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ORIGINAL ARTICLE

Network meta-analysis of the treatment efficacy of different lasers for peri-implantitis

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Abstract

The aim of this study was comparing different lasers with conventional non-surgical treatment (CNT) for the management of peri-implantitis, regarding probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI). Randomized controlled trials (RCTs) on different lasers and CNT for peri-implantitis were searched. Pairwise and network meta-analyses were performed to analyze the PD, PLI, CAL, and SBI outcomes. The risk of bias, evidence quality, statistical heterogeneity, and ranking probability were also evaluated. Eleven studies were included in this study, involving three types of lasers. Diode + CNT had significantly superior efficacy to CNT alone, regarding PD reduction, while Er:YAG + CNT had significantly superior efficacy than CNT in terms of the PLI, CAL, and SBI. The highest probability of being most effective for PD was diode + CNT (49%), while Er:YAG + CNT had the highest probability of improving the PLI, CAL, and SBI (66%, 53%, and 79%, respectively). Diode + CNT was significantly superior for PD management in peri-implantitis compared with CNT alone, while Er:YAG + CNT significantly improved the PLI, CAL, and SBI. Therefore, Er:YAG + CNT might be recommended methods considered for management of peri-implantitis.

Keywords Lasers · Conventional non-surgical treatment · Peri-implantitis · Network meta-analysis · Randomized controlled trial

Introduction

Implant dentistry has rapidly advanced in recent years, and more implants are now being placed and restored with teeth loss. Moreover, clinicians are beginning to focus on long-term effects and treatment outcomes. Peri-implantitis, which remains an important cause of implant failure, [1] refers to the inflammation of soft and hard tissues around osseointegrated implants, which leads to bone loss around implants and the formation of peri-implant pockets [2]. This pathology can cause failure of dental implants, necessitating removal, and grafting procedures. Previous studies have reported that the incidence of peri-implantitis is 30–70% [2, 3].

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Currently, the basic treatment of peri-implantitis involves plaque removal, infection control, elimination of peri-implant pockets, prevention of bone loss, and induction of bone regeneration. The management of peri-implantitis includes both conventional non-surgical treatment (CNT) and surgical treatment. The first step in peri-implantitis treatment is CNT via mechanical debridement, ultrasonic scaling, and topical drug therapy [4, 5]. However, previous research has shown that it is difficult to remove all of the invading bacteria around an implant by CNT [6, 7]. Rough surfaces and screw-shaped implants are not conducive to plaque removal [8]. Therefore, it may be necessary to use additional methods to treat peri-implantitis [9]. At this situation, laser systems are being used more frequently as a non-surgical treatment modality for peri-implantitis [10]. Several types of lasers have been used to treat peri-implantitis, including Er:YAG, diode, and Nd:YAG lasers. [8, 11, 12] Compared with CNT, the main advantages of laser therapy are minimal invasiveness, ease of use, high acceptability to patients, safety (with respect to hemostatic effects on tissues), and high plaque removal efficiency [13, 14].

Previous studies have analyzed the efficacy of lasers for treatment of peri-implantitis, but the clinical impact remains controversial. Some studies have shown that lasers can control peri-implantitis more effectively than CNT [8, 15, 16], while others found that lasers do not yield outcomes that are significantly different from those of CNT [17–19]. Systematic reviews and meta-analyses focusing on the effect of lasers on peri-implantitis have been published but have certain drawbacks. Previous meta-analyses only analyzed the therapeutic effects of a certain types of lasers used alone, rather than comparing the therapeutic effects of several types of lasers at the same time [9]. In addition, some reports included surgical treatments of peri-implantitis, rather than just comparing lasers with CNT [20, 21]. Moreover, other meta-analyses not only included studies on laser therapy for peri-implantitis but also for peri-implant mucositis, which may have led to biased results [22]. Finally, these studies did not rank the different laser treatments in terms of peri-implantitis treatment efficacy, and no consensus has been reached on the best laser treatment for the condition; thus, there no evidence-based guidelines for laser treatment of peri-implantitis are available to clinicians [23].

Network meta-analysis is a new method of evidence synthesis that is now frequently employed when examining the literature on clinical treatments. Network meta-analysis allows for statistical comparison of multiple treatments [24–27]. This technique can be used to estimate the heterogeneity of outcomes for a given treatment, as well as any inconsistencies in the data for two different treatments among studies [28]. Network meta-analysis also allows for indirect comparison of studies with different research designs. Given the changes in treatment methods, a more comprehensive and up-to-date systematic review and network meta-analysis on the efficacy of different laser systems for peri-implantitis is needed, including correlation ranking of the various laser systems. The present network meta-analysis addresses this gap and should provide guidance for dentists with respect to choosing the most suitable laser treatments for peri-implantitis.

Materials and methods

This study was conducted according to international guidelines for pairwise and network meta-analyses [29, 30] and registered in the International Prospective Register of Systematic Review database (PROSPERO-CRD42019145195).

PICOS question

Based on the recommendations of the Centre for Evidence-Based Medicine (University of Oxford, Oxford, UK), the participants, interventions, comparisons, outcomes, and study design (PICOS) question were as follows: How do lasers compare with CNT as a treatment for peri-implantitis?

Participants

Healthy adult patients with peri-implantitis (titanium implants).

Intervention

Any type of laser system (diode, Nd:YAG, Er:YAG, etc.) applied for peri-implantitis treatment, with no limitations in terms of power or management method.

Comparator

CNT (mechanical debridement, chlorhexidine solution, minocycline hydrochloride, etc.) applied for peri-implantitis treatment with no limitations on drug concentrations or management method.

Outcomes

Quantitative outcomes of laser treatments and CNT on peri-implantitis, i.e., probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI) at the final follow-up.

Studies

Randomized controlled trials (RCTs) only.

Inclusion criteria

Based on the PICOS model, the inclusion criteria were as follows [31]:

i. Clinical studies on systemically healthy adult patients with peri-implantitis (titanium implant)
ii. Peri-implantitis treated by any type of laser (diode, Nd:YAG, Er:YAG, etc.) and CNT
iii. Studies describing quantitative outcomes that assessed the effects of different lasers and CNT on peri-implantitis, in terms of PD, PLI, CAL, and SBI at the final follow-up
iv. RCTs

Exclusion criteria

According to the PICOS model, the exclusion criteria were as follows [31]:

i. Animal and in vitro studies
ii. Studies assessing surgical treatments for peri-implantitis

iii. Studies with qualitative or quantitative outcome measures other than those listed above
iv. Prospective and retrospective cohort studies, case studies, unpublished materials, and review papers

Information sources and literature search

The MEDLINE, EMBASE, Web of Science, CENTRAL (Cochrane Library), CNKI, and China Biology Medicine databases were searched for English and Chinese language studies on the efficacy of different lasers and CNTs for peri-implantitis, from inception to December 10, 2019, using the following MeSH terms: "laser" and "peri-implantitis". The MEDLINE search strategy is detailed in Appendix (S1). ClinicalTrials.gov, the International Clinical Trials Registry Platform, the ProQuest Dissertation Abstracts and Thesis database, and the System for Information on Gray Literature in Europe were also searched for relevant "grey" literature. Furthermore, reference lists of related papers and review articles were searched manually to supplement the electronic search.

Study selection

The RCTs that compared the efficacy of different lasers and CNT for peri-implantitis were reviewed. Two authors screened the study titles and abstracts independently to identify the studies that met the criteria for full-text evaluation. For studies with at least three arms, any arm that was not relevant to our analysis was excluded. A third author was consulted, and agreement reached through discussion, if the two authors disagreed regarding the inclusion of a given study.

Data collection process and data items

The data and information required for this network meta-analysis were extracted from the selected studies independently by the two authors, and included the following: first author of study, publication year, country, follow-up periods, intervention and comparison groups, laser treatment applied, and outcomes. Any disagreements between the two authors were resolved by a third author to achieve a consensus.

Risk of bias of studies and assessment of the quality of the evidence

The Cochrane Collaboration tool's in Review Manager software (version 5.0 for Windows; the Cochrane Collaboration, Oxford, UK) was used to evaluate the quality and risk of bias among the selected RCTs. The risk of study was considered low when all indicators of bias were classified as low risk. If one or more bias indicators were classified as uncertain risk, the risk of study was deemed unclear. All other studies were considered high risk. STATA software (version 14.0; Stata Corp, College Station, TX, USA) was used to analyze the potential publication bias of the included studies [32]. The quality of evidence of the finally selected studies was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. Two authors conducted this process independently, and any difference of opinion was resolved via consultation with a third author.

Summary measures and data synthesis

A random-effects pairwise meta-analysis was performed to synthesize the data of the studies and compare two treatment types (CNT and laser treatments) using the Aggregate Data Drug Information System (ADDIS; Drugis.org). The results are expressed as mean differences (MDs) with 95% confidence intervals (CIs). Heterogeneity across studies was evaluated by the I^2 statistic and a value > 50% was taken to indicate moderate to high heterogeneity [33].

A random-effects network within a Bayesian framework was established by the Markov chain Monte Carlo method in ADDIS [34]. The authors networked the translated binary results and analyzed the relationship among the MDs of the different studies to ensure that the comparisons of laser treatments and CNT were comprehensive. In this manner, both direct and indirect comparisons of different treatments were performed, as detailed in previous reports [27]. A P value < 0.05 was considered statistically significant. The ranking probability of each treatment was also estimated using ADDIS. The MD of each treatment group compared with the control was calculated, and the number of Markov chains required for derivation of the MD-based ranking of the treatments was counted.

Results

Study selection

An electronic search of six databases and manual examination of the reference lists of relevant articles identified 921 and 15 studies, respectively. In total, 268 duplicate studies were excluded; further 629 records were excluded because they were found to not meet the inclusion criteria after filtering the titles and abstracts. The full texts of the remaining 39 articles were reviewed, 28 of which were excluded for not meeting the inclusion criteria. Thus, 11 articles that compared treatment efficacy among different laser methods and CNT for peri-implantitis were ultimately included in the analysis. The study selection process is shown in detail in Fig. 1. Regarding the consistency between the reviewers with respect to title/abstract screening and full-text assessment, the respective

Kappa values were 0.94 and 0.96, corresponding to an "almost prefer" consistency among reviewers [35].

Study characteristics

The basic characteristics of the 11 selected studies are shown in Table 1. All of the included studies were published between 2005 and 2019 and concerned diode, Nd:YAG, and Er:YAG laser treatments and CNT [12, 15, 16, 36–43]. The follow-up time of the studies ranged from 8 weeks to 1 year. A network meta-analysis was performed to compare the different laser systems and CNT for peri-implantitis, in terms of the PD, PLI, CAL, and SBI (Fig. 2). Each node represents one treatment and connections between nodes represent direct comparisons. The size of the nodes and thickness of the connections varied according to the number of studies involved in the comparison.

Risk of bias of studies and quality of evidence

The risk of bias assessment indicated that two studies had a high risk of bias, while the remaining nine studies had an unclear risk (Fig. 3). The most common type of bias pertained to the blinding of participants and study personnel. Figure 4 provides funnel plots of the publication bias. No significant asymmetry was observed in the plots, and there was no obvious publication bias among the included studies. The quality of the evidence with respect to the comparisons of laser treatments and CNT (in terms of the PD, PLI, CAL, and SBI) was poor. Details regarding the quality of the studies are provided in Appendix S2–5.

Results for individual studies and synthesis of results

The results of the pairwise meta-analysis are shown in the Appendix S6–9, and indicate that Er:YAG + CNT

Fig. 1 PRISMA flow program for study selection

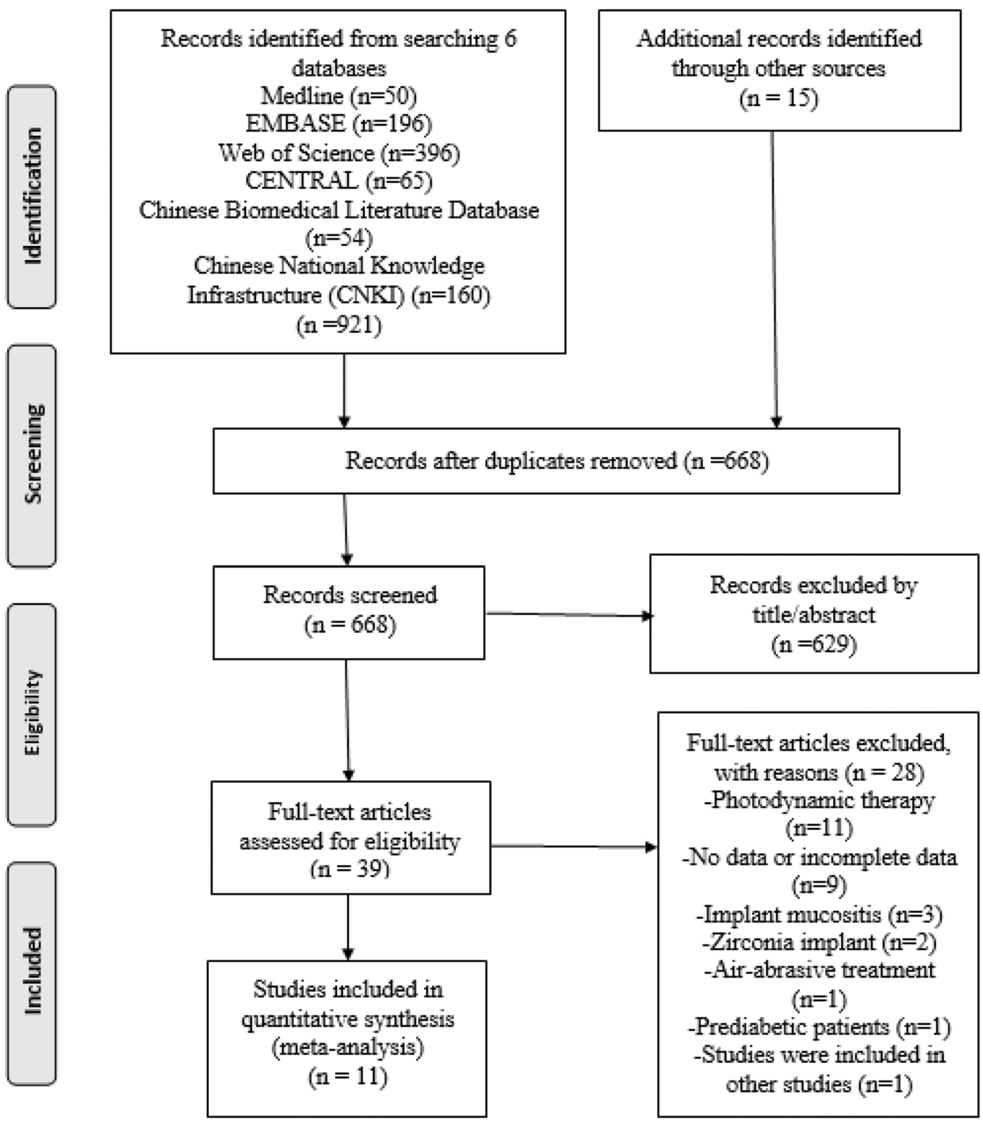

Table 1 Characteristics of studies included in final analysis ($N = 11$)

First author of study	Year	Country	Follow-up times	Intervention group	Comparator group	Number of intervention and comparison	Parameter of lasers	Outcomes
Frank	2005	Germany	0/3/6 months	Er:YAG	CNT	16/16	2.94 um,100 mJ/pulse,10 pps	PD/PLI/CAL
Frank	2006	Germany	0/1 years	Er:YAG	CNT	20/20	2.94 μm,100 mJ/pulse,10 Hz	PD/CAL
Francesco	2015	Italy	0/1 years	Diode+CNT	CNT	101/24	810 nm, 1 W, 50 Hz, 100 ms	PD
Volkan	2015	Turkey	0/1/6 months	Diode	CNT	24/24	810 nm,3 J/cm2, 1 W	PD
Li	2016	China	0/3/6 months	Er:YAG+ CNT	CNT	12/15	2940 nm,160 mJ/pulse,10 Hz	PD/PLI/CAL/SBI
Liu	2016	China	0/8 weeks	Nd:YAG+ CNT	CNT	20/20	1064 nm,0.25~12 W	PD/PLI/SBI
Jiang	2018	China	0/3/6 months	Er:YAG+ CNT	CNT	10/10	2940 nm,160 mJ/pulse,10 Hz	PD/PLI/CAL/SBI
Ren	2018	China	0/2/8 weeks	Diode+CNT	CNT	25/25	808 nm,80 mW,4 J/cm2	PD/PLI/SBI
Wu	2018	China	0/3/6/12 months	Diode+CNT	CNT	19/17	810 nm,5 W,2500 mW	PD/PLI
Shen	2019	China	0/1 weeks/1/3 months	Er:YAG+ CNT	CNT	27/25	SP40 mJ, 20 Hz, 0.8 W	PD/PLI/SBI
Zhou	2019	China	0/3/6 months	Er:YAG+ CNT	CNT	32/30	2.94 um,160 mJ/pulse,10 Hz	PD/PLI/CAL/SBI

CNT conventional nonsurgical treatment, *PD* probing depth, *PLI* plaque index, *CAL* clinical attachment level, *SBI* sulcus bleeding index

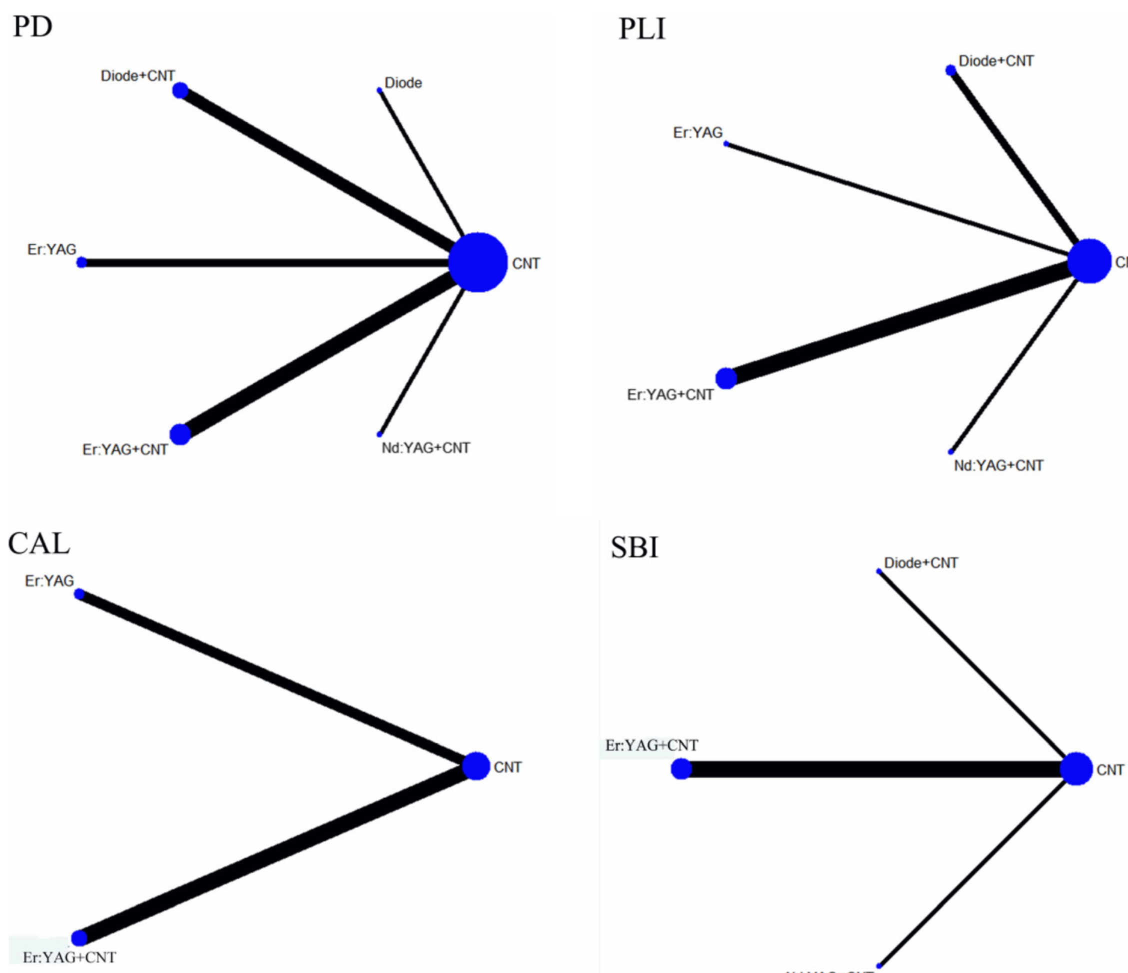

Fig. 2 Network comparing the different lasers and conventional non-surgical treatment (CNT) for the treatment of peri-implantitis in terms of probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI)

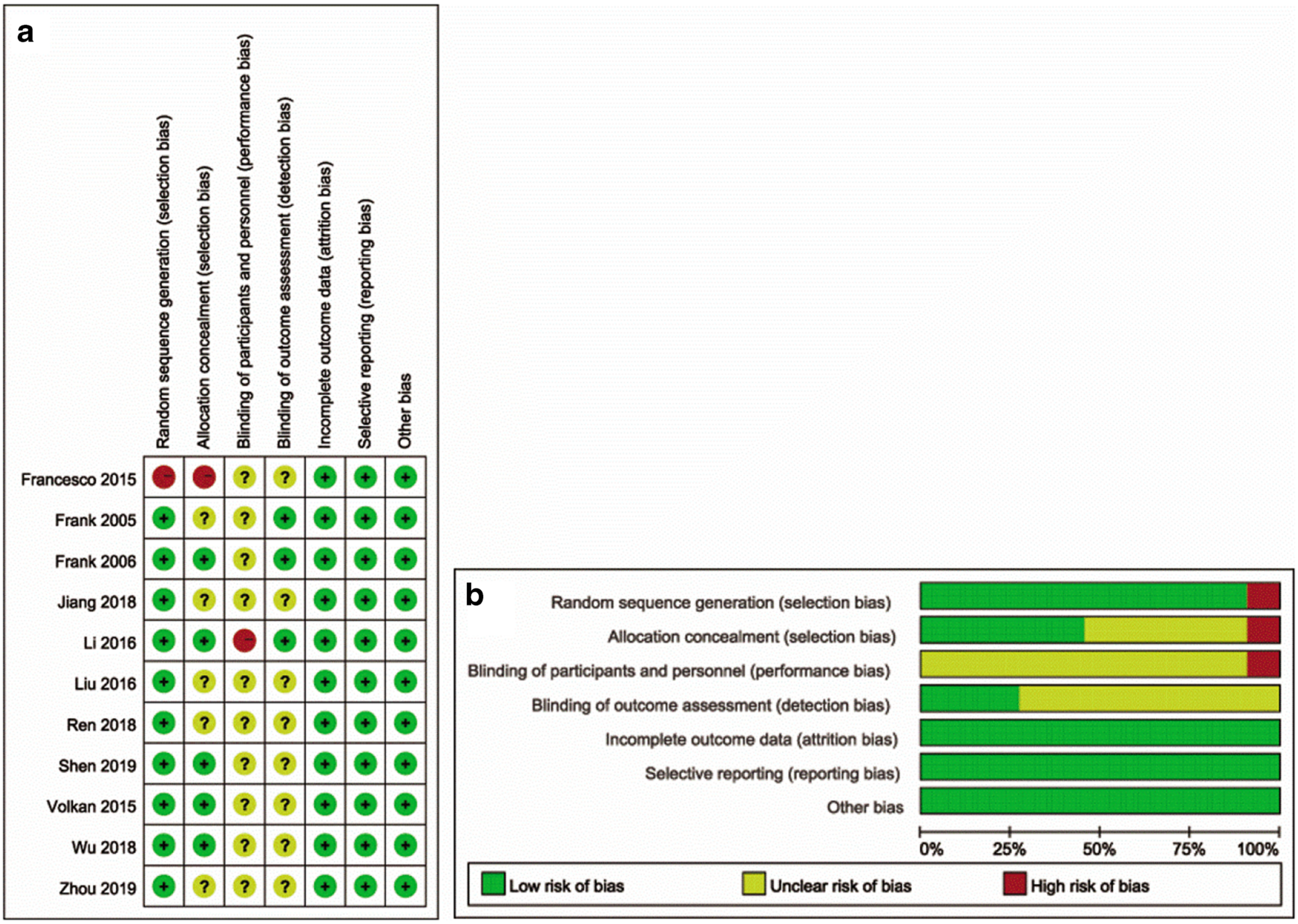

Fig. 3 The risk of bias summary (**a**) and graph (**b**) of all the final included studies

was significantly better than CNT alone in terms of improving the PD, PLI, and SBI ($P < 0.05$). The Nd:YAG + CNT treatment was found to be significantly superior to CNT in terms of reducing the PD ($P < 0.05$), while the diode + CNT treatment was significantly better than CNT alone for improving the SBI ($P < 0.05$). However, there were no significant differences among the various laser system and CNT modalities in terms of the PD, PLI, CAL, or SBI.

The results of our network meta-analysis are summarized in Table 2. The diode + CNT treatment was significantly superior to CNT for reducing the PD ($P < 0.05$), while Er:YAG + CNT was significantly better than CNT in terms of improving the PLI and SBI ($P < 0.05$). However, there were again no significant differences among the various laser system and CNT modalities in terms of the PD, PLI, CAL, and SBI.

Rank probabilities

The treatment efficacy rankings of the different laser treatments and CNT are provided in Fig. 5 and Appendix S10. The rank of each treatment, in terms of the likelihood of efficacy, is shown on a histogram. Lower ranks indicate higher treatment efficacy.

The treatment most likely to be efficacious in terms of reducing the PD was diode + CNT (49%), followed by Er:YAG + CNT, Nd:YAG +CNT, CNT, Er:YAG, and diode. Regarding the PLI, the most efficacious treatment was Er:YAG + CNT (66%), followed by diode + CNT, CNT, Er:YAG, and Nd:YAG + CNT. The treatment most likely to improve the CAL was Er:YAG + CNT (53%), followed by CNT and Er:YAG. Finally, the most efficacious treatment for decreasing SBI was Er:YAG + CNT (79%), followed by diode + CNT, Nd:YAG +CNT, and CNT.

Discussion

The removal of plaque and prevention of recurrence are key for successful peri-implantitis treatment. Dentists should apply multiple treatments for peri-implantitis, with non-surgical treatment being the first step. While many types of lasers are

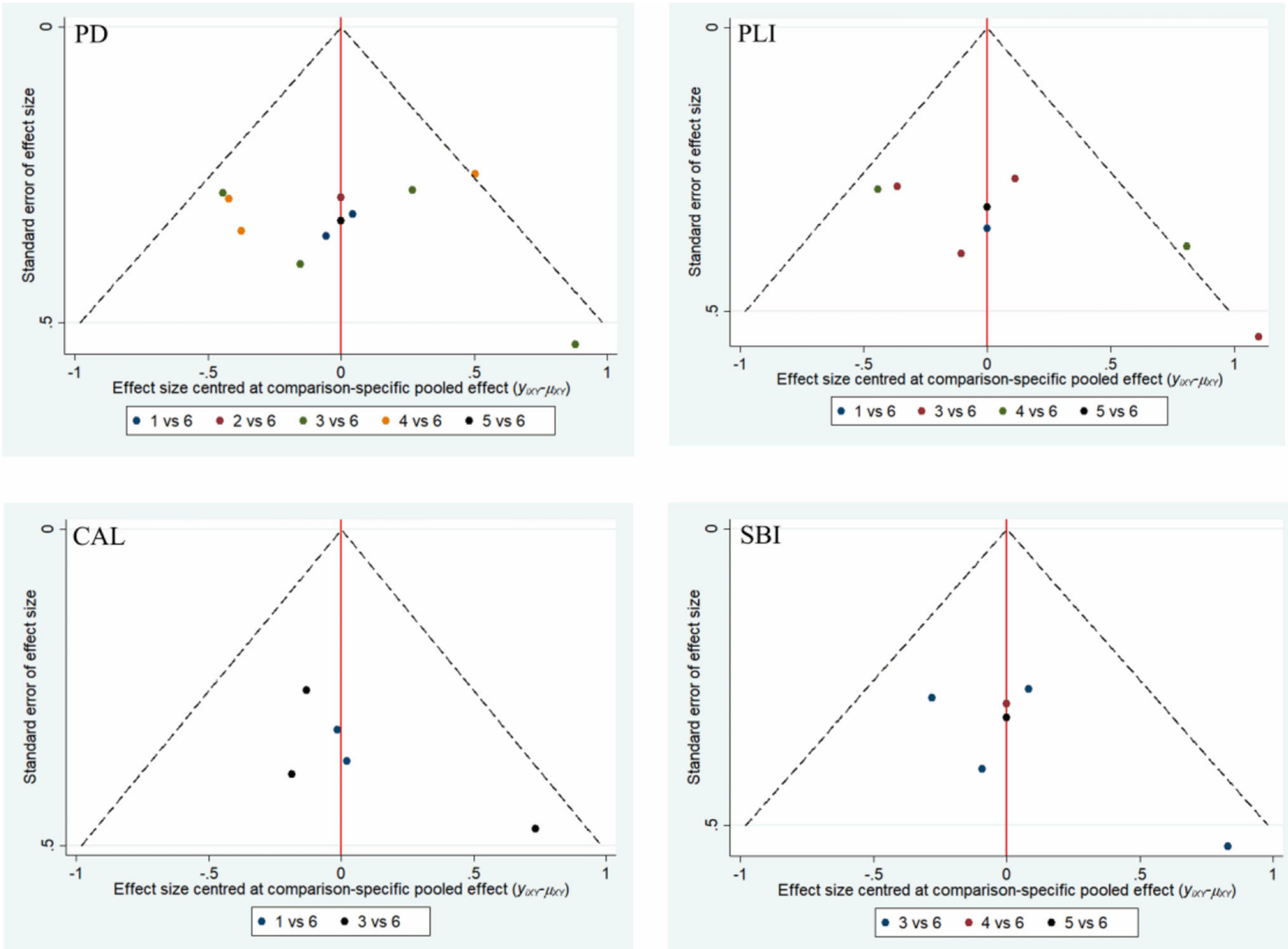

Fig. 4 Comparison-adjusted funnel plots for assessing publication bias and comparing the different lasers and conventional non-surgical treatment (CNT) for the treatment of peri-implantitis in terms of probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI)

used to treat peri-implantitis, their efficacy is not currently clear, and the best laser system for treating peri-implantitis has yet to be determined. Therefore, it is vital to evaluate and compare the efficacy of different laser treatments for peri-implantitis.

The purpose of this meta-analysis was to synthesize direct and indirect evidence to determine the optimal laser treatment for peri-implantitis. It has been argued that indirect comparisons are less biased than direct comparisons and better reflect real-life results [44]. Pairwise meta-analysis is limited to “head-to-head” trials, and is difficult to apply when several different treatments are not compared directly. Thus, indirect comparisons of different treatments via network meta-analysis may be useful for generating data to support clinical decision-making.

Bacteria and their by-products are responsible for peri-implantitis. Controlling and reducing plaque is important for treating and preventing peri-implantitis [45]. In this study, the PD, PLI, CAL, and SBI were the outcomes of interest; all four are key parameters in the diagnosis of peri-implantitis and are well-established indicators of reduced inflammation after peri-implantitis treatment [46].

Our network meta-analysis showed that diode + CNT was significantly superior for reducing the PD in peri-implantitis compared with CNT, consistent with a previous study [47]. It has been reported that laser treatment can promote stable attachment of the junctional epithelium to implants [48]. Lasers can promote the growth of fibroblasts, allowing a dense fibrous envelope to form around the neck of the implant and reducing the PD. However, although diode lasers used at peri-implantitis sites can immediately reduce inflammation, their long-term healing efficacy has not been demonstrated [49, 50]. It is important to note that the penetration of the periodontal probe tip is affected by various factors, such as the probe angle and diameter, implant design at the macro- and micro-level, and the texture of the mucosa around the implant [46]. However, these factors may vary from study to study, which could influence the PD results.

Our network meta-analysis demonstrated that the PLI was improved significantly more by Er:YAG + CNT compared

Table 2 Network comparing the different lasers and conventional non-surgical treatment (CNT) for the treatment of peri-implantitis in terms of probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI)

PD					
CNT	−0.05(−1.46, 1.36)	0.90(0.09, 1.78)	0.13(−1.00, 1.20)	0.61(−0.09, 1.38)	0.56(−0.89, 1.97)
0.05(−1.36, 1.46)	Diode	0.95(−0.70, 2.66)	0.18(−1.68, 1.98)	0.65(−0.91, 2.28)	0.60(−1.42, 2.62)
−0.90(−1.78, -0.09)	−0.95(−2.66, 0.70)	Diode+CNT	−0.77(−2.22, 0.56)	−0.29(−1.41, 0.83)	−0.35(−2.04, 1.27)
−0.13(−1.20, 1.00)	−0.18(−1.98, 1.68)	0.77(−0.56, 2.22)	Er:YAG	0.48(−0.86, 1.86)	0.42(−1.37, 2.23)
−0.61(−1.38, 0.09)	−0.65(−2.28, 0.91)	0.29(−0.83, 1.41)	−0.48(−1.86, 0.86)	Er:YAG+CNT	−0.06(−1.69, 1.55)
−0.56(−1.97, 0.89)	−0.60(−2.62, 1.42)	0.35(−1.27, 2.04)	−0.42(−2.23, 1.37)	0.06(−1.55, 1.69)	Nd:YAG+CNT
PLI					
CNT	0.28(−0.03, 0.61)	0.01(−0.52, 0.52)	0.38(0.12, 0.61)	−0.07(−0.62, 0.45)	
−0.28(−0.61, 0.03)	Diode+CNT	−0.27(−0.89, 0.33)	0.10(−0.33, 0.48)	−0.36(−0.99, 0.24)	
−0.01(−0.52, 0.52)	0.27(−0.33, 0.89)	Er:YAG	0.37(−0.20, 0.95)	−0.08(−0.83, 0.65)	
−0.38(−0.61, −0.12)	−0.10(−0.48, 0.33)	−0.37(−0.95, 0.20)	Er:YAG+CNT	−0.45(−1.03, 0.12)	
0.07((−0.45, 0.62)	0.36(−0.24, 0.99)	0.08(−0.65, 0.83)	0.45(−0.12, 1.03)	Nd:YAG+CNT	
CAL					
CNT	0.07(−0.59, 0.76)	0.16(−0.27, 0.67)			
−0.07(−0.76, 0.59)	Er:YAG	0.08(−0.70, 0.94)			
−0.16(−0.67, 0.27)	−0.08(−0.94, 0.70)	Er:YAG+CNT			
SBI					
CNT	0.33(−0.31, 0.93)	0.59(0.28, 0.93)	0.14(−0.49, 0.78)		
−0.33(−0.93, 0.31)	Diode+CNT	0.26(−0.43, 1.00)	−0.19(−1.05, 0.67)		
−0.59(−0.93, −0.28)	−0.26(−1.00, 0.43)	Er:YAG+CNT	−0.45(−1.16, 0.24)		
−0.14(−0.78, 0.49)	0.19(−0.67, 1.05)	0.45(−0.24, 1.16)	Nd:YAG+CNT		

with CNT. Several studies have shown that the Er:YAG laser has a sterilization effect, removing bacteria from the surface of titanium implants without significantly raising the temperature of the implant or surrounding tissue. This allows Er:YAG laser irradiation to effectively remove plaque and calculus from the surface of the implant [51–53]. Nevertheless, the oral hygiene and dietary habits of patients still play an important role in the control of periodontal bacteria, which must be reinforced during maintenance visits.

The network meta-analysis revealed that Er:YAG + CNT was better than Er:YAG or CNT alone for improving the CAL, but not significantly; this result differed from that of a previous study, which indicated that Er:YAG + CNT was significantly superior to CNT alone [54]. The reason for this difference may due to the small study samples. Elsewhere, laser treatment was shown to improve the CAL due to removal of diseased peri-implant tissue, thereby, promoting healing and regeneration [55].

Our network meta-analysis also showed that Er:YAG + CNT was significantly better than CNT alone for improving the SBI, consistent with previous studies [8, 56, 57]. The efficacy of Er:YAG + CNT may be related to the removal of plaque around and on implant surfaces by the laser. Besides, studies have found that Er:YAG combined with CNT for peri-implantitis, which can obviously improve all kinds of index [58].

CNT serves as the basis for the treatment of peri-implantitis, with lasers currently viewed as an auxiliary treatment. Our systematic review indicated that lasers combined with CNT are better than CNT alone in treating peri-implantitis. Besides, Er:YAG+CNT might be a recommended method to treat peri-implantitis.

To the best of our knowledge, this is the first network meta-analysis to compare the efficacy of different lasers and CNT for peri-implantitis. However, there were some limitations to this study. The number of included studies (and their sample sizes) was small, so some results may have been biased. Also, the included studies were limited to those published in English and Chinese in six literature databases. Furthermore, the follow-up periods of the included studies varied, and we only included titanium implant treatments; zirconia implants were not considered. Finally, the surface properties of implants produced by different manufacturers may influence treatment outcomes, but this was not considered in our study. Further high-quality, well-designed RCTs with larger sample sizes are required to accurately address some of these limitations.

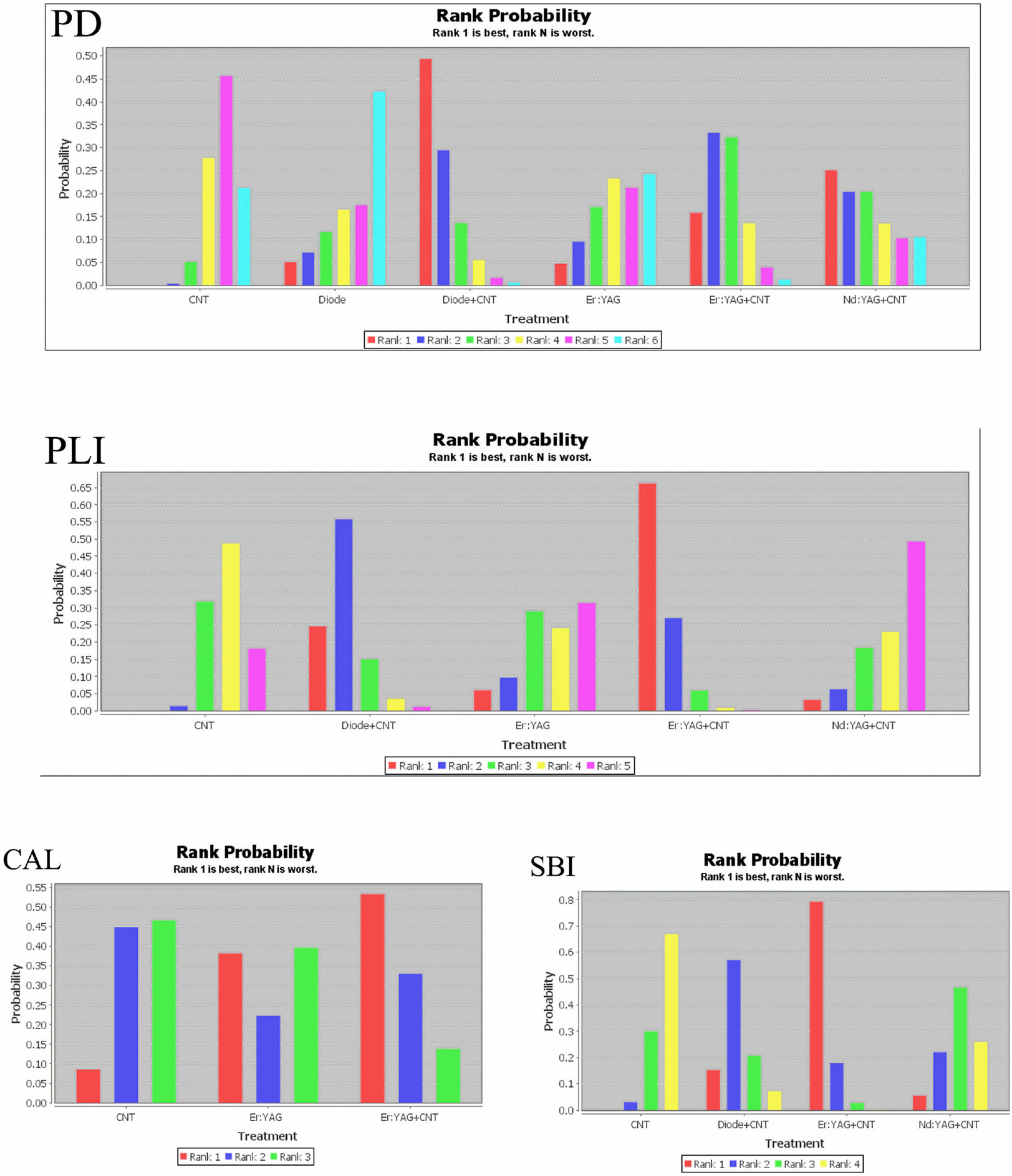

Fig. 5 Ranking probability of each treatment effect on peri-implantitis in terms of probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and sulcus bleeding index (SBI)

Conclusions

We demonstrated an advanced method of evidence synthesis, i.e., combining direct and indirect evidence, to compare several laser systems and CNT for peri-implantitis in a single meta-analysis. Diode + CNT was significantly superior as a peri-implantitis treatment than CNT, in terms of reducing the PD, while Er:YAG + CNT showed significantly better PLI, CAL, and SBI outcomes. Thus, Er:YAG + CNT might be the recommended methods considering the treatment of peri-implantitis.

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Compliance with ethical standards

This was a network meta-analysis which did not require an informed consent.

Conflict of interest The authors declare that they have no conflict of interest.

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