narrow angles in cohorts inclusive of a large Black population.

MATERIALS AND METHODS

Study Design

A review of electronic medical records of patients who received LPI at the University of Pennsylvania Department of Ophthalmology between August 2010 and April 2018 was conducted. This study was approved by the Institutional Review Board at the University of Pennsylvania and all methods adhered to the tenants of the Declaration of Helsinki. Inclusion criteria were: (1) age 18 years or older, and (2) at least 1 eye with a diagnosis of anatomical narrow angle/PACS. See Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/IJG/A597 for the full list of International Classification of Diseases (ICD) codes used in this study. Exclusion criteria were: (1) prior diagnosis of PAC, PACG or chronic angle closure glaucoma; and (2) prior LPI in the same eye.

Age, sex, self-identified race, history of iritis or uveitis, and histories of diabetes, hypertension, and autoimmune diseases were collected for each patient. Autoimmune diagnoses included Behcet's disease, Sjogren's syndrome, lupus, psoriasis, rheumatoid arthritis, sarcoidosis, and gout. In addition, data were collected on laser type (Nd:YAG or sequential argon-Nd:YAG), laser energy (Nd:YAG, argon, and total energy), surgeon, the total number of pulses for each laser type, average IOP within 30 days before the procedure (baseline IOP), IOP within the first hour postprocedure (post-LPI IOP), and the incidence of a new iritis diagnosis within the first 30 days postprocedure. Total argon energy (in millijoules, mJ) was calculated by multiplying laser energy (milliwatts) with laser duration (seconds) and the number of laser pulses. Argon-only LPIs were few in number (n = 24 eyes/19 patients) and were excluded from statistical analysis. Consistent with previous studies, post-LPI IOP elevation was defined as either IOP elevation ≥ 8 mm Hg over baseline or any post-LPI IOP measurements > 21 mm Hg.[17–20,24] A secondary analysis of post-LPI IOP elevation ≥ 8 mm Hg over baseline was also performed.

The majority of LPIs were performed by 5 individual glaucoma specialists (Surgeons A to E, Table 1). All other surgeons were analyzed together as "Other" (n = 22 surgeons), and consisted of fellowship-trained glaucoma specialists, general ophthalmologists, and glaucoma fellows, but did not include ophthalmology residents.

Baseline IOP was the average of all IOP measurements made by applanation within 30 days before LPI. Post-LPI IOP was measured between 45 and 60 minutes after the laser procedure by applanation. Each post-LPI IOP value represented a single measurement by applanation.

LPI

Briefly, patients received 1 drop of apraclonidine 1% and 1 drop of either pilocarpine 1% or 2% based on surgeon preference in the operative eye before the procedure. After topical proparacaine 0.5% was instilled into the operative eye, an Abraham iridotomy contact lens (Ocular Instruments, Bellevue, WA) with Goniosol (Akorn, Lake Forest, IL) was placed on the cornea. LPIs were located either between 2 and 4 o'clock or between 8 and 10 o'clock on the iris per surgeon preference. For sequential argon-Nd:YAG LPI, argon laser was applied first, followed by Nd:YAG laser in the same region of the iris. The argon laser was used starting at a setting of 400 mW, and was increased up to 900 mW based on tissue response, with a spot size of 50 to 200 μm for a duration of 0.1 to 0.3 seconds depending on surgeon preference. As soon as the iris thinned to a honeycomb-like appearance, the Nd:YAG laser was used starting at an initial setting of 1.5 to 6.0 mJ per surgeon preference and then increased up to 7 mJ until an iridotomy of 0.3 to 0.5 mm was created. The patient was given a drop of apraclonidine 1% immediately after the procedure and prescribed topical prednisolone acetate 1% to be used 4 times a day for 4 to 14 days per surgeon preference after the procedure.

Statistical Analysis

Comparisons between the Nd:YAG LPI cohort and Nd:YAG + Argon LPI cohort were performed using 2-sample t test for continuous variables and Pearson χ^2 test for categorical variables. Univariate and multivariate logistic regression models that accounted for the intereye correlation by generalized estimating equation were used to assess factors associated with incidence of post-LPI IOP elevation and iritis.[25] Multivariate models included laser type, age, sex, race, surgeon, baseline IOP (for evaluation of post-LPI IOP elevation), autoimmune disease (for evaluation of post-LPI iritis), and history of diabetes and hypertension. All statistical analyses were performed in SAS, version 9.4 (SAS Institute Inc., Cary, NC), and a 2-sided P value <0.05 was considered statistically significant.

RESULTS

A total of 2407 eyes of 1485 patients met inclusion criteria for primary analysis. The mean ± SD age was 66.8 ± 12.6 years, 1045 patients (70.4%) were female, 454 (43.4%) were Black, and 514 (45.6%) were non-Hispanic White (White). A total of 1066 patients (71.8%) underwent Nd:YAG LPIs, and 419 patients (28.2%) underwent sequential argon-Nd:YAG LPIs. Surgeon was associated with the type of laser procedure performed ($P < 0.001$). The same type of laser procedure was performed in both eyes in all patients. 126 eyes were excluded from analysis of post-LPI IOP elevation because of lack of baseline IOP measurements.

Patients who underwent Nd:YAG LPIs or argon-Nd:YAG LPIs were comparable with respect to sex, baseline IOP, and histories of diabetes or hypertension. Patients who received Nd:YAG LPIs (67.2 ± 12.3 y) were older than those who received sequential argon-Nd:YAG LPIs (65.7 ± 12.5 y,

TABLE 1. Comparisons of Baseline Characteristics Between Nd:YAG and Sequential Argon-Nd:YAG LPI Cohorts

Baseline Characteristics	Nd:YAG LPI (n = 1066 Patients; 1783 Eyes), n (%)	Argon-Nd:YAG LPI (n = 419 Patients; 624 Eyes), n (%)	*P*
Age (y), mean ± SD	67.2 ± 12.3	65.7 ± 12.5	0.03
Female	752 (70.5)	293 (69.9)	0.82
Race/ethnicity			< 0.001
White	514 (48.2)	163 (38.9)	
Black	454 (42.6)	191 (45.6)	
Asian	34 (3.2)	17 (4.1)	
Other	64 (6)	48 (11.5)	
Diabetes	559 (52.4)	227 (54.2)	0.55
Hypertension	629 (59)	254 (60.6)	0.57
Autoimmune disease*	90 (8.4)	53 (12.6)	0.01
Baseline IOP (mm Hg), mean ± SD	17.1 ± 5.8	17.2 ± 5.6	0.60
Nd:YAG energy (mJ), mean ± SD	86.3 ± 194.5	85.3 ± 171.4	0.93
Argon energy (mJ), mean ± SD	—	3247.3 ± 4228.3	—
Total energy (mJ), mean ± SD	86.3 ± 194.5	3331.0 ± 4244.4	< 0.001
Surgeon			< 0.001
Surgeon A	75 (4.2)	301 (48.2)	
Surgeon B	495 (27.8)	36 (5.8)	
Surgeon C	271 (15.2)	7 (1.1)	
Surgeon D	169 (9.5)	7 (1.1)	
Surgeon E	477 (26.8)	10 (1.6)	
Other	296 (16.6)	263 (42.1)	

*Behcet's disease, Sjogren's syndrome, prior uveitis or iritis, lupus, psoriasis, rheumatoid arthritis, sarcoidosis, and/or gout.
IOP indicates intraocular pressure; LPI, laser peripheral iridotomy; Nd:YAG, neodymium-doped yttrium-aluminum-garnet.

$P = 0.03$; Table 1). Patients who received Nd:YAG LPIs were more likely to self-identify as White compared with those who received sequential argon-Nd:YAG LPIs (48.2% vs. 38.9%, $P < 0.001$). A history of uveitis and other autoimmune diagnoses was more common in the sequential argon-Nd:YAG LPI cohort compared with the Nd:YAG LPI cohort (12.6% vs. 8.4%, $P = 0.01$).

Sequential argon-Nd:YAG was associated with higher total laser energy compared with Nd:YAG alone (3331 mJ vs. 86.3 mJ, $P < 0.001$). Nd:YAG energy was comparable between cohorts ($P = 0.91$). Immediate post-LPI IOP elevation occurred in 213 of 2281 eyes, with a total incidence of 9.3% [95% confidence interval (CI): 8.1%-10.5%]. In multivariate regression adjusted for age, sex, surgeon, and history of diabetes and hypertension, Black patients had significantly higher rates of post-LPI IOP elevation compared with White patients [13.3% vs. 5.5%; adjusted odds ratio (OR): 2.08, 95% CI: 1.31-3.3, $P = 0.002$; Table 2). The rate of IOP elevation in Asian patients (3.6%) was comparable to that of White patients ($P = 0.19$). Patients who racially self-identified as "Other" also had higher rate of post-LPI IOP elevation compared with White patients (11.3% vs. 5.5%; adjusted OR: 2.02, 95% CI: 1.03-3.98, $P = 0.04$). Higher baseline IOP was a risk factor for post-LPI IOP elevation in primary analysis (adjusted OR: 1.19, 95% CI: 1.13-1.25, $P < 0.001$). When IOP > 21 mm Hg was removed from the definition of post-LPI IOP elevation in secondary analysis, Black race, but not higher baseline IOP, remained a significant risk factor (Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/IJG/A597). Interestingly, neither the type of laser nor total laser energy was associated with the rate of immediate post-LPI IOP elevation (Table 2).

Post-LPI iritis occurred in 62 of 2407 eyes, at a rate of 2.6% (95% CI: 1.9%-3.2%; Table 3). In multivariate analysis adjusted for age, sex, surgeon, and history of diabetes and hypertension, Black patients experienced higher rates of post-LPI iritis compared with White patients (4.4% vs. 1.1%; adjusted OR: 5.07, 95% CI: 2.07-12.38, $P < 0.001$). Although sequential argon-Nd:YAG compared with both Nd:YAG (4.3% vs. 2.0%, $P = 0.03$) and total laser energy ($P = 0.03$) was associated with a higher incidence of post-LPI iritis in univariate analysis, statistical significance for both were lost in multivariate analysis ($P = 0.11$ and 0.17, respectively). In addition, the incidence of post-LPI iritis was not associated with a history of autoimmune disease including uveitis, diabetes, or other racial self-identification categories.

DISCUSSION

In a single-center retrospective study, we evaluated risk factors for postprocedure IOP elevation and iritis in patients who underwent either Nd:YAG or sequential argon-Nd:YAG LPI for anatomical narrow angles/PACS. Self-identified Black race was a risk factor for both immediate IOP elevation and post-LPI iritis. This is consistent with the results of a recent retrospective study, which showed higher rates of immediate IOP elevation in African-Americans following LPI for angle closure.[21] A greater degree of pigment dispersion in thicker, darkly pigmented irides has been suggested to impact IOP elevation and iritis following LPI.[26–30] Consistent with this, patients who racially self-identified as "Other" also experienced higher rates of post-LPI IOP elevation compared with Whites, which could similarly be because of differences in postlaser pigment dispersion resulting from differences in iris characteristics. However, the lack of additional racial identifying information in the "Other" category prevents further interpretation of this finding.

Interestingly, Asian race, which is similarly associated with dark iris pigmentation and increased iris thickness,[30,31]

TABLE 2. Risk Factors Associated With Post-LPI IOP > 21 mm Hg or IOP Elevation ≥ 8 mm Hg From Baseline

		Univariate Analysis		Multivariate Analysis*	
	Eyes, n (%) (n = 2281)†	Unadjusted Odds Ratio (95% CI)	*P*	Adjusted Odds Ratio (95% CI)	*P*
Laser type					
Nd:YAG	153 (9)	Reference	—	Reference	—
Nd:YAG+Argon	60 (10.3)	1.14 (0.80, 1.62)	0.47	0.74 (0.44, 1.3)	0.31
Race			< 0.001		0.01
White	59 (5.5)	Reference	—	Reference	—
Black	127 (13.3)	2.70 (1.87, 3.92)	< 0.001	2.08 (1.31, 3.3)	0.002
Asian	8 (3.6)	1.92 (0.72, 5.13)	0.19	1.77 (0.65, 4.79)	0.26
Other‡	19 (11.3)	2.07 (1.16, 3.82)	0.02	2.02 (1.03, 3.98)	0.04
Baseline IOP	—	1.18 (1.13, 1.23)	< 0.001	1.19 (1.13, 1.25)	< 0.001
Hypertension					
Present	142 (10.4)	1.37 (0.98, 1.93)	0.06	1.16 (0.72, 1.88)	0.55
Absent	71 (7.8)	Reference	—	Reference	—
Total laser energy§	—	1.001 (0.996, 1.01)	0.73	—	—
Nd:YAG energy§	—	1.001 (0.99, 1.01)	0.84	—	—
Argon energy§	—	1.04 (0.99, 1.10)	0.15	—	—

*Adjusted for age, sex, surgeon, and history of diabetes and hypertension.
†126 eyes were excluded from the analysis of post-LPI IOP elevation because of lack of baseline IOP measurements.
‡Includes Hispanic individuals and unspecified race.
§Odds ratios were calculated based on every 100 mJ increase in energy.
CI indicates confidence interval; IOP, intraocular pressure; LPI, laser peripheral iridotomy; Nd:YAG, neodymium-doped yttrium-aluminum-garnet.

was not found to be significantly associated with either immediate post-LPI IOP elevation or iritis. This suggests the presence of other clinically significant risk factors for both conditions in addition to iris thickness and pigmentation. While a history of autoimmune disease, prior ocular inflammation, and diagnosis of diabetes were factors associated with postoperative iritis following cataract surgery,[8] none were risk factors for post-LPI iritis in our study.

The incidence of post-LPI IOP elevation, defined as either an IOP increase of ≥ 8 mm Hg from baseline or post-LPI IOP > 21 mm Hg, was 9.3% in our study, a rate in the higher end of the 2 to 10.7% range reported in the literature.[17–19,24] We found higher baseline IOP to be a risk factor for IOP elevation when elevation is defined by IOP > 21 mm Hg after LPI. Perhaps not surprisingly, when we separately analyzed post-LPI IOP elevation ≥ 8 mm Hg from baseline, the association with baseline IOP disappeared while Black race remained a significant risk factor. By electing to include eyes with IOP > 21 mm Hg in our definition of post-LPI IOP elevation, we sought to encompass all individuals that may require additional IOP management after LPI.

TABLE 3. Risk Factors Associated With Post-LPI Iritis

		Univariate Analysis		Multivariate Analysis*	
	Eyes, n (%) (n = 2407)	Unadjusted Odds Ratio (95% CI)	*P*	Adjusted Odds Ratio (95% CI)	*P*
Laser type					
Nd:YAG	35 (2.0)	Reference	—	Reference	—
Argon-Nd:YAG	27 (4.3)	2.19 (1.12, 4.28)	0.03	1.88 (0.8, 4.42)	0.11
Race			0.001		0.003
White	12 (1.1)	Reference	—	Reference	—
Black	45 (4.4)	4.68 (2.09, 10.46)	< 0.001	5.07 (2.07, 12.38)	< 0.001
Asian	3 (3.6)	3.99 (0.81, 19.63)	0.30	3.21 (0.62, 16.55)	0.16
Other†	2 (1.1)	1.29 (0.26, 6.47)	0.78	1.04 (0.2, 5.42)	0.95
Autoimmune disease‡					
Present	7 (3)	0.74 (0.14, 3.84)	0.64	0.61 (0.12, 3.17)	0.43
Absent	55 (2.5)	Reference	—	Reference	—
Diabetes					
Present	28 (2.2)	0.74 (0.41, 1.35)	0.34	0.55 (0.25, 1.21)	0.16
Absent	34 (3)	Reference	—	Reference	—
Total laser energy§		1.005 (1, 1.01)	0.03	1.004 (1, 1.01)	0.17
Nd:YAG energy§		1.03 (1, 1.07)	0.04	1.004 (0.99, 1.06)	0.17
Argon energy§		1.005 (1, 1.01)	0.04	1.03 (0.99, 1.01)	0.2

*Adjusted for age, sex, surgeon, and history of diabetes and hypertension. Adjusted odds ratios for total energy and argon energy were based on model without laser type.
†Includes Hispanic individuals and unspecified race.
‡Behcet's disease, Sjogren's syndrome, prior uveitis or iritis, lupus, psoriasis, rheumatoid arthritis, sarcoidosis, and/or gout.
§Odds ratios were calculated based on every 100 mJ increase in energy.
CI indicates confidence interval; IOP, intraocular pressure; LPI, laser peripheral iridotomy; Nd:YAG, neodymium-doped yttrium-aluminum-garnet.

Nd:YAG laser photodisruption has been shown to increase hemorrhage and pigment dispersion compared with argon,[13] and it has been proposed that deposition of blood and pigment may obstruct aqueous outflow at the trabecular meshwork to cause IOP elevation.[18] Nd:YAG laser has also been associated with other adverse events including uveitis, corneal decompensation, and cystoid macular edema,[6,32,33] while reduction in Nd:YAG energy has been described as one of the advantages of sequential argon-Nd:YAG LPI in dark irides.[13,34] In this study, however, the amount of Nd:YAG energy utilized during LPI did not differ between Nd:YAG and sequential argon-Nd:YAG LPIs, suggesting that laser selection does not impact Nd:YAG energy expenditure. Further, consistent with prior studies, immediate post-LPI IOP elevation was not found to be associated with either laser type or energy.[6,13,19,22,35] Results suggest that mechanistic differences between Nd:YAG and argon lasers may exhibit low clinical relevance at the population level, and that innate ocular responses following laser procedures play a bigger part in determining immediate IOP elevation.

Because of the retrospective design of this study, postprocedure medication regimens and laser procedures were not standardized. Our multivariate analysis, however, adjusted for surgeon to account for these and other surgeon-associated factors. Although post-LPI IOP was only measured within the first hour after the procedure, and it is possible that IOP elevation could have occurred at a later timepoint in some patients, a prior study examining prophylactic LPI showed that late IOP elevation between 1 hour and 2 weeks after the procedure only occurred in a very small number (0.82%) of cases.[18]

In a demonstration of practice pattern changes in response to salient patient factors, many surgeons in this study reported adjusting the type and duration of post-LPI medication regimens based on iris pigmentation, the amount of laser energy used, and baseline IOP. Specifically, 1 surgeon uses a topical steroid taper of 2 weeks instead of 7 days for patients with dark iris pigmentation, 2 use a 2-week-long topical steroid taper if Nd:YAG energy ≥ 100 mJ, and another uses a 2-week-long steroid taper if the patient had a prior history of recurrent post-LPI iritis in the fellow eye. Two of the 5 surgeons with the greatest number of cases also reported initiating a glaucoma medication in patients with baseline IOP > 22 mm Hg undergoing LPI. None, however, reported routinely adjusting post-LPI medications based on patient race.

In summary, we found the incidence of immediate IOP elevation following LPI for PACS to be higher in patients self-identified as Black and in those with higher preprocedure IOP. The incidence of iritis following LPI was also higher in Black patients independent of laser type and total laser energy. Results suggest that Black patients and those with higher preprocedure IOP would benefit from additional medications to mitigate the effects of immediate IOP elevation and decrease the incidence of iritis. Further investigation with a prospective trial is necessary to not only verify these results, but to yield insight into the optimal management, duration, and long-term sequelae of post-LPI IOP elevation and iritis in Black patients.

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