

Systematic Review

Er:YAG laser versus scaling and root planing as alternative or adjuvant for chronic periodontitis treatment: a systematic review

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Abstract

Aim: To perform a systematic review to evaluate the erbium-doped: yttrium, aluminium and garnet (Er:YAG) laser versus scaling and root planing (SRP) as alternative or adjuvant for chronic periodontitis treatment.

Material and Methods: We performed a literature search using six electronic databases and completed by manual searches up to July 2013. We conducted a meta-analysis as well as heterogeneity, sensitivity, subgroup and power analyses to clarify and validate the pooled results. The 3-, 6- and 12-month clinical outcomes were evaluated.

Results: Twelve eligible randomized clinical trials were finally included. Our meta-analysis showed that Er:YAG laser resulted in similar clinical improvements as SRP 3 months postoperatively. For subgroups by laser level, quality of trials and fluorescence feedback device, the results remained consistent. The 6- and 12-month observations between Er:YAG laser and SRP demonstrated no difference but inconclusive, due to large heterogeneity. The advantage of Er:YAG laser adjuvant to SRP for periodontitis treatment was not significant.

Conclusions: This systematic review indicated that the clinical efficacy of Er:YAG laser was similar to SRP 3 months postoperatively. The clinical benefits of Er:YAG laser as adjuvant to SRP was still lacking. Since Er:YAG laser has certain advantages, it could be expected to be a novel short-term alternative choice for chronic periodontitis.

Key words: chronic periodontitis; Er:YAG laser; meta-analysis; non-surgical periodontal treatment; scaling and root planing

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Conflict of interest and source of funding statement

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Since the introduction of lasers in dentistry, the erbium-doped: yttrium, aluminium and garnet (Er:YAG) laser has gained increasing attention as an adjuvant or alternative treatment method for chronic periodontitis (Aoki et al. 2004, Ishikawa et al. 2009). Compared with conventional methods, debridement with an Er:YAG laser (ERL) holds great promise because of its bactericidal and detoxification effects against peri-

odontal pathogens (Ando et al. 1996, Folwaczny et al. 2003), its removal of endotoxins from diseased root surfaces without major injury to tooth substances (Schwarz et al. 2006, Herrero et al. 2010), and easy access to complicated anatomical sites because of its specific design and light beam radiations (Soo et al. 2012). More recently, a subgingival calculus detection system with fluorescence has been included in an Er:

YAG laser device (Folwaczny et al. 2002a, Krause et al. 2003). Using this system, subgingival calculus may be removed more effectively, and a more predictable root surface is preserved compared with hand instruments (Schwarz et al. 2006).

However, despite these potential advantages, the clinical efficacy of Er:YAG laser as an alternative therapy to scaling and root planing for chronic periodontitis remains a matter of debate. Up to now, two systematic reviews centred on Er:YAG laser therapy for chronic periodontitis are available (Schwarz et al. 2008, Sgolastra et al. 2012). Schwarz et al. (2008) qualitatively analysed the clinical effect and safety of all potential laser applications in non-surgical periodontal therapy, concluding that the Er:YAG laser produced similar clinical outcomes compared with mechanical debridement, both in short- and long-term evaluations. However, evidence from evaluated studies in Schwarz's review was inadequate (Schwarz et al. 2008). With a limited number of studies and high heterogeneity, the authors could not perform a comprehensive meta-analysis. Meanwhile, according to the subsequent consensus report of the sixth European workshop on periodontology, stronger evidence was required to support the clinical recommendation of this novel intervention (Sanz & Teughels 2008). More recently, another systematic review was conducted using updated evidence up to January 2012, with a quantitative meta-analysis (Sgolastra et al. 2012). This review came to the same conclusions as the previous one, indicating no potential difference between Er:YAG laser and scaling and root planing (SRP) in any of the investigated clinical parameters. Nevertheless, this finding should be interpreted with caution, because of the moderate to high heterogeneity observed. Furthermore, because of the limited number of studies, none of the previous systematic reviews included subgroup and sensitivity analysis in their study. These procedures, strictly recommended by PRISMA guidelines (Moher et al. 2009), not only help to detect sources of heterogeneity but rule out the effects of different laser settings parameters or other confounders on the real estimates. On the other

hand, Er:YAG laser debridement has also been reported to serve as an adjuvant therapy for chronic periodontitis: it was able to offer rapid and effective disinfection of the colonized periodontal tissues, even at the low energy (Ando et al. 1996, Folwaczny et al. 2002b). Nevertheless, this evidence was also inconclusive among published randomized clinical trials. To obtain more rigorous evidence, an up-to-date systematic review is warranted.

Thus, we performed a systematic review of all eligible studies published so far. The main aims of this review were: (1) to evaluate clinical outcomes of the Er:YAG laser alternative to SRP for chronic periodontitis in 3-, 6- and 12-month observations; (2) to evaluate whether Er:YAG laser adjuvant to SRP has an additional advantage for chronic periodontitis. The null hypothesis was that there would be no significant difference in clinical outcomes in the effectiveness of the Er:YAG laser compared with SRP as alternative or adjuvant for initial chronic periodontitis therapy.

Material and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al. 2009). To define a patient centred clinical inquiry, we also developed a well-built protocol of population, intervention, comparison and outcomes (PICO) (Richardson et al. 1995) format in this systematic review.

Population or participants: Adult patients with chronic periodontitis who needed non-surgical periodontal treatment.

Intervention: Er:YAG laser debridement alone or combined with SRP treatment

Comparison: Conventional SRP treatment, including scaling with hand curettes and/or ultrasonic scalers

Outcome: Changes in clinical outcomes

Searching strategy

We performed a detailed search for potential eligible publications in the

following biomedical electronic databases:

- PubMed (1969 to July 2013)
- Embase (1980 to July 2013)
- The Cochrane Central Register of Controlled Trials (CENTRAL)
- ISI Web of Science (1950 to July 2013)
- Science Direct (1823 to July 2013)
- Scopus (1960 to July 2013)

All search strategies were carried out with both medical subheadings (MeSH) and free terms, using a combination of the following phrases: ("periodontitis" OR "periodontal diseases") AND ("treatment" OR "therapy" OR "intervention" OR "non-surgical periodontal therapy" OR "scaling" OR "root planing" OR "debridement" OR "SRP") AND ("Er:YAG laser" OR "erbium-doped yttrium aluminum garnet laser"). We conducted a hand search to retrieve the major periodontology and laser journals from 2000 to 2013: *Journal of Clinical Periodontology*, *Journal of Periodontology*, *Periodontology 2000*, *Journal of Periodontal Research*, *International Journal of Periodontics and Restorative Dentistry*, *Lasers in Medical Sciences*, *Lasers in Surgery and Medicine and Photomedicine and Laser Surgery* (2004–2013). Furthermore, we scanned reference lists of all selected full-text publications and review articles to obtain any other pertinent papers. No language restrictions were applied.

Selection criteria

Two reviewers (Zhao Y. and Tao L.) screened the selection process of the studies independently and in duplicate. Any disagreement was resolved by arbitration until a consensus was reached. The eligibility of studies between the reviewers showed good agreement, with a kappa score of 0.9. Studies were eligible for inclusion in this review if they complied with the following predefined criteria: (1) Study design: randomized clinical trials with a parallel-group or split-mouth design; (2) Participants: adult subjects who were ≥ 18 years old diagnosed with chronic periodontitis; (3) Intervention: Er:

YAG laser with and without SRP versus SRP alone; (4) Outcomes: with sufficient clinical data to calculate weighted mean differences (WMDs) and their corresponding 95% confidence intervals (CIs). In addition, we restricted studies to those that provided follow-up for at least 3 months. We excluded studies that exclusively reported supportive periodontal treatment. We also excluded studies that involved participants with systemic diseases, those who were pregnant or those who received antimicrobial treatment within the past 3 months.

Data extraction and outcomes of interest

Two reviewers (Zhao Y. and Tao L.) independently extracted the data from included full-text publications, using standardized Excel 2007 worksheets (Microsoft Corporation, Redmond, WA, USA). Discrepancies were resolved by discussions between the reviewers. The following items were sought from each included publication: author; publication year; region/country where the study was conducted; study design; the interventions and comparisons for participants; period of follow-up; and periodontal outcomes. In addition, we also recorded items as potential sources of heterogeneity that might have confounded the pooled estimates (e.g. the inclusion criteria and samples for each study population; the age, gender distributions; smoking percentage in populations; settings for the Er:YAG laser; and the application of a fluorescence feedback system).

For the clinical periodontal parameters, we extracted those that were extensively investigated in the selected studies, as well as those presented routinely in clinical practice, at both baseline and during the follow-up period. The primary outcome of interest was changes in clinical attachment level (CAL); the secondary outcome variables included probing depth (PD), plaque index (PI) and gingival recession (GR).

Quality assessment

Two review authors (Zhao Y. and Tao L.) independently assessed the quality of each study, and resolved any discrepancies by consensus. The

methodological quality was assessed using a modified questionnaire from Tu et al. (2010) for evaluating randomization methods, allocation concealment, blinding, and intention to treat, as well as sample size and statistical power calculations. Trials with adequate generation of allocation sequence (e.g. computer or random-number table), adequate allocation concealment (e.g. central randomization or sealed envelopes), adequate follow-ups (i.e. the accounts for dropouts and withdrawals in all interventions were described if necessary), and clear blinding were regarded as high-quality and low risk of bias (Kjaergard et al. 2001). Trials with one or more inadequate or unclear components were low-quality and high risk of bias (Kjaergard et al. 2001).

Statistical analysis

Changes in periodontal parameters between baseline and the follow-up period were calculated using the following formulae;

- 1 For clinical outcomes such as probing depth, $\Delta PD = PD_2 - PD_1$, where ΔPD stands for the reduction of probing depth; PD_2 stands for the post-treatment probing depth value, while PD_1 is the pre-treatment probing depth value.
- 2 If the standard deviation (SD) of the pre- and post-intervention mean difference was not reported in the studies, then it was calculated according to the following formula: $SD = \sqrt{(SD_1^2 + SD_2^2 - 2r \times SD_1 \times SD_2)}$; the coefficient r was assumed as 0.5 (Follmann et al. 1992).

The results for continuous data of each intervention were measured by WMDs with their 95% CIs. For the meta-analysis, the statistical significance for pooled WMDs was determined using a Z -test; $p_Z < 0.05$ was considered significant. The Cochrane Q statistic was applied to evaluate the heterogeneity among studies. When a significant Q statistic was achieved ($p < 0.1$) (Lau et al. 1997), a random-effects model was selected to calculate the pooled WMDs (DerSimonian & Laird 1986); otherwise, a fixed-effects

model was applied. In this study, we also introduced another measurement, I^2 , for more quantitatively analysis of the potential heterogeneity. I^2 stands for the proportion of inter-study variability attributed to heterogeneity, which ranges from 0% to 100% (Lau et al. 1997). Moderate and high risk of heterogeneity is detected if I^2 is larger than 50% and 75% respectively (Lau et al. 1997).

In addition, we performed a subgroup analysis to control the potential confounding factors, as possible heterogeneity that may have distorted the results. Sensitivity analysis was conducted by the leave-one-out method to detect the sources of heterogeneity across the studies, both in the overall pooled estimate and within the subgroups (Galbraith 1988). A Galbraith plot was used to identify outliers as the potential major sources of heterogeneity (Galbraith 1988).

In addition, publication bias was evaluated by Begg's funnel plot (Begg & Mazumdar 1994) and Egger's linear regression (Egger et al. 1997). A p value < 0.1 represented the existence of publication bias. The above statistical analyses were undertaken using Stata 11.1 (Stata Corp, College Station, TX, USA) with two-sided p values.

Finally, to detect if the sample size in the pooled analysis was adequate to confer a reliable result, we performed a power analysis for each synthesized estimate using SAS 9.13 (SAS Institute Inc., Cary, NC, USA), with the level of significance (α) set at 0.05.

Results

Search results

Using the search strategy described above, 482 citations were identified by database searching and hand retrieval. By evaluating the titles and abstracts, we excluded all duplicated references, and those related to other topics, review articles, book chapters, index/contents, animal trials, in vitro studies/histological observations and studies for surgical treatment. Twenty-six potentially relevant studies were selected for further full-text evaluations. Fourteen studies were then excluded based on the

selection criteria. Ultimately, 12 RCTs were included in this systematic review (Schwarz et al. 2001, 2003a,b, Sculean et al. 2004, Crespi et al. 2007, Lopes et al. 2010, Rotundo et al. 2010, Feng et al. 2011, Malali et al. 2012, Soo et al. 2012, Yilmaz et al. 2012, 2013) (Fig. 1).

Study characteristics

The main characteristics of the studies are summarized in Table 1. A total of 225 participants were randomized in 12 pooled studies, of which 214 finished the trials. The total dropout rate was assessed at 4.9%. One study (Schwarz et al. 2003b) was the long-term follow-up of another study (Schwarz et al. 2001) and included 20 subjects. As a

result, these subjects were not added to the total sample. Malali et al. (2012) compared two single methods of SRP with ERL; therefore, this study was treated as two separate studies in the pooled analysis. Finally, eight studies were included to compare the therapeutic outcomes of the Er:YAG laser and SRP treatment at 3-month follow-up (Schwarz et al. 2003b, Sculean et al. 2004, Crespi et al. 2007, Lopes et al. 2010, Rotundo et al. 2010, Malali et al. 2012, Soo et al. 2012); four were included to compare the interventions at 6-month follow-up (Schwarz et al. 2001, Sculean et al. 2004, Lopes et al. 2010, Rotundo et al. 2010); while at 12-month follow-up, only three studies were included (Schwarz et al. 2003b, Crespi et al.

2007, Lopes et al. 2010). On the other hand, four studies were selected to compare the periodontal outcomes between Er:YAG laser + SRP and SRP at 3-month follow-up (Lopes et al. 2010, Rotundo et al. 2010, Yilmaz et al. 2012, 2013). The smoking rate varied among selected studies, with five including non-smoking populations. The lasers in seven studies were set at 160 mJ/pulse for energy level and 10 Hz for frequency rate, while the others applied a lower energy level in their designs.

Quality assessment

As shown in Table 2, a certain bias in methodology was detected across studies. Limited to the procedures of intervention, all the studies had blinded allocation restricted to patients. Only two trials (Rotundo et al. 2010, Soo et al. 2012) conformed to the CONSORT statement were of high quality, which reported adequate randomization methods, allocation concealment, follow-ups and clear blinding in their papers.

Er:YAG laser versus SRP as an alternative treatment

At 3 months postoperatively, eight RCTs analysed the potential effects on CAL and PD changes between ERL and SRP treatments (Fig. 2; Table 3). Although certain changes for both treatment modalities were reported in almost all the trials, our meta-analysis showed that Er:YAG laser treatment resulted in similar CAL gains as SRP at the 3-month follow-up point (WMD = 0.135 mm, 95% CI = -0.486-0.756, $p_Z = 0.670$). Similar conclusions were also observed between the two novel therapies with regard to PD reduction (WMD = 0.113 mm, 95% CI = -0.336-0.562, $p_Z = 0.622$), as well as changes of PI ($p_Z = 0.826$, $I^2 = 0.0\%$) and GR ($p_Z = 0.587$, $I^2 = 0.0\%$) (Fig. 2, Table 3). However, a great heterogeneity was found in the synthesized data (i.e. for both CAL and PD, $I^2 = 87\%$); therefore, we conducted a sensitivity analysis to further test the robustness of our results. In addition, a Galbraith plot was performed to identify the outliers of heterogeneity (Fig. S1). The results showed that

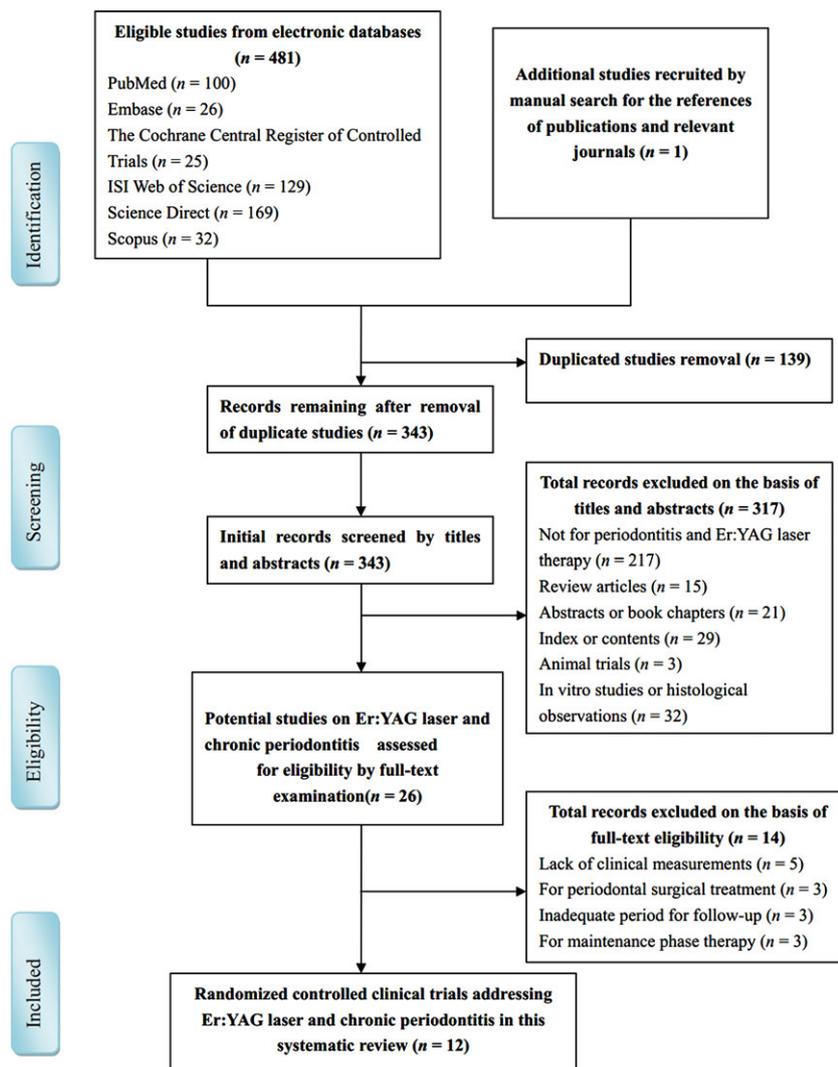


Fig. 1. Flow chart for selecting publications.

Table 1. Characteristics for randomized clinical trials that included in this systematic review

Study, year	Country	Design	Samples	Age	Gender ratio (M/F)	Smoking %	Interventions		Er:YAG laser setting	With LIF	Follow-up	Periodontal outcome evaluated
							Experiment	Control				
Yilmaz et al. (2013)	Turkey	RCT	30	37-67	N.A.	0	1: SRP + ERL 2: SRP + O ₃	SRP	50 mJ/pulse; 20 Hz	No	3 months	PI,SBI,PD,RAL
Malali et al. (2012)	Turkey	RCT	30	48.83 ± 7.23	19/11	N.A.	ERL	1: Hand curettes 2: Ultrasonic scalers	160 mJ/pulse; 10 Hz	No	3 months	PR,RAL
Yilmaz et al. (2012)	Turkey	RCT	27	35-65	13/14	N.A.	1:SRP + ERL; 2: SRP + systemic metronidazole;	SRP	30 mJ/pulse; 10 Hz	No	3 months	PI,GI,PD,RAL
Soo et al. (2012)	New Zealand	RCT, SM	28 (22 finish)	≥30	11/11	45.5	ERL	SRP (Hand + ultrasonic scaling)	160 mJ/pulse; 10 Hz	Yes	1.5, 3 months	PI,PD,BOP, GR,CAL
Feng et al. (2011)	China	RCT, SM	17 (15 finish)	41.7 ± 9.3	11/6	0	ERL	SRP (Hand + ultrasonic scaling)	140-160 mJ/pulse; 10 Hz	No	2, 4 months	PLI,PD,BI,AL
Sculean et al. (2004)	Germany	RCT, SM	20	29-62 Mean: 51	N.A.	N.A.	ERL	SRP (Ultrasonic)	160 mJ/pulse; 10 Hz	Yes	3, 6 months	PI,BOP,PD, GR,CAL
Rotundo et al. (2010)	Italy	RCT, SM	27 (26 finish)	50.5 ± 11.7	N.A.	44.4	1:SRP + ERL; 2: ERL	1: Supragingival prophylaxis; 2: Hand + ultrasonic scaling	150 mJ/pulse; 10 Hz	No	3, 6 months	PD,CAL,BOP, PI,GR,
Lopes et al. (2010)	Brazil	RCT, SM	21 (19 finish)	31-55 Mean: 43	7/14	0	1:SRP + ERL; 2: ERL	1: SRP; 2: No treatment	100 mJ/pulse; 10 Hz	No	1, 3, 6, 12 months	PD,CAL,BOP, PI,GR,GI
Crespi et al. (2007)	Italy	RCT, SM	25	37-65 Mean:53	10/15	N.A.	ERL	SRP (Ultrasonic)	160 mJ/pulse; 10 Hz	No	3, 12, 24 months	PD,CAL,PI,GI
Schwarz et al. (2001)	Germany	RCT, SM	20	28-79 Mean:54	N.A.	0	ERL	SRP (Ultrasonic)	160 mJ/pulse; 10 Hz	No	3, 6 months	PD,CAL,BOP, PI,GR,GI
Schwarz et al. (2003b)	Germany	RCT, SM	20	28-79 Mean:54	6/14	0	ERL	SRP (Ultrasonic)	160 mJ/pulse; 10 Hz	No	12, 24 months	PD,CAL,BOP, PI,GR,GI
Schwarz et al. (2003a)	Germany	RCT, SM	20	28-79 Mean:54	N.A.	N.A.	ERL + SRP	ERL	160 mJ/pulse; 10 Hz	No	3, 6, 12 months	PD,CAL,BOP, PI,GR,GI

RCT, randomized clinical trial; SM, split-mouth design; PD, probing depth; BOP, bleeding on probing; CAL, clinical attachment level; PI, plaque index; GI, gingival index; GR, gingival recession; SBI, sulcus bleeding index; SPT, supportive periodontal treatment, M/F, male versus female ratio; ERL, Er:YAG laser; LIF, laser-induced fluorescence; SRP, subgingival scaling and root planing; N.A., not available.

Table 2. Quality assessment of randomized clinical trials (RCTs) included for meta-analysis

Study	Described as randomized	Randomization methods	Allocation concealment method	Examiner blinding	All patient accounted for at end of study	Analysis accounts for patient losses	Sample size/statistical power calculation
Yilmaz et al. (2013)	Yes/Abstract	Yes/computer-assisted randomization table	Unclear	Yes/adequate	Yes	Not applicable	Not reported
Malali et al. (2012)	Yes/Abstract	Unclear	Unclear	Unclear	Yes	Not applicable	Not reported
Yilmaz et al. (2012)	Yes/Abstract	Yes/computer-assisted randomization table	Unclear	Yes/adequate	Yes	Not applicable	Not reported
Soo et al. (2012)	Yes/Title	Yes/using random sequences by Excel	Yes/adequate concealed in serially numbered opaque envelopes	Yes/adequate	No	Yes/adequate	Yes, statistical power = 90%
Feng et al. (2011)	Yes/Abstract	Unclear	Unclear	Yes/adequate	No	Yes/adequate	Not reported
Sculean et al. (2004)	Yes/Abstract	Unclear	Unclear	Yes/adequate	Maybe yes (Not explicit)	Not applicable	Yes, post hoc power analysis = 75%
Rotundo et al. (2010)	Yes/Title	Yes/computer-generated random permuted block	Yes/adequate concealed in serially numbered opaque envelopes	Yes/adequate	No	Yes/adequate	Yes, statistical power = 80%
Lopes et al. (2010)	Yes/Text	Yes/computer-generated table	Unclear	Yes/adequate	Yes	Not applicable	Yes, statistical power = 95%
Crespi et al. (2007)	Yes/Text	Unclear	Unclear	Yes/adequate	Yes	Not applicable	Yes, statistical power = 99%
Schwarz et al. (2001)	Yes/Abstract	Unclear	Unclear	Yes/adequate	Yes	Not applicable	Yes, statistical power = 99%
Schwarz et al. (2003b)	Yes/Abstract	Unclear	Unclear	Yes/adequate	Yes	Not applicable	Yes, statistical power = 99%
Schwarz et al. (2003a)	Yes/Abstract	Unclear	Unclear	Yes/adequate	Yes	Not applicable	Yes, statistical power = 99%

Note: Since the patient blinding was not reported in all included trials and caregiver blinding was not applicable, we did not list these items in this tables.

Table 3. Meta-analysis for comparison of Er:YAG laser and SRP in the treatment of chronic periodontitis

Follow-up	Periodontal outcomes	Variables	Study number	Stat. model	WMD (mm)	95% Confidence Interval		Z	p_z	$H_{het} \chi^2$	p_{het}	\hat{I}^2 (%)		
						Lower	Upper							
3 months	CAL	Total	8	R	0.135	-0.486	0.756	0.43	0.670	54.38	<0.001	87.1		
		Ex. Crespi et al.	7	F	-0.062	-0.315	0.191	0.48	0.632	5.80	0.447	0.0	0.0	
	PD	With LIF	2	F	-0.117	-0.489	0.254	0.62	0.536	0.34	0.558	0.0	0.0	
		Without LIF	5	F	-0.014	-0.359	0.331	0.08	0.937	5.29	0.259	24.4	24.4	
	6 months	CAL	High-level laser	6	F	0.016	-0.249	0.280	0.12	0.908	1.85	0.869	0.0	0.0
			High quality	2	F	-0.222	-0.782	0.337	0.78	0.436	0.12	0.733	0.0	0.0
		PI	Low quality	5	F	-0.021	-0.304	0.263	0.14	0.886	5.28	0.260	24.3	24.3
			Total	8	R	0.113	-0.336	0.562	0.49	0.622	53.92	<0.001	87.0	87.0
		GR	Ex. Crespi et al.	7	F	-0.024	-0.204	0.155	0.27	0.789	4.63	0.592	0.0	0.0
			With LIF	2	F	-0.133	-0.434	0.168	0.87	0.386	0.23	0.629	0.0	0.0
12 months	CAL	Without LIF	5	F	0.035	-0.188	0.259	0.31	0.756	3.62	0.459	0.0	0.0	
		High-level laser	6	F	0.005	-0.178	0.189	0.06	0.955	2.45	0.784	0.0	0.0	
	PD	High quality	2	F	-0.222	-0.782	0.337	0.93	0.436	0.07	0.733	0.0	0.0	
		Low quality	5	F	0.017	-0.184	0.217	0.17	0.868	3.75	0.440	0.0	0.0	
6 months	CAL	Total	4	F	-0.007	-0.072	0.057	0.22	0.826	1.71	0.634	0.0	0.0	
		Total	5	F	0.021	-0.055	0.097	0.54	0.587	2.82	0.589	0.0	0.0	
	GR	Total	4	R	0.017	-0.606	0.639	0.05	0.958	10.94	0.012	72.6	72.6	
		High level laser	3	R	0.234	-0.430	0.897	0.69	0.490	6.92	0.031	71.1	71.1	
	PD	Total	4	R	-0.049	-0.455	0.356	0.24	0.812	6.96	0.073	56.9	56.9	
		High-level laser	3	F	0.087	-0.155	0.329	0.70	0.482	3.76	0.153	46.8	46.8	
12 months	PD	Total	3	R	0.868	-1.018	2.755	0.90	0.367	55.58	<0.001	96.4	96.4	
		Total	3	R	0.662	-1.033	2.357	0.77	0.444	60.35	<0.001	96.7	96.7	

CAL: clinical attachment level; PD: probing depth; PI: plaque index; GR: gingival recession; LIF: laser-induced fluorescence; Ex.: exclusion; Stat.: Statistics; R: random-effects model; F: fixed-effects model; WMD: weighted mean difference; p_z : p value of heterogeneity chi-squared; p_{het} : p value of heterogeneity chi-squared; $p_z < 0.05$ was regarded as significant; $p_{het} < 0.1$ was regarded as significant.

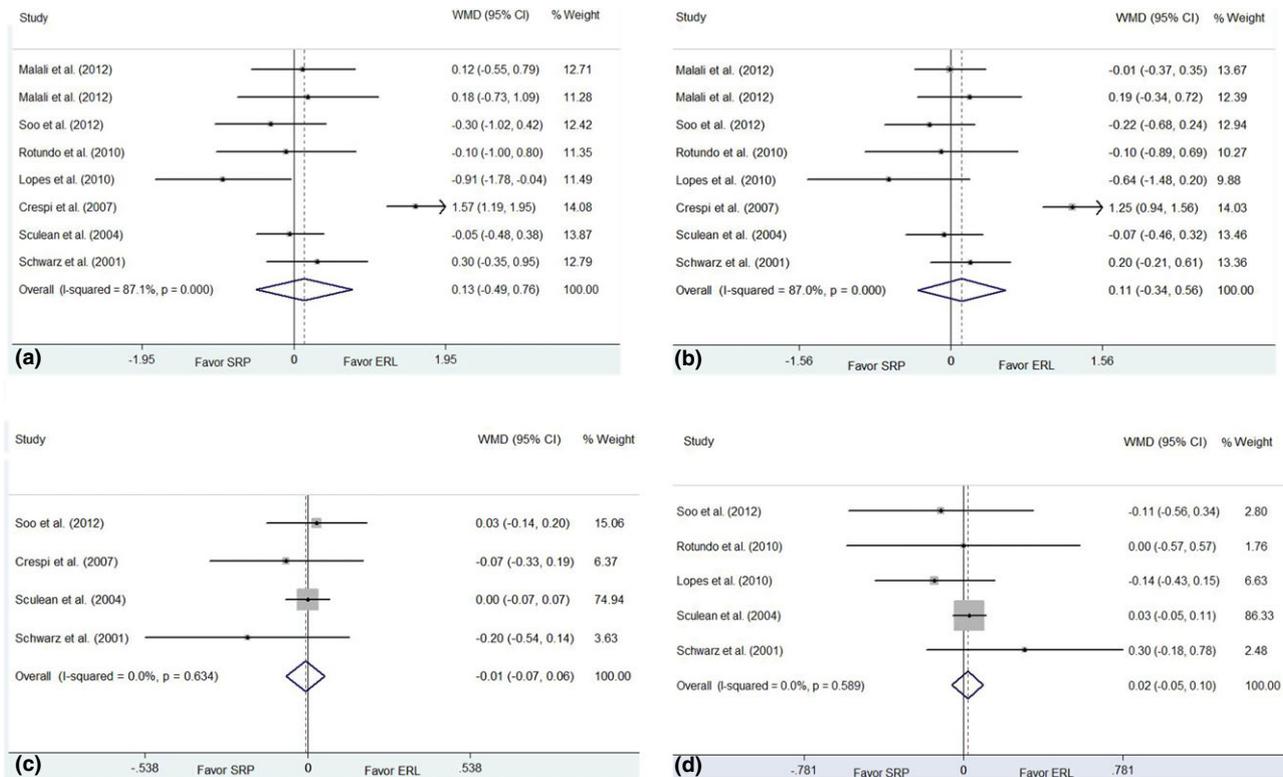


Fig. 2. Forest plots for changes in CAL, PD, PI and GR when Er:YAG laser compared with SRP at 3-month follow-up. (a) forest plot for changes in CAL; (b) forest plot for changes in PD; (c) forest plot for changes in PI; (d) forest plot for changes in GR.

the study by Crespi et al. (2007), with a more positive result favouring ERL, was the main origin of heterogeneity (Fig. S1). By excluding this study, the pooled results remained consistent but lacked heterogeneity (Table 3).

At 6 months postoperatively, significant improvements of PD and CAL were observed in both treatments in four selected RCTs, when compared with baseline scores. However, any differences between ERL and SRP treatments in terms of either changes of CAL ($p_Z = 0.958$) or PD ($p_Z = 0.812$) were not significant, with moderate to high heterogeneity for both measurements (for CAL, $I^2 = 72.6\%$; for PD, $I^2 = 56.9\%$) (Table 3). For the 12-month re-evaluations, only three RCTs reported the clinical outcomes between ERL and SRP treatments. Comparison of the two treatment modalities demonstrated no statistically significant differences in the improvement of CAL ($p_Z = 0.367$, $I^2 = 96.4\%$) and PD ($p_Z = 0.444$, $I^2 = 96.7\%$) (Table 3).

To detect the potential confounding factors that may have influenced

the pooled results, we performed a subgroup analysis by stratification of different laser energies, the groups with or without application of fluorescence feedback system and the quality of trials. No statistical difference was found between ERL and SRP treatments, regardless of switching on/off the feedback system ($p_Z > 0.05$) (Table 3). Only one trial (Lopes et al. 2010) reported lower energy level treatment; therefore, the comparison of pooled results concerning high-level versus low-level lasers could not be performed. The quality of trials did not confound the pooled results. The pooled results of high-quality trials showed similar results as low-quality trials (Table 3).

Er:YAG laser versus SRP as an adjuvant treatment

Four RCTs highlighted short-term evaluations regarding Er:YAG laser adjuvant to SRP in the treatment of chronic periodontitis (Lopes et al. 2010, Rotundo et al. 2010, Yilmaz et al. 2012, 2013) (Fig. S2). The

pooled results revealed that both of the treatments were equally effective in bringing about successful outcomes in CAL gain 3 months postoperatively, with a mean difference 0.082 mm (95% CI = -0.367 – 0.531 , $p_Z = 0.720$). However, comparison of the two treatments indicated a significant reduction in PD within the ERL + SRP group, compared with the SRP group (WMD = 0.337 mm, 95% CI = 0.191 – 0.483 , $p_Z < 0.001$). No heterogeneity across the studies was detected for both outcomes ($I^2 = 0.0\%$ for PD & CAL).

Publication bias

Publication bias was analysed using Begg's funnel plots and Egger's linear regression, which found no evidence of publication bias for Er:YAG laser versus SRP in terms of both PD and CAL changes ($p > 0.05$). The Begg's funnel plots were symmetrical, and the results of Begg's test and Egger's test did not reveal any publication bias ($p > 0.05$ for the PD and CAL).

Discussion

With a 99% statistical power to detect a true difference of 0.5 mm, our systematic review revealed that the Er:YAG laser debridement provided similar clinical outcomes as SRP in terms of improvement of CAL and PD at 3 months postoperatively. The heterogeneity across studies was unbiased after exclusion of the study by Crespi et al. (2007). In addition, we evaluated the changes of PI and GR because they were extensively reported in the selected trials; however, no statistical difference was observed between ERL and SRP treatments. These pooled results were supported by a variety of published trials, although two earlier trials (Schwarz et al. 2001, 2003b) and a recent one (Crespi et al. 2007) came to different conclusions. We agree with the previous point of view that these controversies concerning divergent results could be mainly attributed to the different standards of selection criteria, the design methodology, the settings for the lasers and certain other factors that may have confounded the results across these studies (Sgolastra et al. 2012). Despite these robust results, evidence from the current systematic review concerning clinical outcome evaluations at 6 months and 12 months postoperatively remain inadequate, because of the limited number of studies and large heterogeneity. A random-effects model was adopted to pool the data, showing no difference between the two treatments; however, this result should be interpreted with caution.

In addition, we performed a subgroup analysis to rule out factors that may potentially confound the synthesized results. Recently, an InGaAsP 655-nm diode laser beam has been coupled with Er:YAG laser to detect calculus (Folwaczny et al. 2002a, Krause et al. 2003). Histological and *in vivo* results showed that fluorescence-controlled Er:YAG laser radiation enables a more effective removal of subgingival calculus and preserves a predictable root surface compared with hand instruments (Schwarz et al. 2006, Herrero et al. 2010). Furthermore, in Beagle dog models, periodontal regeneration was more pronounced in the group

that received laser treatment compared with ultrasonic debridement (Schwarz et al. 2007). As a result, clinical trials with or without the application of a fluorescence feedback system were expected to be different in terms of improvements in clinical outcomes. However, in the subgroups of our meta-analysis, we did not find a positive association between clinical outcomes and the application of a fluorescence feedback system. Only two RCTs (Sculean et al. 2004, Soo et al. 2012) were included to evaluate clinical outcomes with Er:YAG laser using a fluorescence feedback system; therefore, this result should be verified with further well-designed RCTs with larger samples.

Our systematic review also provided important insights into the application of Er:YAG laser as an adjuvant therapy for chronic periodontitis. The pooled results from our primary outcome indicated that Er:YAG laser in combination of SRP led to significant gain in CAL, similar to SRP. This finding, which was not highlighted in the previous systematic review (Sgolastra et al. 2012), was in accordance with those obtained by several investigators (Dominguez et al. 2010, Lopes et al. 2010, Rotundo et al. 2010). For instance, Dominguez et al. (2010) found that both groups of ERL + SRP and SRP treatment resulted in significant difference improvement for PI, PD and bleeding on probing between baseline and 4 and 8 weeks postoperatively, but there is no statistical difference between the groups. Similarly, Rotundo et al. (2010) reported that an Er:YAG laser did not show an adjunctive benefit in clinical evaluations. Lopes et al. (2010) observed a significant CAL gain in ERL + SRP, ERL, and SRP groups at 3 months postoperatively ($p < 0.05$); however, they reported no significant differences among these groups. Based on the results above, we assume that as a non-surgical periodontal treatment, the Er:YAG laser alone was effective in providing a prospective clinical outcome. Additional scaling and root planing on the laser-treated sites was unnecessary following laser therapy. In contrast to a recent systematic review (Karlsson et al. 2008), which presented weak evi-

dence to support the efficacy of laser treatment as an adjunct to conventional SRP therapy, no substantial evidence of additional benefit was found by this systematic review.

The current systematic review evaluated the potential effectiveness of the Er:YAG laser in the treatment of chronic periodontitis by means of clinical outcomes. Unlike previous systematic reviews, our results were robust in providing a strong evidence to indicate that Er:YAG laser was as effective as SRP treatment in dealing with chronic periodontitis during short-term follow-up. Nevertheless, evidence of clinical outcomes from long-term observations remains insufficient. In addition, this systematic review has some limitations that should be considered: first, the potential heterogeneity and confounding factors (e.g. the varied inclusion and exclusion criteria, age, gender distributions, smoking percentage and settings for ERL among studies) may have distorted the analysis. Second, with limited data, an interaction of Er:YAG laser with SRP could not be considered in the current review. Third, Er:YAG laser treatment is relatively expensive (Chanthaboury and Irinakakis 2005). As the high financial cost of a laser apparatus is a significant barrier for laser application in clinical practice, an economic analysis to validate its clinical value would be useful. However, such data were not contained in this paper because of a lack of original data in published studies.

In conclusion, our systematic review provided compelling evidence that there was no difference in clinical outcomes between Er:YAG laser and SRP for chronic periodontitis in the 3-month follow-up. Evidence concerning clinical outcome evaluations at 6 and 12 months postoperatively remained insufficient. Furthermore, clinical benefits of Er:YAG laser as adjuvant to SRP were still lacking. Since Er:YAG laser has certain benefits compared with SRP, we conjecture that it could be expected to be a novel short-term alternative choice for chronic periodontitis.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Galbraith plots of Er:YAG laser versus SRP in the treatment of chronic periodontitis at 3-month follow-up. A. The studies by Crespi et al. (2007) and Lopes et al. (2010) were the outliers of Er:YAG laser versus SRP in the treatment of chronic periodontitis in terms of changes of CAL; B. The study by Crespi et al. (2007) was the outliers of Er:YAG laser versus SRP in the treatment of chronic periodontitis in terms of changes of PD.

Figure S2. Forest plots for changes in CAL and PD when Er:YAG laser + SRP compared with SRP at 3-month follow-up. A. forest plot for changes in CAL; B. forest plot for changes in PD.

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Clinical Relevance

Scientific rationale for the study: Current evidence addressing Er:YAG laser adjuvant to or alternative to scaling and root planing for chronic periodontitis remained inadequate; therefore, we performed a systematic review with all eligible randomized clinical trials published so far on this topic.

Principal findings: Compelling evidence had been reached to support that as an alternative choice for chronic periodontitis, Er:YAG laser was capable of providing significant improvements of clinical outcomes in the short-term follow-up as conventional SRP therapy. However, evidence from long-term clinical assessment remained questionable.

The advantage of Er:YAG laser adjuvant to SRP in the treatment for periodontitis was insufficient.

Practical implications: The Er:YAG laser monotherapy could provide short-term improvement in clinical outcomes as SRP for chronic periodontitis.