Effects of Non-surgical Periodontal Therapy on Periodontal Clinical Data in Periodontitis Patients With Rheumatoid Arthritis: a Meta-analysis

Yu Huang
Hospital of Stomatology, Jilin University
Zheng Zhang
Tianjin Stomatological Hospital,School of Medicine, Nankai University
Youli Zheng
Hospital of Stomatology,Tianjin Medical University
Zhulan Zhao
Hospital of Stomatology, Jilin University
Yang Zhong
Hospital of Stomatology, Jilin University
Qingyu Zhang
Hospital of Stomatology, Jilin University
Degeng Xia
Hospital of stomatology, Jilin University
Ning Ma (man@jlu.edu.cn)
Hospital of stomalogy, Jilin University
Li Zhang
Hospital of stomalogy, Jilin University

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Abstract

Backgrounds: To date, there is still no consensus about the clinical efficacy of non-surgical periodontal therapy in rheumatoid arthritis (RA) patients with periodontitis. Therefore, the overall aim of this study was to summarize available data regarding the clinical efficacy of scaling and root planing (SRP) in patients with RA and periodontitis compared to patients with periodontitis alone.

Methods: A meta-analysis of existing randomized controlled clinical trials (RCTs) was conducted. The eligible RCTs were selected through Embase, PubMed and Cochrane Central Register of Controlled Trials and manual retrieval from the earliest records to March 15, 2020 to extract data. The overall effect size of plaque index (PI), gingival index (GI), attachment loss (AL), probing depth (PD) and bleeding on probing (BOP) were calculated by either a fixed or random-effect model, and subgroup analyses were conducted according to the different time points of follow-up. Cochrane Collaboration's tool was responsible for the evaluation of the literature quality and the inter-study heterogeneity was evaluated by Q test and I^2 statistic. The authors applied sensitivity analysis for results with heterogeneity. Publication bias was determined by Begg's test, Egger's test and the trim-and-fill method.

Results: Eight RCTs eventually met the inclusion criteria for the study. The overall outcomes concerned PI, GI, PD, Al and BOP were 0.42(95% CI 0.02, 0.81), 0.03(95% CI -0.03, 0.10),-0.06mm (95% CI -0.18, 0.06), 0.16mm (95% CI-0.03, 0.36) and 4.15(95% CI -0.26, 8.55), respectively. In subgroup analysis, a larger BOP reduction at 3 months, PI and AL reduction at 6 months were observed in patients with RA and periodontitis group. The results of sensitivity analyses had no significant effect. No evidence of potential publication bias was tested.

Conclusions: The authors conclude that SRP is equally effective in patients with periodontitis and RA than in periodontitis ones. This result suggests RA does not affect the clinical efficacy of non-surgical periodontal therapy.

Background

Periodontitis is a chronic inflammation of the periodontal tissues, with negative impact on both local and systemic health. It is well known that the inflammatory state gives rise to a multitude of damage of periodontal tissue, of which the most critical are in alveolar bone, as well as in periodontal ligament [1, 2]. In a comprehensive epidemiological report in 1990 and 2010 of severe periodontitis (SP), a global age-standardized rate of severe periodontitis was reported to be high around 11.2% [3]. It suggested a growing global health threat from severe periodontitis. In addition, many modifiable and non-modifiable risk factors, such as rheumatoid arthritis (RA), diabetes, obesity, high blood pressure, atherosclerosis and other cardiovascular diseases and so on, can modify the individual's risk of developing periodontitis, as well as the response to periodontal therapy [4-8].

RA is a chronic autoimmune disorder and can ultimately lead to the irreversible damage to cartilage in joints and loss of function even, which is closely related to the production of autoantibodies, synovial

inflammation and hyperplasia [9, 10]. The interplay between RA and periodontitis has long been studied, with evidence showing complex associations between these two distinct diseases [11, 12]. The pathogenesis of the two diseases are characterized by local destruction of hard and soft tissues as a consequence of inflammation [13, 14]. Additionally, there is strong evidence that people with RA have elevated risk for inflammation of periodontal ligament, respiratory mucosa and intestinal mucosa to some extent[15]. Studies among people with RA demonstrate significantly higher prevalence levels in patients with periodontitis [16-18]. To date, the mechanisms accounting for the aggravation of periodontitis by RA are not completely clarified.

The representative of non-surgical periodontal therapy as scaling and root planing (SRP) has been considered as the traditional treatment regime in managing periodontitis. Conventional clinical indices and parameters of periodontal health, namely plaque index (PI), gingival index (GI), attachment loss (AL), probing depth (PD) combined with bleeding on probing (BOP), are usually calculated to determine the efficacy of SRP. In recent years, there have been several works discussing effects of periodontal treatment on RA markers [19-21]. Additionally, in a recent meta-analysis, the bidirectional relationship between periodontitis and RA was also analyzed [22]. However, to our knowledge, a comprehensive meta-analysis attempted to establish the clinical efficacy of SRP in periodontitis patients with RA has not yet emerged. In light of these considerations, meta-analysis is now imperative to assess the difference in the clinical efficacy of SRP between patients with periodontitis and RA and those with periodontitis alone.

Methods

Search strategy

In this meta-analysis, we followed the guidelines in accordance with the 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analysis –PRISMA statement [23]. Online Embase, PubMed and Cochrane Central Register of Controlled Trials from the earliest records to December, 2020 were systematically screened for the desired publications. The search keywords included (Rheumatoid arthritis OR RA) AND (periodontitis OR periodontal disease) AND (treatment OR therapy). Additionally, reference lists of related studies and some journals were manually searched for completeness. We didn't place any restrictions on the language of publications when searching these online databases and the unpublished works were not accounted.

Eligibility criteria

The following study designs were included: (1) Type of study design must be randomized controlled trial (RCT); (2) Articles that evaluated the clinical efficacy of SRP in RA patients with periodontitis; (3) SRP was the only treatment; (4) Changes at least in one of the five clinical periodontal indices/parameters (PI, GI, AL, PD and BOP) were recorded in the study.

The excluded criteria for our study were: (1) The study design was not RCT; (2) Potential participants who had any other disease or combined with systemic antibiotic therapy; (3) Studies lacked of control group;

(4) Studies did not record any one of the five periodontal indices/parameters; (5) Articles where the full text and date was not available.

Data extraction

Two investigators (Z Zhang and Y Huang) screened the titles, abstracts, and full articles independently according to eligibility criteria for study selection. The data extracted from each article including the following data: periodontal indices/parameters included in the results, first author, year of publication, location, sample size, gender and age, duration of RA, and time point of follow-up. A third researcher addressed all remaining discrepancies after consultation between the two investigators.

Quality assessment

The quality of the RCTs was assessed in accordance with the Cochrane Collaboration's tool, including the following aspects of evaluations: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete of the outcome data; 6.selective reporting and the other bias (i.e. non-objective therapy and completeness of follow up) [24]. Following the Cochrane Collaboration guidelines, each RCT was classified as being at low, unclear or high risk of bias.

Statistical analysis

The differences (experimental minus control) of the changes (final values minus baseline values) were employed to calculate the net changes between the two groups. The pooled effect was expressed as mean difference (MD) with their associated 95% confidence intervals (CIs). It was defined as statistically significant if p-value was less than 0.05. The Cochran's Q test and I^2 statistic were employed to calculate heterogeneity among the included studies. $P < 0.05$ (Q test) or $I^2 > 50\%$ represented a substantial high level of heterogeneity, in which case the random-effect model was performed [25, 26], while the fixed-effect model was used when $P > 0.05$ and $I^2 < 50\%$ [27]. Sensitivity analysis was conducted to explore, quantify, and control for sources of heterogeneity and stability of results across studies by excluding eligible studies by sequence. Begg's test [28], Egger's test [29] and the trim-and-fill method [30] were employed to identify the statistical significance of publication bias. All above statistical analyses were conducted by Stata (version 12.0, Stata Corp, College Station, TX, USA).

Results

Literature selection

At the beginning, a total of 1,151 records were identified from the electronic and manual search, including 509 in PubMed database, 593 in Embase database, 41 in Cochrane Central Register of Controlled Trials and 8 of manual search. After removal of the duplicates, 1048 publications remained for independent screening, of which 1001 were deemed irrelevant on the basis of their title and abstract and 47

publications were eligible for full-text evaluation. Of these articles, 39 were excluded, mostly because of being meta-analysis, case report, review studies (n=9), without full text (n=9), the combination of systemic antibiotic therapy (n=2), being overlapping study (n=1), without available date (n=2) and the lack of control group (n=16). Finally, 8 RCTs met the eligibility criteria in this meta-analysis. (Supplementary figure S1)

Characteristics of the included studies

As shown in Table 1, main characteristics of the included trials are presented. They were published between 2009 and 2019. There was little variation in the number of participants enrolled in the 8 RCTs (24–36), reaching a total of 247 with mean age ranging between 41.4 and 51.6 years. The studies were carried out in the following countries: Brazil (n=2), Turkey (n=4), China (n=1) and Germany (n=1). The percentages of female participants in the studies were summarized, which ranged between 40.0% and 100%. All studies reported the percentage of female participants, Five of these studies reported a duration of RA from 6 weeks to 14.9 years and three did not provide the duration information. Length of follow-up period varied amongst the 8 included studies, ranging from 1 to 6 months duration. Seven of the studies included outcomes of PI, PD and BOP, four of AL and three of GI.

Risk of bias within studies

The quality of evidence for each outcome was based on six domains: Selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. Results were presented graphically by study (Fig. 1A) and proportion chart of bias was set across all studies (Fig. 1B). It is noteworthy that only one of the studies was judged to be at high risk of selection bias, which was observed in Roman-torres 2015. Three studies had an unclear risk of bias in blinding of participants and personnel, 4 studies had an unclear risk of bias in blinding of outcome assessment, and 6 studies had an unclear risk of bias in selective reporting. In addition, with regard to allocation concealment, all studies showed unclear risk.

Meta-analysis of clinical indices

The overall effect size showed that the PI value in periodontitis patients with RA changed more significantly compared with periodontitis control patients (MD: 0.42; 95% CI: 0.02, 0.81) (Fig. 2A). Substantial heterogeneity was observed for PI (I^2=50.8%, P =0.06). No statistically significant difference was showed between the two groups for the GI (MD: 0.03; 95% CI: -0.03, 0.10) (Fig. 2B). No evidence of heterogeneity was detected for GI (I^2=20.8%, P =0.29).

Meta-analysis of clinical parameters

Compared with periodontitis control patients, the changes of the PD (MD: -0.06; 95% CI: -0.18, 0.06), AL (MD: 0.16; 95% CI: -0.03, 0.36) and BOP (MD: 4.15; 95% CI: -0.26, 8.55) were not obvious in periodontitis patients with RA. No heterogeneity was observed for PD (I^2=0.0%, P =0.84) and AL (I^2=0.6%, P=0.39), and substantial heterogeneity was observed for BOP (I^2=50.8%, P =0.06) (Fig. 3A-C).

Sensitivity analysis

Sensitivity analyses were performed in order to assess the potential source of heterogeneity of PI and BOP outcomes. We evaluated the influence of individual dataset on the pooled effect by sequential removal of each eligible study. However, the findings were corroboratively robust and no significant change was detected for all primary outcomes (Fig.4).

Publication bias

Begg's and Egger's test revealed that there was no publication bias for the changes of PI, GI, AL and BOP (*P*0.05), but Egger's test manifested that there was publication bias for PD (Egger's test P=0.04). The trim-and-fill analysis suggested no evidence of significant difference between the adjusted value and the original value of PD changes, but revealed a missing study for BOP changes. At the same time, the adjusted value for BOP changes was also not significantly different from the original value (Table 2).

Subgroup analysis

To determine the potential influence of follow-up time on the clinical efficacy of SRP, we performed analyses separately for different follow-up time points. Compared with periodontitis control patients, the reduction of BOP (MD: 5.93; 95%CI: 0.28, 11.58) was significantly larger in periodontitis patients with RA at the 3rd month after SRP. Similarly, the changes of PI (MD: 0.60; 95% CI: 0.08, 1.13) and AL (MD: 0.36; 95% CI: 0.06, 065) of periodontitis patients with RA were slightly larger at the 6th month than periodontitis control patients (Table 3).

Discussion

To the best of our knowledge, available evidence was summarized in an effort to specifically estimate the clinical efficacy of SRP in periodontitis patients with RA for the first time of meta-analysis. Eight RCTs were included, and all the studies evaluated the changes associated to treatment of the periodontal inflammation, based on the measurement of different clinical indices and parameters (PI, GI, PD, AL and BOP). The findings from the present meta-analysis failed to find significant difference in the clinical efficacy of SRP between RA patients with periodontitis and patients with periodontitis alone. This provides evidence that RA does not affect the clinical efficacy of SRP in periodontitis.

It has been confirmed that periodontitis patients with RA were found to have higher plaque scores compared to individuals without RA [31]. Our meta-analysis showed that SRP resulted in 0.42 of additional PI reduction in periodontitis patients with RA. SRP appears to be more effective in improving oral hygiene in periodontitis patients with RA than that in patients with periodontitis alone. This finding could be linked to the evidence that a higher prevalence of severe periodontitis in RA patients [32, 33]. A further study from Van der Weijden et al indicated that severe periodontitis yielded greater PI reduction after SRP as compared to mild periodontitis [34]. Thus, the results we obtained may be partly attributed to the SRP efficacy for SP rather than the improvement by RA.

Recent report showed that the duration of RA is likely to have a significant impact on the association between RA and periodontitis [35]. What's more, Qiao et al declared that periodontitis might be more closely related to disease duration >5 years of RA patients [36]. Also, a significantly higher clinical AL was found in moderately-to-highly active RA patients, compared to those in remission [35]. Unfortunately, information about the RA duration was not available in the studies enrolled in our meta-analysis. In addition, we did not confirm a significant difference of AL reduction in the two groups. We speculate that an imprecise duration of RA is likely to contribute to no difference in the SRP- related outcomes between groups. Clearly, this needs further investigation in well-designed studies taking this variable into account.

Likewise, several parameters failed to show difference between groups in this meta-analysis. The results showed that the effects of SRP on the GI, PD, BOP of patients with RA and periodontitis were almost consistent with those with periodontitis alone. It is pertinent to mention that previous research demonstrated the application of the mechanical periodontal treatment as SRP could effectively improve periodontal parameters [37]. But whether this effect will change in the presence of RA is unclear. Thus, these findings confirmed that SRP is an effective treatment for periodontitis and the clinical benefits of SRP could not be affected by RA in periodontitis patients in this regard.

Cosgarea et al observed a significant reduction in some clinical periodontal parameters within 3 and 6 months after treatment in patients with periodontitis and RA [38]. However comparisons of efficacy differences were not achieved. In our study, when stratified by the points of follow-up, the periodontitis patients with RA showed a higher BOP reduction at 3 months and an overall improvement for PI and AL at 6 months in comparison to periodontitis patients. However, it did not show significantly statistical differences in other parameters and follow-up time points. Besides, research reported no difference in clinical parameter outcomes when studying periodontal treatment effects of patients with low and high disease activity of RA [39]. Therefore, the difference in the efficacy of SRP between groups has not been well demonstrated by the outcomes for follow-up within 6 months after treatment.

Although the study was designed seriously and data was processed carefully, we still identified several limitations in this meta-analysis. First, the study is likely to lack the statistical power to detect differences between groups due to the limited number of studies and subjects. Second, 3 studies did not publish RA duration. As a result, potential confounding factors could lead to some bias in the outcomes. Third, there may also be some heterogeneity between the two groups in terms of gender and demographic data, which were not analyzed in the subgroup. Finally, some clinical criteria for disease assessing are not entirely consistent and tend to introduce non-differential misclassification of the two diseases, with a potential effect of driving the results towards no difference.

Conclusions

Taken together, in spite of these limitations, we conclude that SRP is equally effective in patients with periodontitis and RA than in periodontitis ones. This result suggests RA does not affect the clinical

efficacy of non-surgical periodontal therapy. We are looking forward to additional scientific researches to elucidate the clinical efficacy of SRP in RA patients with periodontitis of various severities further.

List Of Abbreviations

RA, rheumatoid arthritis, SRP, scaling and root planning, RCTs, randomized controlled clinical trials, SP, severe periodontitis, PI, plaque index, GI, gingival index, AL, attachment loss, PD, probing depth, BOP, bleeding on probing, PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses, MD, mean difference, CI, confidence intervals

Declarations

Ethics approval and consent to participation

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The detailed data supporting the study are available upon reasonable request.

Competing interests

All the authors declare no conflict of interest.

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Authors' contributions

Y.H conceived this study and prepared the manuscript. Z.Z downloaded the data. Y.Z statistically analyzed and summarized the data, and Z.Z helped in the data analysis. N.M and L.Z designed the study and developed the search strategy. Z.Z and Y.Z reviewed drafts of the paper. Q.Z and D.X helped find the books and materials. All authors read and approved the final version of the manuscript.

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Tables

Table 1.

Characteristics of eligible studies included in this meta-analysis.

First author, year	Location	Subjects	Gender (%Female)	Age	RA duration (years)	Follow-up time	Outcomes
Pinho et al., 2009	Brazil	Test: 15 Control: 15	60.0%	35-60	0.5-10	3, 6 months	PI, PD, BOP
Bıyıkoğlu et al., 2013	Turkey	Test: 15 Control: 15	Test: 60.0% Control: 40.0%	Test: 46.6 Control: 46.7	6.4	1,3,6 months	PI, PD, AL, BOP
Roman-Torres et al.,2015	Brazil	Test: 12 Control: 12	100%	Test: 45.4 Control: 46.8	10.0	3 months	PI, PD, BOP
Kurgan et al., 2016	Turkey	Test: 13 Control: 13	Test: 69.2% Control: 46.2%	Test: 48.5 Control: 41.4	NA	3 months	PI, GI, PD, BOP
Yuce et al., 2017	Turkey	Test: 17 Control: 18	Test: 64.7% Control: 50.0%	Test: 51.0 Control: 49.5	NA	6 weeks	PI, GI, AL
Kurgan et al., 2017	Turkey	Test: 15 Control: 15	Test: 60.0% Control: 53.3%	Test: 49.3 Control: 42.1	NA	3 months	PI, GI, PD, AL, BOP
Zhao et al., 2018	China	Test: 18 Control: 18	Test: 77.8% Control: 77.8%	Test: 42.8 Control: 44.8	>6 weeks	1 month	PI, GI, PD, BOP
Cosgarea et al., 2019	Germany	Test: 18 Control: 18	Test: 77.8% Control: 55.6%	Test: 51.6 Control: 43.6	14.9	3,6 months	PD, AL, BOP

AL, attachment loss; BOP, bleeding on probing; GI, gingival index; PD, probing depth; PI, plaque index; RA, rheumatoid arthritis.

Table 2.

Quantitative analysis of publication bias.

Outcome	Studies trimmed/ total studies	Trim-and-fill analysis		Begg's test (*P*-value)	Egger's test (*P*-value)
		MD	95%CI		
PI	0/7	0.42	0.02, 0.81	0.55	0.99
GI	0/4	0.03	-0.03, 0.10	0.73	0.56
PD	0/7	-0.06	-0.18, 0.06	0.07	0.04
AL	0/4	0.16	-0.03, 0.36	0.73	0.99
BOP	1/8	2.74	-2.10, 7.58	0.76	0.34

AL, attachment loss; BOP, bleeding on probing; CI, confidence interval, GI, gingival index; MD, mean difference; PD, probing depth; PI, plaque index.

Table 3.

Subgroup analysis according to different follow up time points.

Follow-up time	No. of studies	Meta-analysis			Heterogeneity		Publicaton bias(*P*-value)	
		MD	95%CI	*P*-value	I^2(%)	*P*-value	Begg's test	Egger's test
PI								
1-1.5mo	3	0.39	-0.66, 1.43	0.47	84.8	0.001	1.00	0.87
3mo	5	0.31	-0.03, 0.64	0.08	17.0	0.31	0.46	0.59
6mo	2	0.60	0.08, 1.13	0.02	29.7	0.23	1.00	NA
GI								
1-1.5mo	2	0.05	-0.03, 0.12	0.20	0.0	0.76	1.00	NA
3mo	2	-0.05	-0.36, 0.26	0.76	61.2	0.11	1.00	NA
PD								
1mo	2	-0.14	-0.47, 0.20	0.43	50.5	0.16	1.00	NA
3mo	6	-0.05	-0.20, 0.09	0.43	0.0	0.59	0.13	0.05
6mo	3	-0.14	-0.35, 0.06	0.17	0.0	0.49	0.30	0.26
AL								
1-1.5mo	2	0.01	-0.31, 0.33	0.94	0.0	0.82	1.00	NA
3mo	3	-0.02	-0.24, 0.20	0.85	0.0	0.77	0.30	0.20
6mo	2	0.36	0.06, 0.65	0.02	0.0	0.78	1.00	NA
BOP								
1mo	2	-0.77	-4.35, 2.81	0.67	0.0	0.80	1.00	NA
3mo	6	5.93	0.28, 11.58	0.04	54.2	0.05	0.71	0.32

	6mo	3		5.02	-1.28, 11.32	0.12	6.0	0.35	0.30	0.28

AL, attachment loss; BOP, bleeding on probing; CI, confidence interval, GI, gingival index; MD, mean difference; PD, probing depth; PI, plaque index.

Figures

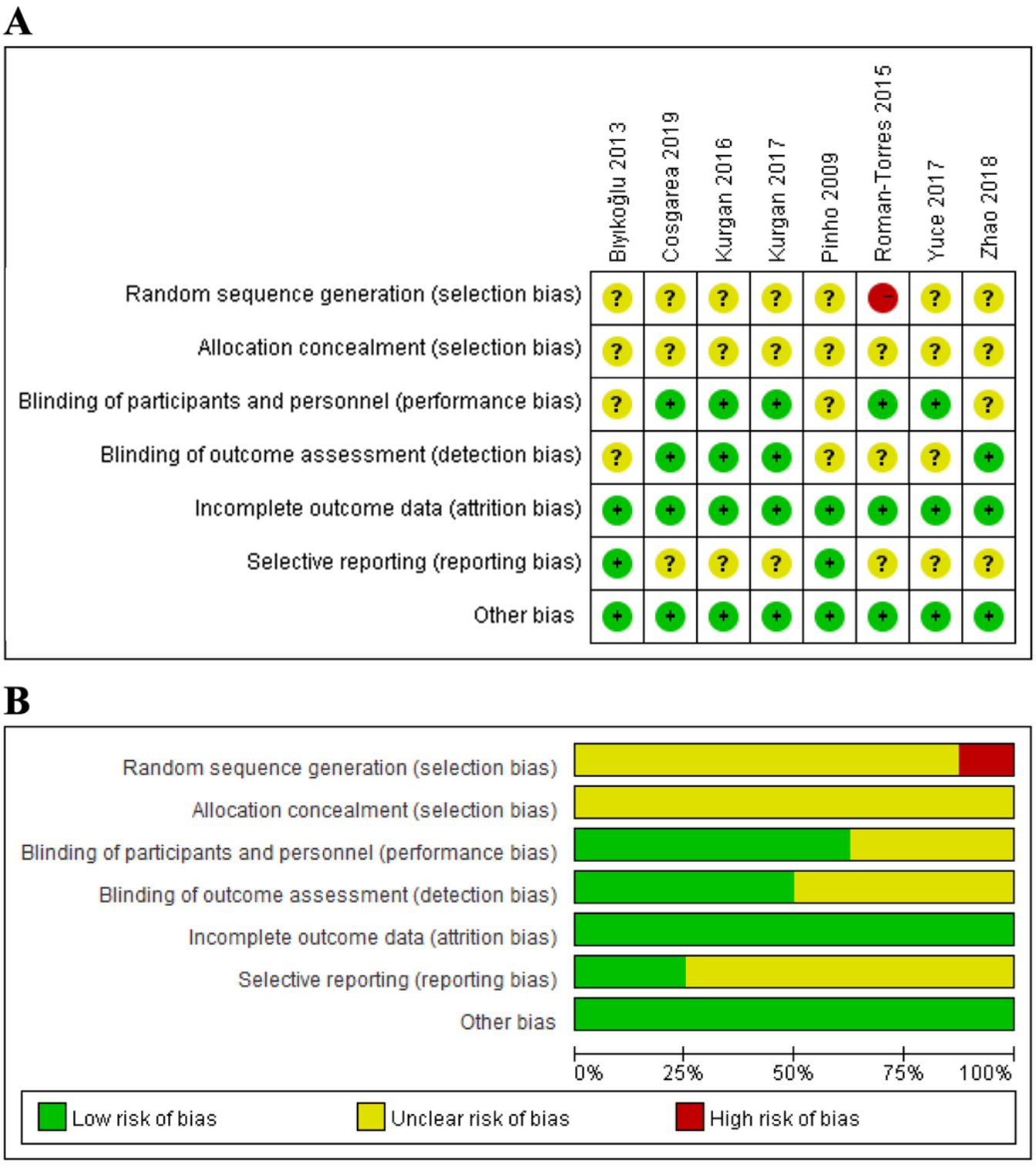

Figure 1

Risk of bias assessment for the studies included in the meta-analysis. A, risk of bias summary; B, risk of bias graph. (+): low risk of bias; (?): unclear risk of bias; (−): high risk of bias.

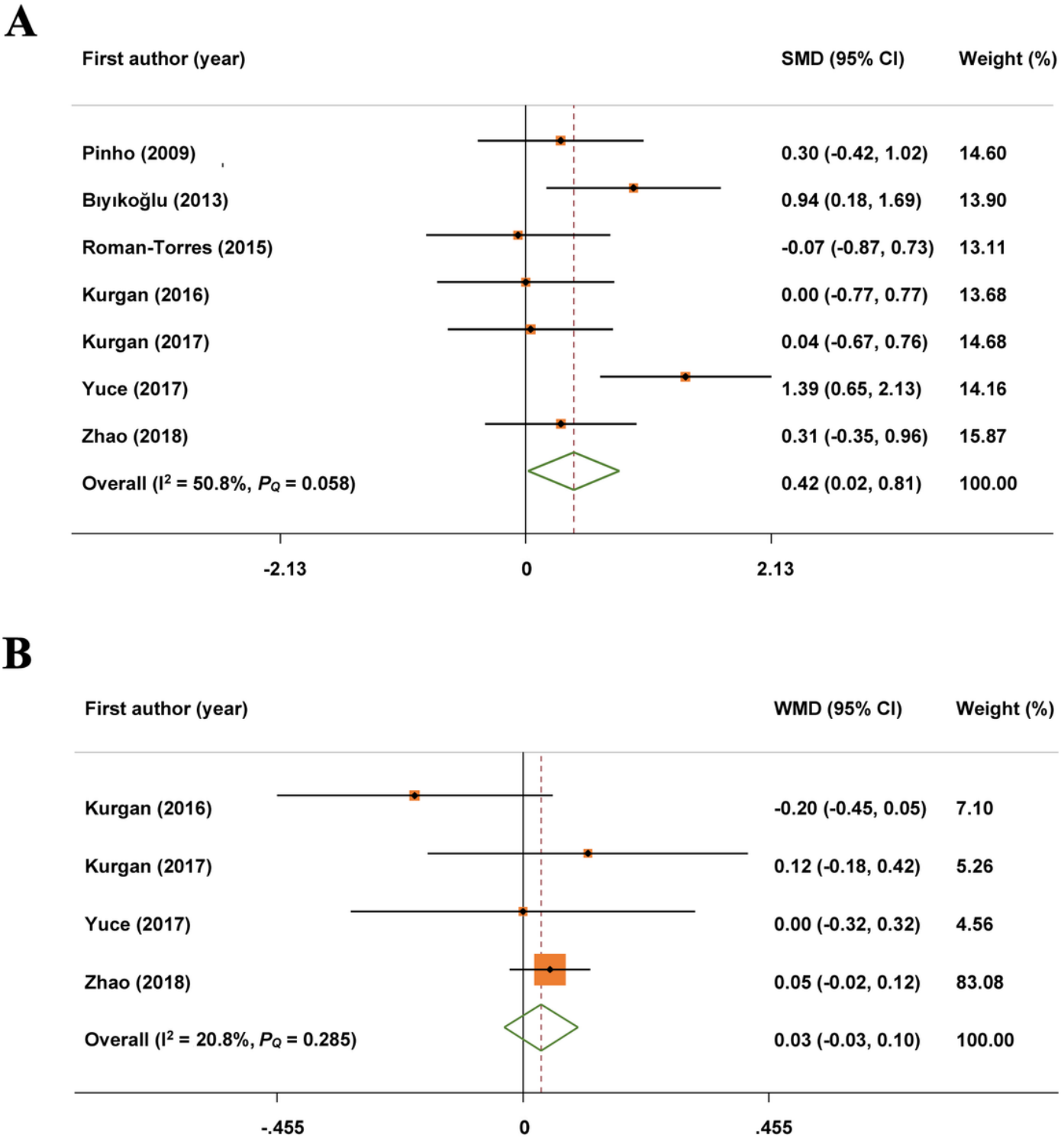

Figure 2

Forest plot of changes in plaque index and gingival index reduction. A, plaque index; B, gingival index.

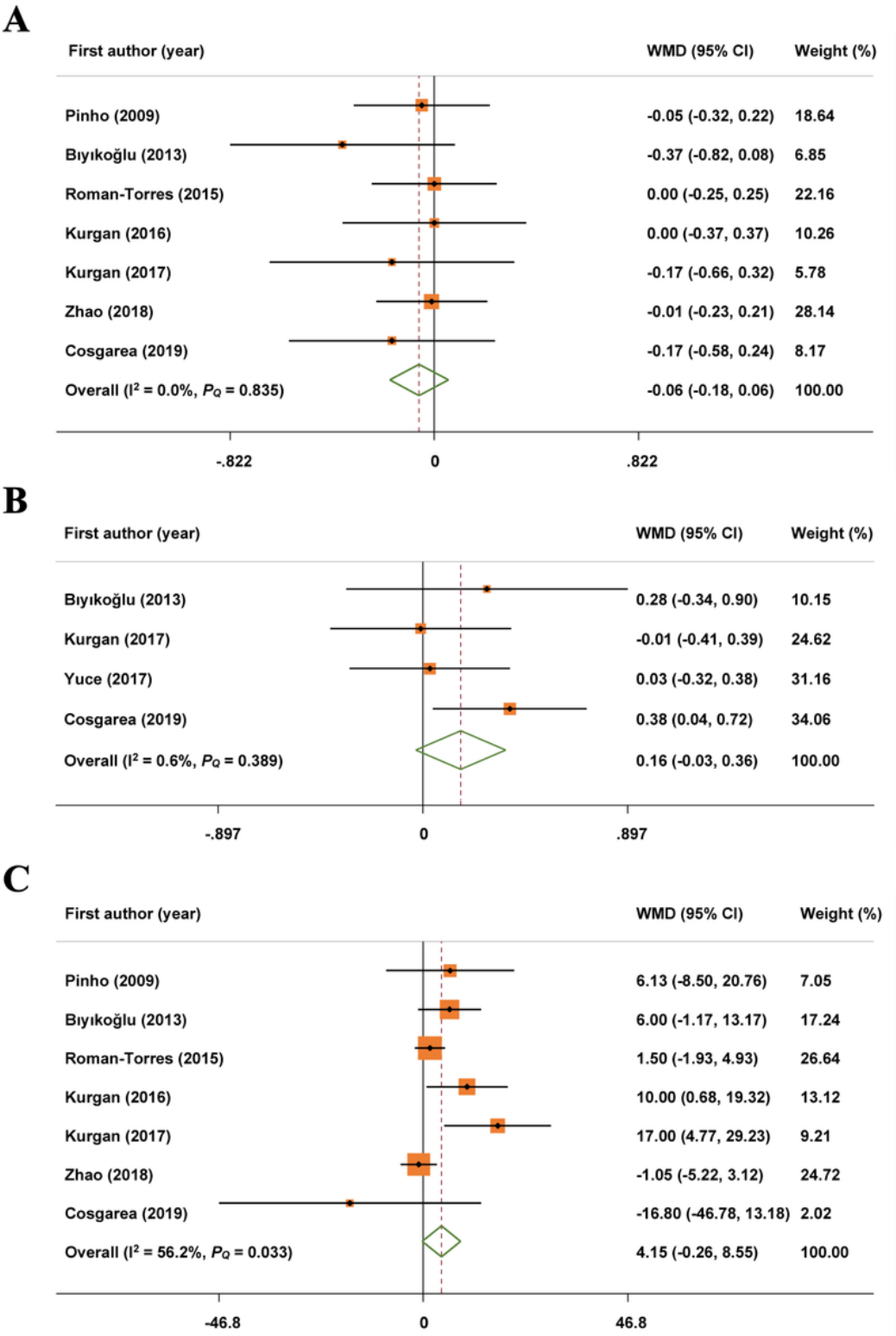

Figure 3

Forest plot of changes in probing depth, attachment loss and bleeding on probing reduction. A, probing depth; B, attachment loss; C, bleeding on probing.

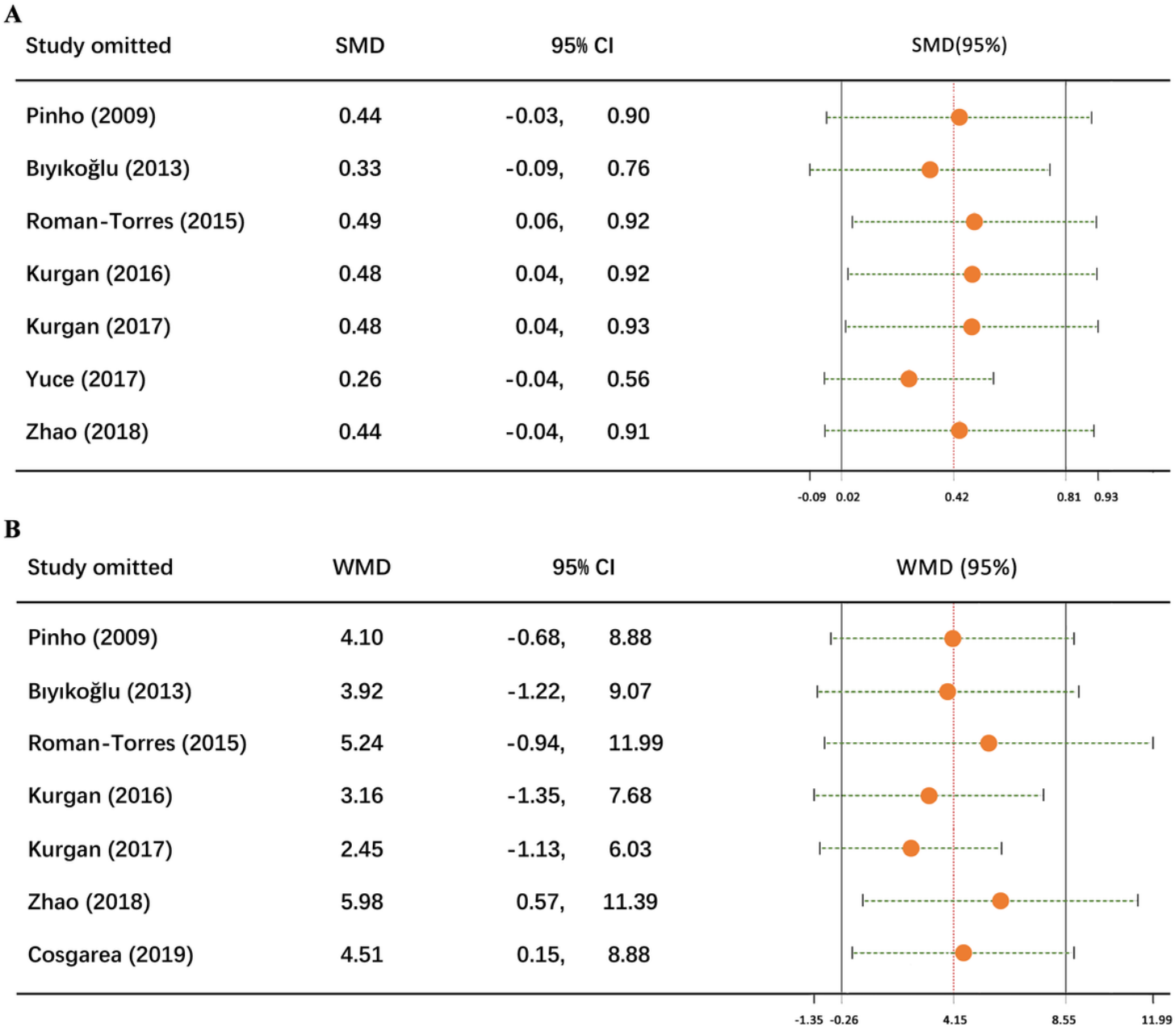

Figure 4

Sensitivity analysis of changes in plaque index and bleeding on probing reduction. A, plaque index; B, bleeding on probing.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigureS1.png