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Selective Laser Trabeculoplasty as First-Line Treatment in Primary Open Angle Glaucoma: A Meta-Analysis

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ABSTRACT
Introduction: For primary open-angle glaucoma (POAG), selective laser trabeculoplasty (SLT) is a non-invasive therapeutic approach that provides an alternative to conventional operations and medications. The effectiveness and safety profile of SLT as a primary treatment for newly diagnosed POAG were evaluated by a meta-analysis.
Methods: A systematic review and meta-analysis were performed using databases including PubMed, ScienceDirect, ProQuest, and Scopus from inception to March 2025, adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Analyses were executed via Review Manager 5.4.1. Subgroup analyses were performed on SLT compared with medical therapy and categorized SLT as initial or adjunctive therapy.
Results: Out of twelve qualifying trials, 2.248 patients were combined. In newly diagnosed POAG, the results showed no significant differences in IOP reduction between SLT and topical medications as first line modality (Mean Difference (MD): 0.21, 95% CI 0.81 to 1.83, p=0.69, I2 = 70%); however, initial SLT performed better than adjunctive SLT (MD: 0.57, p=0.05, I2: 37%). Antiglaucoma drug use, glaucoma surgery rates, and ocular side effects were all markedly lower in the SLT group.
Conclusion: SLT has the potential to transform glaucoma management due to its enhanced efficacy, minimal adverse effects, reduced medication burden, and cost-effectiveness.
Keywords: glaucoma, primary open-angle glaucoma, selective laser trabeculoplasty

ABSTRAK
Pendahuluan: Laser Trabekuloplasti Selektif (SLT) sebagai terapi non-invasif glaukoma primer sudut terbuka telah menjadi alternatif dari operasi dan pengobatan konvensional. Meta-analisis ini dilakukan untuk mengevaluasi efektivitas dan profil keamanan SLT sebagai terapi pertama glaukoma primer sudut terbuka (POAG) yang baru terdiagnosis.
Metode: Review sistematis dan meta-analisis dilakukan menggunakan basis data PubMed, ScienceDirect, ProQuest, dan Scopus dari awal hingga Maret 2025, dengan pedoman PRISMA. Analisis menggunakan Review Manager 5.4.1, dengan Analisis subgrup SLT dibandingkan dengan terapi medis dan mengkategorikan SLT sebagai terapi lini pertama dan adjuvant.
Hasil: Sebanyak 2.248 pasien dikumpulkan dari 12 studi yang memenuhi kriteria inklusi. Tidak ada perbedaan signifikan dalam penurunan TIO antara SLT dan pengobatan topikal sebagai modalitas lini pertama POAG yang baru terdiagnosis (MD: 0,21, 95% CI -0,81 hingga 1,83, p=0,69, I^2 =70%), namun SLT primer menunjukkan hasil lebih baik dibandingkan SLT adjuvant (MD: 0,57, p= 0,05, I^2: 37%). Kelompok SLT menunjukkan tingkat operasi glaukoma, jumlah pengobatan antiglaukoma, dan efek samping okular yang menurun secara signifikan.
Kesimpulan: SLT berpotensi mengubah tatalaksana glaukoma karena efektivitas, efek samping yang minimal, beban pengobatan menurun, dan biaya yang lebih terjangkau.
Kata Kunci: glaukoma, glaukoma sudut terbuka primer, laser trabekuloplasti selektif

INTRODUCTION

Glaucoma, marked by optic neuropathy, is a major cause of global irreversible visual impairment.[1] A *meta-analysis* indicates a global incidence rate of glaucoma is 23.46 per 10,000 person-years for individuals aged 40–79.[2] The estimated global population of Primary Open-Angle Glaucoma (POAG) is 68.56 million, constituting the most common subtype.[3] Data from Indonesia remains limited, though a prevalence of 0.46% was reported in 2007.[4]

While glaucoma is incurable, reducing intraocular pressure (IOP) can mitigate progression and vision loss.[5] The National Glaucoma Guideline of The Indonesian Ophthalmologist Association endorses IOP-lowering therapy as the primary effective treatment for POAG, demonstrating benefits in disease progression and visual field preservation.[4] Despite their efficacy, topical medications present ocular and systemic side effects, leading to poor compliance and increased medical costs, which contribute significantly to treatment failures.[6]

Recent research suggests selective laser trabeculoplasty (SLT) as a viable primary treatment for glaucoma. The Laser in Glaucoma and Ocular Hypertension Trial (LiGHT) found SLT to be as effective as topical medications.[7] Moreover, SLT reduces the need for topical glaucoma medications for extended periods.[8] SLT is safe, repeatable, and does not harm the trabecular meshwork.[9] Additionally, SLT may enhance patients' quality of life by decreasing medication reliance and is cost-effective compared to conventional treatments.

However, prior systematic reviews and meta-analyses have evaluated SLT primarily as an adjunct to topical therapy[6,10–12], with limited evidence in treatment-naïve POAG and inconsistent reporting of long-term outcomes compared with first-line pharmacological treatment. Furthermore, although the 2024 Report of The American Academy of Ophthalmology (AAO) provides Level 1 evidence supporting SLT as a primary intervention[13], its effectiveness across diverse populations and healthcare settings has not been comprehensively evaluated. This meta-analysis synthesizes the latest high-quality studies to evaluate SLT exclusively as initial therapy, providing updated data on efficacy, safety, cost-effectiveness, and patient's quality of life.

METHOD

The study was performed in alignment with Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines and the protocol has been registered in the international prospective register of systematic reviews (PROSPERO) under: CRD420251030926.

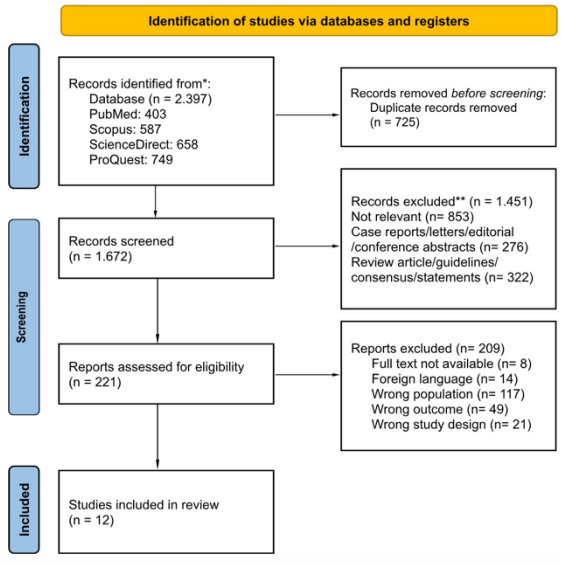

Figure 1. Flowchart of study selection

Studies were eligible for inclusion if they reported SLT use and compared with other modalities as first-line treatment in POAG among human participants and published in the English language. The exclusion criteria were as follows: (1) the study recruited patients with Acute Closure Glaucoma (ACG), (2) grey literature, not reporting details, (3) letters, comments, editorials, and case reports.

We conducted the literature search using online databases, including PubMed, Science Direct, Scopus and ProQuest, from inception to March 31, 2025. The keywords used were “primary open angle glaucoma” and “selective laser trabeculoplasty”. All retrieved citations were imported into the Rayyan web platform for systematic review management. After removing duplicates, two reviewers (AZFR and FDH) independently screened titles and abstracts to determine eligibility. Full-text articles of potentially relevant studies were then reviewed in detail. Any disagreements between reviewers are resolved through discussion or, when necessary, by consultation with a third reviewer (F) as an ophthalmologist.

The risk of bias in the individual observational studies was independently assessed by the two reviewers with the Risk of Bias 2 (ROB-2) and Risk of Bias in Non-Randomized Studies - of Interventions (ROBINS-I) assessment tool. All perceptional disparities are discussed in order to reach a consensus. No permission from an ethics board was required because the primary data had been previously published.

Review Manager Software version 5.4.1 was used to perform the meta-analysis; the dichotomous outcomes were measured as odds ratio (OR) with the corresponding 95% confidence intervals (CIs) were used to measure the overall adjusted odd’s ratio of the outcomes with a 95% confidence interval. Logarithmic odd’s ratio (OR) was obtained for each study and used to pool the results. A random effects model was used to account for heterogeneity among studies. Heterogeneity was assessed with the Higgins I^2 statistic. I^2 >50% indicated significant heterogeneity. Forest plots were used to graphically display the effect size in each study and the pooled estimates.[14]

RESULT

Of the 2.397 articles retrieved from the initial search, 725 duplicates were removed. A total of 1.672 studies underwent title and abstract screening. The full texts of 221 studies were retrieved for assessment of eligibility, with 12 studies remaining in the final quantitative meta-analysis, as shown in **Figure 1**.

Characteristics of Included Studies

Baseline characteristics of the included studies are presented in **Table 1.** A total of 2.248 patients were pooled from twelve eligible studies. The studies consisted of 5 randomized control trials,[7,15–18] 3 cohort studies,[19–21] and 4 observational studies.[22–25] The studies had the following geographic distribution: two in the America continent,[17,20] four in Asia, [15,16,21,23] three in Europe,[7,19,25] and three in Africa.[18,22,24] The mean duration of follow-up ranged from 3–60 months. The mean baseline IOP ranged from 18.9 mmHg to 27.07 mmHg in primary SLT groups, from 15.57 mmHg to 27.0 mmHg in the medication control group and from 18.29 mmHg to 22.92 mmHg in SLT as adjunctive group.

Characteristics of Intervention

In the studies, SLT was applied for 100 laser spots, lasting 3 nanoseconds, starting energy level was 0.3-0.9 mJ, which was continuously titrated in steps of 0.1 mJ. In three studies [20,21,25] 180 degrees trabecular meshworks was treated, and 360 degrees were treated in eight studies [7,15–19,22,23] as presented in **Table 2**. The topical medication regimen group starts with ocular prostaglandin analog: latanoprost, bimatoprost, or travoprost. If the target IOP is not met, but initial medication is deemed effective, add a b-blocker (or substitute, if the first drug used was ineffective or not tolerated): timolol or betaxolol. Then a step-

up regime is followed by an α2-agonist, and carbonic anhydrase inhibitor.[16,17,21] However, some studies only use one regimen, such as timolol 0.5%,[18] 0.005% latanoprost.[15]

Table 1. Baseline characteristics of included studies

Author, year	Country	Study design	Total POAG	No of Eyes		Age (years)		Male %	IOP Pre-treatment		Follow up (mo)
				p-SLT	Control	p-SLT	Control		p-SLT	Control	
Primary SLT vs Topical Medication											
Gazzard, 2019	UK	RCT, MC	718	418	437	63.4	62.7	55.3	24.5	24.4	36
Shi, 2023	China	RCT, SC	45	23	22	47.8	53.9	65	20.4	21.0	3
Lai, 2004	China	RCT, SC	64	32	32	51.9	51.9	44.8	26.8	26.2	60
McIlraith, 2006	Canada	Cohort, SC	61	74	26	62	63	44.2	26.0	24.6	12
Philippin, 2021	Tanzania	RCT, SC	840	101	100	67.4	65.09	58.7	26.4	27	12
Hsien, 2020	Malaysia	Cohort, SC	17	10	7	67.4	67.4	52.9	18.9	15.57	6
Katz, 2012	US	RCT, MC	69	67	60	NA	NA	48.1	25.0	24.5	12
Primary SLT vs Adjunctive SLT											
Yener, 2020	Turkey	OS, SC	81	39	40	64.8	64.02	52.4	23.8	22.9	12
Goosen, 2016	South Africa	OS, SC	84	29	119	NA	NA	51.1	27.07	18.97	12
Abdelrahman, 2012	Egypt	OS, SC	65	41	65	53.2	53.2	47	21.54	18.29	18
Gracner, 2018	Slovenia	OS, SC	61	28	31	67.50	72.23	39.9	21.43	21.97	24
De Keyser, 2017	Belgium	Cohort, SC	143	64	61	68.59	72.07	50.4	23.21	22.92	12

POAG: primary open angle glaucoma, p-SLT: primary selective laser trabeculosplasty, RCT: randomized controlled trial, MC: multicenter, SC: single center, OS: observational studies, NA: not available

Table 2. Characteristics of intervention

Author, year	Angle (°)	Initial Energy (mJ)	IOP reduction (mmHg)	
			p-SLT	Control
Gazzard, 2019	360	0.3	9.1	9.1
Shi, 2023	360	0.8	2.6	5.5
Lai, 2004	360	0.6	8.6	8.7
McIlraith, 2006	180	0.8	8.3	7.7
Philippin, 2021	360	0.6	6.3	3.2
Hsien, 2020	180	0.5	4.30	2.71
Katz, 2012	360	0.8	6.3	7.0
Yener, 2020	360	0.8	9.6	7.9
Goosen, 2016	NA	NA	13.33	12.9
Abdelrahman, 2012	360	0.4	17.4	14.89
Gracner, 2018	180	0.8	6.20	5.55
De Keyser, 2017	360	0.9	12.15	11.99

IOP: intraocular pressure, p-SLT: primary SLT

Results of Meta-Analysis

We divided into subgroup meta-analysis 2 subgroups based on the control group that compared with primary SLT modalities. SLT as primary treatment reduced IOP by 0.21 mm Hg (95% CI: -0.81 to 1.23 mm Hg), which was less than the statistically significant difference (p=0.69) between it and topical medicine, in **Figure 2A.** When only including the RCTs, the differences in IOPR (Intra Ocular Pressure Reduction) were also statistically non-significant, **Figure 2B.**

Based on figure 3, the pooling results revealed a significant difference between the two groups, with a MD for the IOPR comparing primary SLT with adjunctive of 0.57 mmHg (95% confidence interval [CI]: 0.00 to 1.33 mm Hg), with p= 0.05. Additionally, there was no significant heterogeneity in these analyses, with I^2 37%.

Adverse events

Concerning adverse events, three studies reported the types and incidences. However, we did not perform a meta-analysis because there were so few cases. In general, adverse events were transient and minor, there were no sight-threatening complications reported

of selective laser trabeculoplasty. Transient IOP spike after SLT treatment has been reported in some studies, 2-6 patients.[7,15,16,18] Adverse effect non ocular related was found higher in medication group than the SLT group.[7,18] Transient anterior chamber reaction, discomfort, redness, and pain were noted as common side effects without sequelae in all studies.

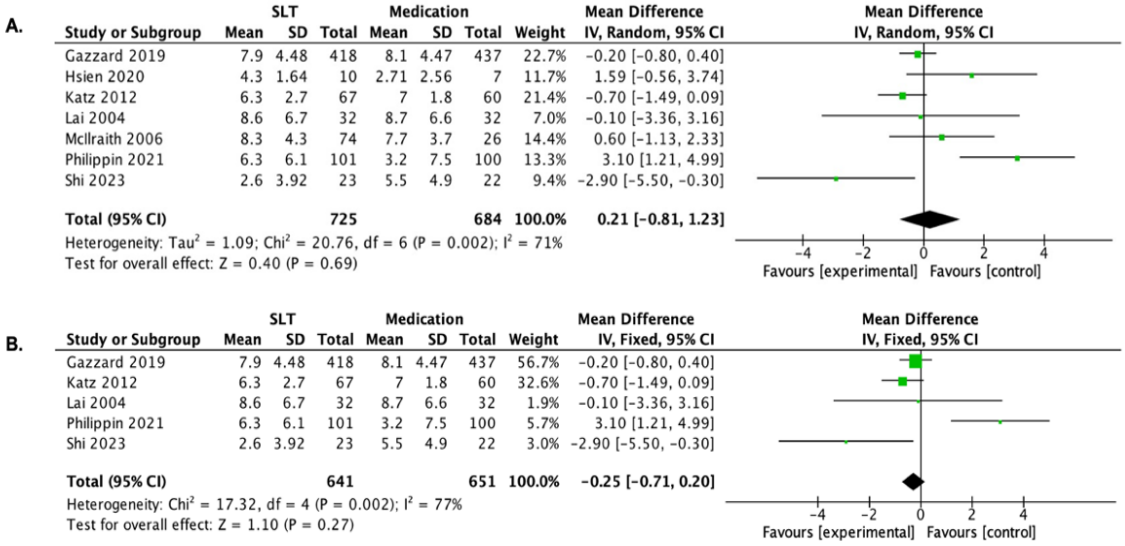

Figure 2. Comparison of IOPR of primary SLT vs topical medication: (A) all studies, (B) RCT subgroup analysis

Cost effectiveness

The application of selective laser trabeculoplasty as an initial treatment modality has been demonstrated to be more cost-effective than the administration of eye drops in three distinct studies,[7,18,21] which considered varying currencies and healthcare systems. The mean cost per patient for ocular surgery over a 36-month period was significantly lower for the selective laser trabeculoplasty group in comparison to the eye drops group.[7]

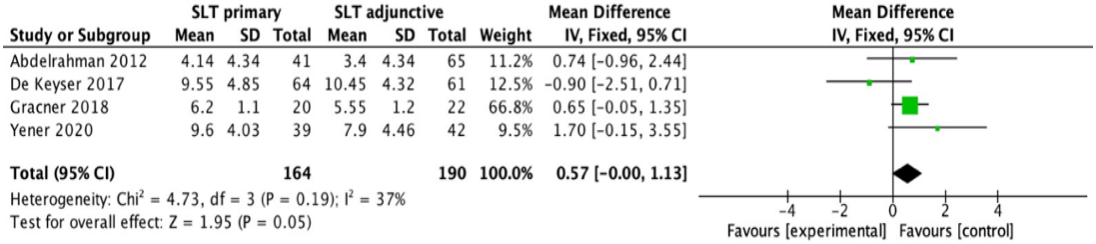

Figure 3. Comparison of IOPR of Primary SLT vs Adjunctive SLT

Quality of life

In evaluating quality of life, various assessment tools have been employed, including the Light Trial, which utilized the EuroQol (EQ-5D) with a p-value of 0.23. Another study utilized the 20-item cross-cultural WHO visual functioning questionnaire (WHO/PBD-VF20) alongside the Glaucoma Quality of Life 36 Item (GlauQoL36), Assessment of Quality of Life-

7D (AQoL-7D), and Vision-related Quality of Life (VisQo), all of which indicated no significant differences between the groups examined.[18,21]

Assessment Quality

Overall, all studies included were shown to be of good quality with acceptable risk of bias, as assessed by the ROBIN-I and ROB-2 classification systems.[26,27] Two distinct systems were employed based on their randomization in accordance with Cochrane guidelines. The outcomes of these analyses are illustrated in **Figures 4.**

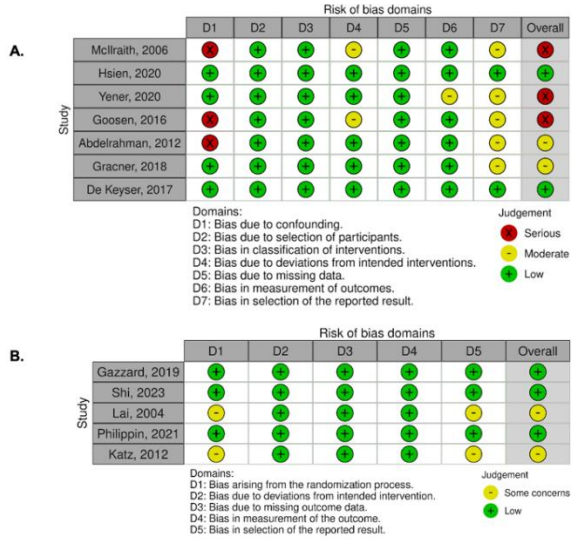

Figure 4. Risk of bias assessment; A) ROBIN-I analysis of non-randomised trials B) ROB-2 risks of bias analysis of the randomised trial

Discussion

While several studies indicate SLT effectively reduces IOP as adjunct therapy, its efficacy as a primary treatment for open-angle glaucoma remains ambiguous. In line with the LIGHT Trial findings on the effectiveness and safety of primary SLT,[7] we conduct this meta-analysis to validate and strengthen these findings.

The precise mechanism by which SLT lowers IOP is not completely elucidated. Current understanding suggests SLT lowers intraocular pressure primarily through mechanical and cellular mechanisms.[28] This mechanism involves coagulative damage to trabecular meshwork cells, resulting in collagen contraction and scarring, thus tightening the meshwork. This tightness facilitates the opening of adjacent intertrabecular spaces, promoting aqueous humor outflow.[29] Furthermore, the disruption of pigment granules incites macrophage migration and subsequent phagocytosis, thereby cleansing the trabecular meshwork.[28]

This meta-analysis encompasses five randomized controlled trials and seven observational studies. To the best of our knowledge, this is the first systematic review and meta-analysis that compares primary SLT to topical medications and adjunctive SLT based on holistic approach; IOP reduction, adverse event, cost effectiveness, and quality of life.

Findings indicate that primary SLT in newly diagnosed individuals yields comparable IOP reduction to medications, aligning with prior reviews.[30] However, primary SLT demonstrates significantly fewer adverse events, lower costs, and enhanced quality of life relative to topical medication. A common transient adverse effect noted post-SLT is an IOP spike, but sustained IOP elevation post-treatment was absent. Patients undergoing primary SLT maintain drop-free control of intraocular pressure for a minimum of three years,[7] potentially diminishing annual treatment costs and improving quality of life. Nonetheless, this study did not yield significant statistical data on quality of life. Extended follow-up durations are requisite to better elucidate potential QoL changes associated with chronic conditions like glaucoma.[21] In the comparison between

primary and adjunctive SLT groups, primary SLT demonstrates superiority in IOP reduction and reduction in eye drop medication. These results support the finding that SLT can reduce the medication burden in medically controlled eyes or can be an adjunctive treatment to medication.[23]

The conclusions drawn from this meta-analysis necessitate cautious interpretation due to the strengths and limitations inherent in the included trials. A notable strength lies in the publication of all studies by reputable centers of excellence employing a prospective comparative controlled design. However, some limitations must be acknowledged despite the rigorous methodology employed, particularly the potential for publication bias. Second, our analysis of IOPR utilized data from trials of varying durations due to incomplete follow-up data, potentially influencing our findings. A 2024 report by the American Academy of Ophthalmology's committee has provided level 1 evidence endorsing SLT as a primary intervention strategy.[13] This high-grade recommendation favors early laser therapy for patients intolerant to or seeking to avoid long-term medication. Consistent with this recommendation, our meta-analysis demonstrates that SLT produces significant and sustained IOP reduction, has an excellent safety profile, reduces medication dependence, and didn't affect in quality of life. Given its procedural simplicity, tolerability, and strong evidence base, SLT is a viable first-line option for appropriately selected POAG patients.

CONCLUSION

In conclusion, this meta-analysis indicates that SLT could revolutionize glaucoma treatment through improved effectiveness, reduced side effects, decreased medication reliance, and cost efficiency. Additional research is necessary to refine SLT protocols and explore additional or alternative treatments that could enhance long-term efficacy.

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