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Research article

Clinical efficacy and pain control of diode laser-assisted flap surgery in the treatment of chronic periodontitis:A systematic review and meta-analysis

Qiaoyu Hu[a,1], Xuanning Liu[a,1], Zirui Zhao[a], Zhijiao Guo[a], Qing Liu[a,**], Na Liu[b,*]

[a] Hebei Key Laboratory of Stomatology, Hebei Clinical Research Center for Oral Diseases, School and Hospital of Stomatology, Hebei Medical University, Shijiazhuang, 050017, PR China

[b] Department of Preventive Dentistry, School and Hospital of Stomatology, Hebei Medical University, Shijiazhuang, 050017, PR China

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ABSTRACT

Objective: To assess the diode laser-assisted periodontal flap surgery's clinical effectiveness and postoperative pain management in treating chronic periodontitis, and to offer evidence-based medical justification for the procedure's clinical use.

Data sources and study selection: In this study, a computer combined with manual search was used to search for articles on diode laser-assisted periodontal flap surgery for the treatment of chronic periodontitis published from the establishment of the database to September 2023. The databases searched included China Academic Journal Full Text Database (CNKI), China Biomedical Literature Database (CBM), Chinese Science and Technology Journal Database (VIP), Wanfang Database, PubMed, Web of science, Cochrane Library, Embase, and Scopus. Two researchers independently performed the screening and study selection, following the inclusion and exclusion standards to extract basic information and required data. Meta-analysis of the included literature was performed using Revman V5.4 software.

Result: Thirteen articles were analyzed. Meta-analysis showed that the use of the diode laser was effective in reducing patients' probing pocket depth (PPD) at 3 and 6 months postoperatively (3 months: MD = −0.46, 95 % CI = [−0.89, −0.03], $P = 0.04$; 6 months: MD = −0.35, 95 % CI = [−0.63, −0.06], $P = 0.02$), was able to effectively improve 3 month clinical attachment level (CAL) (MD = −0.36, 95 % CI = [−0.66, −0.06], $P = 0.02$), and was able to promote wound healing and reduce patients' early postoperative pain (MD = 0.67, 95 % CI = [0.01, 1.32], $P = 0.05$; MD = −1.67, 95 % CI = [−2.23, −1.00], and $P < 0.001$), while for gingival index (GI), the use of diode laser did not have a significant effect.

Conclusions: The available evidence suggests that the use of a diode laser adjunct is effective in reducing PPD, improving CAL, promoting wound healing, and reducing early postoperative pain in patients compared with flap application alone; however, for GI, diode lasers did not show any improvements.

* Corresponding author. Department of Preventive Dentistry, School and Hospital of Stomatology, Hebei Medical University, No. 383, Zhongshan East Road, Shijiazhuang, 050017, PR China.

** Corresponding author. Hebei Key Laboratory of Stomatology, Hebei Clinical Research Center for Oral Diseases, School and Hospital of Stomatology, Hebei Medical University, No. 383, Zhongshan East Road, Shijiazhuang, 050017, PR China.

E-mail addresses: liuqing@hebmu.edu.cn (Q. Liu), liuna@hebmu.edu.cn (N. Liu).

[1] These authors contributed equally to this work.

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Clinical significance: Periodontal flap surgery fails to eliminate microorganisms from the soft tissue wall, potentially leading to recolonization, reinfection, and accompanying side effects such as pain and swelling. The use of a diode laser reduces PPD, improves CAL, and relieves early postoperative pain.

1. Introduction

Periodontitis is a chronic infectious disease caused by plaque microorganisms that cause the destruction of periodontal supporting tissues, resulting in loosening and loss of teeth [1]. The primary objective of periodontal therapy is not solely to halt tissue deterioration but also to promote the regeneration and rejuvenation of tissues lost owing to the disease [2]. Subgingival scaling and root planning (SRP) are effective treatments for periodontal disease [3]. However, surgical intervention is required in deep periodontal pockets and narrow root bifurcation areas, where the removal of calculus and necrotic root surface tissue is difficult because of inaccessible instruments [4].

While the flap procedure facilitates root surface flattening and exposes root bifurcation directly, it does not eliminate microorganisms from the soft tissue walls of periodontal pockets. Recolonization and reinfection may result from residual periodontal pathogens that continue to exist in the lateral gingiva and soft tissue epithelial cells [5]. Soft tissue scraping methods, including ultrasound or chemical agents (such as antimicrobials and antiseptics) and drugs, have been used with varying degrees of success in evaluating their efficacy in the treatment of periodontitis [6]. However, the predictability of these therapeutic procedures remains uncertain and may increase the risk of developing resistant microbial strains [7]. Additionally, surgical treatment can cause numerous side effects such as pain, swelling, and inflammation.

In recent years, lasers have received increasing attention as adjunct or alternative therapies for the treatment of periodontitis. Different types of lasers, including diodes, Nd:YAG, Er:YAG, Er, Cr:YSGG, and CO2, have been used to treat periodontal diseases [8]. Compared to traditional surgical techniques, the diode laser is an effective tool for the control of bleeding, sterilization of the wound or target site, and reduction of post-treatment tissue edema and swelling [9]. Diode lasers typically target soft tissue lesions at wavelengths of 810 nm or 910–980 nm. They do not interact with the hard tissues of the dentition and have a sterilization effect on periodontal pathogens invading the soft tissue wall of the periodontal pockets [10].

Although laser therapy has potential advantages such as sterilization, hemostasis, and ablation, its routine use in the treatment of periodontal disease remains controversial. Gokhale et al. [11], and Jonnalagadda et al. [12] conducted studies in which comparisons of test groups and control groups were done and non-significant results were reported suggesting that the diode laser had no additional benefit over conventional flap surgery.

In contrast, Kolamala [13] found that the clinical parameters of diode laser treatment were superior to those of flap surgery alone from the beginning to the 6th month of follow-up. Therefore, the objective of this study was to conduct a meta-analysis of randomised controlled trials (RCTs) with the aim of conducting a systematic evaluation of diode laser-assisted periodontal flap surgery and provide guidance for its clinical application.

2. Materials and methods

According to the PRISMA Statement 2020: Updated Guidelines for Reporting Systematic Reviews [14], this meta-analysis was carried out, addressing the question "Can diode laser-assisted flap surgery effectively treat severe periodontitis and reduce postoperative pain compared with periodontal flap surgery alone?" It is registered with INPLASY (registration number INPLASY2023100009).

H_0: The efficacy of diode laser-assisted flap surgery in the treatment of severe periodontitis is similar to that of flap surgery applied alone.

H_1: the efficacy of diode laser-assisted flap surgery in the treatment of severe periodontitis is better than flap surgery alone.

If $P \leq 0.05$, H_0 is rejected and H_1 is accepted; if $P \geq 0.05$, H_0 is not rejected and the difference is not statistically significant.

2.1. Inclusion criteria

The PICOS principle served as the basis for the inclusion criteria in the study.

P: Patients with severe periodontitis, meeting surgical indications for periodontal flap surgery, having undergone basic periodontal therapy including affected teeth with a probing pocket depth (PPD) > 5 mm in at least two quadrants and showing bleeding on probing.

I:Diode laser combined with periodontal flap surgery.

C:Use of periodontal flap surgery alone.

O:Periodontal parameters: including probing depth, clinical attachment level (CAL), gingival index (GI), wound healing index (WHI) [15].

Pain level: visual analog scale (VAS) [16], rated on a scale from 0 to 10, with 0 = no pain, 1 to 3 = mild pain, 4 to 6 = moderate pain, and 7 to 10 = severe pain. Patients were instructed to rate their pain intensity on a scale of 0–10.

S:RCTs.

Exclusion Criteria: a. Patients with diabetes mellitus, hypertension, atherosclerosis, and other systemic diseases; b. pregnant and lactating women; c. smokers; d. papers published in languages other than English and Chinese; e. duplicates; and f. studies that did not provide original data.

2.2. Search strategy

Computerized and manual searches were combined, covering the period from database inception to September 2023. The China Academic Journal Full Text Database, Chinese Science and Technology Journal Database, China Biomedical Literature Database, Wanfang Database, PubMed, Cochrane Library, Web of Science, Embase, Scopus were searched electronically for published works, and manual searches of the included literature for relevant systematic evaluations were conducted. Search terms are as follows:

(((Periodontitis [Title/Abstract] OR Aggressive Periodontitis [Title/Abstract] OR Chronic Periodontitis [Title/Abstract] OR Periodontal disease [Title/Abstract]) AND (Flap surgery [Title/Abstract] OR open flap debridement [Title/Abstract] OR periodontal surgery [Title/Abstract])) AND (diode laser [Title/Abstract] OR Laser [Title/Abstract])) AND (randomized controlled trial OR randomized OR placebo)

2.3. Literature screening

Two researchers independently screened and cross-checked each section of included research paper, resolving disagreements with input from the supervising physician. Literature was screened rigorously by initially assessing the title and abstract to exclude irrelevant studies, followed by a thorough review of the full text of the remaining literature.

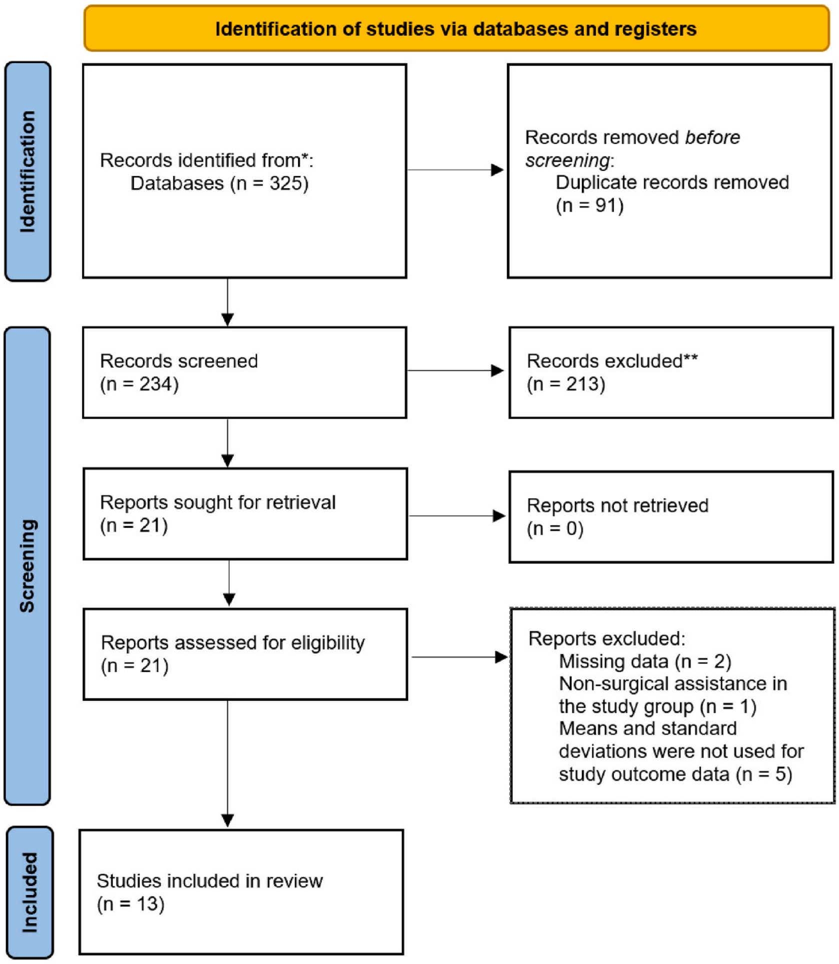

Fig. 1. Flow chart of search.

Table 1
Basic characteristics of the included literature.

Author/Year	Design	Average Age	Gender (M/F)	Sample size		Intervention		Clinical indicators	Follow-up time
				Experimental group	Control group	Experimental group	Control group		
2023Shakoush [19]	RCT (split-mouth)	45	5/5	10	10	DL + OFD	OFD	PI,PPD,CAL, GI,BOP,RGR VAS	3 months
2023Misra [20]	RCT (split-mouth)	–	40	40	40	DL + OFD	OFD	PI,PPD,CAL, GI,WHI	3/6 months
2022Silviya [21]	RCT	–	40	20	20	DL + SFA	SFA	FMPS,PPD, CAL,FMBS EHI	3/6 months
2022Roy [22]	RCT (split-mouth)	34.9 ± 6.38	7/3	10 10	10 10	DL + Kirkland DL + MWF	Kirkland MWF	PPD,CAL, SBI,VAS	6 months
2022Kolamala [13]	RCT (split-mouth)	38.8	10/5	15	15	DL + OFD	OFD	PPD,CAL, mSBI,VAS, WHI	3/6 months
2022Gangolu [23]	RCT (split-mouth)	35 ± 11.36	6/6	12	12	DL + OFD	OFD	PI,PPD,CAL, GI,EHI	3/6 months
2021Khan [24]	RCT (split-mouth)	–	20	20	20	DL + MWF	MWF	PI,PPD,CAL, GI,VAS	3 months
2019Karthikeyan [25]	RCT (split-mouth)	–	12/8	20	20	DL + Kirkland	Kirkland	PI,PPD,CAL, BOP	3/6 months
2018Jonnalagadda [12]	RCT (split-mouth)	40.56 ± 12.22	8/9	17	17	DL+ Flap sugury	Flap sugury	PI,PPD,CAL, GI,GR, VAS,EHI	3/6 months
2018Heidari [26]	RCT (split-mouth)	42.5 ± 9.5	10/16	26	26	DL+ Flap sugury	Flap sugury	VAS	1–8 days
2016Yan, W [27]	RCT (split-mouth)	45.5	32/26	58	58	DL+ Flap sugury	Flap sugury	PI,PPD,SBI	6/ 12months
2015Aena [28]	RCT (split-mouth)	–	13/12	22	22	DL + MWF	MWF	PI,PPD,CAL, PBI	6/9 months
2012Gokhale [11]	RCT (split-mouth)	41,4	30	30	30	DL + OFD	OFD	PI,PPD,CAL, GI	3 months

Author/Year	Laser Type	Wavelength (nm)	Power (W)	Energy Density (J/cm^2)	Laser application methods	Postoperative medication
2023Shakoush	DL	808	2.5	3	output power of 250 mW for 12 s, with an energy density of 3 J/cm^2 in the continuous wave mode (spot size 0.5 cm). The laser beam was directed perpendicularly toward the tissue in contact mode on the buccal and lingual sides. The laser was irradiated at the recipient sites immediately after surgery and again 3 and 7 days later.	antibiotic course (augmentin 1000 mg, amoxicillin 625 mg, and clavulanate potassium) and ibuprofen 600 mg
2023Misra	DL	890	1.5	–	Sweeping movements were made with the tip in the pocket apico-coronally (vertically) and mesiodistally (horizontally). In the test group, laser biostimulation was performed twice a day for 30 s, with a 60-s interval, using a 1.5 W power output in non-contact mode at baseline, the third, and the seventh day following flap surgery.	–
2022Silviya	DL	790–810	0.4-0.7	–	Bio-stimulation using continuous waves for 4–5 min, the buccal and lingual sides of the period were both in contact with the probe tips, which were positioned perpendicularly.	ibuprofen 400 mg
2022Roy	DL	940	1.5	–	Continuous non-contact irradiation on the inner surface of the skin flap, exposed bone and exposed root structures for 30s.	antibiotic (amoxicillin 500 mg and clavulanic acid 125 mg) analgesics (aceclofenac 100 mg with paracetamol 325 mg)

(continued on next page)

Table 1 (*continued*)

Author/Year	Laser Type	Wavelength (nm)	Power (W)	Energy Density (J/cm^2)	Laser application methods	Postoperative medication
2022Kolamala	DL	980	2	–	Continuous mode, using a 320 μm diameter laser tip, horizontal overlapping strokes were used to lase the inner aspect of the flap from the margin to the bottom of the labial/buccal and lingual/palatal flaps.	–
2022Gangolu	DL	980	3	–	Diode laser (980 nm, power: 3.0W; frequency: 2.5 KHz) was used to remove the inflammed soft tissue lining of the pocket for about 30s	antibiotics (amoxicillin 500 mg) and analgesics (diclofenac 50 mg)
2021Khan	DL	980	1.5	–	A 980 nm diode laser unit, 400-μm diameter at 1.5W in contact mode at 45° angle to the inner aspect of the flap was used to remove the remaining epithelium, 10s of irradiation for each part. With a diode laser set at 0.5 W in noncontact mode at baseline and after 7 days, laser biostimulation was performed following suturing. Each site was lased for 10s (60 s/tooth).	–
2019Karthikeyan	DL	970 ± 15	2.5	50	The laser at a power of 2.5W, power density of 10W/cm^2, and dose of 50J/cm^2 in contact mode was used to remove the entire visible epithelium in the inner side of the flap, 10s per tooth.	ibuprofen 400 mg
2018Jonnalagadda	DL	810	1.5		The laser was used in continuous mode with a power setting of 1.5W to irradiate the inside of the flap from the free periodontal margin to the bottom of the flap tip, and the laser emission was interrupted for 30s after irradiation exceeded 10s	ibuprofen 400 mg paracetamol 325 mg
2018Heidari	DL	940	0.5	40	The laser was irradiated to the buccolingual surface of the flap using 940 nm, 0.5 W, continuous mode from a distance of 3 mm. The total energy density received by the buccal and lingual surfaces was 40 J/cm^2	amoxicillin 500 mg Gelofen 400 mg
2016Yan, W	DL	810	2.5		Each tooth was laser sterilized for 30 s, and then Duraphat was repeatedly applied to the roots of the affected teeth with a small brush tip for 2 times, 10 s each time, and the diode laser was used for immediate desensitization treatment, and the irradiation was repeated for a total of 40 s at 10 s intervals.	antibiotics
2015Aena	DL	810	0.1	4	Remove all visible epithelium on the inner side of the flap and interrupt laser emission for 30 s if the exposure time exceeds 10 s. The laser is then held at a 45° angle to the soft tissue flap to avoid laser contact with the root surface or alveolar bone, and a second laser irradiation is performed using the same laser in 0.1 W continuous mode.	–
2012Gokhale	DL	980	2.5	50	A continuous contact pattern is used. The fiber was used to perform a "brushing" motion on the lower surface of the flap to remove the pocket lining.	antibiotics were not prescribed

DL: diode laser; OFD: open flap debridement, SFA: single flap approach, MWF: modified Widman flap, PI: plaque index, PPD: probing pocket depth, CAL: clinical attachment level; GI: gingival index, BOP: bleeding on probing, VAS: visual analogue scale, SBI: sulcus bleeding index, WHI: wound healing index, EHI: early healing index.

2.4. Data extraction

The authors, study type, sample size, periodontal parameters, laser application method, and follow-up duration were gathered from the included studies. The data collection procedure was carried out independently by two researchers using an Excel sheet to collect data electronically.

2.5. Literature quality evaluation

Each study's risk of bias was evaluated in accordance with version 5.1.0 of the Cochrane Handbook for the Systematic Evaluation of Interventions. [17], and consisted of six aspects and seven entries: method of randomization (selection bias), concealment of the allocation scheme (selection bias), blinding of subjects and researchers (implementation bias), blinding of the outcome evaluations (measurement bias), completeness of the outcome data (follow-up bias), selective publication (reporting bias), and other sources of bias (other bias). The level of risk of bias for each included study was evaluated according to the above seven entries, including "low risk”, “unknown risk”, and “high risk”.

2.6. Statistical analysis

With the use of the Cochrane Community’s Review Manager (RevMan, version 5.4), a meta-analysis of the included literature was conducted; all clinical parameters in this study were continuous variables, and effect sizes are represented by mean difference (MD) and 95 % confidence intervals (CI). If $P > 0.1$ and $I^2 \leq 50$ %, it suggests minimal or no statistical heterogeneity among the studies, prompting the use of a fixed-effects model for analysis. Conversely, if there is statistical heterogeneity among the studies, indicated by $P \leq 0.1$ and $I^2 > 50$ %, a random-effects model was employed for analysis, after accounting for significant clinical heterogeneity.

2.7. GRADE Quality of Evidence Assessment

Citing the GRADE quality of evidence grading system [18] for outcome indicators, which has three factors that are upgraded and five factors that are downgraded, the studies included in this review consisted entirely of RCTs, representing the highest level of evidence; thus, no upgrading was necessary. Four levels of evidence quality were identified based on five dimensions: risk of bias, inconsistency, indirectness, imprecision, and publication bias. These levels were identified as high, moderate, low, and very low.

3. Results

3.1. Literature search and screening results

Through a combination of computer and manual searches, 325 articles were initially retrieved. After removing 91 duplicates, 213 were excluded based on the title and abstract. Following a full-text review, an additional eight were excluded. Finally, as indicated by Fig. 1 and 13 articles satisfied the inclusion requirements. The search strategies used in each database and the reasons for excluding articles after reading the full text are shown in Tables 2 and 3.

3.2. Characteristics of the included literature

Twelve split-mouth studies and one parallel controlled experiment comprised the 13 published literatures. Regarding the type of surgery, five studies used open flap debridement （OFD）; three, modified Widman flap （MWF）; two, Kirkland; one, single flap approach （SFA）; and the remaining three did not specify the surgery type. The details of the laser wavelengths, powers, and application methods are shown in Table 1.

3.3. Literature quality evaluation

All 13 studies used randomized controlled methods; four of them used allocation scheme concealment, seven clearly stated that patients and principal investigators were blinded, five blinded the study outcome measures, and three did not. The results of the quality assessment are shown in Fig. 2.

3.4. Meta-analysis results

3.4.1. PPD

Twelve papers were included and the test for heterogeneity at PD baseline showed no heterogeneity between studies ($p = 0.29$, $I^2 =$ 15 %), and meta-analysis was performed using a fixed-effects model (MD = 0.04, 95 % CI = [−0.05, 0.13], $P = 0.35$), with no

Table 2
Search strategy used for each database.

Database	Search strategy	No. of results
PubMed	(((Periodontitis[Title/Abstract] OR Aggressive Periodontitis[Title/Abstract] OR Chronic Periodontitis[Title/Abstract] OR Periodontal disease[Title/Abstract]) AND (Flap surgery[Title/Abstract] OR open flap debridement[Title/Abstract] OR periodontal surgery[Title/Abstract])) AND (diode laser[Title/Abstract] OR Laser[Title/Abstract])) AND (randomized controlled trial OR randomized OR placebo)	26
Web of science	TS= (Periodontitis OR Aggressive Periodontitis OR Chronic Periodontitis OR Periodontal disease) AND TS=(Flap surgery OR open flap debridement OR periodontal surgery) AND TS=(diode laser OR Laser) AND TS=(randomized controlled trial OR randomized OR placebo)	98
Cochrane	TS= (Periodontitis OR Aggressive Periodontitis OR Chronic Periodontitis OR Periodontal disease) AND TS=(Flap surgery OR open flap debridement OR periodontal surgery) AND TS=(diode laser OR Laser) AND TS=(randomized controlled trial OR randomized OR placebo)	207
Embase	TS= (Periodontitis OR Aggressive Periodontitis OR Chronic Periodontitis OR Periodontal disease) AND TS=(Flap surgery OR open flap debridement OR periodontal surgery) AND TS=(diode laser OR Laser) AND TS=(randomized controlled trial OR randomized OR placebo)	25

Table 3
List of excluded full-text papers and reasons for exclusion following full-text screening.

Citation	Exclusion reason
Rathod2023 [29]	Missing data
Patila2022 [30]	Non-surgical assistance in the study group
Dogan2022 [31]	Incomplete data
Nagaraj2020 [32]	Incomplete data
Doshi2014 [33]	Incomplete data
Sanz-Moliner2013 [34]	Incomplete data
Gaspirc2012 [35]	Missing data
Ozcelik2008 [36]	Incomplete data

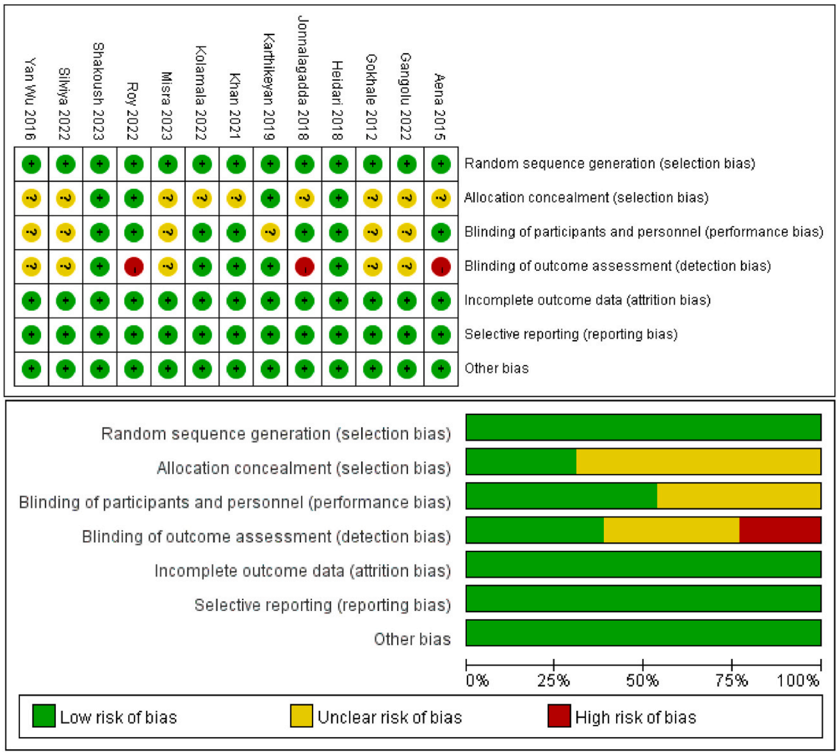

Fig. 2. Risk bias graph of the included literature.

statistically significant difference. A random-effects model was used for the meta-analysis, and the results showed a statistically significant difference (MD = −0.46, 95 % CI = [−0.89, −0.03], $P = 0.04$). Heterogeneity between studies was observed at 3 months ($P < 0.001$, $I^2 = 83$ %). A significant heterogeneity was observed between studies at six months ($P < 0.001$, $I^2 = 88$ %), necessitating the use of a random effects model (MD = −0.35, 95 % CI = [−0.63, −0.06], $P = 0.02$). This difference was found to be statistically significant. The results showed that after 3 and 6 months of treatment, diode laser-assisted flap surgery was more effective than flap surgery alone in reducing PPD (Fig. 3).

3.4.2. CAL

Eleven papers were included and the test for heterogeneity at CAL baseline showed heterogeneity between studies ($P = 0.07$, $I^2 =$ 41 %). A meta-analysis was conducted using a random effects model (MD = 0.02, 95 % CI = [−0.25, 0.29], $P = 0.88$), and the difference was found to be not statistically significant. There was significant heterogeneity between studies at three months ($P = 0.06$, I^2 = 47 %), and a random effects model was employed (MD = −0.36, 95 % CI = [−0.66, −0.06], $P = 0.02$), resulting in a statistically significant difference. Heterogeneity existed between studies at 6 months ($P < 0.001$, $I^2 = 85$ %), random effects model was used for Meta-analysis (MD = −0.24, 95 % CI = [−0.67, 0.19], $P = 0.28$), with no statistically significant differences (Fig. 4).

3.4.3. GI

The heterogeneity test at baseline revealed heterogeneity between studies ($P = 0.02$, $I^2 = 67$ %) for the five papers that were included. A random effects model was used in the meta-analysis (MD = 0.07, 95 % CI = [−0.16, 0.31], $P = 0.53$), and the difference

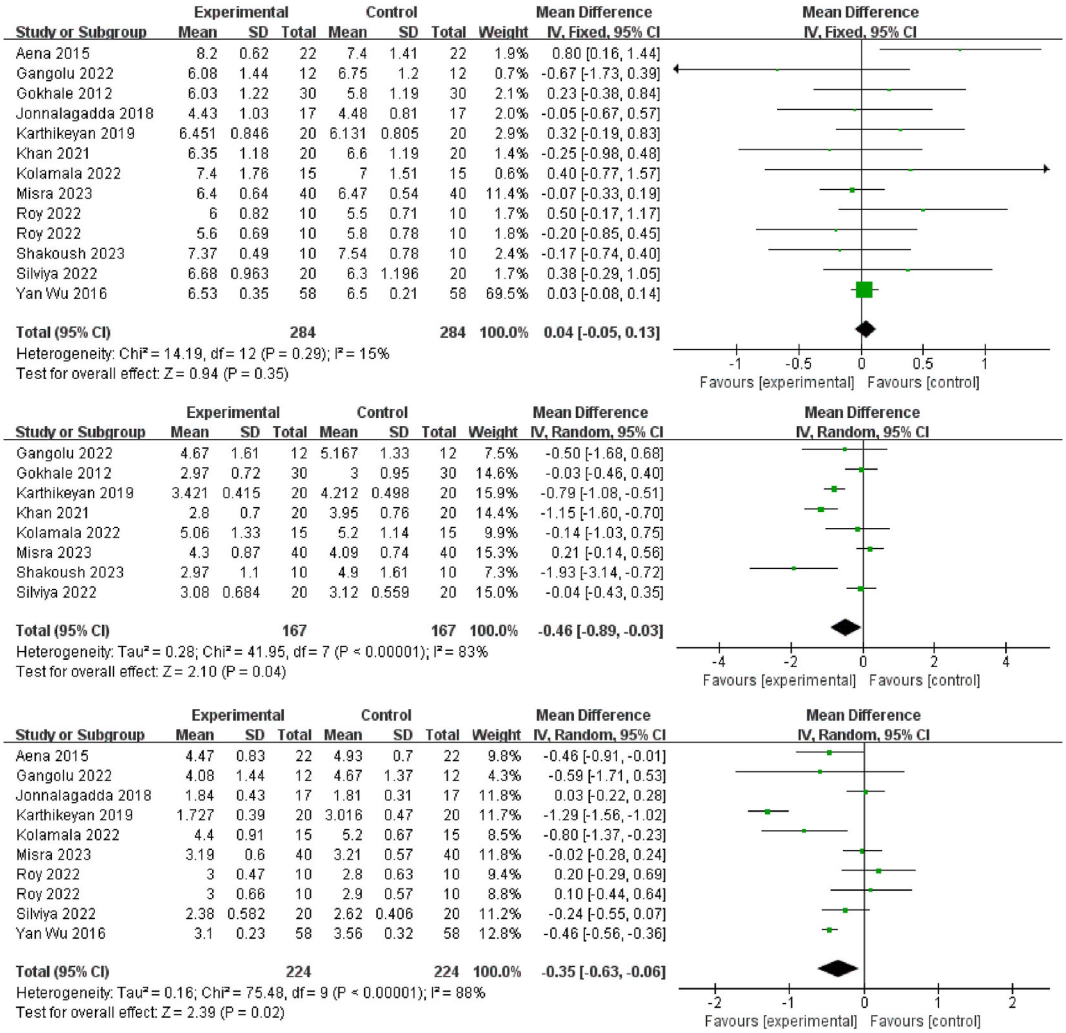

Fig. 3. PPD forest plot at baseline, 3 months, 6 months.

was not statistically significant. There was no heterogeneity between studies at 3 months (P = 0.6, I^2 = 0 %). Meta-analysis was conducted using a fixed-effects model (MD = −0.11, 95 % CI = [−0.24, 0.02], P = 0.10), with no statistically significant differences. There was no heterogeneity between studies at 6 months (P = 0.67, I^2 = 0 %), and a fixed-effects model was used (MD = 0.05, 95 % CI = [−0.09, 0.18], P = 0.48); the difference was not statistically significant. Diode laser-assisted flap surgery improved the GI of patients to a similar extent as flap surgery alone after 3 and 6 months (Fig. 5).

3.4.4. WHI

Two papers were included and the heterogeneity test on postoperative day 7 showed heterogeneity between studies (P = 0.0006, I^2 = 91 %). Consequently, the meta-analysis was performed using a random-effects model (MD = 0.67, 95 % CI = [0.01, 1.32], P = 0.05), which was statistically significant, and the diode laser promoted wound healing after periodontal flap surgery (Fig. 6).

3.4.5. VAS

Five papers were included and the heterogeneity test on postoperative day 1 showed heterogeneity between studies (P = 0.09, I^2 = 58 %), and meta-analysis was performed using a random-effects model (MD = −1.67, 95 % CI = [−2.23, −1.00], P < 0.001), revealing statistically significant differences. Heterogeneity existed between studies on day 3 (P < 0.001, I^2 = 95 %), and a random effects model was used (MD = −0.42, 95 % CI = [−1.81, 0.97], P = 0.56), with no statistically significant differences. Day 7 studies showed heterogeneity (P < 0.001, I^2 = 92 %), and no statistically significant differences were found when the random effects model (MD = −0.71, 95 % CI = [−1.64, 0.22], P = 0.14) was applied. A diode laser reduced the pain and discomfort caused by flap surgery on the 1st postoperative day, while there was no significant effect on the 3rd and 7th days (Fig. 7).

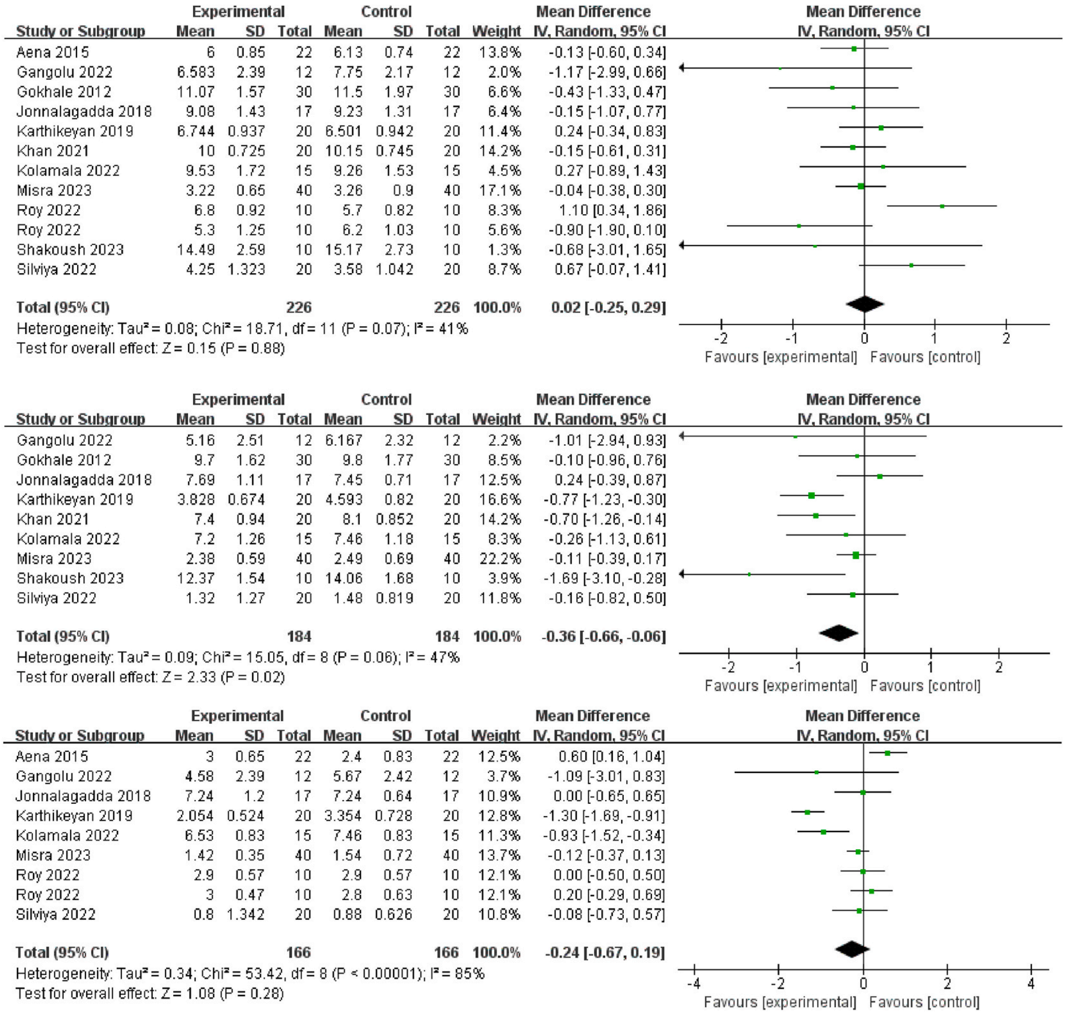

Fig. 4. CAL forest plot at baseline, 3 months, 6 months.

3.5. *Sensitivity analysis and publication bias*

For each inclusion indicator, both the random-effect model and fixed-effect model were alternately used, or each study was systematically removed one by one followed by Meta-analysis, demonstrating no significant alterations in results. This suggests that the statistical results of the corresponding effect sizes in this study were stable and reliable. Using the baseline PPD as the analysis index, a funnel plot analysis was performed for the included literature, and the results showed that the graph was more symmetrical, which suggests that the bias of this study was minimal (Fig. 8).

3.6. *GRADE Quality of Evidence Assessment*

The GRADEpro GDP program was used to categorize the quality of the evidence, and the results indicated that the PPD baseline, CAL baseline, GI at 3 and 6 months, and VAS at 1 day were all of moderate quality (moderate). CAL at 3 months was determined to have high quality evidence (high), while the remaining indicators were classified as having low (low) or very low quality evidence (very low) (Fig. 9).

4. Discussion

Lasers have become an integral part of periodontal therapy and have successfully assisted almost every periodontal procedure over the past decade. Diode lasers offer the advantages of high efficiency, low thermal damage, stable output power, and ease of use [37]. Soft tissue surgery using lasers allows for hemostasis and disinfection with minimal postoperative pain when compared with conventional surgery [20]. PPD has a significant impact on the results' long-term stability, and CAL is the gold standard for assessing the

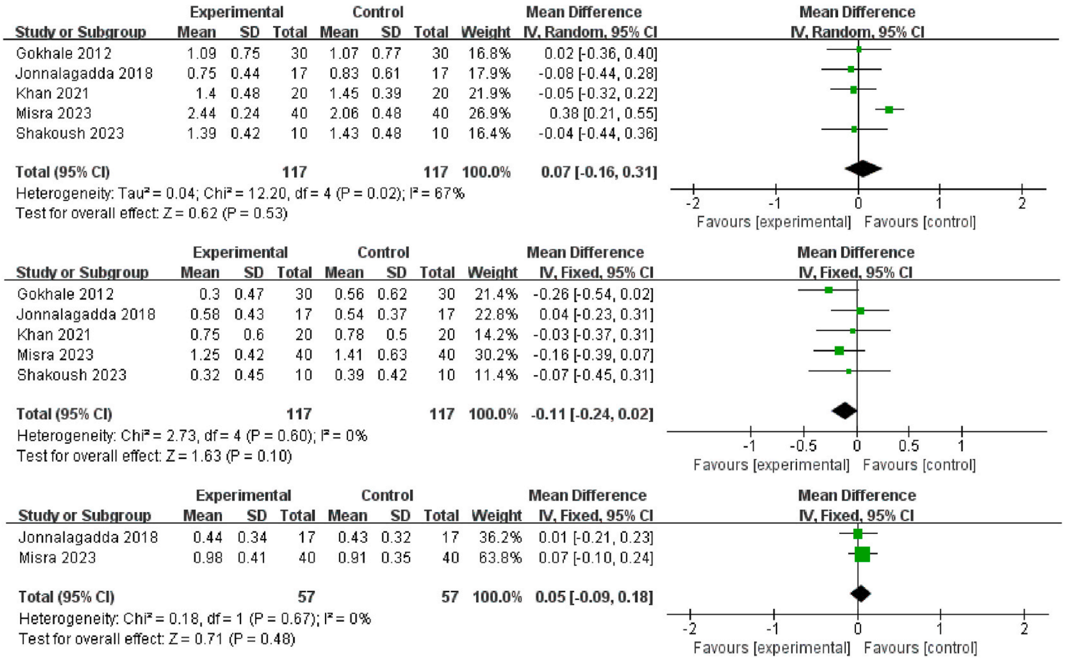

Fig. 5. GI forest plot at baseline, 3 months, 6 months.

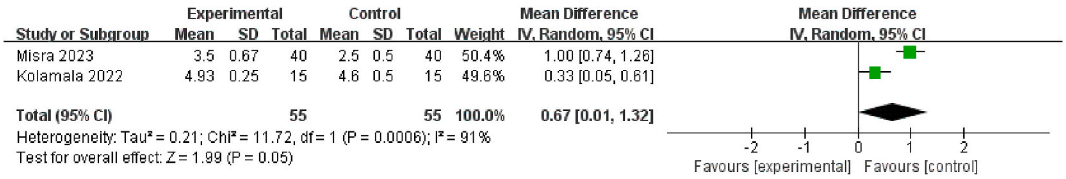

Fig. 6. WHI forest plot at 7 days.

efficacy of periodontal therapy. This meta-analysis evaluated the value of diode lasers in periodontal flap surgery using the PPD, CAL, GI, WHI, and VAS.

Diode laser-assisted periodontal flap surgery resulted in a better reduction in PPD in patients at the 3- and 6-month follow-up periods, which may be related to elevated levels of anti-inflammatory cytokines and enhanced microcirculation after laser irradiation [38]. The increase in attachment levels in the laser-assisted flap-surgery group at 3 months was significantly higher than that in the control group, and the difference was statistically significant. New connective tissue attachments were formed as a result of the diode laser's ability to remove the epithelium more thoroughly. A study by Fisher et al. [39] found that laser de-epithelialization delayed the downward growth of epithelial cells after periodontal surgery by up to 14 days compared to the traditional flap technique. This is because the laser causes thermal necrosis of the wound edges and the formation of a crust that prevents epithelialization, leading to a delay in epithelialization. The effectiveness of a laser is influenced by its mode of use (laser applied inside or outside the periodontal pocket) [40]. By inserting the laser tip inside the periodontal pocket, the internal mode uses high levels of laser light to generate a photothermal effect that ablates the epithelial tissue and inflammatory lesions in the soft tissue walls of the periodontal pockets, slowing the migration of the epithelium and promoting the regeneration of periodontal tissues [41]. Meanwhile, the external mode is based on photo-biomodulation using low levels of laser light, which regulates cell behavior by affecting "membrane calcium channels" or "mitochondrial respiratory chain," thus assisting in the processes of angiogenesis, growth factor release, and collagen synthesis [42].

The GI reflects the condition of the gingiva, including changes in morphology and texture. There was a statistically significant decrease in the GI scores in both the laser and control groups in the four included studies [11,20,19,24], demonstrating the effectiveness of periodontal flap surgery in removing inflammation caused by tartar and infected granulation tissue. One of the studies by Shakoush et al. [19] showed that laser-assisted flap surgery at 3 months resulted in better gingival condition. Diode lasers can inhibit interleukin (IL)-6, monocyte chemotactic protein-1, IL-10, and tumor necrosis factor (TNF) to exert anti-inflammatory effects [43]; reduce edema by restoring the circulation of microcapillaries; and normalize the permeability of the vascular wall [44]. The remaining studies [11,12,20] showed statistically significant decreases, but comparisons between groups did not show statistical differences, probably because the participants in both groups followed proper oral hygiene practices and performed effective oral cleaning.

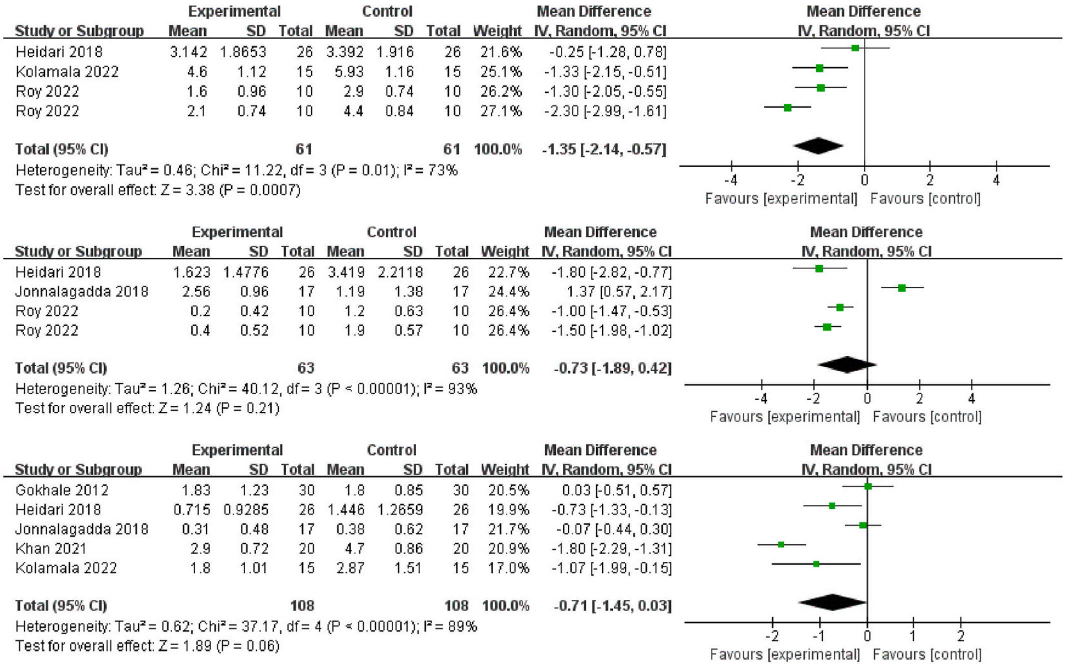

Fig. 7. VAS forest plot at 1 day, 3 days, 7 days.

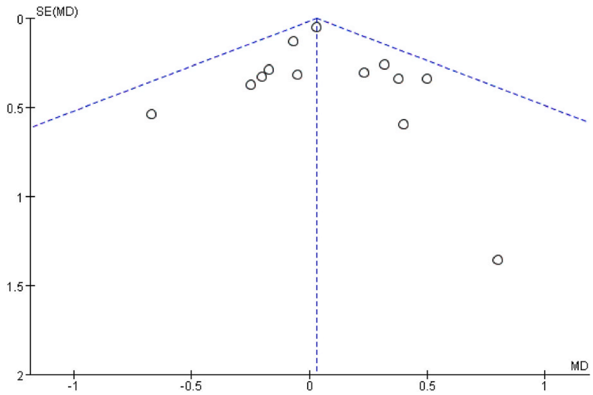

Fig. 8. Funnel plot of PPD baseline.

The dose applied when using the laser is an important therapeutic parameter; the therapeutic window dose for biostimulation is between 0.001 J/cm^2 and 10 J/cm^2, and a dose of approximately 1–2 J/cm^2 is necessary to determine its effect on wound healing [45]. The results of this systematic evaluation indicate that 1 week postoperatively, the diode laser can promote wound healing. Wound healing is a complex process that involves the proliferation, differentiation, migration, and adhesion of various cell types. Different growth factors regulate the functions of these cells, which ultimately determine the rate and quality of healing [21]. Diode lasers exert additional effects on fibroblasts by promoting proliferation, increasing cell number, secreting growth factors, and differentiating fibroblasts into myofibroblasts. Growth factors such as transforming growth factor-β1 (TGF-β1) and basic fibroblast growth factor (bFGF) regulate various aspects of wound healing, including the inflammatory response of fibroblasts, synthesis of specific extracellular matrix molecules, angiogenesis, epithelial regeneration, and remodeling [46]. Transforming growth factor β1 stimulates fibroblast proliferation, increases synthesis of extracellular matrix molecules and matrix metalloproteinase (MMP) inhibitors, and inhibits MMP synthesis. bFGF is a potent stimulant of the angiogenic response in wounds, acting as a chemoattractant for fibroblasts and endothelial cells. It also activates neutral proteases in fibroblasts and epithelial cells, resulting in enhanced wound contraction and a reduction in inflammatory mediators [47].

The pain rating scales used in the included studies are highly subjective, relying on individual patient perception and experience. Inflammatory chemical intermediates released by periodontal disease or tissue damage caused during surgical treatment play an important role in postoperative pain [48] The release of these inflammatory intermediates has been controlled using a variety of

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	diode laser-assisted flap surgery	flap surgery	Relative (95% CI)	Absolute (95% CI)		
PD base line												
12	randomised trials	not serious	not serious	not serious	serious[a]	none	284	284	-	MD 0.03 higher (0.06 lower to 0.12 higher)	⊕⊕⊕◯ Moderate	IMPORTANT
PD 3 month												
8	randomised trials	not serious	very serious[b]	not serious	not serious	none	167	167	-	MD 0.46 lower (0.89 lower to 0.03 lower)	⊕⊕◯◯ Low	IMPORTANT
PD 6 month												
9	randomised trials	not serious	very serious[b]	not serious	not serious	none	224	224	-	MD 0.35 lower (0.63 lower to 0.06 lower)	⊕⊕◯◯ Low	IMPORTANT
CAL base line												
11	randomised trials	not serious	not serious	not serious	serious[a]	none	226	226	-	MD 0.02 higher (0.25 lower to 0.29 higher)	⊕⊕⊕◯ Moderate	IMPORTANT
CAL 3 month												
9	randomised trials	not serious	not serious	not serious	not serious	none	184	184	-	MD 0.36 lower (0.66 lower to 0.06 lower)	⊕⊕⊕⊕ High	IMPORTANT
CAL 6 month												
8	randomised trials	not serious	very serious[b]	not serious	serious[a]	none	166	166	-	MD 0.24 lower (0.67 lower to 0.19 higher)	⊕◯◯◯ Very low	IMPORTANT
GI base line												
5	randomised trials	not serious	serious	not serious	serious[a]	none	117	117	-	MD 0.17 higher (0.06 higher to 0.29 higher)	⊕⊕◯◯ Low	IMPORTANT
GI 3 month												
5	randomised trials	not serious	not serious	not serious	serious[a]	none	117	117	-	MD 0.11 lower (0.24 lower to 0.02 higher)	⊕⊕⊕◯ Moderate	IMPORTANT
GI 6 month												
2	randomised trials	not serious	not serious	not serious	serious[a]	none	57	57	-	MD 0.05 higher (0.09 lower to 0.18 higher)	⊕⊕⊕◯ Moderate	IMPORTANT
WHI 7 day												
2	randomised trials	not serious	very serious[b]	not serious	not serious[a]	none	55	55	-	MD 0.67 higher (0.01 higher to 1.32 higher)	⊕⊕◯◯ Low	IMPORTANT
VAS 1 day												
3	randomised trials	not serious	serious[b]	not serious	not serious	none	61	61	-	MD 1.35 lower (2.14 lower to 0.57 lower)	⊕⊕⊕◯ Moderate	IMPORTANT
VAS 3 day												
3	randomised trials	not serious	very serious[b]	not serious	serious[a]	none	63	63	-	MD 0.73 lower (1.89 lower to 0.42 higher)	⊕◯◯◯ Very low	IMPORTANT
VAS 7 day												
5	randomised trials	not serious	very serious[b]	not serious	serious[a]	none	108	108	-	MD 0.71 lower (1.45 lower to 0.03 higher)	⊕◯◯◯ Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference

Explanations

a. Inclusion of studies with small sample sizes and too wide confidence intervals
b. Large heterogeneity exists

Fig. 9. Grade quality of evidence assessment.

techniques, including the use of non-steroidal anti-inflammatory medicines (NSAIDs); however, they can cause digestive problems and platelet dysfunction [49]. Although newer NSAIDs greatly reduce digestive problems by selectively inhibiting the cyclooxygenase-2 enzyme, they also increase the risk of myocardial infarction and nephrotoxicity [50].

The four studies that were included in the analysis reported that patients felt less pain at the site of laser treatment than at other sites, which may be owing to the inhibitory effect of laser therapy on peripheral neurons by slowing down conduction velocities and decreasing the amplitude of compound action potentials, preventing the transmission of pain signals from the site of injury to the brain [51] Photobiomodulation with diode lasers can inhibit the production of pain-related substances, such as histamine or bradykinin [52]. Additionally, diode lasers inhibit the secretion of inflammatory cytokines [53]. In a clinical study by Calderín et al. [54], the levels of IL-1β and TNF-α in the diode laser combined with SRP (scaling and root planning) group were significantly lower than those of SRP alone group, and the study by Misra et al. [20] showed reduced levels of several inflammatory cytokines, including TNF-α and MMP8, after diode laser-assisted flap debridement. However, a study by Jonnalagadda [12]et al. found that the use of diode lasers as an adjunct to periodontal flap surgery did not relieve overall postoperative pain in patients. On day 3 after treatment, patients felt more pain at the test site than at the control site, and the pattern of analgesic consumption was similar in both groups, i.e., the test group had a higher level of post-surgical pain, and the reason for this discrepancy may be due to differences in the type of surgery or the pattern of laser application between the different studies.

This meta-analysis had certain limitations that need to be considered. First, the effect of laser irradiation on periodontal tissues vary according to the laser irradiation protocol (wavelength, power, mode). Because the laser parameters and type of procedure are not exactly the same between studies, a categorized discussion based on the laser irradiation protocol has not been made. Second, The length of follow-up varied so much between studies that subgroup analyses could be biased as a result. Finally, we limited our search to articles written in English and Chinese, and the language inclusion criteria may have created a language selection bias.

More high-quality studies on the combination of laser wavelength and power should be carried out to form a unified standard to reduce clinical heterogeneity and provide guidance for the wide application of semiconductor lasers in clinical practice. For the lack of test efficacy due to the small sample size, more RCTs with larger samples should be conducted, and more RCTs with parallel and split designs should be conducted in the future for research. Since most of the studies had a follow-up time of 3 and 6 months, the lack of studies with longer follow-up time is not conducive to our understanding of the long-term efficacy of laser-assisted flap surgery, future RCTs should have a longer follow-up time and focus on the differences between short- and long-term efficacy of lasers in periodontitis.

5. Conclusion

Available evidence suggests that the use of diode laser adjuncts is effective in reducing PPD and improving CAL, promoting wound healing, and reducing early postoperative pain compared with flap surgery alone; however, for GI, diode lasers did not show any improvements.

Availability of data and materials

All data generated or analyzed during this study are included in this article.

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Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Qiaoyu Hu: Writing – original draft, Software, Methodology, Conceptualization. **Xuanning Liu:** Software, Methodology, Conceptualization. **Zirui Zhao:** Data curation. **Zhijiao Guo:** Software. **Qing Liu:** Writing – review & editing, Conceptualization. **Na Liu:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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