Factors Associated With Laser Trabeculoplasty Response Duration: Analysis of a Large Clinical Database (IRIS Registry)

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Original Study

Received for publication March 24, 2021; accepted July 11, 2021.

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Supported by the NIH Center Core Grant P30-EY014801, Research to Prevent Blindness Unrestricted Grant, The University of Miami Institute for Advanced Study of the Americas 2019 Pilot Grant and the 2019 American Glaucoma Society IRIS Registry-AGS Research Initiative Grant.

Disclosure: The authors declare no conflict of interest.

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Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.glaucomajournal.com.

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DOI: 10.1097/IJG.0000000000001918

Précis: In eyes with trabeculoplasty response, those with lower baseline pressure, angle recession or uveitis had shorter survival. Eyes without medications before treatment remained medication-free for a median of 197 days.

Purpose: We examined patients in a large clinical registry to assess factors associated with laser trabeculoplasty (LTP) response durations.

Methods: This is a retrospective cohort study with LTP patients in the Intelligent Research in Sight Registry. Data were extracted if the eye had a LTP procedure code and a glaucoma diagnosis. In responders [≥20% intraocular pressure (IOP) reduction], any post-LTP IOP that was above 80% of baseline was considered a failure event. Eyes were censored if IOP-lowering medication/procedure was added/performing, or if the eye reached the end of follow-up. First eye of bilaterally treated patients were included.

Results: A total of 79,332 patients/eyes were included; 53.2% female; mean age 71.5 years; 64.5% White; 71.2% primary open angle glaucoma. Mean baseline IOP was 21.6 ± 5.3 mm Hg (2.1 ± 1.5 medications). Eyes without medications before treatment remained medication-free for a median of 197 days (interquartile range 106, 395 d).

Conclusions: Angle recession and uveitis increased the risk of failure (hazard ratios 1.69 and 1.80, respectively). Eyes without medications at baseline remained medication-free for a median of 197 days (interquartile range 106, 395 d).

Key Words: IRIS Registry, uveitis, angle recession, laser trabeculoplasty (J Glaucoma 2021;30:902–910)

Laser trabeculoplasty (LTP) is one of the most frequently performed ophthalmic procedures and comprised ~40% of all glaucoma interventions in 2014.1 Recently, several studies have demonstrate adequate efficacy and safety of LTP as initial treatment in primary open angle glaucoma,2–4 while others suggest cost-saving implications of LTP either as initial or adjunctive therapies.5,6 Prior studies of modestly sized cohorts have shown LTP efficacy to be maintained in about 80% of patients after 2 years,7 with younger age and higher baseline intraocular pressure (IOP) associated with failure.8 As the utilization of LTP is likely to increase, the characterization of its treatment effect duration is a priority,1,9 and analysis of a larger cohort is needed to assess these potential predictive factors.

The Intelligent Research in Sight (IRIS) Registry is an electronic health record-based clinical data registry that includes data submitted by >2300 ophthalmology practices in the United States. In 2016, the registry contained ~17.4 million unique patient entries that captured patient demographics, payer types, social history, ocular examination laterality and values, diagnoses, procedures and medications.10 Recently, analyses of the IRIS Registry have provided “real-world” clinical insight to several important ophthalmologic diagnoses and treatments including: the prevalence and treatment patterns of myopic choroidal neovascularization, the incidence of postcataract surgery endophthalmitis, and outcomes of age-related macular degeneration treatment, macular hole surgery, and strabismus surgery.11–17 In this study, we performed an analysis of a large cohort of eyes that initially responded to LTP using the IRIS Registry to assess potential predictive factors of LTP treatment survival.

METHODS

The study protocol has been reviewed and was exempted by the Institutional Review Board of the University of Miami Miller School of Medicine as it did not meet the criteria of research involving human subjects as defined by the Department of Health and Human Services and Food and Drug Administration regulations.

Data Source

The IRIS Registry data acquisition have been described elsewhere (www.aao.org/iris-registry/about).10 Study eyes met the following inclusion and exclusion criteria:

Inclusion

1. Current Procedural Terminology (CPT) code for LTP (65855); (2) All entries between January 1, 2013 and August 31, 2019; (3) Eyes with a glaucoma or glaucoma
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Exclusion

(1) Entries without LTP laterality (coded as “unspecified”) in a patient with 2 sighted eyes; (2) LTP eye that had angle-closure International Classification of Diseases codes (9th and 10th editions; ICD-9: 364.2X, H40.2X; (3) Eyes with no light perception; (4) Eyes without visual acuity and/or pretreatment baseline IOP measurements (defined below) before LTP; and (5) Eyes that have reached an “exclusion event,” as defined below.

All data referred to below were for the study eyes, except as noted. The inclusion criteria did not distinguish between selective and argon trabeculoplasty, as the 2 procedures share the same CPT code. Separate from the glaucoma or glaucoma suspect diagnosis, the presence of “angle recession” (ICD-9 364.77, ICD-10 H21.55X) and/or “uveitis” (ICD-9 364.65, ICD-10 H20.XX, H30.XX, H44.XX) codes designated the eyes as having “angle recession” and/or “uveitis,” respectively. If neither code was present, since “glaucoma secondary to eye inflammation (H40.43XS),” “glaucoma secondary to ocular inflammation (365.62),” and “glaucoma secondary to drugs (H40.6XX)” were nonspecific and many instances of “glaucoma secondary to drugs” may be due to steroid use to treat ocular inflammation, these diagnoses were grouped as “glaucoma due to inflammation/drugs.” Similarly, since “glaucoma associated with ocular trauma (365.65),” “glaucoma secondary to eye trauma (H40.3),” and “glaucoma secondary to other eye disorders (H40.5XX)” may in fact be part of the same continuum (eg, iris sphincter tear without angle recession), these diagnoses were grouped as “glaucoma due to trauma/other eye disorders.” The lens status of the study eyes were inferred from diagnostic codes. If codes for “pseudophakia,” “aphakia,” or “cataract” were present, the eyes were labeled as such. Otherwise, the lens status was categorized as “unknown.” If the glaucoma diagnosis code had specified mild, moderate, severe or indeterminate, the eye was designated as such. If the glaucoma diagnosis code had severity available but no severity information was coded, the glaucoma severity for the eye was designated as “missing/unspecified.” Otherwise, the glaucoma severity was “not applicable.” An eye was considered to have prior glaucoma procedure if, within the IRIS Registry study period and before LTP treatment date (TD), the treated eye had undergone glaucoma procedure (CPT 658XX, 661XX, 665XX, 666XX, 667XX). The number of medications refer to the number of topical or systemic IOP-lowering agents, with fixed-dosed combination medications counted based on their constituent agents. Medications recorded in the IRIS Registry database are not eye-specific, and every glaucoma medication for a patient was attributed to the study eye. Presence of diabetes/hypertension were based on diagnostic codes and/or presence of medications commonly used to treat diabetes/hypertension.

Defining Treatment Groups

Each study eye was classified into 1 of 2 groups based on the sequence of LTP procedures. “Treatment” refers to the entirety of the management protocol; “procedure” refers to each individual LTP episode. (1) “Single LTP” was 1 LTP procedure without an additional LTP within 8 weeks. TD was the date of the procedure. (2) “Double LTP” was an initial LTP procedure followed by 1 or more additional LTP procedures within 8 weeks. Dates of the first and last procedures were recorded, as “early procedure date” and “late procedure date.” Late procedure date was designated as the TD. If > 1 TD is available per eye during the IRIS Registry study period, only the earliest TD was included in the analysis.

Defining IOP Baseline and Treatment Responses

Pretreatment baseline IOP was defined as the average of the immediate 2 (or more if they were all on the same day) measurements before LTP TD (before the LTP procedure in “single LTP,” before early procedure date in “double LTP”). Following LTP TD, responders were those who were not censored within the first 8 weeks, but whose first day’s mean IOP measurement on or after 8 weeks post-treatment (as long as this IOP measurement was within 6 mo of LTP TD) was at or below 80% of the pretreatment baseline IOP. An analysis of factors associated with responders versus nonresponders was reported previously. Only responders were included in the present analysis.

Defining Censoring Event

Censoring occurred on the date following LTP TD when: (1) IOP-lowering medication was added and/or (2) IOP-lowering procedure (CPT 658XX, 661XX, 665XX, 666XX, 667XX) was performed on the study eye (or if procedure laterality was unspecified) and/or (3) cataract surgery (CPT 668XX, 669XX) was performed on the study eye (or if the procedure laterality was unspecified) and/or (4) reaching the end of IRIS Registry follow-up. Since medication is not laterality specific, to censor whenever medication was added ensured a conservative assessment of LTP efficacy. If the IOP-lowering procedure or cataract surgery was coded as “unspecified” laterality, then censoring occurred.

Defining Failure Event

Following LTP TD+8 weeks, when the mean post-LTP IOP of any single day was above 80% of the pretreatment baseline IOP, a failure event had occurred. If a failure event and censoring event occurred on the same date, the former was declared. The failure criterion was purposely stringent to provide a conservative estimate of LTP response duration. While alternative proposed endpoints, such as obtaining 2 consecutive IOP measurements above 80% of pretreatment baseline IOP (1 index measurement followed by 1 confirmatory measurement) may more closely resemble real-world practice patterns, this approach risks overestimating response duration if medical treatment were added after the index measurement in such a way that was not captured by the IRIS registry (eg, using a medication previously prescribed only for the fellow eye in the study eye). In this context, “failure event” was considered for its technical meaning particular to this study and not equated as “treatment failure.”

Defining Provider Status

The providers were examined and categorized based on number and types of procedures captured by the IRIS Registry. Group 1—glaucoma surgeon—at least 25 of trabeculectomy and/or tube shunts each year when there is IRIS data for the provider (based on Association of University Professors of Ophthalmology/Fellowship Compliance Committee requirement for glaucoma fellowship.
training; https://aupofcc.org/system/files/resources/2017-08/glaucoma_guidelines.pdf, accessed May 25, 2021). Group 2—other anterior segment surgeon—those who were not in group 1 but had at least 85 cataract surgeries each year when there is IRIS data for the provider. Group 3—unknown—those who are not group 1 nor group 2. Provider LTP count per year was arbitrarily grouped into <50, 50 to 99, 100 to 499, and >500.

**Statistical Methods**

Continuous data were summarized as mean ± SD and/or 5-number summary (5NS: minimum, 25th percentile, median, 75th percentile, and maximum), while categorical data were summarized with counts and/or percentages. Mean times were compared using analysis of variance. Univariable and multivariable Cox proportional hazards regression (proc PHREG) was used to estimate hazard ratios (HRs), and Kaplan-Meier survival analysis was used to produce survival curves. For patients who had bilateral LTP during the study period, the sample include only the first eye that received LTP or a randomly selected eye if a patient had a bilateral LTP on the same date. Each eye for all patients who had unilateral LTP was also included in the sample. All statistical analyses were performed using SAS (Cary, NC) version 9.4. The figures were produced with R version 4.0.2 (www.r-project.org/). A P-value of <0.050 was considered to be statistically significant.

**RESULTS**

**Responder Baseline and Demographics**

The initial CPT code search yielded 668,128 eyes. After applying the exclusion criteria, 380,957 eyes were included. The main reasons of exclusion were: no pre-LTP IOP

| Variables | n (%) |
|-----------|-------|
| Age       |       |
| 18-39     | 928 (1.2) |
| 40-64     | 19,237 (24.3) |
| 65-79     | 37,715 (47.5) |
| 80+       | 21,090 (26.6) |
| Unknown/missing | 362 (0.5) |
| Sex       |       |
| Male      | 36,883 (46.5) |
| Female    | 42,222 (53.2) |
| Unknown   | 227 (0.3) |
| Race      |       |
| Asian     | 1530 (1.9) |
| Black     | 9487 (12.0) |
| Unknown   | 5779 (7.3) |
| White     | 51,143 (64.5) |
| Hispanic  | 3810 (4.8) |
| Other/multiracial | 7583 (9.6) |
| Insurance |       |
| Dual Medicaid and Medicare | 10,196 (12.9) |
| Medicaid  | 1761 (2.2) |
| Medicare advantage | 9140 (11.5) |
| Medicare fee-for-service | 35,036 (44.2) |
| Military  | 491 (0.6) |
| Other government | 131 (0) |
| Private   | 16,519 (20.8) |
| Unknown/no payment listed | 6058 (7.6) |
| Region    |       |
| Midwest   | 18,255 (23.0) |
| Northeast | 14,153 (17.8) |
| South     | 30,910 (39.0) |
| West      | 14,258 (18.0) |
| Unknown   | 1756 (2.2) |
| Diabetess |       |
| Yes       | 14,546 (18.3) |
| Hypertension | 3.1 |
| Yes       | 14,546 (18.3) |
| LTP type  |       |
| Single    | 77,354 (97.5) |
| Double    | 1978 (2.5) |
| Angle recession | 46 (0.1) |
| Yes       | 46 (0.1) |
| Uveitis   |       |
| Yes       | 552 (0.7) |
| Prior glaucoma procedure | 1463 (1.8) |
| Prior lens surgery | 4978 (6.3) |
| Prior intravitreal injection/surgery | 2254 (2.8) |
| Provider status |       |
| Group 1    | 16,118 (20.3) |
| Group 2    | 33,601 (42.4) |
| Group 3    | 28,406 (35.8) |
| No provider information | 1207 (1.5) |
| Provider LTP count per year |       |
| 50 or fewer | 30,204 (38.1) |
| 51-99      | 15,812 (19.9) |
| 100-499    | 30,175 (38.0) |
| 500 or more | 3141 (4.0) |
| Glaucoma type |       |
| Glaucoma suspect | 15,850 (20.0) |
| POAG       | 56,457 (71.2) |
| Trauma/other eye disorders | 408 (0.5) |
| Inflammation/drugs | 297 (0.4) |
| Other glaucoma | 172 (0.2) |
| Unspecified glaucoma | 6148 (7.8) |

**TABLE 1. Baseline Descriptive Statistics of the 79,332 IRIS Registry LTP Responder Eyes**

| Variables | n (%) |
|-----------|-------|
| Severity  |       |
| Mild      | 13,442 (16.9) |
| Moderate  | 17,566 (22.1) |
| Severe    | 11,434 (14.4) |
| Indeterminate | 2065 (2.6) |
| Missing/unspecified | 12,655 (16.0) |
| Not applicable | 22,170 (28.0) |
| Lens status |       |
| Cataract  | 25,505 (32.2) |
| Pseudophakia | 4042 (5.1) |
| Aphakia   | 219 (0.3) |
| Unknown   | 49,566 (62.5) |

| Variables | n (%) |
|-----------|-------|
| Baseline Intraocular pressure (mmHg) |       |
| Mean (SD) | 21.6 (5.3) |
| Minimum-maximum | 4-68 |
| Baseline visual acuity (logMAR) |       |
| Mean (SD) | 0.23 (0.3) |
| Minimum-maximum | −0.12 to 2.00 |
| Baseline number of glaucoma medications* |       |
| Mean (SD) | 2.1 (1.5) |
| Minimum-maximum | 0-7 |
| Age (y) |       |
| Mean (SD) | 71.5 (11.8) |
| Minimum-maximum | 18-99 |

Only 1 eye per patient is included.

*Fixed-dose combination medications were counted as the number of their constituents.

IRIS indicates Intelligent Research In Sight; LogMAR, logarithm of minimum angle of resolution; LTP, laser trabeculoplasty; POAG, primary open angle glaucoma.
TABLE 2. Time to Failure or Censoring Event After Treatment (Days Between Treatment Date and When Failure or Censor Events Occurred)

|                          | Mean (SD)   | Median | Minimum-Maximum | Q1-Q3 | P       |
|--------------------------|-------------|--------|-----------------|-------|---------|
| For all eyes             |             |        |                 |       |         |
| Overall                  | 410.50 (346.62) | 301    | 56-2371         | 181-516 | <0.0001* |
| IOP categories           |             |        |                 |       |         |
| For baseline IOP <18 mm Hg | 323.80 (250.91) | 256    | 56-2300         | 168-385 |
| For baseline IOP 18-24 mm Hg | 412.08 (338.72) | 309    | 56-2371         | 186-520 |
| For baseline IOP > 24 mm Hg | 480.41 (410.38) | 349    | 56-2360         | 182-644 |
| Glaucoma categories      |             |        |                 |       |         |
| Glaucoma suspect         | 464.47 (391.58) | 332    | 56-2371         | 189-608 |
| POAG                     | 388.88 (321.21) | 294    | 56-2360         | 178-488 |
| Trauma                   | 416.63 (380.65) | 279    | 56-2070         | 149-552 |
| Inflammation/drugs       | 379.78 (352.02) | 260    | 57-2220         | 158-476 |
| Other glaucoma           | 390.20 (356.65) | 263.5  | 57-2321         | 173-447.5 |
| Unspecified glaucoma     | 471.58 (415.76) | 320    | 56-2334         | 188-609 |
| Angle recession status   |             |        |                 |       |         |
| No                       | 410.53 (346.63) | 301    | 56-2371         | 181-516 |
| Yes                      | 362.26 (328.79) | 287.5  | 62-1932         | 153-428 |
| Uveitis status           |             |        |                 |       |         |
| No                       | 411.08 (347.07) | 302    | 56-2371         | 181-517 |
| Yes                      | 327.44 (261.10) | 254    | 57-1932         | 144-406 |
| For eyes in the analysis that reached fail event | | | | | |
| Overall                  | 574.85 (453.85) | 441    | 56-2371         | 248-782 |
| IOP categories           |             |        |                 |       |         |
| For baseline IOP <18 mm Hg | 431.79 (360.93) | 331    | 56-2300         | 163-566 |
| For baseline IOP 18-24 mm Hg | 563.23 (441.94) | 433    | 56-2371         | 248-758 |
| For baseline IOP > 24 mm Hg | 650.35 (488.54) | 511    | 56-2360         | 291-901 |
| Glaucoma categories      |             |        |                 |       |         |
| Glaucoma suspect         | 675.27 (501.94) | 533    | 56-2371         | 279-1008 |
| POAG                     | 527.15 (414.69) | 414    | 56-2360         | 238-699 |
| Trauma                   | 633.21 (492.04) | 522    | 56-2070         | 215-886 |
| Inflammation/drugs       | 643.95 (466.90) | 518    | 71-2220         | 324-871 |
| Other glaucoma           | 603.64 (528.48) | 352    | 57-2321         | 251-830 |
| Unspecified glaucoma     | 835.20 (599.96) | 744    | 56-2334         | 275-1296 |
| Angle recession status   |             |        |                 |       |         |
| No                       | 574.99 (453.84) | 441    | 56-2371         | 248-782 |
| Yes                      | 411.76 (451.93) | 322    | 66-1932         | 171-390 |
| Uveitis status           |             |        |                 |       |         |
| No                       | 575.58 (454.66) | 441    | 56-2371         | 248-783 |
| Yes                      | 489.35 (336.88) | 385.5  | 60-1932         | 244-703 |
| For eyes in the analysis that did not reach failure event | | | | | |
| Overall                  | 353.52 (278.88) | 273    | 57-2340         | 173-434 |
| IOP categories           |             |        |                 |       |         |
| For baseline IOP <18 mm Hg | 302.42 (216.49) | 248    | 57-2194         | 168-357 |
| For baseline IOP 18-24 mm Hg | 360.98 (277.77) | 281    | 57-2296         | 180-446 |
| For baseline IOP > 24 mm Hg | 390.86 (328.88) | 290    | 57-2340         | 160-508 |
| Glaucoma categories      |             |        |                 |       |         |
| Glaucoma suspect         | 385.09 (305.26) | 293    | 57-2227         | 179-490 |
| POAG                     | 339.53 (263.39) | 266    | 57-2340         | 170-414 |
| Trauma                   | 328.51 (281.24) | 245.5  | 58-1840         | 133-409 |
| Inflammation/drugs       | 272.11 (214.96) | 208    | 57-1185         | 125-341 |
| Other glaucoma           | 327.62 (258.80) | 252    | 57-1604         | 168-385 |
| Unspecified glaucoma     | 401.37 (326.08) | 297    | 57-2212         | 183-510 |
| Angle recession status   |             |        |                 |       |         |
| No                       | 353.53 (278.90) | 273    | 57-2340         | 173-434 |
| Yes                      | 333.24 (233.82) | 259    | 62-959          | 153-428 |
| Uveitis status           |             |        |                 |       |         |
| No                       | 354.17 (279.32) | 273    | 57-2340         | 173-434 |
| Yes                      | 254.16 (174.99) | 208    | 57-992          | 126-329 |

*Statistically significant.

All P values are from analysis of variance.

IOP indicates intraocular pressure; POAG, primary open angle glaucoma; Q1-Q3, first and third quartiles.
categorized as "responders." From the responder cohort, we included only the first treated eye (if both eyes were treated on different dates) or a randomly selected eye (if both eyes treated on the same date), as well as all unilaterally treated eyes, which resulted in the 79,332 patients/eyes included in the present analysis.

Among the responders, there was a slight female predominance (53.2%), with mean ± SD age of 71.5 ± 11.8 years. The majority were White (64.5%) or Black (12.0%), and the most common glaucoma diagnoses were primary open angle glaucoma (71.2%), glaucoma suspect (20.0%) and unspecified (7.8%). Baseline mean visual acuity was 0.23 ± 0.29 logarithm of the minimal angle of resolution (logMAR, Snellen equivalent of ~20/34), mean IOP was 21.6 ± 5.3 mm Hg on 2.1 ± 1.5 IOP-lowering medications (Table 1).

Follow-up and Response Duration
Median follow-up time (from LTP TD+8 wk, which was defined as time = 0 for the survival analysis) to the last date in the IRIS Registry for 79,332 responder eyes was 245 days (5NS: 0, 125, 215, 245 d; mean of 354.5 ± 346.6 d).

Overall, 20,423 eyes (25.7%) failed with a median follow-up of 385 days (5NS: 0, 192, 385, 726, 2315 d), while 58,909 (74.3%) were censored with a median follow-up of 217 days (5NS: was 1, 117, 217, 378, 2284 d); 6625 (8.4%) were censored due to addition of IOP-lowering medications, 3323 (4.2%) due to additional IOP-lowering procedures, 3845 (4.8%) due to cataract surgery, 45,116 (56.9%) by reaching the end of IRIS follow-up. Eyes with higher baseline IOP had longer time to failure event compared with eyes with lower baseline IOP (> 24 mm Hg median 349 d; 18 to 24 mm Hg median 309 d; <18 mm Hg median 256 d, \( P < 0.001 \) for all comparisons). Time to failure event in other subgroups are outlined in Table 2.

Responder Survival Analysis
The proportions that reached failure event for the overall cohort at 0, 6, 12, 18, and 24 months following LTP were 0.2%, 6.1%, 16.8%, 29.1%, and 40.8%. The proportion of eyes with angle recession and eyes with uveitis that failed at various time-points are outlined in Table 3. In univariable analyses (Supplemental Table 2, Supplemental Digital Content 2, http://links.lww.com/IJG/A576) of the 79,332 responders, angle recession \([HR: 1.69; 95\% \text{ confidence interval (CI): } 1.05-2.73; \ P=0.0299]\) and uveitis \([HR: 1.80; 95\% \text{ CI: } 1.55-2.09; \ P<0.0001]\) significantly increased the risk of failure (Figs. 1, 2). In multivariable analyses (Table 4), the effects of uveitis remained significant.

For eyes that were not on any IOP-lowering medications at the time of LTP (n=1488), they remained

| Cohort                  | 0 Month* | 6 Months | 12 Months | 18 Months | 24 Months |
|-------------------------|----------|----------|-----------|-----------|-----------|
| Overall                 | 0.2      | 6.1      | 16.8      | 29.1      | 40.8      |
| Angle recession         | 0        | 20.9     | 41.6      | 47.5      | 55.2      |
| Uveitis                 | 0        | 9.8      | 31.5      | 48.3      | 67.7      |

*Treatment response is assessed after TD+8 weeks. Any responders who reached failure between TD+8 weeks and TD+12 weeks is considered to have failed after “0 month.”
LTP indicates laser trabeculoplasty; TD, treatment date.
medication-free for a median of 197 days (SNS: 57, 106, 197, 395, 2211 d; mean of 317.6 ± 311.6 d).

DISCUSSION

LTP has been shown to be safe and efficacious as initial glaucoma therapy,4,19 while several studies that compared LTP to medication as initial treatment showed comparable efficacies.2,3,20 The ability to identify factors associated with different response durations in LTP responders is crucial in planning follow-up and setting treatment expectations.

Our findings of 0.2% failure at 6 months, 6.1% failure at 12 months and 40.8% failure at 24 months are better than previously published literature, which ranged between 25% to 33% failure by 6 months and 47% to 73% failure by 24 months.21–26 This may be due either the IRIS Registry cohort being older and/or our study defining a technical failure event separate from “treatment failure.” Khawaja et al24 analyzed a large database of LTP patients and defined failure clinically based insufficient IOP reduction, IOP > 21 mm Hg or addition of IOP-lowering procedures and/or medications. In contrast, our survival analysis included only patients who had initially responded with adequate IOP reduction, such that the “nonresponders” that were excluded from our study would have been counted as “failures” by prior studies.18 Furthermore, since the goal of our study was to assess the longevity of the LTP treatment effect, rather than the ability of LTP to stave off the addition of medications (which can occur despite a 20% or more IOP reduction from LTP), the addition of IOP-lowering medications after LTP treatment was a censoring rather than a failure event. This strategy perhaps better reflects the therapeutic effect of LTP in the context of medication confounders, although it limits the prognostic value of LTP in delaying additional IOP-lowering medication and/or procedures.

The analysis of angle recession and uveitis failures following LTP treatment may imply different mechanisms of trabecular dysfunction in these diseases. At 6 months post-LTP, a larger proportion of angle recession eyes had failed compared with uveitic eyes (20.9% vs. 9.8%, Table 3). However, by 18 months, the proportion of failures in both groups were comparable (47.5% angle recession vs. 48.3% uveitic). The mechanism behind the earlier failure in eyes with angle recession compared to uveitis remains uncertain, and may be attributed to the different ways the trabecular tissues are affected in angle recession (irreversible metaplasia)27 versus uveitis (partially reversible trabecular dysfunction).28 Furthermore, as IOP fluctuations may be associated with uveitis flare-up (not captured by the IRIS Registry), the LTP failure rates may vary greatly in different types of uveitis. Due to the small proportion of eyes with either angle recession or uveitis in our cohort, the generalizability of these observations remain uncertain.

Previously, we have reported higher odds of favorable IOP responses to LTP treatment with high baseline IOP,18 and the current cohort with highest baseline IOP (> 24 mm Hg) had the longest time to failure. However, baseline IOP had only a modest effect on time to failure (HR: 1.01; 95% CI: 1.01-1.01; \( P < 0.0001 \)) for eyes that initially responded to LTP. Thus, while the effect of high baseline IOP was significant, we did not feel it be strong enough to be clinically important. This finding is similar a previous multicenter retrospective study in which baseline IOP conferred a failure HR of 0.96, which is statistically, but not clinically, significant.24

In eyes without medications at baseline, following LTP, they remained medication-free for a median of 197 days (mean 317.6 d). When a medication is added, since laterality is not specified, it may or may not apply to the study eye. Thus, the duration reported here is a conservative estimate with the actual medication-free period to be possibly longer. The cost comparison of LTP versus topical prostaglandins in the United States favors LTP,29 and the IRIS Registry data suggests that the relative longevity of the LTP treatment effect may have cost-saving implications when performed in medication-free eyes (a subset of which would be as initial therapy in eyes with newly diagnosed...
TABLE 4. Multivariable Survival Analysis of Laser Trabeculoplasty Outcomes

| Parameters                          | Hazard Ratio | 95% Hazard Ratio Confidence Limits | P       | Comments                                                                 |
|-------------------------------------|--------------|------------------------------------|---------|--------------------------------------------------------------------------|
| Age (y)                             |              |                                    |         |                                                                           |
| 18-39                               | 1.37         | 1.22                               | 1.53    | <0.0001* Age: per patient eye, 5 levels: 18-39, 40-64, 65-79 (reference), 80+ |
| 40-64                               | 0.96         | 0.93                               | 1.00    | 0.0738                                                                   |
| 80+                                 | 1.44         | 1.39                               | 1.49    | <0.0001*                                                                 |
| Unknown                             | 1.60         | 1.33                               | 1.93    | <0.0001*                                                                 |
| Sex                                 |              |                                    |         |                                                                           |
| Female                              | 0.93         | 0.90                               | 0.95    | <0.0001* Sex; per patient, 3 levels: male (reference), female, unspecified |
| Unspecified                         | 1.19         | 0.93                               | 1.48    | 0.1345                                                                   |
| Region                              |              |                                    |         |                                                                           |
| Midwest                             | 0.92         | 0.89                               | 0.95    | <0.0001* Region: per patient eye, provider region, 5 levels: Midwest, Northwest, West, South |
| Northeast                           | 0.91         | 0.88                               | 0.95    | <0.0001*                                                                 |
| West                                | 0.94         | 0.90                               | 0.98    | 0.0046*                                                                  |
| Unknown                             | 1.22         | 1.05                               | 1.42    | 0.0103* (reference), unknown                                             |
| Race                                |              |                                    |         |                                                                           |
| Asian                               | 1.15         | 1.04                               | 1.28    | 0.0092* Race: per patient, 6 levels: White (reference), Asian, Black, Hispanic, multirace/other, unknown |
| Black                               | 1.10         | 1.05                               | 1.15    | <0.0001*                                                                  |
| Hispanic                            | 0.91         | 0.85                               | 0.98    | 0.0088*                                                                  |
| Multi/other                         | 0.97         | 0.92                               | 1.02    | 0.2722                                                                   |
| Unknown                             | 1.54         | 1.46                               | 1.62    | <0.0001*                                                                  |
| Insurance type                      |              |                                    |         |                                                                           |
| Dual Medicare and Medicaid          | 0.72         | 0.68                               | 0.76    | <0.0001* Insurance: per patient, 8 levels: dual Medicare/Medicaid, Medicaid, Medicare advantage, Medicare fee-for-Service, military, other government, unknown, private (reference) |
| Medicaid                            | 1.01         | 0.92                               | 1.11    | 0.8087                                                                   |
| Medicare advantage                  | 0.82         | 0.77                               | 0.86    | <0.0001*                                                                  |
| Medicare FFS                        | 0.77         | 0.74                               | 0.80    | <0.0001*                                                                  |
| Military                            | 1.28         | 1.10                               | 1.49    | 0.0016*                                                                  |
| Other Government                    | 1.31         | 0.96                               | 1.79    | 0.0864                                                                   |
| Unknown                             | 1.13         | 1.07                               | 1.19    | <0.0001*                                                                  |
| No. glaucoma medications            | 0.96         | 0.95                               | 0.97    | <0.0001*                                                                  |
| Mean baseline IOP                   | 1.01         | 1.01                               | 1.01    | <0.0001*                                                                  |
| Mean baseline VA                    | 1.18         | 1.13                               | 1.24    | <0.0001*                                                                  |
| Provider status                     |              |                                    |         |                                                                           |
| Group 2                             | 1.10         | 1.05                               | 1.14    | <0.0001* Provider status: per patient eye, 3 levels: group 1 (glaucoma surgeon) (reference), group 2 (other anterior segment surgeon), or group 3 (unknown) |
| Group 3                             | 1.25         | 1.20                               | 1.31    | <0.0001*                                                                  |
| No provider information             | 0.72         | 0.60                               | 0.88    | 0.001*                                                                   |
| Prior glaucoma procedures           | 1.03         | 0.92                               | 1.14    | 0.6224                                                                   |
| Prior lens surgery                  | 1.28         | 1.21                               | 1.36    | <0.0001*                                                                  |
| Prior intravitreal injections       | 1.05         | 0.96                               | 1.16    | 0.2983                                                                   |
| Diabetes                            |              |                                    |         |                                                                           |
| Yes                                 | 1.07         | 1.03                               | 1.11    | 0.0003*                                                                   |
| Hypertension                        | 0.93         | 0.85                               | 1.01    | 0.0765                                                                   |
| Angle recession                     | 0.91         | 0.55                               | 1.50    | 0.7104                                                                   |
| Uveitis                             | 1.30         | 1.10                               | 1.52    | 0.0009*                                                                   |
| Provider LTP count in preceding year|              |                                    |         |                                                                           |
| 51-99                               | 1.10         | 1.06                               | 1.15    | <0.0001* No. LTP performed by provider in the year preceding treatment date, per patient eye, 4 levels: < 50 (reference), 50-99, 100-499, 500+ |
| 100-499                             | 1.21         | 1.17                               | 1.25    | <0.0001*                                                                  |
| 500+                                | 1.24         | 1.14                               | 1.34    | <0.0001*                                                                  |
| Glaucoma type                       |              |                                    |         |                                                                           |
| Inflammation/drugs                  | 1.62         | 1.30                               | 2.01    | <0.0001* Glaucoma type: per patient eye, 6 levels: suspect (reference), POAG, trauma, inflammation, other, unspecified |
| POAG                                | 1.71         | 1.64                               | 1.79    | <0.0001*                                                                  |
| Trauma/other eye disorders          | 1.59         | 1.32                               | 1.93    | <0.0001*                                                                  |
| Other glaucoma                      | 1.10         | 0.80                               | 1.50    | 0.5712                                                                   |
| Unspecified glaucoma                | 0.66         | 0.61                               | 0.70    | <0.0001*                                                                  |
| Glaucoma severity                   |              |                                    |         |                                                                           |
| Moderate                            | 0.91         | 0.88                               | 0.95    | <0.0001* Glaucoma Severity: per patient eye, stage closest to LTP date, 6 levels: mild (reference), moderate, severe, indeterminate, unspecified/missing, not applicable |
| Severe                              | 0.89         | 0.85                               | 0.94    | <0.0001*                                                                  |
| Indeterminate                       | 1.06         | 0.98                               | 1.16    | 0.1557                                                                   |
| Missing/unspecified                 | 0.37         | 0.35                               | 0.39    | <0.0001*                                                                  |
glaucoma), in addition to the benefits of the therapy not being compliance-dependent.

This study has several notable limitations. First, as with all studies involving very large sample sizes, many associations that are statistically significant may not necessarily be clinically significant. As there are no accepted consensus on the magnitude of HR that renders a finding clinically significant, we have decided to present the entire output of univariable and multivariable analyses (Supplemental Table 2, Supplemental Digital Content 2, http://links.lww.com/IJG/A576; Table 4) such that the readers can determine for themselves the importance of each association, while limiting our discussion to a few findings we believed to be particularly relevant clinically. Second, this study is subjected to the limitations inherent to all retrospective cohort studies using large clinical database, namely observational data not subjected to the same rigorous validation as those produced by a clinical trial. Similarly, the variabilities inherent in ICD-9/ICD-10 coding in clinical practice may limit the Registry’s ability to provide precise glaucoma type, stage, and nomenclature beyond the large categories which we have utilized. However, the direct extraction of longitudinal clinical information from the electronic health records at a scale that would not be practical through other means makes IRIS Registry a useful large-scale real-world database for assessing ophthalmology treatment outcomes and practice patterns. Multiple publications in high-impact journals using the IRIS Registry and similar registries has established this mode of research as relevant and impactful. Nevertheless, clinicians should recognized the limitations of such registries, as information, selection and confounding biases are possible.31

In conclusion, this analysis of 79,332 eyes that had undergone LTP in the IRIS Registry and had initially responded to this treatment revealed a median duration of 385 days (mean 518.9 d) before reaching failure events, with 84.2% survival at 1 year and 59.2% survival at 2 years. Uveitis and angle recession significantly increased the risk of reaching failure events, while eyes with high baseline IOP (>24 mm Hg) had the longest survival compared with eyes with lower baseline IOP. Eyes not receiving glaucoma medications at the time of LTP treatment remained medication-free for a median of 197 days (mean 317.6 d). Overall, this data supports offering LTP to medication-free eyes as a means of obviating medication burden to optimize medical resource utilization in glaucoma therapeutics. Future studies that analyze LTP practice patterns and implementation lag would facilitate resource optimization in glaucoma therapy.

### ACKNOWLEDGMENTS

The authors thank Dr Charles Nenner and Mrs. Elisa Krassner for their generous philanthropic support of The Samuel & Ethel Balkan International Pediatric Glaucoma Center research efforts.

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