• Meta-Analysis •

Micropulse laser therapy at 532, 577, and 810 nm for chronic central serous chorioretinopathy: a systematic review and Meta-analysis

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Abstract

● **AIM:** To evaluate the effectiveness of 532, 577, and 810 nm lasers as an initial treatment for non-resolving central serous chorioretinopathy (CSC).

● **METHODS:** Following the Cochrane Collaboration Handbook and Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines, randomized clinical trials (RCTs), non-randomized cohorts, observational studies, and case series (>10 cases) assessing these lasers for non-resolving CSC with ≥3mo of follow-up were included. Non-resolving CSC was defined as persistent subretinal fluid (SRF) for >3-6mo. Searches were conducted in PubMed, the Cochrane Library, and Embase (January 17, 2025). Two authors independently performed data extraction and assessed the risk of bias. The primary outcome was SRF resolution on optic cherence tomography (OCT) at 3-6mo. Central retinal thickness (CRT) and best-corrected visual acuity (BCVA) were secondary outcomes. A random-effects model was employed to calculate pooled proportions with 95% confidence intervals (CIs), and heterogeneity was assessed using I^2 and *Q* statistics.

● **RESULTS:** Twenty-four studies (3 RCTs, 21 non-RCTs) involving 829 non-resolving CSC eyes (77.6% male, mean age 45.36y) were included. SRF resolution was 59% (95%CI: 0.51-0.67; I^2=72.6%), showing no significant difference between lasers. Trim-and-fill adjustment raised SRF resolution to 65% (95%CI: 0.44-0.81). CRT significantly decreased by 126.32 μm (95%CI: 95.99-156.65; *P*<0.0001; I^2=95.7%), with the largest reduction noted for the 810 nm laser. BCVA change was 0.10 logMAR (95%CI: -0.03 to 0.22; *P*=0.13; I^2=96.6%), indicating no significant visual improvement.

● **CONCLUSION:** This Meta-analysis supports the use of 532, 577, and 810 nm subthreshold micropulse lasers as equally effective in resolving SRF in non-resolving CSC.

● **KEYWORDS:** central serous chorioretinopathy; subretinal fluid resolution; micropulse laser; optical coherence tomography; systematic review; Meta-analysis
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INTRODUCTION

Central serous chorioretinopathy (CSC) is recognized as one of the stages of the pachychoroid disease spectrum, which is a group of ocular conditions characterized by choroidal thickening, dysfunction of the retinal pigment epithelium (RPE), neurosensory retinal detachment, and accumulation of subretinal fluid (SRF). Although various treatments have been proposed for CSC, identifying an effective and consistent treatment remains a critical challenge[1].

Laser therapy is frequently used to treat CSC. However, significant uncertainties persist regarding its effectiveness, particularly in non-resolving cases[2-31]. The impact of different laser wavelengths, such as 532, 577, and 810 nm, on the resolution of SRF is not well established, limiting the

optimization of laser-based treatments. While 577 nm and 810 nm lasers have shown promising outcomes in preserving retinal integrity, the efficacy of 532 nm lasers as an alternative remains underexplored and requires evidence[6-7].

Previous studies have investigated the effectiveness of subthreshold micropulse laser (SML) and photodynamic therapy for chronic CSC[26-29]. However, these studies do not directly compare the impact of 532, 577, and 810 nm wavelengths. By focusing on these wavelengths, our study provides a practical and applicable perspective to optimized clinical decision-making.

Therefore, we conducted a systematic review and a proportional Meta-analysis to evaluate the effectiveness of 532, 577, and 810 nm lasers as an initial treatment strategy in patients with non-resolving CSC. This study aims to address the evidence gap, clarify the role of these laser wavelengths, and inform more targeted and effective clinical practices.

MATERIALS AND METHODS

This systematic review and Meta-analysis were performed and reported in accordance with the Cochrane Collaboration Handbook for Systematic Review of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement guidelines[32-33]. The prospective Meta-analysis protocol was registered on PROSPERO on January 5, 2025, under protocol #CRD42025630436.

Inclusion in this Meta-analysis was restricted to studies that met all the following eligibility criteria: 1) randomized clinical trials (RCTs), nonrandomized cohorts, observational studies, and case series with more than 10 cases; 2) enrolling patients who underwent laser treatment with 532, 577, and 810 nm for non-resolving CSC; 3) with follow-up of at least 3mo. In addition, studies were included only if they reported any of the clinical outcomes of interest.

We excluded studies involving 1) other types of lasers, 2) chronic CSC with atypical characteristics (*e.g.*, RPE atrophy), 3) studies lacking quantitative outcomes or data. Non-resolving CSC was defined as the persistence of SRF for more than 3 to 6mo without spontaneous resolution.

The safety outcome of interest at 3 to 6mo was the resolution of SRF, which was defined as the complete absence of detectable SRF under the neurosensory retina, as assessed by optical coherence tomography (OCT). This criterion was applied during follow-up examinations after the therapeutic intervention was initiated. OCT imaging was conducted at predefined intervals to monitor the anatomical response, with SRF resolution as a primary anatomical outcome measure for treatment efficacy.

We conducted searches in PubMed, Cochrane Library, and Embase using the following search strategy: ("Central Serous Chorioretinopathy" OR CSC OR CSCR) AND (laser OR micropulse OR STMP OR "532 nm" OR "577 nm" OR "810 nm"). The searches were performed on 17 January 2025. The references from all included studies, previous systematic reviews, and Meta-analyses were also searched manually for any additional studies.

Two authors (Fuganti RM and Cadide DM) independently extracted the data following predefined search criteria and quality assessment.

We evaluated the risk of bias in randomized studies using version 2 of the Cochrane Risk of Bias assessment tool (RoB 2). Non-randomized studies were assessed with the risk of bias in non-randomized studies of interventions tool (ROBINS-I)[34-35]. Two independent authors completed the risk of bias assessment. Disagreements were resolved through consensus after discussing the reasons for discrepancies.

The primary measure of association was the proportion of eyes achieving SRF resolution, defined as the complete absence of detectable SRF on OCT[36]. Subgroup analyses were performed to compare SRF resolution rates across micropulse laser characteristics, including 532, 577, and 810 nm wavelengths. A random-effects model was employed to calculate pooled proportions and their respective 95% confidence intervals (CIs), accounting for heterogeneity across studies. Heterogeneity was assessed using the I^2 statistic, with values greater than 25% indicating significant heterogeneity, complemented by the Q statistic, where $P<0.10$ were considered indicative of significant heterogeneity.

The central retinal thickness (CRT) and best-corrected visual acuity (BCVA) were analyzed as secondary outcomes to assess the effects of 532, 577, and 810 nm lasers. For each included study, we calculated the mean difference (MD) between baseline and the last follow-up measurements for CRT and BCVA using a random-effects model to account for interstudy variability. Heterogeneity was quantified using the I^2 statistic, with values above 25% indicating significant heterogeneity, and the Q statistic, with a significance threshold of $P<0.10$. Publication bias was assessed using a funnel plot. All statistical analyses were conducted in *R* using the Meta package, and results were presented in forest plots to facilitate the comparison of the effects of different laser wavelengths on CRT and BCVA.

Prespecified subanalysis included data restricted to 1) RCTs; 2) studies with follow-up periods exceeding 3mo; 3) interventions utilizing 532 nm, and/or 577 nm micropulse laser, and/or 810 nm micropulse laser; 4) outcomes explicitly reporting SRF resolution; 5) studies with clearly defined inclusion and exclusion criteria to ensure consistency and comparability of the analyzed patient population.

Sensitivity analyses were conducted to ensure the robustness of the results. These included leave-one-out analyses to evaluate

the influence of individual studies on the overall estimates and exclusions of studies with a high risk of bias. Subgroup analyses further explored potential sources of heterogeneity, focusing on laser wavelengths (532, 577, and 810 nm) and follow-up periods exceeding 3mo. These analyses aimed to provide deeper insights into factors influencing treatment outcomes and refine the understanding of laser efficacy under varying conditions.

Publication bias was assessed through funnel plot analysis and Egger's test for funnel plot asymmetry, with a $P<0.05$ indicating significant asymmetry. The trim-and-fill method was applied to address potential bias, estimating the number of missing studies and recalculating pooled proportions. This adjustment revealed a slightly lower pooled proportion of SRF resolution compared to the unadjusted analysis, reflecting the impact of publication bias on the initial estimates. The adjusted pooled proportion was calculated using a logit transformation to stabilize variance, while the random-effects model incorporated the restricted maximum likelihood estimator to account for between-study variance.

RESULTS

The initial search yielded 2280 results. After removing duplicate records and ineligible studies, 163 remained and were fully reviewed based on inclusion criteria. Of these, 24 studies were included, comparing the efficacy of 532, 577, and 810 nm SMLs for the treatment of non-resolving CSC from 3 RCTs and 21 non-RCTs (Figure 1 and Table 1[2-25]).

The analysis summarized data from twenty-four studies investigating the efficacy of 532, 577 and 810 nm SML's for the treatment of non-resolving CSC. These studies collectively included 829 eyes, predominantly male (77.6%), with an average age of 45.36y (range: 31.1-53.19) and a mean follow-up duration of 7.16mo. Most studies required persistent SRF for over 3mo as an inclusion criterion, while exclusion criteria typically encompassed prior invasive treatments or coexisting retinal pathologies.

The overall proportion of SRF resolution was 59% (95%CI: 0.51-0.67; $P=0.6592$; $I^2=72.6\%$), with no statistically significant differences observed between the lasers (532, 577 and 810 nm lasers) within 6mo. In the subgroup analysis, the resolution rate was 62% for the 532 nm laser (95%CI: 0.54-0.70; $I^2=57\%$), 59% for the 577 nm laser (95%CI: 0.53-0.65; $I^2=46.3\%$), and 47% for the 810 nm laser (95%CI: 0.17-0.80; $I^2=92.6\%$), indicating similar efficacy. These findings suggest that 532, 577, and 810 nm lasers are effective and interchangeable therapeutic options for managing SRF in patients with CSC (Figure 2).

The overall mean reduction in CRT following laser treatment was 126.32 μm (95%CI: 95.99-156.65; $P<0.0001$; $I^2=95.7\%$), indicating a significant decrease in retinal thickness. Subgroup

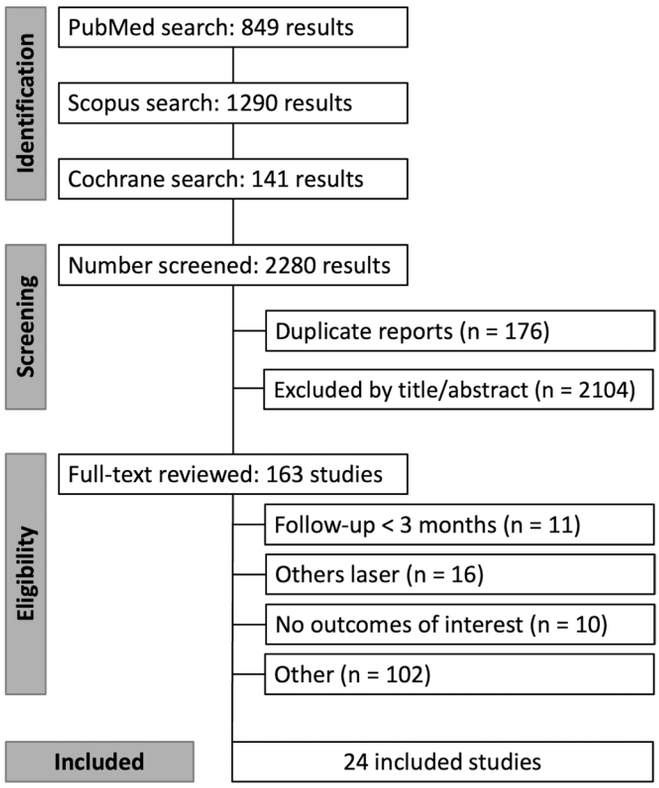

Figure 1 PRISMA flow PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analysis.

analysis by laser wavelength demonstrated a mean CRT reduction of 158.64 μm for the 532 nm laser (95%CI: 10.98-306.30; $I^2=98.6\%$), 178.40 μm for the 810 nm laser (95%CI: 158.69-198.11; $I^2=0$), and 112.90 μm for the 577 nm laser (95%CI: 80.09-145.72; $I^2=93.4\%$). These results suggest that all three lasers effectively reduce CRT, with the 810 nm laser demonstrating the largest and most consistent reduction across studies (Figure 3).

The overall mean change in BCVA following laser treatment was 0.10 logMAR (95%CI: -0.03 to 0.22; $P=0.13$; $I^2=96.6\%$), indicating no statistically significant improvement in visual acuity across all laser treatments. In the subgroup analysis, the mean BCVA change was 0.16 logMAR for the 810 nm laser (95%CI: -0.11 to 0.43; $I^2=85.8\%$), 0.07 logMAR for the 577 nm laser (95%CI: -0.02 to 0.15; $I^2=91.3\%$), and 0.21 logMAR for the 532 nm laser (95%CI: -0.91 to 1.33; $I^2=99.7\%$). These results suggest that while all three lasers were associated with slight improvements or stabilization of BCVA, the changes were not statistically significant (Figure 4).

Due to the high heterogeneity observed across analyses, we conducted a leave-one-out sensitivity analysis by iteratively removing one study at a time to ensure that any single study did not disproportionately influence the results. Overall, the pooled estimates for SRF resolution, CRT reduction, and BCVA change remained stable, reinforcing the robustness and reliability of the findings. Despite minor fluctuations

Table 1 Characteristics of included studies

Authors	Laser (nm)	Study	Country/ region	Complete SRF resolution (*n*)	Total eyes (*n*)	Gender (male)	Age (mean)	FU (mo)
Khatri *et al* 2018[2]	532	Retrospective observational	Nepal	12	13	12	42.91	5.00
Piasecka *et al* 2020[3]	532	Retrospective observational	Poland	19	35	NA	48.50	12.00
Lanzetta *et al* 2008[4]	810	Prospective observational	Italy	9	24	18	46.43	14.00
van Dijk *et al* 2018[5]	810	RCT	Europe	11	80	69	48.60	7.00
Ambiya *et al* 2024[6]	532	RCT	India	63	99	83	37.44	6.00
Ambiya *et al* 2024[6]	810	RCT	India	60	99	76	36.48	6.00
Roisman *et al* 2013[7]	810	RCT	Brazil	9	10	7	39.50	6.00
Ntomoka *et al* 2018[8]	577	Retrospective observational	India	13	23	12	48.90	6.00
Altinel *et al* 2021[9]	577	Retrospective observational	Türkiye	14	23	34	50.48	24.00
Liu *et al* 2024[10]	577	Retrospective observational	China	24	33	25	51.72	7.35
Kaderli *et al* 2022[11]	577	Prospective observational	Türkiye	10	14	10	48.50	3.00
Kiraly *et al* 2023[12]	577	Prospective interventional	Slovenia	15	31	NA	NA	3.00
Viggiano *et al* 2024[13]	577	Retrospective observational	Italy	18	18	16	51.11	12.00
Ambiya *et al* 2016[14]	577	Prospective interventional	India	6	10	10	38.20	6.00
Ilhan *et al* 2023[15]	577	Retrospective interventional	Türkiye	18	23	15	48.68	8.78
Zheng *et al* 2022[16]	577	Retrospective observational	China	31	58	47	47.72	3.00
Yamada-Okahara *et al* 2023[17]	577	Retrospective interventional	Japan	13	22	16	50.10	3.00
Zhou *et al* 2024[18]	577	Retrospective observational	China	16	30	25	47.00	3.00
Mercuri *et al* 2024[19]	577	Prospective interventional	England	13	31	NA	48.95	12.00
Vignesh *et al* 2020[20]	577	Prospective interventional	India	12	28	NA	31.10	8.00
Kustryn *et al* 2024[21]	577	Prospective observational	Ukraine	15	30	27	43.00	6.00
Gao *et al* 2024[22]	577	Quasi-randomized controlled	China	22	37	35	46.95	3.00
Abd Elhamid 2015[23]	577	Retrospective observational	Egypt	13	15	11	36.40	6.00
Lee *et al* 2024[24]	577	Retrospective observational	Korea	15	31	21	53.19	6.00
Volodin and Ivanova 2020[25]	577	Prospective interventional	Russia	12	12	9	46.75	3.00

SRF: Subretinal fluid; FU: Follow-up months; NA: Not available; RCT: Randomized controlled trial.

in the effect sizes, the overall trends remained consistent, supporting the therapeutic role of laser treatment in reducing macular thickness and managing SRF in patients with CSC. However, the persistently high heterogeneity (I^2) across iterations suggests substantial variability among the included studies, likely stemming from differences in patient demographics, disease severity, baseline measurements, laser protocols, and follow-up durations. Notably, heterogeneity was particularly high in the 532 and 577 nm subgroups for CRT and BCVA, indicating greater variability in response to these laser wavelengths. Additionally, the funnel plot for BCVA suggested potential publication bias, with asymmetry indicating the possibility of missing studies with less favorable outcomes. Despite these limitations, the findings suggest that laser treatment effectively promotes SRF resolution and CRT reduction, though its impact on BCVA remains inconsistent (Figures 5-10).

The risk of bias (RoB 2 and ROBINS-I) tool was employed for quality assessment[34-35,37]. No studies were considered at high risk of bias (Figures 11-12).

On funnel plot analysis, studies occupied an asymmetrical distribution, indicating a potential risk of publication bias or variability in study outcomes (Figures 8-10). The asymmetry was confirmed by the Egger' test (t=3.37, P=0.00099), indicating statistically significant bias for SRF. The trim-and-fill method was applied to address potential biases, imputing 12 hypothetical missing studies, resulting in an adjusted proportion estimate. This adjustment revised the overall SRF resolution proportion to 65% (95%CI: 0.44-0.81) accounting for potential publication bias.

DISCUSSION

CSC primarily affects individuals during their most productive years, significantly impairing their quality of life and daily activities. Without a clear consensus on the most effective laser wavelength for treatment, this Meta-analysis provides valuable insights by synthesizing data from 24 studies involving 829 non-resolving CSC eyes. The findings demonstrate that 532, 577, and 810 nm SMLs have comparable efficacy, offering safe and reliable therapeutic options.

Over 6mo, the pooled resolution rate of SRF was 59% (95%CI: 0.51-0.67; P=0.6592; I^2=72.6%), despite substantial heterogeneity among studies. Subgroup analyses by wavelength

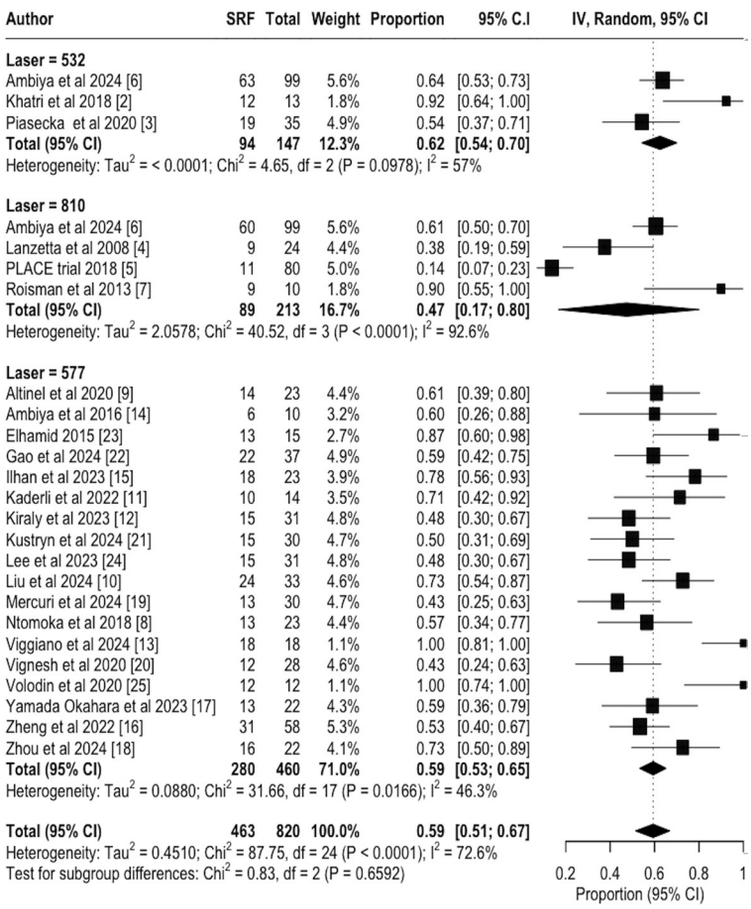

Figure 2 Forest plot of resolution of the SRF within 6mo SRF: Subretinal fluid; SML: Subthreshold micropulse laser; CI: Confidence interval; IV: Inverse variance.

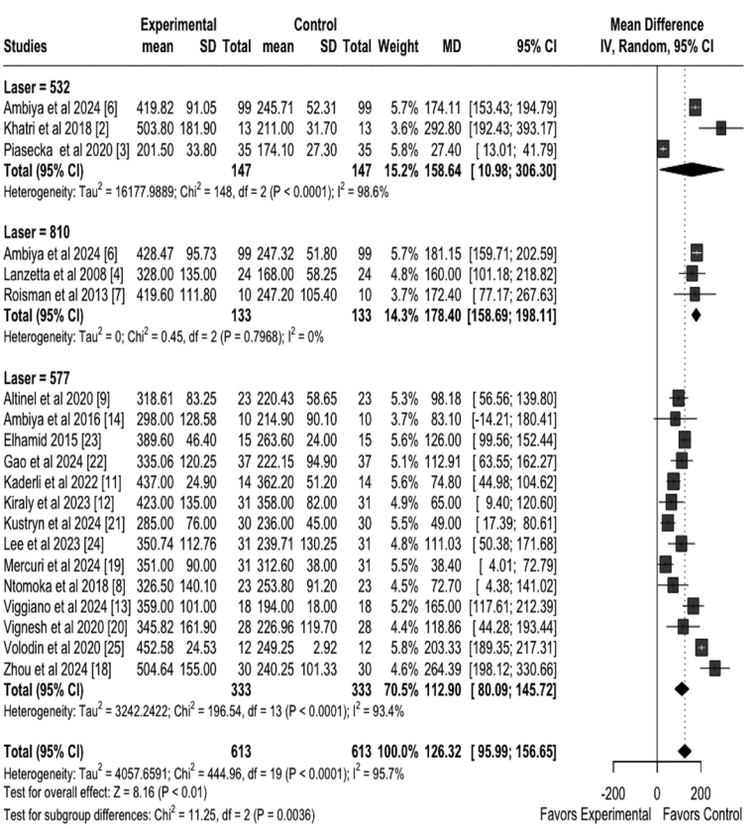

Figure 3 Forest plot of central retinal thickness during follow-up period SD: Standard deviations; MD: Mean difference; CI: Confidence interval; IV: Inverse variance.

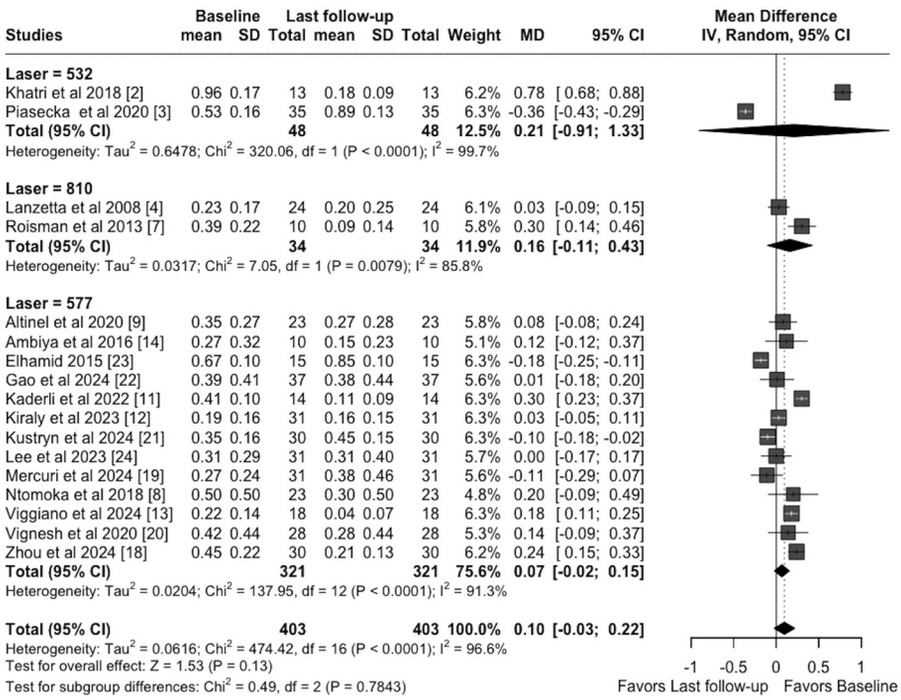

Figure 4 Forest plot of best-corrected visual acuity during follow-up period SD: standard deviation; MD: Mean difference; CI: Confidence interval; IV: Inverse variance.

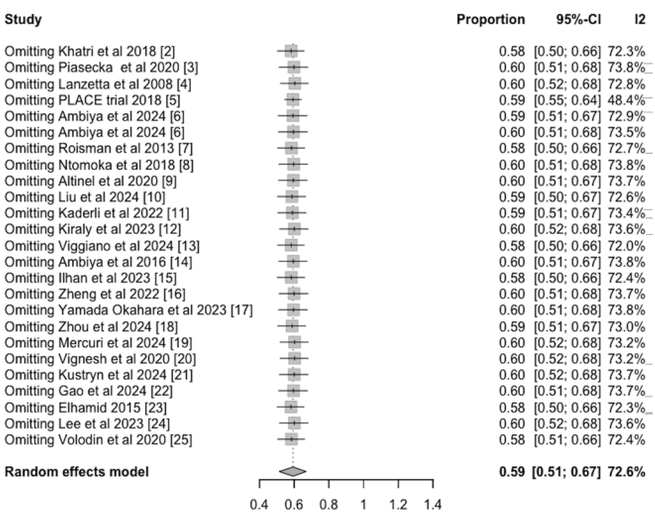

Figure 5 Leave-one-out sensitivity analysis for subretinal fluid CI: Confidence interval.

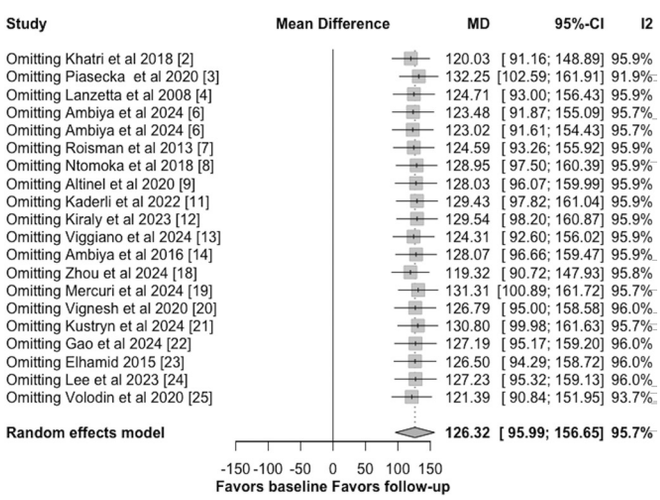

Figure 6 Leave-one-out sensitivity analysis for central retinal thickness MD: Mean difference; CI: Confidence interval; I^2: Inconsistency index.

revealed resolution rates of 62% for the 532 nm laser (95%CI: 0.54-0.70; I^2=57%), 59% for the 577 nm laser (95%CI: 0.53-0.65; I^2=46.3%), and 47% for the 810 nm laser (95%CI: 0.17-0.80; I^2=92.6%). No statistically significant differences were found between the groups (P=0.6592), underscoring the comparable effectiveness of these wavelengths in the treatment of CSC.

SMLs deliver brief laser pulses spaced apart to allow for sufficient heat dissipation. This controlled application minimizes the risk of thermal damage to the targeted tissue and surrounding structures, ensuring precise and safe treatment[37]. The 532 nm laser, often referred to as the "green laser", is widely recognized for its accessibility, cost-effectiveness, and versatility, making it a practical first-line choice for managing various retinal conditions, including CSC. Its energy is efficiently absorbed by the melanin in the RPE and hemoglobin in blood vessels. This targeted absorption allows the laser to stimulate the RPE and promote the reabsorption of SRF without causing significant thermal damage to adjacent retinal layers[2-3,6,37].

On the other hand, the 577 nm laser offers greater specificity for the RPE, with minimal absorption by hemoglobin, making it particularly effective and safe for treating lesions near the fovea, where precision is crucial. This wavelength focuses its

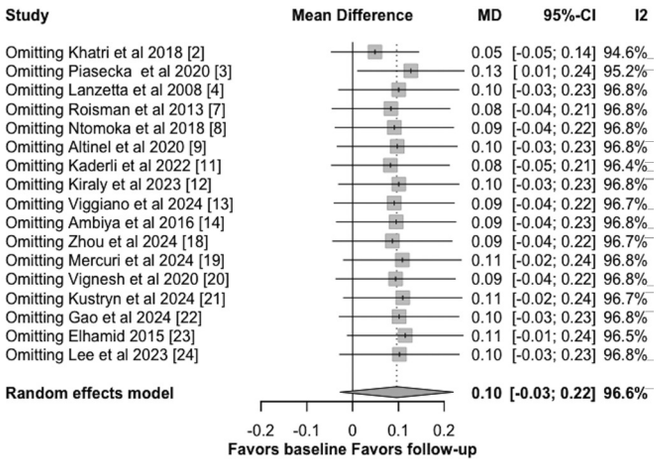

Figure 7 Leave-one-out sensitivity analysis for best-corrected visual acuity MD: Mean difference; CI: Confidence interval; I^2: Inconsistency index.

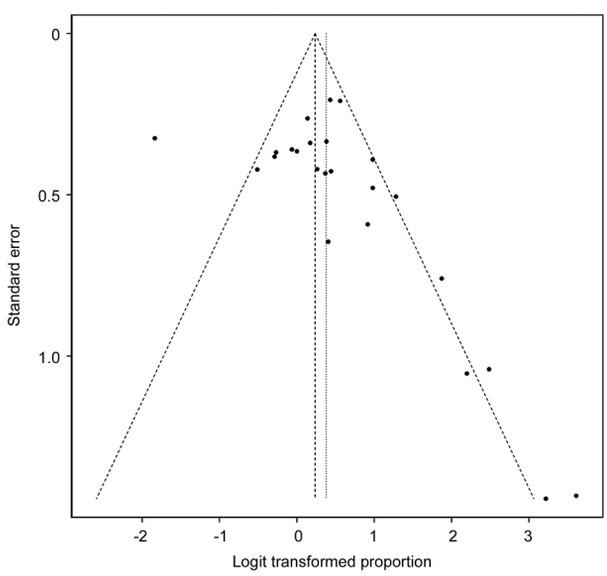

Figure 8 Funnel plot of studies for subretinal fluid.

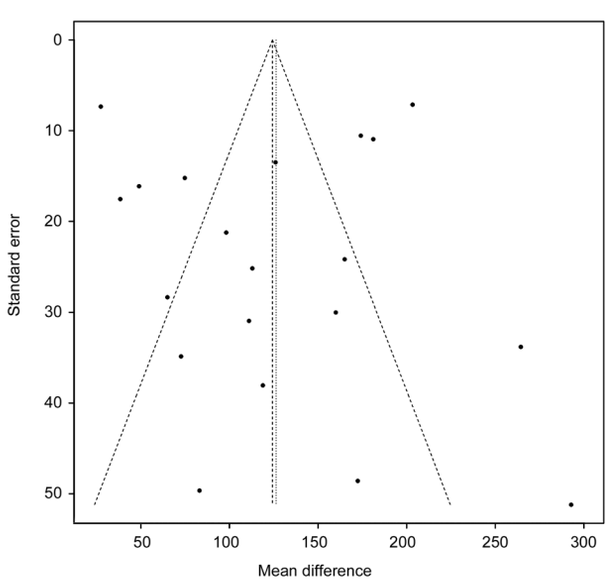

Figure 9 Funnel plot of studies for central retinal thickness.

energy primarily on the RPE, reducing the risk of unwanted thermal damage to outer retinal layers and effectively

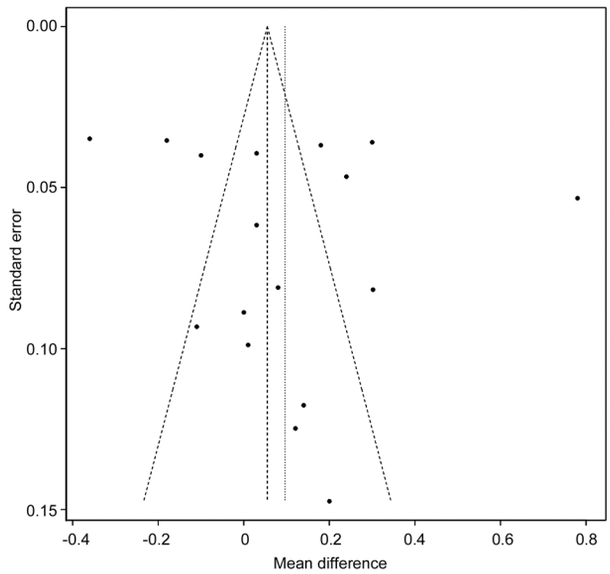

Figure 10 Funnel plot of studies for best-corrected visual acuity.

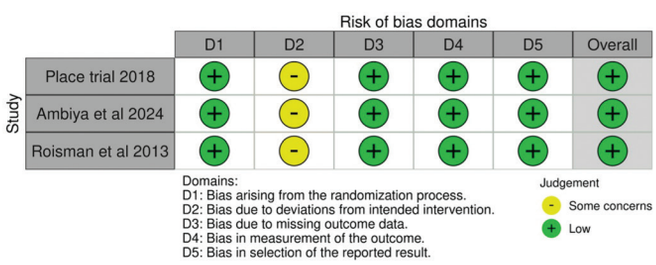

Figure 11 Quality assessment, using version 2 of the Cochrane Risk of Bias assessment tool (ROB 2).

promoting the resolution of SRF. Furthermore, the micropulse mode allows for better titration of laser power, as the individual threshold can be calibrated in the more peripheral retina. In this mode, the power can be adjusted to higher levels, producing visible burns in controlled environments, enabling safer and more efficient treatment even in delicate retinal regions[6,9-12,37].

The 810 nm laser, due to its longer wavelength, is particularly suitable for complex CSC cases, especially those involving choroidal thickening. Its deeper penetration enables it to target the choroid and deeper retinal structures, making it effective for refractory or persistent cases. Utilizing the laser in subthreshold mode is essential to maximize therapeutic benefits while minimizing thermal effects[4,6,37]. Notably, the studies included in this Meta-analysis consistently reported no evidence of RPE alterations or atrophy during follow-up, reinforcing its safety and reliability in managing challenging CSC presentations.

The significant reduction in CRT across all laser wavelengths indicates that laser treatment confirms the structural benefits of laser treatment in CSC. The 810 nm laser demonstrated the most consistent CRT reduction, likely due to its deeper penetration, while the 532 nm and 577 nm lasers also proved effective despite greater variability. These findings support

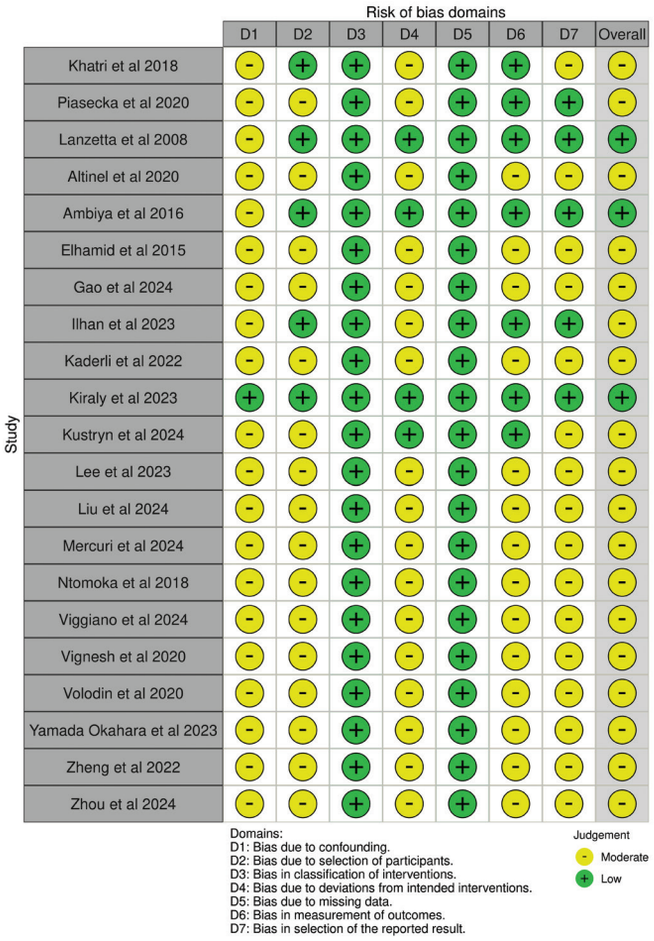

Figure 12 Quality assessment, using risk of bias in non-randomized studies of interventions tool (ROBINS-I).

the role of laser therapy in reducing macular thickness and resolving SRF.

However, the improvement in BCVA was not statistically significant, highlighting the complex relationship between structural changes and functional recovery. Given that all patients were treatment-naïve, variability in visual outcomes may be influenced by baseline disease severity, the duration of fluid accumulation, or subtle photoreceptor dysfunction present before treatment. Additionally, potential publication bias suggests that studies with less favorable BCVA improvements may be underrepresented. Variability in visual acuity measurement methods across studies likely also contributes to inconsistent findings regarding visual outcomes. While laser treatment effectively reduces CRT and SRF, its impact on vision remains uncertain, warranting further research with standardized protocols and longer follow-up.

The robustness of this Meta-analysis is supported by the leave-one-out sensitivity analysis, which consistently produced stable pooled estimates for SRF resolution, CRT reduction, and BCVA change. Although minor fluctuations in effect sizes were observed, the overall trends remained unchanged, confirming the reliability of the findings and the therapeutic role of laser treatment in reducing macular thickness and managing SRF in CSC. However, the persistently high heterogeneity (I^2) observed across analyses suggests substantial variability among studies, likely influenced by differences in patient demographics, disease severity, baseline measurements, laser protocols, and follow-up durations. Notably, heterogeneity was particularly pronounced in the 532 nm and 577 nm subgroups for CRT and BCVA, indicating greater variability in response to these wavelengths. Additionally, the funnel plot indicated potential publication bias, raising the possibility of underreporting less favorable BCVA outcomes. Despite these limitations, the findings confirm that laser treatment effectively reduces CRT and promotes SRF resolution, though its impact on BCVA remains uncertain.

Although some studies presented moderate concerns regarding specific risk of bias domains, the overall methodological quality was deemed low risk in most cases (Figures 11-12). No substantial variation in SRF resolution or CRT reduction was observed between studies with low versus moderate risk of bias, which supports the robustness and consistency of the findings despite minor methodological limitations. However, it should be noted that the trim-and-fill method assumes that funnel plot asymmetry is solely due to missing studies, which may also result from between-study heterogeneity or small-study effects.

Future research should prioritize the development of standardised treatment protocols and implementing more rigorous inclusion criteria to enhance comparability and strengthen the synthesis of findings. Conducting well-designed RCTs will mitigate bias and enhance the quality of evidence in this field. The test for subgroup differences (Chi^2=0.83, *df*=2, *P*=0.6592) found no statistically significant variation among the laser wavelengths, suggesting comparable effectiveness in CSC treatment. Clinicians may thus select a laser wavelength based on availability, safety, and practical considerations, as all three options appear similarly effective.

Looking ahead, refining patient selection criteria and prioritizing treatment standardization are crucial for optimizing clinical outcomes. These findings hold relevance for resource-limited settings, where access to specialized treatments may be constrained. Large-scale RCTs are needed to validate these results and establish clearer guidelines. Additionally, identifying reliable biomarkers for predicting treatment response and disease progression should be a research priority, paving the way for more personalized therapeutic strategies in CSC management.

In conclusion, this Meta-analysis demonstrates that 532, 577, and 810 nm SML's are equally effective in resolving SRF in cases of non-resolving CSC. Among these, the 532 nm laser emerges as a particularly practical choice due to its widespread

availability, robust safety profile, and affordability, making it a reliable option in routine clinical practice. By focusing on standardising treatment protocols, improving study designs, and ensuring consistent follow-up, SML therapy can be further refined into an even more impactful tool. Such advancements will not only enhance its effectiveness and safety but also provide tailored care to patients, ultimately improving long-term outcomes for individuals affected by this condition.

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