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ORIGINAL ARTICLE

The effects of Er:YAG on the treatment of peri-implantitis: a meta-analysis of randomized controlled trials

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Abstract The clinical effectiveness of the erbium-doped yttrium-aluminum-garnet (Er:YAG) laser in patients with peri-implantitis remains unclear. The aim of this meta-analysis was to investigate the efficacy and safety of Er:YAG laser (ERL) compared to subgingival mechanical debridement (SMD) for the treatment of peri-implantitis. A systematic electronic literature search was conducted to identify randomized clinical trials (RCTs), followed by a manual search. Results were expressed as weighted mean differences (WMDs) with accompanying 95 % confidence intervals (CIs). The primary outcome measurements were changes in clinical attachment level (CAL) and probing depth (PD). Secondary outcome measurements included changes in gingival recession (GR). The meta-analysis was performed with fixed-effect or random-effect model according to the heterogeneity assessed by I^2 test. Visual asymmetry inspection of the funnel plot, Egger's regression test, and the trim-and-fill method were used to investigate publication bias. At 6 months, significant difference in PD reduction (p=0.018) was observed for Er:YAG laser compared to SMD treatment, while no significant differences were detected in CAL gain and GR change; at 12 months, no significant difference was observed for any investigated outcome. The findings of this meta-analysis suggest that use of the Er:YAG laser as alternative to SMD could potentially provide short-time additional benefits, while there is no evidence of long-time superior effectiveness. As all included studies were not at low risk of bias, and only four studies were included in the meta-analysis, future long-term and well-designed RCTs reporting clinical and microbiological outcomes, considering the cost/effectiveness ratio, and having a high methodological quality are needed to clarify the effectiveness of Er:YAG laser.

Keywords Peri-implantitis · Laser · Er:YAG · Meta-analysis

Introduction

Peri-implantitis was defined as an inflammatory process affecting the soft and hard tissues around a functioning osseointegrated implant, resulting in loss of supporting bone [1]. Nowadays, considerable evidence has supported a cause-effect relationship between microbial colonization and pathogenesis of peri-implantitis [2–5]. Hence, it is a prerequisite for the treatment of peri-implantitis to remove bacterial biofilms and calculus from the implant surface [6, 7].

The current principles for the treatment of peri-implantitis were primarily derived from principles established for the treatment of periodontitis [8]. However, recent study showed that using conventional means of treatment, eradication of pathogens by mechanical means on implant surfaces with threads and often with rough surface structures is difficult [9]. Furthermore, the implant rough surface structure may provide the bacteria with "protected areas" inaccessible to conventional mechanical removal [10]. Additionally, some other studies also showed that subgingival mechanical debridement (SMD) did not demonstrate significant clinical improvements or significant microbiologic changes [4, 10–13]. Thus, other effective methods for the treatment of

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peri-implantitis by managing the infection must be established.

Recently, different kinds of lasers have been suggested as alternative or adjunctive treatment to conventional debridement. Various advantageous characteristics, such as easy handling, hemostatic effects, effective calculus ablation, or bactericidal effects against periodontopathic pathogens have been proposed to improve treatment outcomes [14–17]. Data from an in vitro study [18] suggested that, at low-energy densities, the erbium-doped yttrium-aluminum-garnet (Er:YAG) laser had a high bactericidal potential on common implant surfaces without causing morphologic changes of the implant surface or inducing excessive heat. Er:YAG laser treatment can debride the implant surface effectively and safely [19]. Despite the potential benefits, contrasting results have been obtained in clinical trials [20, 21]. A previous review has highlighted the need for further scientific evidence and stated that the long-term clinical effectiveness of the Er:YAG laser remains unclear [22]. Furthermore, important issues related to the safety of the Er:YAG laser and its effects on peri-implant pathogens should be evaluated. None of the previous studies included a meta-analysis. Therefore, there is a need to evaluate the scientific literature on this topic.

The first aim of this study was to determine the efficacy of Er:YAG when used as alternative treatment to conventional debridement in the treatment of patients with peri-implantitis. A secondary aim was to survey the literature in relation to the clinical safety of Er:YAG treatment.

Materials and methods

The present meta-analysis was conducted according to the guidelines of the Cochrane Collaboration [23] and the Preferred Reporting Items for Systematic Reviews and Meta-analysis [24] (PRISMA) guidelines.

Search strategy

PubMed, Cochrane Controlled Clinical Trial Register (CCCTR), and EMBASE databases (from inception to November 2013) were searched to identify randomized clinical trials (RCTs) comparing the use of Er:YAG laser with a control in patients with peri-implantitis. The structured search strategies used the following format of search terms: (Laser* OR Erbium OR erbium yag OR erbium yttrium aluminum garnet OR erbium-yttrium-aluminum-garnet OR er yag) AND (periimplantitis OR peri-implantitis OR peri-implant disease* OR Peri-implant Bacterial Infection OR Peri-implant Bone Loss). The search was limited to human subjects. To be as inclusive as possible, no restrictions were applied with regard to the year of publication of the studies or to language. In addition, the reference lists of identified studies were manually checked to identify other potentially eligible trials. This process was performed iteratively until no additional articles could be identified.

Additionally, several journals were searched manually up to and including November 2013, reported in alphabetical order as follows: Clinical Oral Implants Research, Clinical Oral Investigations, The International Journal of Oral and Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, The International Journal of Periodontics and Restorative Dentistry, The International Journal of Prosthodontics, The Journal of the American Dental Association, Journal of the Canadian Dental Association, Journal of Clinical Periodontology, Journal of Cranio-Maxillofacial Surgery, Journal of Oral and Maxillofacial Surgery, Journal of Periodontology, The Journal of Prosthetic Dentistry, Journal of Prosthodontics, and Oral Surgery.

To minimize the potential for reviewer bias, screening was performed independently by two reviewers (M.-D. Y. and M.-M. L.). The level of agreement between reviewers was determined by the Cohen k test, assuming $k=0.61$ as an acceptable agreement score [25]. Disagreement regarding inclusion or exclusion of the retrieved papers was resolved by discussion. If consensus could not be reached, a third reviewer (M. W.) could be consulted.

The references of all selected full-text articles and related reviews were scanned. If the information of the included studies was not incomplete, we would contact the first author or corresponding author.

Inclusion and exclusion criteria

Studies were considered acceptable for inclusion in the meta-analysis if they met the following criteria:

1. Randomized controlled clinical trials
2. Studies comparing Er:YAG laser with SMD
3. Studies involving human adult subjects (age ≥18 years)
4. Patients with peri-implantitis

The exclusion criteria unanimously agreed upon were as follows:

1. Data not reported as mean±SD
2. History of radiotherapy in the head and neck region of the patients
3. Absent or uncompleted periodontal therapy before dental implant placement
4. Follow-up of <6 months
5. No outcome of interests
6. Insufficient information on laser device and energy settings
7. Duplicate studies

Table 1 Categories of quality assessment of selected studies

Category	Description	Grading
A	Sample size calculation, estimating the minimum number of participants required to detect a significant difference among compared groups	0=did not exist/not mentioned/not clear 1=was reported, but not confirmed 2=reported and confirmed
B	Randomization and allocation concealment methods	0=clearly inadequate 1=possibly adequate 2=clearly adequate
C	Clear definition of inclusion and/or exclusion criteria	0=no 1=yes
D	Completeness of follow-up (specified reasons for withdrawals and dropouts in each study group)	0=no/not mentioned/not clear 1=yes/no withdrawals or dropouts occurred
E	Experimental and control groups comparable at study baseline for important prognostic factors	0=no 1=unclear/possibly not comparable for one or more important prognostic factors 2=clearly adequate
F	Presence of masking	0=no 1=unclear/not complete 2=yes
G	Appropriate statistical analysis	0=no 1=unclear/possibly not the best method applied 2=yes

Data extraction and outcome measurements

Two authors (M.-D. Y. and M.-M. L.) independently extracted the following data: first author, year of publication, number of patients and implants, population, study design, intervention, inclusion criteria, diagnostic criteria, laser characteristics, and follow-up. Extracted data were entered into a standardized Excel file. Any disagreements were resolved by discussion and consensus, and a third reviewer (M. W.) would be included when necessary. The primary outcome measurements were probing depth (PD) reduction (mm) and clinical attachment level (CAL) gain (mm) between the test and control groups. Secondary outcome measurement included changes in gingival recession (GR). Microbiological changes and laboratory findings were evaluated as reported by the authors. Frank Schwarz was contacted to offer the detailed data for variables of his published study [26].

Quality assessment

The methodological quality of each selected study was evaluated independently by two blinded reviewers (M.-D. Y. and M.-M. L.) based on the revised recommendation of the CONSORT statement [27] (Table 1). When there is any disagreement that could not be resolved by discussion, the third reviewer (M. W.) would be consulted to make a decision. After the scores of each trial were calculated, an overall estimate of the plausible risk of bias (low, moderate, or high) was made for each study. The studies stand for low risk of bias if all of the criteria were met, a moderate risk if one or more criteria were partly met, and a high risk of bias if one or more criteria were not met (Cochrane Handbook for Systematic

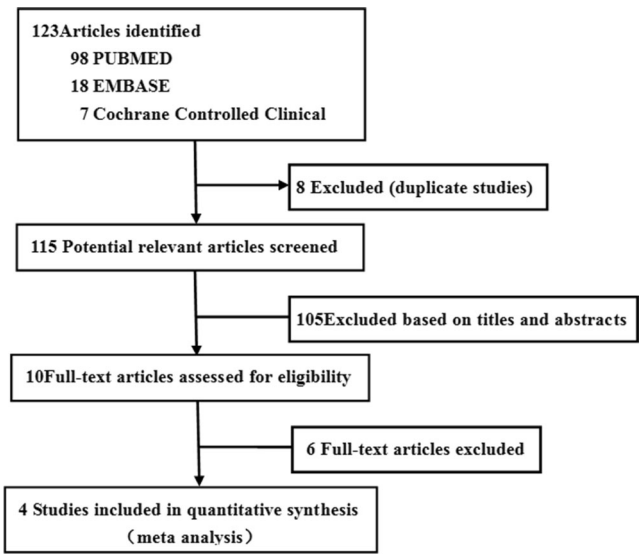

Fig. 1 Flowchart of studies included in meta-analysis. *RCT*, randomized controlled trial

Table 2 The studies excluded in the second phase of selection and the reason for the exclusion of each study

Excluded study (authors/publication year)	Reason for exclusion
Schwarz et al. (2003) [37]	Not a randomized controlled clinical trial
Schwarz et al. (2006) [38]	Not a controlled or comparative study (case series)
Persson et al. (2011) [39]	Comparative group was not mechanical debridement
Renvert et al. (2011) [10]	Comparative group was not mechanical debridement
Kianimanesh et al. (2012) [40]	A case report
Perez et al. (2012) [41]	Not a controlled or comparative study (case series)

Reviews of Interventions, Version 5.1.0, http://www.cochrane-handbook.org/).

Statistical analyses

For both test and control groups, the differences between the pre- and post-intervention means of the outcomes of interest were counted according to the following formulas [28]: $\Delta CAL = CAL2 - CAL1$, where ΔCAL is CAL gain, CAL2 is the mean value of CAL at the end of follow-up, and CAL1 is the mean value of CAL at baseline; $\Delta PD = PD2 - PD1$, where ΔPD is PD reduction, PD2 is the mean value of PD at the end of follow-up, and PD1 is the mean value of PD at baseline. For the secondary outcomes, changes between pre- and post-intervention were counted from $\Delta GR = GR2 - GR1$, where ΔGR is the change in gingival recession, GR1 is the mean value of GR at baseline, and GR2 is the mean value of GR at the end of follow-up.

If the standard deviation of the pre- and post-intervention mean difference was not showed in the study, then it was counted with the following formula: $SD = \sqrt{(SD1^2 + SD2^2 - 2r \times SD1 \times SD2)}$, where SD is the standard deviation of the

Table 3 Characteristics of the included studies

First author (year of publication)	Study design	Population	Inclusion criteria	Intervention	Laser type	ERL parameters	Evaluation intervals
[20]	RCT, PS	30 patients (60.8±10.9 years) 35 implants test: 15 patients, 19 implants control: 15 patients, 16 implants	PD>6 mm and an intrabony component of >3 mm, non-smokers or light smoking status	Test: ERL control: CPS (plastic curets+cotton pellets+sterile saline)	Er: YAG device	Wavelength 2.94 μm, frequency 10 Hz, energy level 100 mJ/pulse	6 months
[21]	RCT, PS	20 patients (laser: 48 years mechanical debridement: 51 years) 32 implants test: 10 patients, 16 implants control: 10 patients, 16 implants	PPD≥4 mm with BOP, no related systemic disease, nonsmoker	Test: ERL control: mechanical debridement	Er:YAG	Wavelength 2.94 μm, 10 pps, energy level 100 mJ/pulse	3, 6 months
[26]	RCT, PS	20 patients (mean age: 56±14 years) 40 implants, 240 sites test: 10 patients, 20 implants versus control: 10 patients, 20 implants (2 patients, 4 implants excluded)	PD>4 mm, signs of acute peri-implantitis, non-smokers	Test: ERL control: mechanical debridement and antiseptic treatment	Er:YAG cone-shaped fiber tip	Wavelength 2.94 μm, frequency 10 Hz, energy level 100 mJ/pulse	3, 6, 12 months
[35]	RCT, PS	24 patients (62.3±10 years) 26 implants test: 10 patients control: 14 patients	PD>6 mm, non-smokers or light smoking status	Test: ERL control: CPS (plastic curets+cotton pellets+sterile saline)	Er:YAG	Wavelength 2.94 μm, frequency 10 Hz, energy level 100 mJ/pulse	12, 24 months

RCT randomized controlled trial, *PS* parallel-designed study, *PD/PPD* probing depth, *BOP* bleeding on probing, *ERL* Er:YAG laser

Table 4 Outcome data of randomized controlled trials included in the meta-analysis of Er:YAG in patient with peri-implantitis

First author (year of publication)	CAL gain	PD reduction	Changes in GR
[20]	ERL 1.5±1.4 versus control 2.2±1.4 (6 months)	ERL 1.7±1.4 versus control 2.4±1.5 (6 months)	ERL 0.2±0.2 versus control 0.2±0.3 (6 months)
[21]	ERL 0.7±0.9 versus control 0.6±1.4526 (6 months)	ERL 0.8±1.1533 versus control 0.7±1.4526 (6 months)	ERL 0.1±0.6 versus control 0.1±0.8 (6 months)
[26]	Moderate ERL 0.52±0.34 versus control 0.23±0.46 (6 months) ERL 0.23±0.1109 versus control 0.05±0.4641 (12 months)	Moderate ERL 0.78±0.21 versus control 0.32±0.41 (6 months) ERL 0.5±0.28 versus control 0.15±0.41 (12 months)	Moderate ERL 0.3±0.28 versus control 0.08±0.17 (6 months) ERL 0.23±0.11 versus control 0.05±0.46 (12 months)
	Advanced ERL 0.37±0.57 versus control 0.33±0.82 (6 months) ERL 0.18±0.58 versus control 0.23±0.81 (12 months)	Advanced ERL 0.68±0.39 versus control 0.48±0.85 (6 months) ERL 0.49±0.40 versus control 0.39±0.85 (12 months)	Advanced ERL 0.33±0.29 versus control 0.16±0.22 (6 months) ERL 0.18±0.58 versus control 0.23±0.81 (12 months)
[35]	ERL 1.3±1.2 versus control 1.5±1.6 (12 months) ERL 1.0±2.2 versus control 1.2±2.2 (24 months)	ERL 1.7±1.2 versus control 2.0±1.6 (12 months) ERL 1.1±2.2 versus control 1.5±2.0 (24 months)	ERL 0.4±0.2 versus control 0.5±0.4 (12 months) ERL 0.1±0.4 versus control 0.3±0.6 (24 months)

difference between the pre- and post-intervention mean values, SD1 is the standard deviation of the mean value at baseline, SD2 is the standard deviation of the mean value at the end of follow-up, and r is the correlation coefficient (assumed to be 0.5). If studies provided the standard errors of the mean (SE), then the SD was calculated based on the sample size (N), with the following formula: $SE=SD/\sqrt{N}$.

Differences were expressed as weighted mean differences (WMDs), and 95 % confidence intervals (CIs) were calculated. I^2 statistic, a quantitative measure of inconsistency across studies, was used to test heterogeneity across studies. Studies with an I^2 statistic of 25–50 % are considered to have low heterogeneity, those with an I^2 statistic of 50–75 % have moderate heterogeneity, and those with an I^2 statistic of >75 % have a high degree of heterogeneity [29]. An I^2 value greater than 50 % indicates significant heterogeneity [30].

A fixed-effect model was used, and a random-effect model was used in the case of significant heterogeneity (I^2>50 %) [31]. In addition, the presence of publication bias was investigated for each outcome of interest using two methods: visual detection was used to analyze the funnel plot [32], while quantitative analysis was performed using the regression asymmetry test [33] and the trim-and-fill method [34].

The pooled effect was judged as statistically significant if p was <0.05. Data were combined for the meta-analysis with STATA version 12.0 (StataCorp, College Station, TX).

Results

Study identification and selection

The flowchart of studies included in the meta-analysis is shown in Fig. 1. An initial database search identified a total of 123 studies. No additional articles were identified through the manual search. Eight articles were excluded because of duplicate studies, and 105 articles were excluded based on the titles and abstracts (inter-reviewer agreement k=0.83). The remaining ten full-text articles were reviewed for more detailed evaluation; six of them were also excluded because they did not fulfill the inclusion and exclusion criteria (k=1), as is shown in Table 2. Finally, a total of four studies [20, 21, 26, 35] fulfilled the required selection criteria of both phases and were included in the present study.

Table 5 CONSORT-based risk of bias analysis

Study	A (0–2)	B (0–2)	C (0–1)	D (0–1)	E (0–2)	F (0–2)	G (0–2)	Estimated risk of bias
[20]	2	1	1	1	2	2	2	Moderate
[21]	0	1	1	1	2	2	2	High
[26]	0	1	1	1	2	2	2	High
[35]	2	1	1	1	2	2	2	Moderate

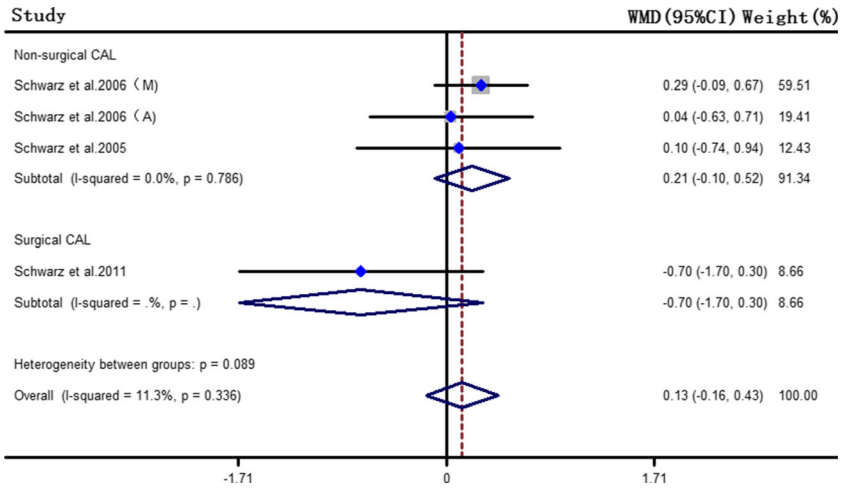

Fig. 2 Forest plot for CAL gain at 6 months for Er:YAG laser vs. SMD

Characteristics of the studies

The main characteristics of the four RCTs included in the meta-analysis are presented in Table 3, and the outcome data of each included trial are described in Table 4. These studies were published between 2005 and 2012. Among the four studies included here, three studies [20, 21, 26] reported CAL gain, PD reduction, and GR changes at 6 months, while two studies [26, 35] reported these outcomes at 12 months. Changes in PI, GI, and BOP were evaluated in all studies. No laser-related side effects or adverse events were reported by the included studies.

Risk of bias in included studies

The risk of bias analysis revealed that two studies were at high risk of bias, while the other two were at moderate risk (Table 5). The most frequently unsatisfied criteria were sample size calculation (criteria A) and the adequacy of the methods used for randomization and allocation concealment (criteria B).

Outcomes

The primary outcomes were the changes in CAL and PD between the test and control groups 6 and 12 months after baseline. The secondary outcomes were the changes in GR at 6 and 12 months. Three studies [20, 21, 26] reported the outcomes above 6 months, and two studies [26, 35] showed the outcomes in the control and test groups at 12 months. Subgroup effects were studied comparing surgical and non-surgical groups, while meta-regression was not attempted given the small number of included studies.

Primary outcome

The mean differences of CAL changes at 6 and 12 months were included in the meta-analysis respectively. At 6 months, a greater gain in CAL for the ERL was found. However, the difference between the two groups was not statistically significant (weighted mean difference 0.13 mm, 95 % CI −0.16 to 0.43, p=0.379; Fig. 2), with

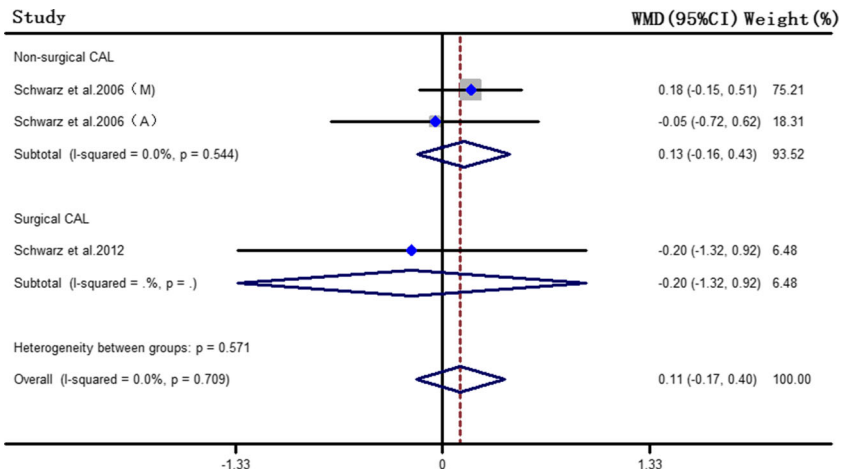

Fig. 3 Forest plot for CAL gain at 12 months for Er:YAG laser vs. SMD

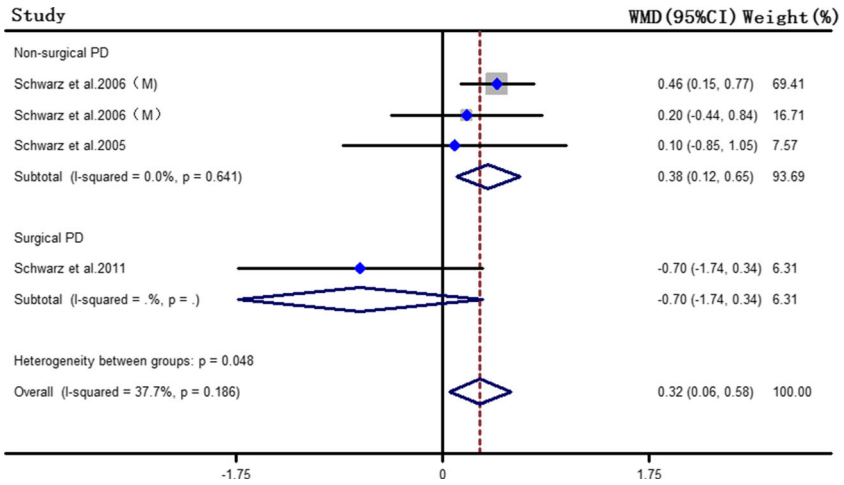

Fig. 4 Forest plot for PD reduction at 6 months for Er:YAG laser vs. SMD

a low heterogeneity between studies (χ^2=3.38, p=0.336, I^2=11.3 %). Similar results were found at 12 months, with a WMD of 0.11 mm (95 % CI range −0.17 to 0.40, p=0.436; Fig. 3) with I^2 for heterogeneity of 0.0 % (p=0.709, χ^2=0.69).

At 6 months, a statistically significantly greater gain in PD for the ERL treatment was found. This amounted to a weighted mean difference of 0.32 mm (95 % CI 0.06 to 0.58, p=0.018; Fig. 4) with low heterogeneity across the studies (χ^2=4.82, p=0.186, I^2=37.7 %). However, no significant difference was observed at 12 months (WMD=0.26, 95 % CI=−0.03 to 0.54, p=0.079; Fig. 5) and no evidence of heterogeneity was detected (χ^2=1.48, p=0.478, I^2=0.0 %).

Secondary outcomes

The changes in GR at 6 months were extracted from three studies [20, 21, 26], while at 12 months, it was extracted from only two studies [26, 35]. No statistically significant difference was detected between groups at 6 months (WMD=0.11, 95 % CI range=−0.01 to 0.22, p=0.069), and no evidence of heterogeneity was found (χ^2=2.86, p=0.413, I^2=0.0 %) (Fig. 6). The result at 12 months was comparable to that at 6 months (WMD=0.10, 95 % CI range −0.09 to 0.29, p=0.290) with I^2=51.8 % (p=0.125, χ^2=4.15) (Fig. 7).

Publication bias

The funnel plots for GR changes (Fig. 8) and other outcomes of interest did not show asymmetry. The regression asymmetry test did not suggest publication bias for the investigated outcomes of interests (Table 6). The trim-and-fill method did not show significant differences between the original estimate and the adjusted effect size for all calculated outcomes of interest at 6 and 12 months. No evidence of publication bias was detected (Table 6,

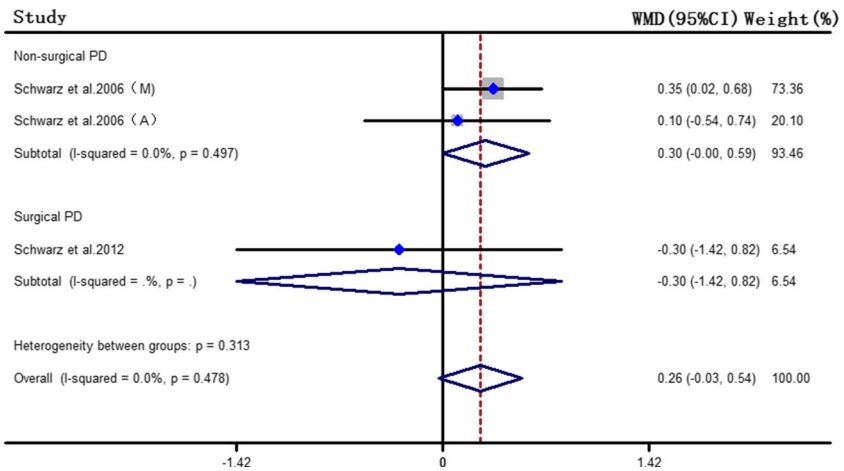

Fig. 5 Forest plot for PD reduction at 12 months for Er:YAG laser vs. SMD

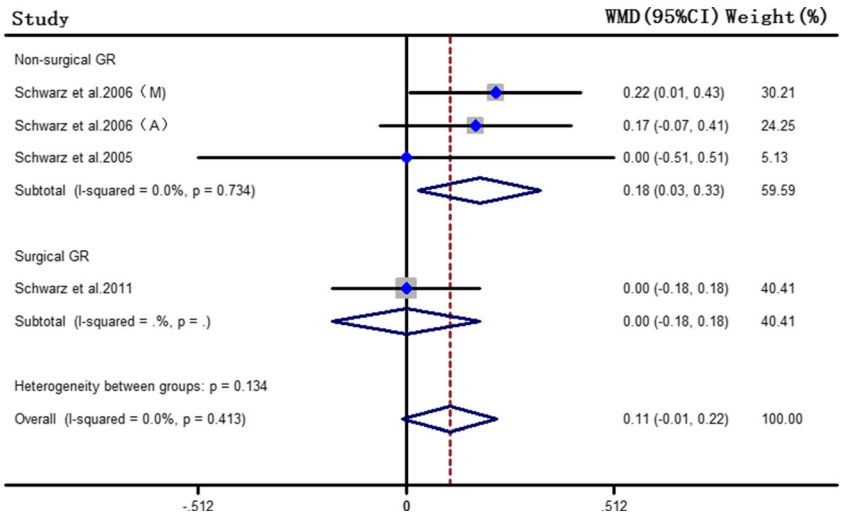

Fig. 6 GR changes at 6 months for Er:YAG laser vs. SMD

Fig. 9), as each outcome had a funnel plot that exhibited no significant asymmetry.

Discussion

Summary of main results

To the best of our knowledge, this is the first meta-analysis to explore the effect of Er:YAG laser versus SMD on clinical outcomes in patient with peri-implantitis. Four RCTs, with a total of 92 patients and 129 implants, were entered in the meta-analysis to investigate CAL gain, PD reduction, and GR changes between the Er:YAG laser and SMD groups.

One study [21] reported significant intragroup improvement in clinical parameters in patients treated with the Er:YAG laser, while another study [26] indicated that the effectiveness of laser seemed to be limited to a period of 6 months, and three studies [20, 21, 26] failed to reveal significant CAL gains. In addition, two studies [21, 26] showed that treatment with laser resulted in a significant higher BOP reduction than mechanical debridement; however, the other two studies [20, 35] did not get the same results.

The results of our meta-analysis suggest that Er:YAG laser provides short-term benefits in terms of PD reduction (at 6 months, WMD=0.32 mm), while no significant difference was observed at 12 months. Additionally, the overall CAL gains and GR changes were slightly higher in the test group but failed to reach statistical significance over the evaluation period.

Results of the meta-analysis revealed that there was no evidence of superior effectiveness of the Er:YAG laser compared to SMD. However, the use of Er:YAG laser has a higher improvement according to the higher value of PD reduction, CAL gain, and GR changes. The lack of significant results could be attributed to the small number of pooled studies. What is more, when analyzing the results of this meta-analysis, several issues that could have potentially influenced the studies' clinical outcomes must be considered; these issues include the difference of inclusion criteria, treatment design which two studies included combined surgical therapy, and

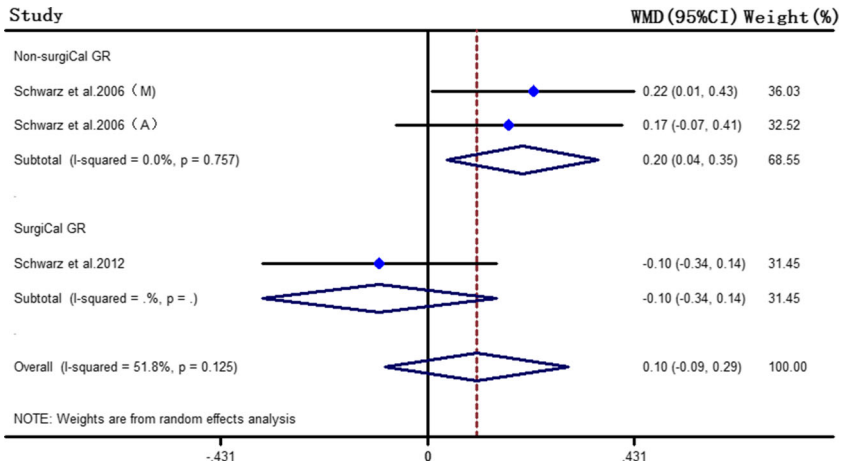

Fig. 7 GR changes at 12 months for Er:YAG laser vs. SMD

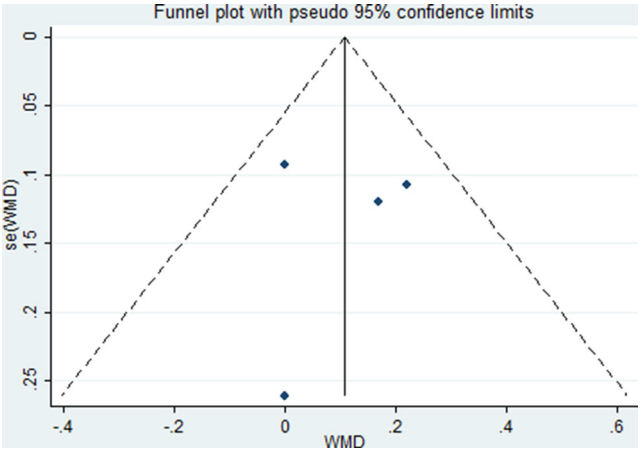

Fig. 8 Funnel plot for GR changes outcome for Er:YAG laser vs. SMD

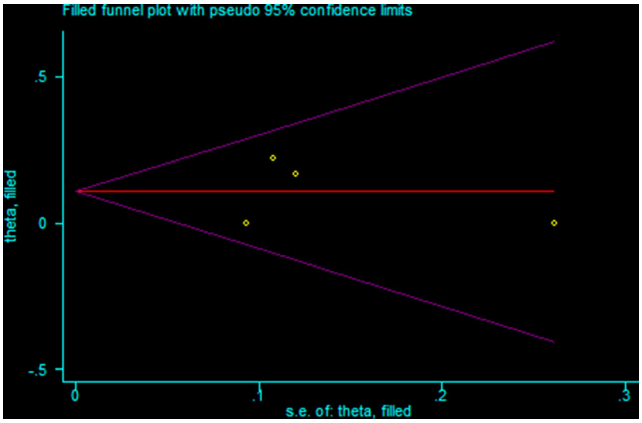

Fig. 9 Funnel plot for GR changes outcome for Er:YAG laser vs. SMD, adjusted with the trim-and-fill method

the variety of surface characteristics of screw-type implants. As it has been verified that the surface characteristic of the implant itself strongly influences reosseointegration after treatment of peri-implantitis defects [36], it must be stressed that different implant types and the variety of surface topographies may influence the generalization of the present results.

Given the limited number of studies included, our findings are consistent with those of a previous review [22] that found insufficient evidence in the literature to support the use of Er:YAG laser. No definitive conclusion could be drawn with regard to the clinical efficacy of Er:YAG in the improvement of clinical parameters. Further RCTs are needed to confirm these findings.

Other treatments have been reported to result in additional improvement in peri-implantitis, such as the use of air-abrasive [42] and photodynamic treatment [43]. However, in terms of safety, Er:YAG laser has no risk of local damage to the adjacent tissue. If used with appropriate energy settings, it does not cause changes to titanium surface and its irradiation does not influence the attachment rate of osteoblasts. In addition, an effective removal of calculus and plaque is even possible on contaminated abutments and of biofilms grown on sand-blasted and acid-etched titanium surfaces [44]. This study confirmed the safety profile of Er:YAG laser as none of the included studies reported any complaints or adverse side effects throughout the entire study period with the employed energy settings.

No cost/effectiveness ratio analysis could be performed, since none of the included studies reported information about this issue. However, since laser represents a more expensive treatment than traditional ones [45], this is an important issue to address. What is more, the ratio is an important matter for both clinicians and patients, as it could influence the need for future treatment sessions. Therefore, cost/effectiveness ratio should be evaluated in future studies.

No meta-analysis of microflora changes could be performed, as none of the included studies monitor the subgingival microfloras. Therefore, it is recommended that future studies address microbiological changes following the application of Er:YAG laser, as well as the possibility of bacterial resistance.

Quality of the evidence

The present evidence-based study included rigorous inclusion/exclusion criteria and used a wide search strategy with no language restrictions. An appropriate meta-analysis was performed that was based on the DerSimonian-Laird random-effect model for data with substantial heterogeneity [30] and publication bias analysis.

Table 6 Quantitative publication bias analysis

Outcome	Original meta-analysis SMD (95 % CI)	*p*	Trim-and-fill analysis SMD (95 % CI)	Studies trimmed/ total studies	Egger regression *p*
PD 6m	0.32 (0.06 to 0.58)	0.018	0.32 (0.06 to 0.58)	0/4	0.11
PD 12m	0.26 (−0.03 to 0.54)	0.079	0.26 (−0.03 to 0.54)	0/3	0.002
CAL 6m	0.13 (−0.16 to 0.43)	0.379	0.13 (−0.16 to 0.43)	0/4	0.14
CAL 12m	0.11 (−0.17 to 0.40)	0.436	0.11 (−0.17 to 0.40)	0/3	0.12
GR 6m	0.11 (−0.01 to 0.22)	0.069	0.07 (−0.16 to 0.32)	0/4	0.99
GR 12m	0.10 (−0.09 to 0.29)	0.29	0.10 (−0.09 to 0.29)	0/3	0.42

Our quality assessment after contacting the authors showed that all included studies exhibited moderate to high risk of bias. Although it is difficult to quantify the influence of the moderate to high risk of bias on study outcomes, such methodological shortcomings must be considered when interpreting the results of this meta-analysis.

Limitations of the meta-analysis

Several limitations should be of concern in this present meta-analysis. The low methodological quality for all four included studies and limited number of studies, as well as the others mentioned above, may prevent us from obtaining unbiased and reliable results.

Implications for research

Future long-term RCTs are needed to clarify the effectiveness of Er:YAG laser compared to SMD. These trials should be well-designed and analyze clinical and microbiological outcomes, consider the cost/effectiveness ratio, and have high methodological quality.

Implications for clinical practice

Given the important methodological shortcomings highlighted in the meta-analysis and the low number of studies included, no clinical recommendations can be suggested.

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Ethical standards All human studies included have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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

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