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REVIEW ARTICLE

Comparison of immediate implant placement in infected and non-infected extraction sockets: a systematic review and meta-analysis

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ABSTRACT

Objective: This review aimed to investigate the feasibility of immediate implant placement in infected extraction sockets.

Material and methods: We performed electronic and manual searches up to March 2017 to obtain data from randomized controlled trials (RCTs) and nonrandomized controlled clinical trials (CCTs). Using a fixed-effects model to assess the difference in survival rate (primary outcome), we evaluated the risk difference for immediate implant placement in infected and non-infected sites. We estimated the weighted mean differences (WMDs) of the change in marginal bone loss (MBL), probing depth (PD), modified bleeding index (mBI), marginal gingival level (MGL) and width of keratinized gingiva (WKG) at baseline and latest follow-up.

Results: In total, five studies (0 RCT, five CCTs) were included in the systematic review and three studies were included in the meta-analysis. The risk difference for immediate implant placement in an infected extraction socket compared with that in a non-infected socket was −0.02. WMDs for MBL, PD, mBI, MGL and WKG between the two groups were 0.32, 0.12, 0.07, −0.06, 0.20 and 0.51, respectively. No statistical differences were observed between the two groups, except for the change in WKG.

Conclusions: Implants can be placed in infected extraction sockets after thorough socket debridement. For aesthetics, WKG should be considered when performing immediate implant placement in infected sites.

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KEYWORDS
Dental infection; tooth extraction socket; gingiva; dental implant; immediate implant

Introduction

According to a conventional protocol, implant placement should be done several months after tooth extraction to allow healing of soft and hard tissue and resolution of infections [1]. In 1989, an immediate implant placement procedure was introduced to reduce treatment time and surgical interventions [2]. Recent studies have shown that immediate implant placement provides predictable survival results and satisfactory aesthetic outcomes [3–5].

As there is a risk for developing a local infection or inflammation when implants are immediately placed in compromised tooth extraction sockets, earlier reports suggested that immediate implant placement should only be done in extraction sockets that are free of infection [6,7]. In addition, bacterial infections may affect implant osseointegration, resulting in peri-implant pathosis or implant failure [8].

Recent animal and human studies on immediate implant placement in infected sites [9–11] suggest that this procedure can be performed in infected extraction sockets after exhaustive debridement of the socket. Although there are several systematic reviews evaluating immediate implant placement in infected extraction sockets [12,13], evidence is limited due to the lack of prospective human studies comparing immediate implant placement in infected and non-infected extraction sockets.

This systematic review aimed to investigate the feasibility of immediate implant placement in infected extraction sockets. We compared the risk difference (primary outcome) for immediate implant placement in infected and non-infected extraction sockets as well as differences in marginal bone loss (MBL), probing depth (PD), modified bleeding index (mBI), marginal gingival level (MGL) and width of keratinized gingiva (WKG) at baseline and latest follow-up between the two groups.

Materials and methods

We developed a detailed protocol on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols 2015 (PRISMA-P 2015) statement guidelines [14].

Types of studies

In this meta-analysis, we included only longitudinal prospective studies, that is, randomized controlled trials (RCTs) or

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Supplemental data for this article can be accessed here.

nonrandomized controlled clinical trials (CCTs) with immediate implant placement in infected extraction sockets (test group) and non-infected extraction sockets (control group).

Populations of studies

Healthy individuals with no age or sex limit who underwent immediate implant placement after tooth extraction were included.

Types of interventions

Test group

In the test group, studies on immediate implant placement interventions in endodontic and periodontal infection sites were included. A minimum of 10 subjects per group were included in the controlled studies.

Control group

In the control group, studies on immediate implant placement in non-infected sites following a traumatic tooth extraction with no other intervention were included.

Outcome variables

One dichotomous (yes/no) and five continuous implant-related outcome variables were evaluated as follows:

1. Implant failure was expressed as the number of implants that failed to achieve osseointegration or removed after functional loading due to pain, mobility and severe peri-implant bone loss.
2. MBL was an average of the mesial and distal bone loss calculated at baseline and the latest follow-up. If the average bone loss decreased (marginal bone gain) compared with that at baseline, the loss was expressed as a negative value.
3. PD*.
4. mBI*.
5. MGL*.
6. WKG*.

*Changes in the above parameters were calculated using the data at baseline and the latest follow-up.

Risk for bias and methodological quality assessment

The Cochrane Collaboration's tool for assessing risk of bias in randomized trials was used to assess the risk for bias and the methodological quality of the included studies [15]. The following parameters were evaluated for each study and were classified as low risk, unclear risk or high risk for bias: allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias (related to the study design or other issues).

Inclusion criteria

1. Prospective studies (RCTs or CCTs) comparing the outcomes of immediate implant placement in infected and non-infected extraction sockets.
2. Studies performed in medically healthy patients with no age limit.

Exclusion criteria

1. Retrospective studies or case reports.
2. Studies on medically compromised patients.
3. Studies lacking details regarding the extraction socket.
4. Studies using the latest data when publications reported data on the same participants.

Search strategy

Two reviewers (JL and DP) independently performed electronic and manual searches for obtaining the data; disagreements regarding inclusion eligibility were resolved by discussion with a third reviewer (Y-ML) to reach a consensus. The MEDLINE, EMBASE and Cochrane Central Register, LILACS and Web of Science electronic databases were searched using a combination of MeSH terms and text words (see Appendix S1). The manual search was performed using the bibliographies of the included articles; all relevant articles and reviews were screened. Furthermore, the following journals were screened from 2001 to March 2017: *Clinical Oral Implants Research; Clinical Implant Dentistry and Related Research; European Journal of Oral Implantology; Implant Dentistry; International Journal of Oral and Maxillofacial Implants; International Journal of Periodontics and Restorative Dentistry; Journal of Clinical Periodontology; Journal of Dental Research; Journal of Investigative and Clinical Dentistry; Journal of Oral and Maxillofacial Surgery; Journal of Periodontology; Oral Surgery, Oral Medicine, Oral Radiology, Oral Pathology, and Endodontics; Journal of Periodontal & Implant Science; The Journal of Advanced Prosthodontics; The Journal of the Korean Dental Association;* and *Implantology*.

There was no language limitation for article selection, and articles were translated when necessary. We also attempted to include unpublished trials and abstracts in the search process.

Data extraction and synthesis

Table 1 shows the extracted data of all included studies according to the author, title, year, study design, number of subjects, age of subjects, number of implants, implant location, implant position, implant type, number of failed implants, implant insertion torque, loading protocols, observation period, implant success rates and implant survival rates. We investigated the secondary outcomes including marginal bone change, PD, mBI, MGL and WKG at baseline and the latest follow-up. Raw data that could be extracted from the studies were processed for meta-analysis. If extracting or obtaining raw data was impossible, mean estimates

Table 1. Characteristics of included studies.

Study	Design	Patients, *n*	Age, years	Follow-up, years	Flap or flapless	Augmentation procedure	Healing protocol	Occlusal protocol: immediate or delayed loading	Failed/placed implants	Implant survival rate
Crespi et al. [17]	Prospective	30 (15, I; 15, N)	34–71, 51.2	2	Flapless	None	One stage	Delayed loading	0/15 (I); 0/15 (N)	100 (I), 100 (N)
Crespi et al. [21]	Prospective	275 (197, I; 78, N)	32–71, 52.5	4	Flapless	None	One stage	Immediate loading	2/197 (I); 0/78 (N)	98.9 (I), 100 (N)
Jung et al. [18]	Prospective	27 (12, I; 15, N)	53 (31–87), I; 60 (28–82), N	5	Flap	Xenograft	One stage	Delayed loading	0/12 (I); 0/15 (N)	100 (I), 100 (N)
Montoya-Salazar et al. [19]	Prospective	36 (18, I; 18, N)	18–50	3	Flap	Xenograft	Two stage	Delayed loading	1/18 (I); 0/18 (N)	94.4 (I), 100 (N)
Blus et al. [22]	Prospective	168 (83, I; 85, N)	26–77	1	Flapless	None	One stage	Delayed loading	2/83 (I); 1/85 (N)	97.6 (I), 98.8 (N)

I: infected group; N: non-infected group; ND: no data.

and standard deviations were used for the differences in each intervention group, which were calculated using a previously defined method [16].

Meta-analysis was conducted using Review Manager software (version 5.3, The Cochrane Collaboration). For a dichotomous outcome (e.g. implant survival rate), the risk ratio was calculated with 95% confidence intervals (CIs). For continuous variables (e.g. marginal bone loss, probing depth, modified bleeding index, marginal gingival level and WKG), weighted mean differences (WMDs) were estimated with 95% CIs. All selected studies [17–19] in the meta-analysis were considered to be homogenous; therefore, a fixed-effects model was used. A statistical homogeneity assessment was conducted along with determining the I^2 index [20]. If I^2 was >75%, a subgroup analysis was performed to determine the reason for heterogeneity.

Results

Study selection

In total, 3615 papers were identified from the electronic and manual searches. After excluding duplicates and screening the titles and abstracts, 10 papers were obtained for full-text assessment. Five papers [17–19,21,22] were included (Figure 1); three papers [23–25] were excluded due to the lack of a control group and two [26,27] due to the publication of subsequent reports on the same subjects.

Furthermore, meta-analysis was performed using three [17–19] of the five included studies. The studies regarding immediate implant placement in periapical infection sites were included in meta-analysis. Two studies were excluded due to the heterogeneity of the origin of infection (Table 1).

Description of studies

Table 1 shows the study design and characteristics of the included studies [17–19,21,22]. No RCTs were found in the database search; only five CCTs were selected. The origin of infection was a periodontal lesion in one study [21], a periapical lesion in three studies [17–19] and a periodontal and/or periapical lesion in one study [22]. The implant location was not limited in any of the studies. External connection-type implants were used in two studies [17,21], and internal connection-type implants were used in three studies [18,19,22]. The implant insertion torque was recorded in two studies [17,21], and flapped surgery and two-stage surgery protocols were performed in two studies [18,19]. Bone graft procedures were conducted in two studies [18,19], and no augmentation was performed in three studies [17,21,22]. Only one study [21] involved immediate loading, whereas the others involved delayed loading. The follow-up period after loading ranged from 1 to 5 years.

In total, 212 implants were placed in infected sites and 326 in non-infected sites. There were two implant failures: two (0.9%) and six (1.8%) implants placed in non-infected and infected sites, respectively. Data regarding marginal bone change were recorded in all studies, except for the study by Blus et al. [22]. Mean estimates and standard

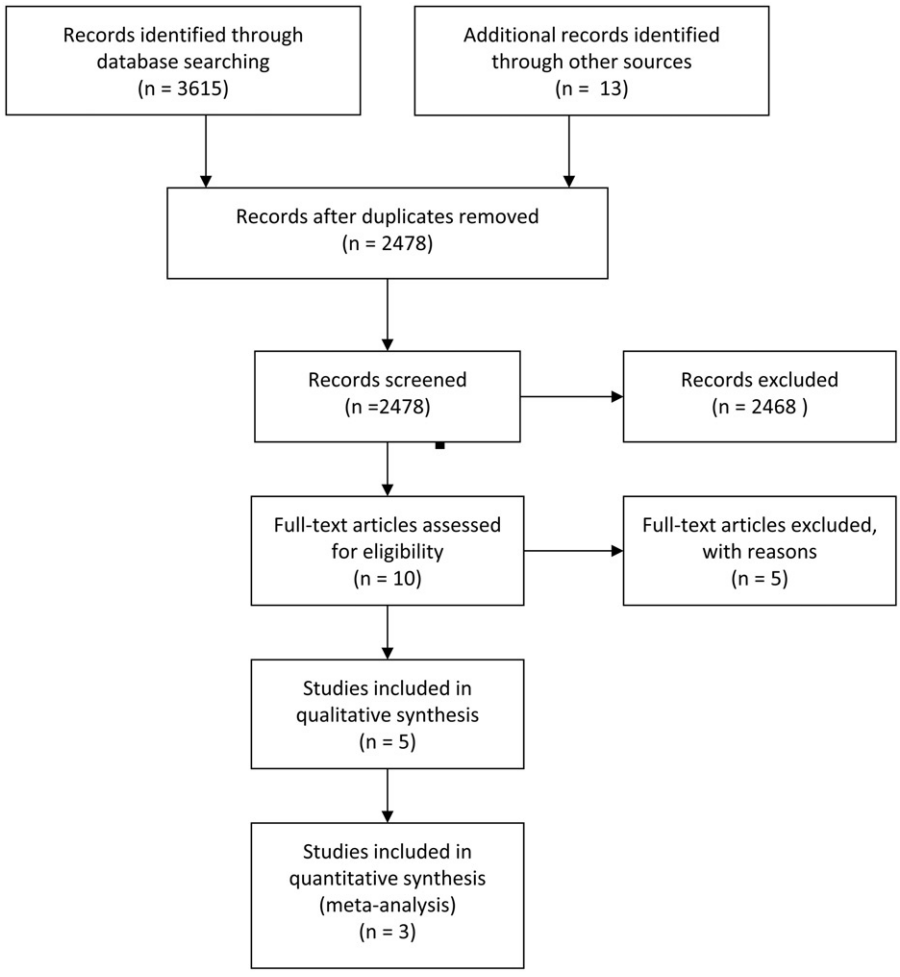

Figure 1. Flow diagram for the study.

Table 2. Mean estimates and standard deviations for the differences at baseline and latest follow-up.

Implant type	Type of infection	Marginal bone loss	Probing depth change	Modified bleeding index change	Marginal gingival level change	With of keratinized gingiva change
Sweden-Martina, external	Chronic Periapical lesion	−0.16 ± 0.47 (I) −0.17 ± 0.45 (N)	0.57 ± 0.51 (I) 0.59 ± 0.58 (N)	0.26 ± 0.32 (I) 0.28 ± 0.31 (N)	0.05 ± 0.11 (I) 0.07 ± 0.16 (N)	0.05 ± 0.11 (I) 0.07 ± 0.16 (N)
Sweden-Martina, external	Chronic Periodontal lesion	−0.22 ± 0.38 (I) −0.25 ± 0.37 (N)	ND	0.25 ± 0.24 (I) 0.26 ± 0.38 (N)	ND	ND
Straumann tissue level, internal	Periapical lesion	1.75 ± 1.22 (I) 1.75 ± 0.95 (N)	ND	ND	ND	−2.10 ± 1.45 (I) −0.60 ± 1.37 (N)
Mis Iberia, C1 implant (internal), Spain	Chronic Periapical lesion	−0.83 ± 0.34 (I) −0.56 ± 0.23 (N)	0.05 ± 0.53 (I) 0.14 ± 0.43 (N)	0.06 ± 0.80 (I) 0.34 ± 0.92 (N)	0.12 ± 0.67 (I) 0.00 ± 0.29 (N)	−0.17 ± 0.98 (I) 0.27 ± 0.82 (N)
Leader (Italy), Bioner (Spain), external	Acute, chronic periodontal/ periapical lesion	ND	ND	ND	ND	ND

I: infected group; N: non-infected group; ND: no data.

deviations for the differences at baseline and the latest follow-up were calculated for changes in marginal bone level, probing depth, modified bleeding index, marginal gingival level and WKG. Table 2 shows the results.

Quality assessment of selected studies

The investigated studies had a low quality and evidence level. Random sequence generation, allocation concealment and blinding of participants and personnel had a high risk for bias. Blinding of the outcome assessment had an unclear risk for bias, whereas incomplete outcome data and selective reporting had a low risk. Figure 2 shows the risk for bias of each included study, and Figure 3 shows a summary of the risk for bias.

Meta-analysis of included studies

No statistically significant differences in implant survival rates were found between the two groups (Figure 4(a)). The risk difference for immediate implant placement in infected extraction sockets compared with that in non-infected

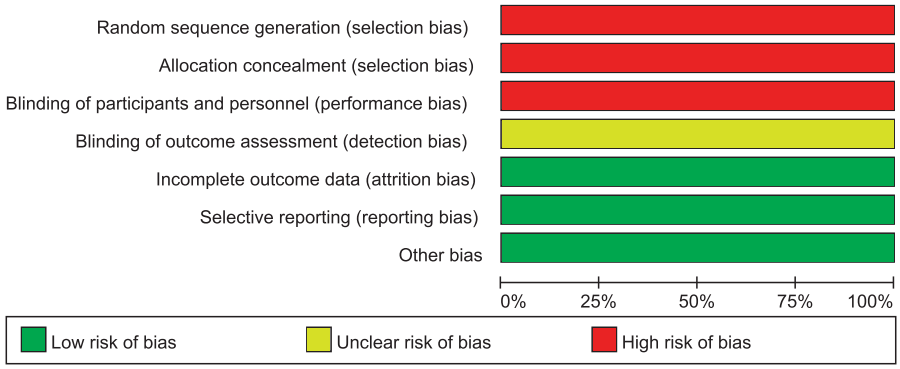

Figure 2. Risk for bias graph, where each item is presented as a percentage across all included studies.

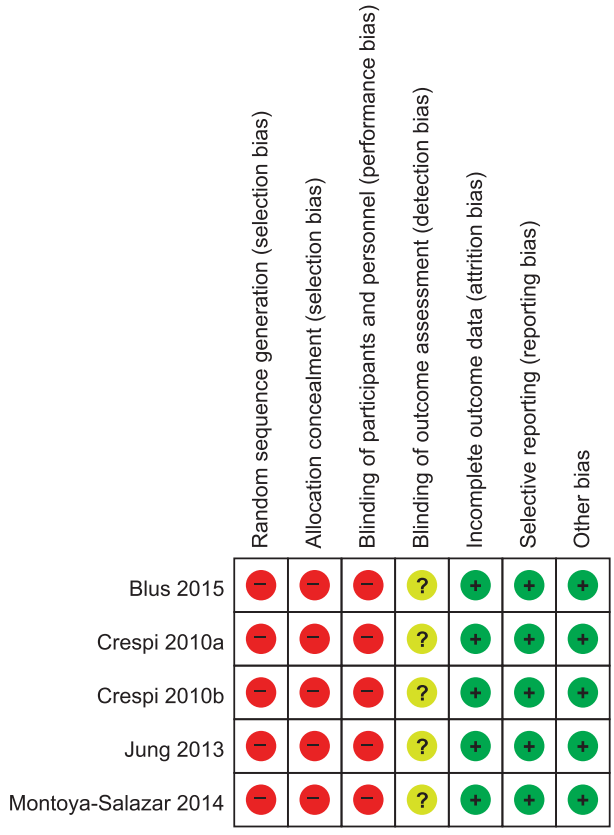

Figure 3. Risk for bias summary of each item for each included study.

extraction sockets was −0.02 (95% CI, −0.10 to 0.06; $p = .61$; heterogeneity $I^2 = 0\%$; $P_{\text{heterogeneity}} = 0.80$).

Three studies were used for evaluating the marginal bone change from baseline to the latest follow-up [17–19,21]; no statistically significant difference was observed between the two groups (Figure 4(b)). The marginal bone loss in the infected versus non-infected sites was 0.32 mm (95% CI, −0.10 to 0.73; $p = .13$; heterogeneity $I^2 = 53\%$; $P_{\text{heterogeneity}} = 0.12$). Two studies [17,19] were used for evaluating the change in probing depth and marginal gingival level from baseline to the latest follow-up, and no statistically significant differences were observed between the two groups (Figure 4(c,d)). The change in probing depth in infected versus non-infected sites was 0.12 mm (95% CI, −0.37 to 0.60; $p = .64$; heterogeneity $I^2 = 0\%$; $P_{\text{heterogeneity}} = 0.77$), and the change in marginal gingival level in infected versus non-infected sites was −0.06 mm (95% CI, −0.54 to 0.42; $p = .81$; heterogeneity $I^2 = 0\%$; $P_{\text{heterogeneity}} = 0.46$).

Two studies [17,19,21] were used for evaluating the change in modified bleeding index from baseline to the latest follow-up; no statistically significant difference was observed between the two groups (Figure 4(e)). The change in modified bleeding index in infected versus non-infected sites was 0.20 (95% CI, −0.28 to 0.68; $p = .42$; heterogeneity $I^2 = 0\%$; $P_{\text{heterogeneity}} = 0.61$).

Three studies [17–19] were used for evaluating the change in WKG from baseline to the latest follow-up, and statistically significant differences were found between the two groups (Figure 4(f)). The change in WKG in infected versus non-infected sites was 0.51 mm (95% CI, 0.09 to 0.93; $p = .02$; heterogeneity $I^2 = 23\%$; $P_{\text{heterogeneity}} = 0.27$).

Discussion

This review did not show any statistically significant differences in survival rates for immediate implants in periapically infected and non-infected extraction sockets possibly due to the improvement in implant fixture over the last few decades. Implant surface topography has been altered to improve osseointegration. Implants with rough versus smooth surfaces have shown superiority in early bone-to-implant contact and in sites with poor bone quality [28,29]. Only rough surface implants were used in the included studies. Despite the unfavourable environment in infected extraction sockets, the implant survival rate did not decrease with the use of rough surface implants. However, we were unable to conclude whether it was safe to immediately place implants in periodontally infected extraction sockets because the related data were superficial and the indication of periodontal infection was vague. For example, data on evidence of an inflammation, proper periodontal examination including PDs, clinical attachment level, bleeding on probing, grade of furcation involvement, tooth mobility and radiographic examination were not included [21,22]. To investigate the safety and feasibility of immediate implant placement in periodontally infected sites, a more detailed case definition should be documented in future studies.

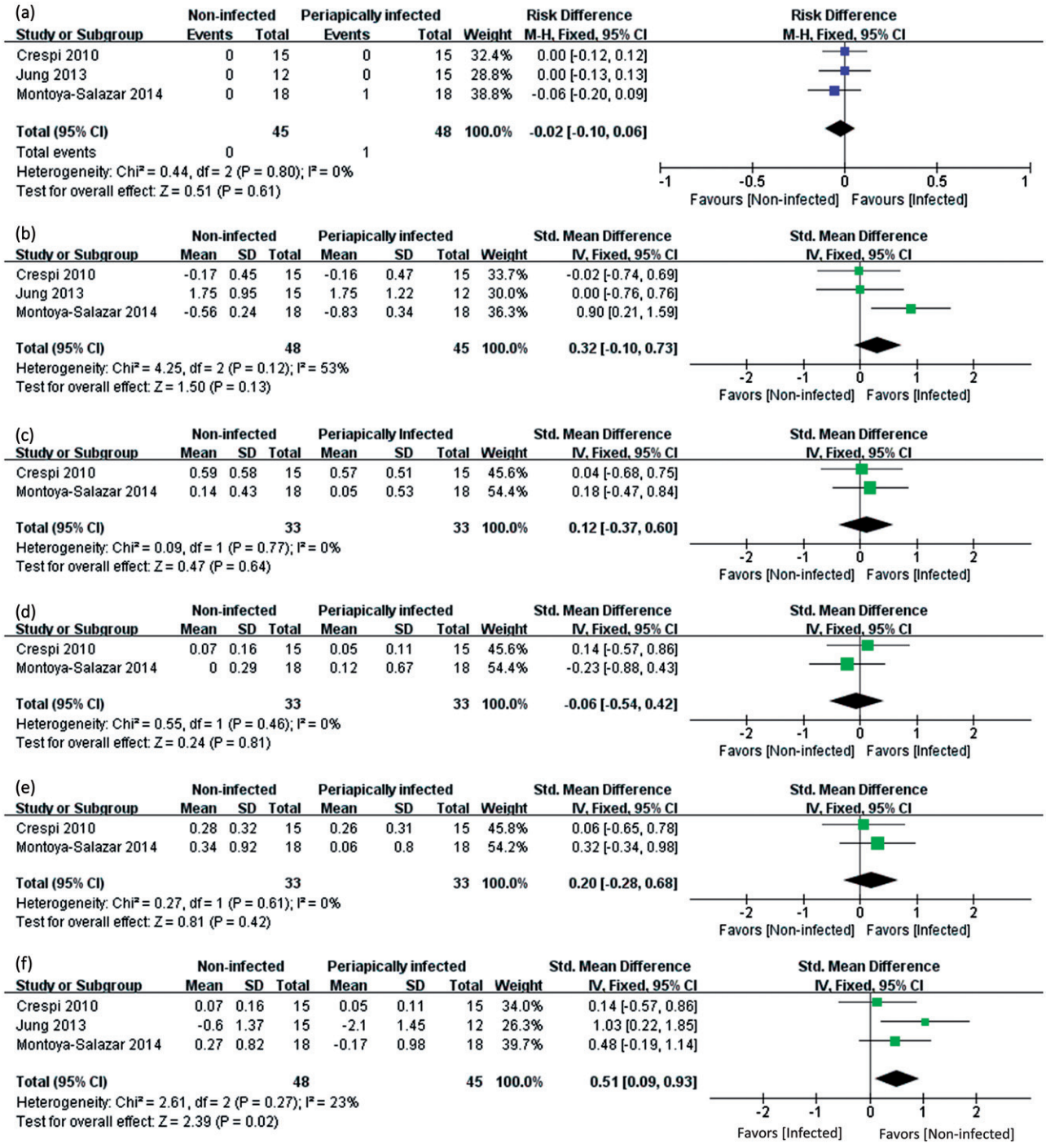

Figure 4. Forest plot for (a) implant survival, (b) marginal bone change, (c) change in probing depth, (d) change in modified bleeding index, (e) change in marginal gingival level and (f) change in width of keratinized gingiva in non-infected and infected extraction sockets.

To our knowledge, there has been no quantitative analysis on soft tissue profile changes around dental implants immediately placed in periapically infected and non-infected sites after tooth extraction. This is the first meta-analysis to assess these changes in both cases. A statistically significant reduction in WKG was observed in periapically infected sites versus non-infected sites, suggesting that there is a potential change in the soft tissue profile when performing immediate implant placement in infected sites, particularly those placed for aesthetic purposes. A systematic review reported that immediate implant placement cannot prevent gingival recession [30] and demonstrated that patients with an intact buccal bone wall and a thick gingival biotype who were treated through a flapless surgery followed by immediate implant placement may have a reduced risk for advanced mid-facial recession. In infected sites, buccal bone is easily destroyed and soft tissue is swollen or in a flabby state due to lack of thickness of the buccal wall compared with the lingual wall; these factors can increase the risk for gingival recession after immediate implant placement. Care must be used when performing immediate implant placement in infected sites with a soft tissue graft to counteract soft tissue reduction.

Lee et al. [31] reported on immediate implant placement combined with connective tissue graft to correct existing gingival recession and revealed predictable success for immediate implant placement in infected sites with aesthetic gingival harmony.

A previous meta-analysis compared the dimensional changes in soft tissue around immediate implant placement sites concomitant with a connective tissue graft with those at baseline [32] and demonstrated that immediate implant placement with a connective tissue graft exhibited no significant change at the midbuccal and interproximal gingival levels; although a change in WKG was observed (1.27 mm; 95% CI, −0.08 to 2.46; $p = .04$) compared with that at baseline. Only two [31,33] of the 10 studies included in the meta-analysis presented reports on immediate implant placement in infected sites. No active infection sites of teeth extraction due to endodontic failure, carious lesions or root or crown fractures were indicated in the other studies. Therefore, more studies investigating the necessity of immediate implant placement with a connective tissue graft in infected sites are needed.

In our study, guided bone regeneration was performed in two [18,19] studies, and connective tissue grafts were not performed in any of the studies. Further investigation is warranted to determine the effect of connective tissue grafts in infected sites where implants are immediately placed after tooth extraction.

We considered the origin and characteristics of infection in the included studies. The origin of infection can be categorized as periodontal or periapical; the characteristics of infection can be classified as acute or chronic. In the current meta-analysis, most included studies investigated immediate implant placement in periapical lesion sites, whereas only one study [21] assessed immediate implant placement in periodontally compromised sites. More studies are required to investigate the effect of periodontal versus periapical lesions in immediate implants. The characteristics of the infections were classified in only one study [22]. No statistical differences were observed in the survival rates of immediate implants in acute infection sites compared with chronic infection or non-infected sites.

Changes in probing depths and modified bleeding indices were investigated to determine the susceptibility of inflammation at implant sites. Many studies showed a positive correlation between periodontitis and peri-implantitis [34–37]. However, we could not determine a relationship between periodontitis and peri-implant inflammation due to the lack of data related to the periodontal infection site. Conversely, some studies reported retrograde peri-implantitis following immediate implant placement in periapically infected extraction sockets [38,39]. In this review, this type of implant failure was not recorded in the included studies. We did not observe an increase in probing depth or modified bleeding index in the periapical infection sites compared with the non-infected sites. Because probing depth and modified bleeding index are related to peri-implant health, the history of periapical infection seems to have a little effect on those parameters.

The current meta-analysis has several limitations. First, the quality of the selected articles is questionable due to the moderate-to-high risk for bias. This might be inevitable to some extent because concealment of the infected extraction sites was not possible at the time of surgery; therefore, blinding and randomization could not be performed. Second, the heterogeneity of the included studies may be attributed to variations in the follow-up periods, origin of the infections and study designs. Well-designed and long-term follow-up studies are required to obtain more reliable results.

Conclusion

The results of our meta-analysis suggest that immediate implant placement in periapically infected extraction sockets is feasible following cautious debridement and the use of proper surgical protocols. In addition, changes in the soft tissue profile and aesthetics should be considered when performing immediate implant placement in infected sites. In future studies, more detailed descriptions and examinations of extraction socket sites, including a more detailed case definition, are necessary to investigate the feasibility of immediate implant placement in infected sites.

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Disclosure statement

The authors report no conflicts of interest related to this study.

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