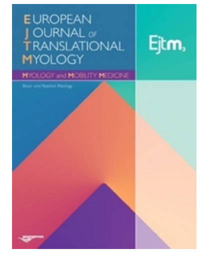
European Journal of Translational Myology



pISSN: 2037-7452 eISSN: 2037-7460

https://www.pagepressjournals.org/index.php/bam/index

Eur J Transl Myol 2024 [Online ahead of print]

To cite this Article:

Sayanjali S, Lima BS. **Effectiveness of laser therapy among patients with open-angle glaucoma: a systematic review and meta-analysis study.** *Eur J Transl Myol* doi: 10.4081/ejtm.2024.12931

Effectiveness of laser therapy among patients with open-angle glaucoma: a systematic review and meta-analysis study

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Abstract

This study aims to evaluate the efficacy of selective laser trabeculoplasty in improving the intraocular pressure in patients diagnosed with open-angle glaucoma. A comprehensive search was performed across electronic databases, including PubMed, Scopus, and Web of Science, until June 2024, using keywords related to "selective laser trabeculoplasty" and "open-angle glaucoma." Studies were chosen based on set eligibility criteria. Data extraction was carried out by two independent reviewers, and statistical analyses were performed using a random-effects model to calculate the pooled mean differences in IOP reduction and overall success rates. The initial search yielded 3111 articles, with 23 studies included in the systematic review and 22 in the meta-analysis. The pooled MD in IOP reduction between the SLT and control groups was -1.44 mm Hg (95% CI: -2.19 to -0.70, $p < 0.01$). Subgroup analyses revealed a MD of -0.76 mm Hg (95% CI: -1.31 to -0.21, $p < 0.01$) when comparing SLT to medication, and -0.42 mm Hg (95% CI: -0.64 to -0.19, $p < 0.01$) when comparing 180-degree SLT to 360-degree SLT. The pooled success rate favored SLT with an odds ratio (OR) of 0.71 (95% CI: 0.51 to 0.99, $p = 0.05$). There was significant heterogeneity among the studies ($I^2 = 71\%$). SLT is effective in lowering IOP in OAG patients, demonstrating significant efficacy compared to medication and different SLT protocols. The findings underscore SLT's potential as a reliable treatment option. However, the observed heterogeneity underscores the necessity for standardized protocols in future research to improve comparability and verify SLT's long-term effectiveness.

Key words: open-angle glaucoma, selective laser trabeculoplasty, intraocular pressure, meta-analysis, laser trabeculoplasty, glaucoma treatment.

Open-Angle Glaucoma (OAG) is one of the most common forms of glaucoma, leading to irreversible blindness globally by affecting millions of individuals. This condition is marked by progressive optic neuropathy, resulting in the degeneration of retinal ganglion cells and subsequent visual field loss.[1,2] Elevated Intraocular Pressure (IOP) is the main risk factor for OAG progression, necessitating effective management strategies to prevent further optic nerve damage. Conventional treatments primarily involve topical IOP-lowering medications, which, although effective, come with challenges such as patient adherence, systemic side effects, and financial costs.[3,4]

Laser trabeculoplasty has become an essential intervention in OAG management, providing an alternative or complement to medication. ALT was initially the standard laser treatment but had significant complications, including thermal damage to the Trabecular Meshwork (TM) and IOP spikes.[5,6] To address these issues, Selective Laser Trabeculoplasty (SLT) was introduced in the mid-1990s. SLT targets pigmented TM cells with a lower-energy laser, minimizing collateral damage and offering a safer profile while effectively lowering IOP. However, the recurrence of elevated IOP and the necessity for retreatment remain significant challenges in the long-term management of OAG.[7,8]

Recent advancements in laser technology have positioned SLT as a promising method with fewer side effects and similar efficacy to traditional approaches. SLT employs a frequency-doubled, Q-switched Nd laser to deliver precise energy bursts that selectively target pigmented cells in the trabecular meshwork, enhancing aqueous humor outflow without causing substantial thermal damage.[9,10] This technique has proven effective in lowering IOP and is particularly beneficial for patients who find it difficult to adhere to pharmacological treatments. Despite the increasing use of SLT, comprehensive assessments of its long-term efficacy and safety across various patient populations are needed. This systematic review and meta-analysis aim to consolidate existing evidence on SLT's role in treating OAG, comparing its outcomes to other treatment modalities to provide a clearer understanding of its clinical utility.

Materials and Methods

The present study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[11]

Systematic search

A comprehensive search was performed across Web of Science, Scopus, and PubMed, covering all available records up to June 2024. We used relevant Medical Subject Headings (MeSH) and relevant keywords, specifically targeting ("selective laser trabeculoplasty" OR "SLT") AND ("open-angle glaucoma" OR "OAG").

Inclusion and eligibility

The eligibility criteria was defined based on the PICO framework: Population (P): Clinical studies on human patients diagnosed with OAG. Intervention (I): SLT. Comparison (C): Medication, argon laser therapy, and 180 vs. 360-degree SLT. Outcome (O): IOP reduction and success rate of SLT. The exclusion criteria were defined as: animal studies, case reports, studies on other types of glaucoma, studies not involving SLT, unclear or undefined SLT protocols, absence of clear clinical outcomes, lack of sufficient data, and histologic and in vitro studies.

Data extraction and outcome measures

Data was extracted independently by two authors using a standardized data collection sheet. Any disagreements were resolved and discussed with a third author. The collected variables included: Authors' names, publication year, design, size, demographics (age, gender), SLT protocols (including laser settings and treatment parameters), Follow-up periods, Mean and standard deviation of IOP measurements, Success rates, Comparison groups (medication, argon laser therapy, 180 vs. 360-degree SLT)

Statistical analysis and data synthesis

The pooled Mean Differences (MD) in IOP reduction between SLT and control groups was calculated using a random-effects model, with Hedges' g and standard deviation estimation. The pooled success rate and Odds Ratio (OR) were determined using the meta package in R. we used the I^2 test to evaluate the heterogeneity. The Mantel-Haenszel method and random-effects model were applied for pooling effect sizes and calculating standard deviations. A z-test was conducted to evaluate the overall significance of the random model and the significance between subgroups. Publication bias was assessed by creating funnel plots for each group. Statistical analyses and the creation of forest and funnel plots were performed using R (R Foundation for Statistical Computing, Vienna, Austria) and RStudio (RStudio Inc., Boston, MA).

Results

Our initial search yielded 3,111 articles from PubMed, Scopus, and Web of Science, from which we eliminated 338 duplicates. After reviewing the titles and abstracts of the remaining 2,493 records, we retrieved 94 full-text articles for further evaluation. Ultimately, 23 studies met our eligibility criteria and were included in the systematic review,[3,9,12-32] with 22 of these studies also included in the meta-analysis (Figure 1). Detailed characteristics of the included studies are summarized in Table 1.

The main focus of the included studies was to evaluate the effectiveness of SLT in lowering IOP in patients with open-angle glaucoma. The studies made several comparisons: SLT versus medication, SLT versus argon laser trabeculoplasty, and 180-degree SLT versus 360-degree SLT. Variations in laser settings and treatment protocols among the studies contributed to the heterogeneity of the outcomes.

Pooled mean difference

The pooled MD in IOP reduction between the SLT and control groups was assessed using a random-effects model. The overall MD was -1.44 mm Hg (95% CI: -2.19 to -0.70, $p < 0.01$), demonstrating a significant decrease in IOP in the SLT groups compared to the control groups (Figures 2 and 3). There was considerable heterogeneity among the studies ($I^2 = 71\%$, $\tau^2 = 0.6742$, $p < 0.01$).

Further subgroup analysis revealed varying MDs: For SLT versus medication, the MD was -0.76 mm Hg (95% CI: -1.31 to -0.21, $p < 0.01$), indicating a statistically significant IOP reduction. For SLT versus ALT, the MD was -1.30 mm Hg (95% CI: -3.77 to 1.17, $p = 0.14$), which was not statistically significant. For 180-degree SLT versus 360-degree SLT, the MD was -0.42 mm Hg (95% CI: -0.64 to -0.19, $p < 0.01$), also showing a statistically significant reduction in IOP.

Pooled success rate

The overall success rate of SLT was evaluated, and the pooled odds ratio (OR) was calculated. The random-effects model indicated an OR of 0.71 (95% CI: 0.51 to 0.99, $p = 0.05$), signifying a statistically significant higher success rate for SLT compared to control treatments (Figures 4 and 5). Significant heterogeneity was observed among the studies ($I^2 = 73\%$, $\tau^2 = 0.3277$, $p < 0.01$). Subgroup analyses provided the following ORs.

For SLT versus medication, the OR was 1.46 (95% CI: 0.88 to 2.40, $p = 0.14$), which was not statistically significant. For SLT versus ALT, the OR was 1.34 (95% CI: 0.73 to 2.45, $p = 0.33$), also not statistically significant. For 180-degree SLT versus 360-degree SLT, the OR was 0.56 (95% CI: 0.20 to 2.51, $p = 0.43$), which was not statistically significant.

Potential publication bias was assessed through funnel plots for the included studies. The observed asymmetry in the funnel plots suggests the presence of publication bias, which may affect the reliability of the pooled estimates.

Discussion

We aimed at evaluating the efficacy of SLT in improving IOP in patients with OAG. We analyzed multiple studies that compared SLT with other treatments, including medication, ALT, and varying SLT protocols (180-degree versus 360-degree). Our findings indicated that SLT significantly reduces IOP, with an overall MDof -1.44 mm Hg (95% CI: -2.19 to -0.70, $p < 0.01$) compared to control groups. Subgroup analyses showed a statistically significant IOP reduction for SLT versus medication and for 180-degree versus 360-degree SLT. However, the comparison between SLT and ALT did not reach statistical significance. Furthermore, the pooled success rate demonstrated a higher success rate for SLT relative to control treatments, despite substantial heterogeneity among the included studies.

A prospective randomized clinical trial compared the effectiveness of SLT and ALT in pseudophakic glaucoma patients. Over a 12-month period, the study observed no significant differences in IOP-lowering effects between SLT and ALT. At the final checkup, the mean IOP reduction was 3.23 mm Hg for ALT and 4.30 mm Hg for SLT, supporting our findings that SLT effectively reduces IOP.[9,28,30] However, unlike our meta-analysis, which found a statistically significant IOP reduction with SLT compared to controls, Rosenfeld et al. did not find a significant difference between SLT and ALT. This suggests that while SLT is effective, its relative advantage over ALT may vary based on patient populations and study designs.[9,28,30,33,34]

A randomized controlled trial compared the efficacy of 180-degree and 360-degree SLT in patients with OAG and glaucoma suspects. The results indicated that 360-degree SLT was more effective in lowering IOP, with reductions of 21.5 mm Hg for 180-degree SLT and 19.9 mm Hg for 360-degree SLT at a 1-year follow-up. This finding is in line with our subgroup analysis, which also demonstrated a statistically significant greater IOP reduction with 360-degree SLT compared to 180-degree SLT. Gazzard *et al.* conducted two studies on the efficacy of SLT for OAG treatment. In their 2019 study, they found that SLT was as effective as medication in reducing IOP over a 3-year period.[3,18] Their 2023 study further confirmed these results, showing sustained IOP reduction with SLT over an extended follow-up period. These findings are consistent with our meta-analysis, which showed a MD in IOP reduction of -0.76 mm Hg (95% CI: -1.31 to -0.21, $p < 0.01$) for SLT compared to medication. The agreement across various studies underscores the reliability of SLT as a treatment option for OAG, particularly for patients who struggle with medication adherence.[9,28,30]

When comparing our results to previous meta-analyses, we observe both similarities and differences. One comprehensive network meta-analysis evaluated the effectiveness of various laser trabeculoplasty techniques, including SLT and ALT, for treating OAG. This study found no statistically significant differences in IOP reduction between any pairs of interventions, consistent with our finding of no significant difference between SLT and ALT (MD -1.30 mm Hg, 95% CI: -3.77 to 1.17, $p = 0.14$). However, the study reported that 180-degree SLT significantly reduced medication use compared to ALT at 12 months (MD -0.28, 95% CI: -0.50 to -0.06, $p = 0.014$), which aligns with our subgroup analysis findings.[35-38]

Another study by Sun *et al.* similarly supported the equivalence of SLT to medication in terms of IOP reduction. This consistency is demonstrated in our findings, where SLT versus medication showed a statistically significant IOP reduction (MD -0.76 mm Hg, 95%CI: -1.31 to -0.21, $p < 0.01$). They also explored the efficacy of newer laser technologies, such as MLT and PSLT, which were not specifically addressed in our analysis. Their results suggested these newer forms of LT are comparable in effectiveness to traditional SLT, indicating potential alternatives for clinical practice. Both studies underscored significant heterogeneity among included studies, a factor also noted in our systematic review ($I^2 = 71\%$). This variability can be attributed to differences in study designs, patient populations, laser settings, and follow-up durations. The two studies emphasized the need for standardized protocols in future research to minimize heterogeneity and enhance comparability. The consistency of findings across our study and these meta-analyses confirms SLT's role as a reliable and effective treatment for OAG, while highlighting areas for further investigation, particularly regarding the long-term efficacy and optimal treatment parameters of newer LT techniques.[35,36,39-41]

The inclusion of multiple subgroup analyses allowed for a detailed understanding of SLT's relative efficacy against various treatments and protocols. However, the study also had limitations, such as the significant heterogeneity. It can be explained by the variability of study designs, sample size, laser settings, and follow-up durations. Additionally, potential publication bias, as suggested by asymmetry in funnel plots, may have influenced the robustness of the pooled estimates. Future research should aim to standardize study protocols and address potential biases to further validate SLT's efficacy.

Conclusions

Our systematic review and meta-analysis study aimed at evaluating the effectiveness of laser trabeculoplasty in the treatment of glaucoma. Based on our results, SLT is leads to reliable treatment outcomes reducing IOP among those with OAG. SLT demonstrates significant IOP reduction compared to control treatments, with 360-degree SLT showing greater efficacy than 180-degree SLT. These findings are consistent with individual studies and other meta-analyses, reinforcing SLT's role as a reliable treatment option. However, the significant heterogeneity among studies highlights the need for standardized protocols in future research. Despite these limitations, our study supports the use of SLT in managing OAG.

List of Abbreviations

IOP, Elevated Intraocular Pressure

SLT:, selective laser trabeculoplasty

OAG, Open-Angle Glaucoma

TM, Trabecular Meshwork

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

MD, Mean Differences

OR, Odds Ratio

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Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval: not applicable.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Acknowledgement

We would like to extend our sincere thanks to Dr. Baseer Khan, MD, Ophthalmologist, FRCS(C), and the team at Clarity Eye Institute, Greater Toronto Area, Canada, for their invaluable support and contributions to this study.

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Figure 1. PRISMA flow diagram of the included studies.

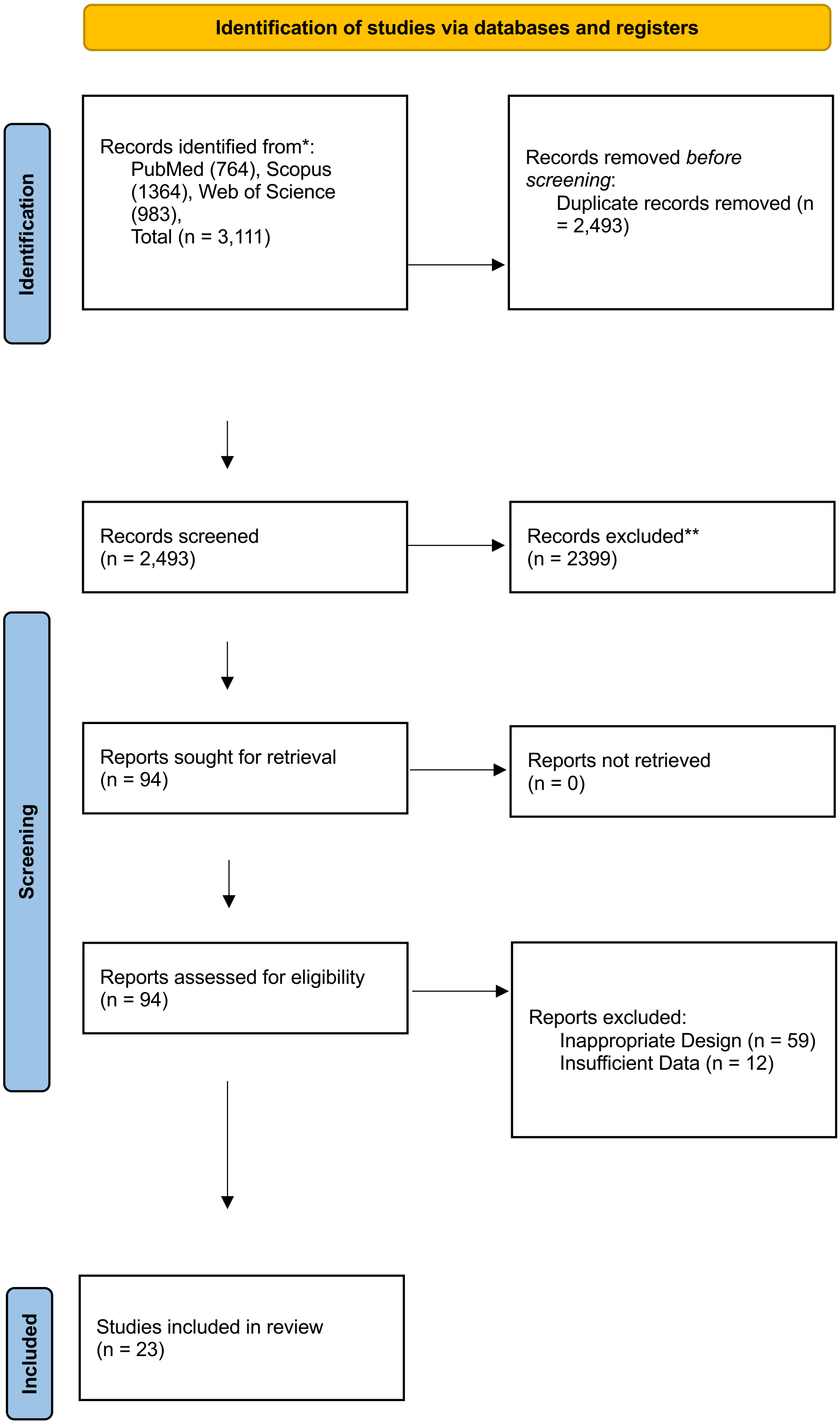

Figure 2. The pooled mean difference between SLT and alternative treatments.

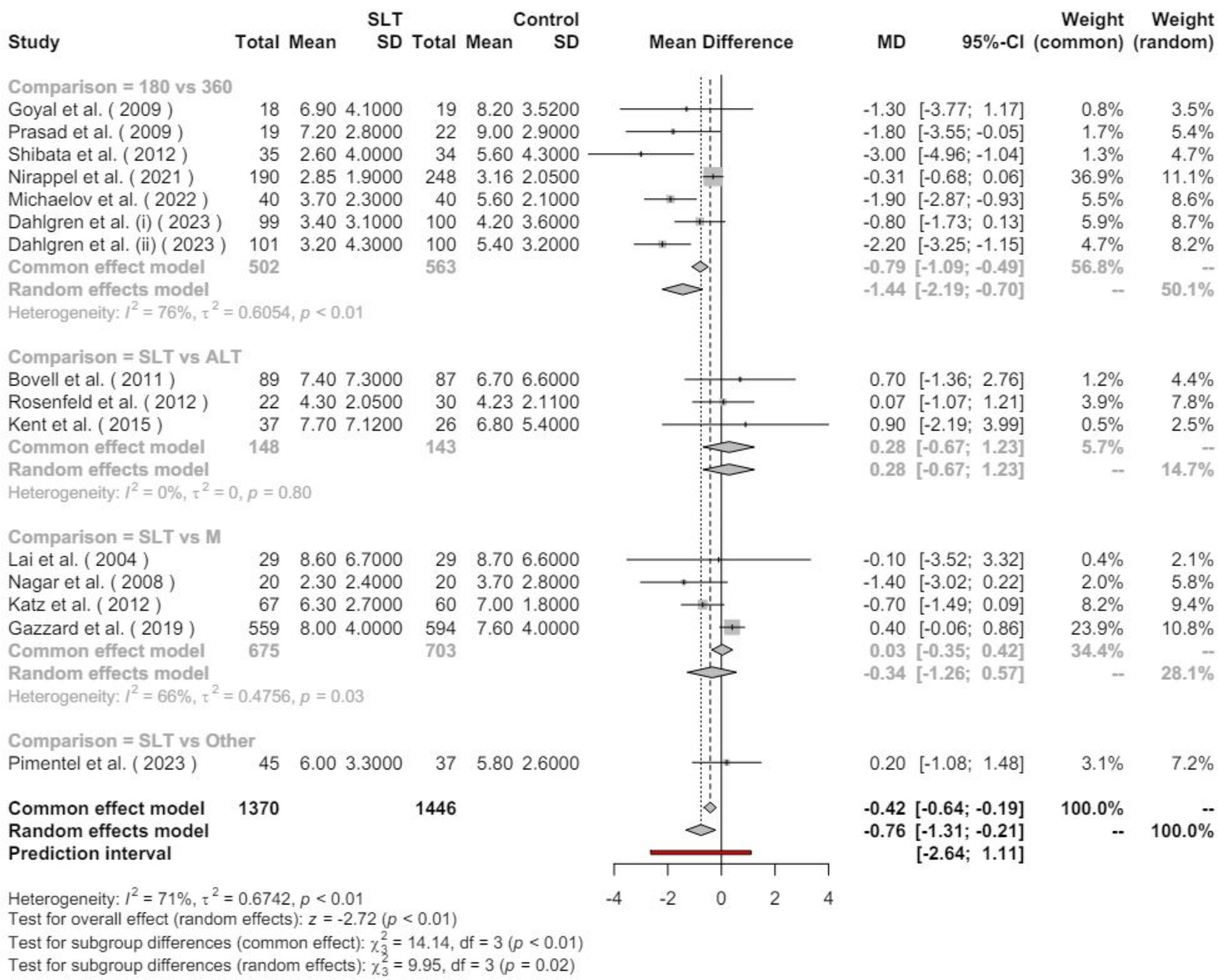

Figure 3. Funnel plot of the mean difference between SLT and alternative treatments.

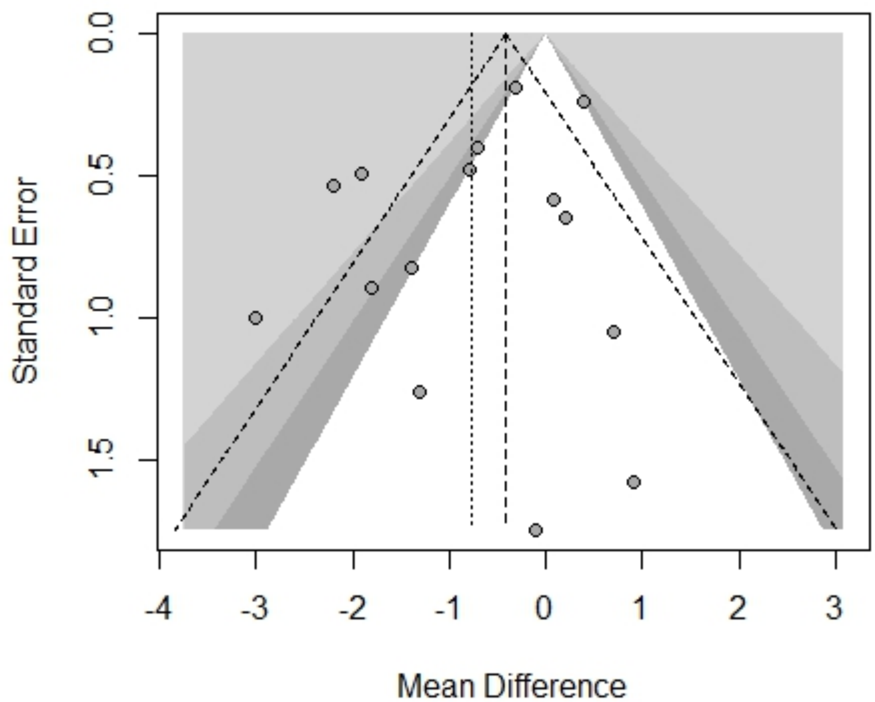

Figure 4. Forest plot of the succus rate and ORs between SLT and alternative treatments.

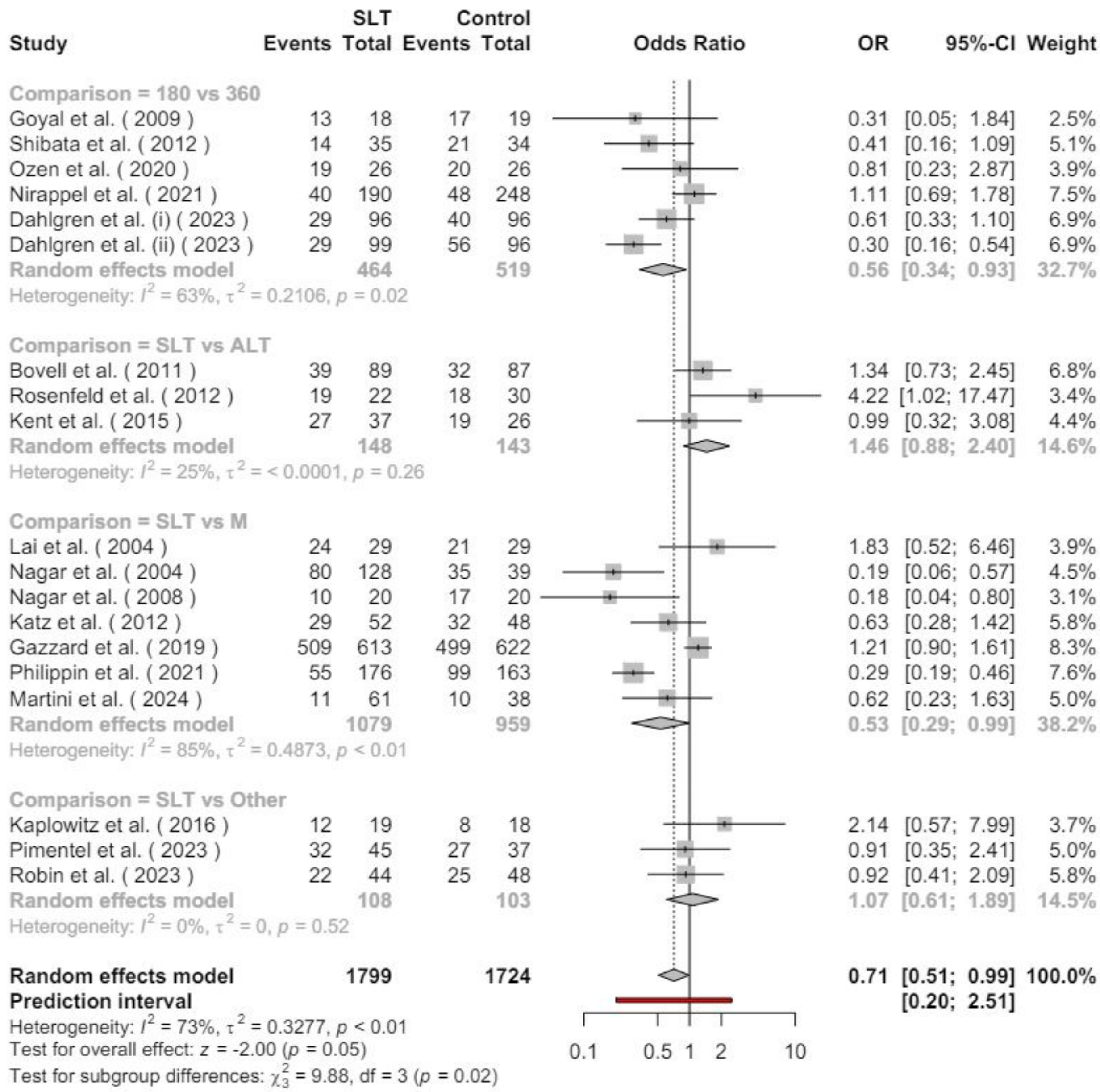

Figure 5. Funnel plot of ORs between SLT and alternative treatments.

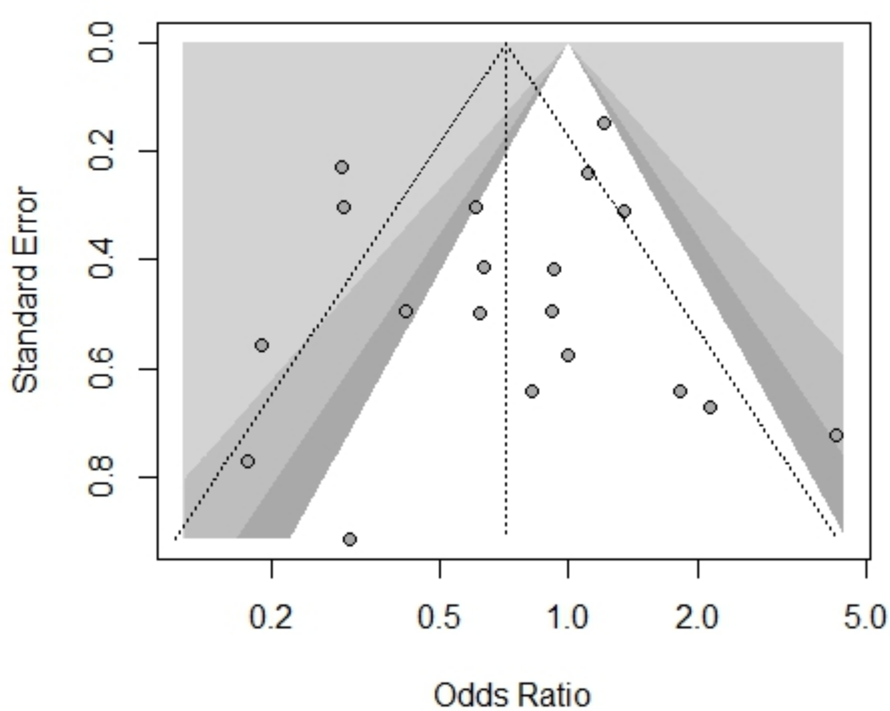

Table 1. Detailed characteristics of the included studies.

Author	Year	Country	Design	Eyes	FD	Age	M/F	Comparison	Control
Lai et al. (20)	2004	China	RCT	58	60	51.9	13/16	SLT vs M	Various
Nagar et al. (25)	2004	UK	RCT	167	10.3	63	77/90	SLT vs M	latanoprost
Nagar et al. (21)	2008	UK	RCT	40	4-6	66.4	21/19	SLT vs M	latanoprost
Goyal et al. (15)	2009	UK	RCT	37	1	57-67	-	180 vs 360	360 as control
Prasad et al. (3)	2009	USA	ROS	41	1-24	65	18/23	180 vs 360	360 as control
Bovell et al. (23)	2011	Canada	RCT	176	36-50	69.5	72/104	SLT vs ALT	ALT as Control
Katz et al. (31)	2012	USA	RCT	127	9-12	-	28/41	SLT vs M	Various
Rosenfeld et al. (18)	2012	Israel	RCT	52	12	71.9	25/27	SLT vs ALT	ALT as Control
Shibata et al. (12)	2012	Japan	ROS	69	17.9-19.5	66.4-70.2	35/34	180 vs 360	360 as control
Kent et al. (26)	2015	Canada	RCT	76	6	73	-	SLT vs ALT	ALT as Control
Kaplowitz et al. (27)	2016	USA	RCT	-	24	62.8-70.3	13/24	SLT vs TLT	TLT as control
Gazzard et al. (30)	2019	UK	RCT	1230	36	62.7-63.4	397/321	SLT vs M	Various
Ozen et al. (14)	2020	Turkey	POS	52	6	62.3	28/24	180 vs 360	360 as control

Nirappel et al. (16)	2021	USA	RCS	258	1.5-24	18-97	215/238	180 vs 360	360 as control
Philippin et al. (29)	2021	Tanzania	RCT	339	12	65.09	118/83	SLT vs M	timolol
Wong et al. (17)	2021	Hong Kong	RCT	132	12	-	-	SLT vs PS-SLT	SLT as control
Christie et al. (24)	2023	Denmark	RCT	144	12	60	77/67	SLT vs M	Bimatoprost as control
Dahlgren et al. (i) (9)	2023	Sweden	RCT	199	6	70-73	-	180 vs 360	360 as control
Dahlgren et al. (ii) (9)	2023	Sweden	RCT	201	6	70-73	-	180 vs 360	360 as control
Michaelov et al. (28)	2022	Australia	RCT	80	12	66.5	-	180 vs 360	360 as control
Pimentel et al. (32)	2023	Brazil	ROS	98	12	61.-62.7	42/56	SLT vs MLT	MLT as Control
Robin et al. (13)	2023	USA	RCS	131	6-12	65.2	63/68	SLT vs MLT	MLT as Control
Schmidl et al. (19)	2023	Austria	RCCS	25	3	72-73	16-Sep	SLT vs ALT	ALT as Control
Martini et al. (22)	2024	France	ROS	73	12	77.7	29/44	SLT vs M	iStent as Control