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The effect of reconstructive techniques as treatment modality for peri-implant osseous defects – a systematic review and meta-analysis

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ABSTRACT

Objectives: The aim of this systematic review is to compare conventional peri-implant flap surgery and reconstructive surgical techniques regarding evidence of remission from peri-implantitis.

Material and methods: Searches were made among randomized controlled trials evaluating clinical aspects and the changes in marginal bone level before and after surgical treatment of peri-implantitis, with and without bone substitute.

Results: Nine published articles and 442 patients were eligible for inclusion in the study. Reconstructive techniques exhibited a greater extent of defect fill than conventional surgical techniques alone. No significant differences could be found for clinical measures of peri-implant disease (bleeding on probing and reduction of probing depth) from baseline to the 12-month follow-up.

Conclusions: With regards to the clinical measures of disease, our review shows that there are no differences between open flap debridement and regenerative surgery. From an esthetic standpoint, it may however be that regenerative measures may lead to improvement but further publications with this focus will be necessary to verify this.

INTRODUCTION

Peri-implant mucositis and peri-implantitis are pathological conditions involving the peri-implant mucosa and additional supporting tissues in response to bacterial load [1]. Peri-implantitis is a local inflammation process involving, at first, the peri-implant mucosa, which may later lead to progressive loss of the peri-implant bone [2]. The clinical characteristic of peri-implant mucositis is bleeding on gentle probing. In the case of peri-implantitis, additional evidence of progressive radiographic bone loss is required [1]. Accordingly, peri-implant health is characterized by the absence of suppuration and bleeding on probing (BoP) [1].

The general prevalence of the disease is commonly estimated to be approximately 14.5–16% [3,4]. Finding a common framework to analyse examination data and to make an evaluation of the general prevalence of peri-implantitis has been strenuous work, given different case definitions and the different extremes adopted for marginal bone loss [5–7].

Different treatment protocols for peri-implantitis have been proposed and can be divided into non-surgical therapies and surgical therapies [8–10]. The aim of the non-surgical therapies is to arrest the infection by removing the biofilm from the implant surface, thereby limiting bacterial penetration into the implant site [8]. Non-surgical therapies are effective and decisive on peri-implant mucositis [1]; however, insufficient in the treatment of peri-implantitis [1].

Currently, the main therapeutic approaches for the surgical treatment of peri-implantitis are access flap surgery sometimes with apical positioning of the mucosa and with or without osseous recontouring for pocket depth (PD) reduction. In conjunction with the surgical treatment of peri-implantitis, various strategies for reconstruction of the peri-implant osseous defect have been suggested [8].

The conventional surgical techniques often result in recessions of the peri-implant mucosa around the dental implants, entailing deterioration of the aesthetics of the dental implants [8,11,12]. With reconstructive techniques, on the contrary, the ambition is to reconstruct lost peri-implant tissue attachment and preserve the aesthetic situation [8].

Dental implants are inserted with the aim to restore missing teeth and the dogmatic understanding among therapists has been that implants will be lasting a life time. In this context, it is unfortunate that most studies evaluating various strategies for treatment of implant complications are short and often with follow-up less than a year. To be able to draw clinical and useful conclusions, the follow-up period needs to be of appropriate length [13]. As far as we know, the most recent and extensive review published on the topic addressed

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exclusively the effectiveness of bone substitutes or bone
grafts calculating the statistical evidence for a successful
result among studies employing such materials [14]. The
present study has a wider approach and addresses all form
of reconstructive materials and consequently a larger count
of studies can be included.

The aim of the present systematic review is to assess the
available scientific literature on the impact of the surgical treat-
ment techniques for peri-implantitis and to evaluate if there are
any beneficial effects of reconstructive techniques. Specifically,
the aim was to answer the following PICOS question: In patients
with peri-implantitis (population), what is the effect of different
approaches of surgical treatment (intervention and comparison)
on the radiographic and clinical aspects of peri-implantitis (out-
comes), in randomized control trials with at least 12 months of
follow-up. The purpose of this systematic review is to compare
reconstructive techniques with conventional flap surgery in terms
of the effect on the outcome (absence of BoP or suppuration, PD
reduction and radiographic evidence of marginal bone level
(Mbl)) in the treatment of peri-implantitis. The review only
includes randomized controlled trials (RCTs) in which surgical
techniques employing measures of reconstruction of lost
peri-implant attachment has been tested.

Materials and methods

This systematic review was conducted according to PRISMA
(Preferred Reporting Items for Systematic Reviews and
Meta-Analyses), an instrument designed to improve the qual-
ity and transparency of systematic reviews [15,16]. PRISMA
relies on detailed and reliable reporting of study results [16].
The review was registered on Prospero with the reference
number CRD42022301820.

A research plan was presented prior to commencing the
review and a PICO was established.

PICO

Population
Patients diagnosed with peri-implantitis.

Intervention
Surgical treatment of peri-implantitis.

Comparison
Reconstructive surgical treatment versus open flap debride-
ment alone.

Outcome
The observed outcome was the absence of BoP or suppura-
tion, PD reduction and radiographic evidence of Mbl/loss.

Search strategy
An electronic search was performed in two databases,
PubMed and Scopus.
reported in the original studies, median was used as a proxy for mean and range. We performed an analysis on the nine included studies focusing on study outcomes: bone level radiographic variation, variation in PPD and BoP [2,17–19,21–24].

Results

Study selection process

The database search produced 210 results on PubMed and 56 results on Scopus. Seven articles were searched manually. Among the selected articles, 35 were removed because of duplicates. Another 175 articles were removed due to lack of relevance to the research question. Among the 65 remaining studies, only nine RCT studies fulfilled the eligibility criteria of the research purpose, as illustrated in the flowchart (Figure 1) [2,17–24].

Characteristics of the included studies

Nine studies that had a follow-up period of at least 12 months were included [2,17–24]. The study by Isheed et al. [21] had an extended follow-up at 3 and 5 years, while the study by Andersen et al. [20] provided a 7 years follow-up.

Table 1 shows the study characteristics and the most significant variations in the clinically measured parameters.

Surface decontamination procedure

The surgical procedure was similar in all studies. A soft tissue flap was elevated in order to provide access and allow proper

Table 1. Characteristics of included studies according to clinical and radiographic measurements.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Definition of peri-implantitis</th>
<th>Follow-up</th>
<th>Principal findings</th>
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<tr>
<td>[17]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Implant with intrabony defect on Rx</td>
<td>12 months</td>
<td>Test 16 (PTG) Δ Mbl + 2.4, p &lt; .001 Δ Mbl + 0.1 p &lt; .001 Δ PPD 1.7 Δ PPD 2.6 Δ BoP 0.38 (sites) Δ BoP 0.56 (sites)</td>
</tr>
<tr>
<td>[18]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Intraosseous defect ≥ 3 mm on Rx</td>
<td>12 months</td>
<td>Test 33 (PTG) Δ Mbl + 3.6, p &lt; .0001 Δ Mbl + 1, p &lt; .0001 Δ PPD 2.8 mm Δ PPD 2.6 mm Δ BoP % 56 Δ BoP % 45 Δ Pus % 23 Δ Pus % 26</td>
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<tr>
<td>[19]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Angular osseous defect ≥ 3 mm on Rx</td>
<td>12 months</td>
<td>Test 9 (EMD) Δ Mbl + 0.9 mm Δ Mbl –0.1 mm Δ PPD 2.8 mm Δ PPD 3 mm Δ BoP 6 Δ BoP 3 (sites) Δ Pus 8 Δ Pus 5 (sites)</td>
</tr>
<tr>
<td>[20]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Angular osseous defect ≥ 4 mm on Rx</td>
<td>12 months</td>
<td>Test 6 (PTG) Δ Mbl + 2.6 mm Δ Mbl + 1.05 mm Δ PPD 2.7 mm Δ PPD + 3.5 mm Δ BoP 15% Δ BoP 17%</td>
</tr>
<tr>
<td>[21]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Angular osseous defect ≥ 3 mm on Rx</td>
<td>36 months</td>
<td>Test 14 (EMD) Δ Mbl + 0.9, p &lt; .109 Δ Mbl –0.1, p &lt; .109 Δ PPD 3.6 Δ PPD 2.5 Δ BoP % 80 Δ BoP % 62.5 Δ Pus % 20 Δ Pus % 33</td>
</tr>
<tr>
<td>[22]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Osseous crater-like defects ≥ 3 mm on Rx</td>
<td>12 months</td>
<td>Test 21 (Endobon) Δ Mbl + 0.7, p &lt; .09 Δ Mbl + 0.2, p &lt; .09 Δ BoP % 32.4 Δ BoP % 32.5 Δ Pus 8 Δ Pus 6</td>
</tr>
<tr>
<td>[23]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Angular osseous defect ≥ 2 mm on Rx</td>
<td>6 months</td>
<td>Test 34 (Bio-Oss + Geistlich) Δ Mbl + 1.08 mm Δ Mbl + 0.24 mm Δ PPD 2.88 mm Δ PPD + 1.64 mm Δ BoP 39% Δ BoP 14% Δ BoP 12 Δ BoP 10</td>
</tr>
<tr>
<td>[24]</td>
<td>PPD ≥ 5 mm, BoP or Pus + Osseous defects ≥ 3 mm on Rx</td>
<td>12 months</td>
<td>Test 39 (Bio-Oss Collagen) Δ Mbl + 2.1, p &lt; .0001 Δ Mbl + 1.0, p &lt; .0001 Δ PPD 2.3 mm Δ PPD 1.9 mm Δ BoP 1 (site) Δ BoP 1 (site) Δ BoP 1 (site) Δ BoP 1 (site) Δ BoP 1 (site)</td>
</tr>
</tbody>
</table>

Δ Mbl (Mbl baseline – Mbl 12 months): marginal bone level; Δ PPD % (PPD baseline – PPD 12 months) %: pocket probing depth; Δ BoP % (BoP baseline – BoP 12 months) %: bleeding on probing; Δ Pus % (Pus baseline – Pus 12 months) %: suppuration on probing.
Figure 1. PRISMA flowchart to demonstrate the methodology applied to a selected article.

Table 2. Summary of risk of bias for all considered studies.

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<td>Allocation concealment</td>
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<tr>
<td>Blinding of participants and personnel</td>
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<td>Blinding of outcome assessment</td>
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<td>Incomplete outcome data</td>
<td>+</td>
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<td>+</td>
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<td>-</td>
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<td>Selective reporting</td>
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Radiographic bone level changes, Forest plot 1.
decontamination of the implant site [2,17–24]. Different decontamination modalities were recorded. Titanium curettes or instruments were used in almost all studies [2,17–21,23,24]. In three studies, titanium curettes and a titanium brush were used [18,23,24]. Emanuel et al. [22] used ultrasonic, sonic or hand instrument but did not specify the material these instruments were made of. Different chemical decontaminant products were used during surgery: 24% ethylenediaminetetraacetic acid [17,20], H₂O₂ [2,18,23] and sterile saline solution [2,18,19,21–24].

**Surgical intervention**

Porous titanium granules (PTGs) were the material of choice in three of the analysed studies [17,18,20]. Emdogain (EMD, Straumann AG, Basel, Switzerland) is another important material composed of an enamel matrix protein-derived gel product with amelogenins that was used by Isehed et al. [19,21].

D-PLEX500, a bone graft made up of medical grade β-tricalcium phosphate (β-TCP) granules, half of them coated with a matrix of poly(lactic-co-glycolic acid) (PLGA), lipids and doxycycline hyclate, was the material elected in one study [22].

Bone filling composed of deproteinized bovine bone mineral (Endobon xenograft granules and DBBM) was used by Renvert et al. [2,23]. Derks et al. [24] used a natural bovine bone mineral (Bio Oss Collagen, Zurich, Switzerland) as bone filling material.

Open flap debridement is the conventional surgical intervention used in the control groups of all studies included in this review [2,17–24].

**Perioperative interventions**

The studies differed in the use of perioperative antibiotic regimes. Amoxicillin 750 mg twice a day was administered by Derks et al. [24] during 10 days starting three days prior to surgery. Amoxicillin 500 mg three times a day and metronidazole 400 mg twice a day were used in three studies [17,18,20]. In the study by Wohlfahrt et al. and Andersen et al. [17,20], it was prescribed three days prior to treatment and continued until seven days after surgery, while in the study by Jepsen et al. [18], it was prescribed one day before surgery and continued for eight days postoperatively. Renvert et al. [2,23] based its perioperative antibiotic regime on Zitromax 500 mg on day 1 and Zitromax 250 mg on day 2–4 postoperatively. In three studies, no perioperative or postoperative antibiotic regime was administered at all [19,21,22].

**The management of implant superstructures**

In four of the analysed studies, the screw retained superstructures were removed prior to surgery [17,19–21,24]. The other studies did not mention removal of the implant superstructures before surgery [2,18,22,23].

**Clinical measurements**

Clinical measurements/assessments (BoP, suppuration and peri-implant PD), and radiographic examinations were carried out at baseline and after 12 months in all studies [2,17–24]. Isehed et al. [21] followed the study group with regard to clinical and radiographic examinations for up to five years. The clinical examinations in Derks et al. [24] were performed at baseline and at 6 and 12 months, while the radiographic examinations were performed at baseline and at 12 months. Emanuel et al. [22] performed all clinical and radiographical examinations at baseline and at 6 and 12 months. Renvert et al. [23] reported clinical examinations at baseline and every 3 months up to 12 months in addition to radiographic assessments at baseline, 6 and 12 months.

**Post-surgical antimicrobial therapy**

Eight of nine studies used chlorhexidine-based mouth rinses and recommended (or instructed) patients to apply modified oral hygiene procedures for two to six weeks postoperatively [2,17–19,21,23,24]. Emanuel et al. [22] did not mention any modified oral hygiene procedures or ordination of chlorhexidine-based mouth rinses.

**Baseline and follow-up radiographic examinations**

Four out of nine studies provided thorough reports on the radiographic instrumentation and techniques that were used [17,18,20,21]. An intraoral analogue radiograph technique was used in three studies [17,18,20], and a digital technique was used by Isehed et al. [19,21]. No information was provided about the kind of radiographs taken in the other studies [2,22–24].

**Marginal bone level**

Marginal bone level is the primary outcome in all nine studies included in the review [2,17–24].

The defect height was clinically measured in millimetres from a well-defined reference point at the most coronal part of the implant body at baseline [17,20]. After 12 months, radiographs from baseline and the 12-month examinations were compared using the same reference points, allowing calculation of the change in defect height and percentage of intrabony defect fill [17,20].

The radiographic measurement of defect height, width, marginal and horizontal bone level was performed at baseline and at 6 and 12 months to obtain data on changes from baseline to 12 months regarding vertical defect depth, Mbl, percentage of defect fill, and percentage of defect resolution [18]. The clinical evaluation and measurement of the bone defect provided information regarding defect depth at the deepest point and defect width in millimetres [18]. The clinical bone defect depth was measured during surgery [19,21], while bone level variations over time were estimated radiographically by comparing radiographs taken at baseline and at 12 months after surgery [19]. The radiographic data on bone defect depth for years 3 and 5 were...
obtained either at the specialist clinic or from the general dentist [21]. All data processing and evaluation was performed by an oral radiology specialist [19]. Intraoral radiographs were studied from baseline to 12 months after the surgical intervention and searched for evidence of radiographic defect fill. The distance from the implant platform to the most coronal bone/defect fill to implant contact was also measured [2]. Intraoral radiographs were evaluated by comparing the deepest site at baseline with intraoral radiographs of the same site 12 months after surgery [23]. The bone defect was clinically examined with a probe and the depth and width were registered, as were defects in geometry [24]. The same defect was examined radiographically and the baseline Mbl was assessed and compared with radiographs taken 12 months after surgery [24]. Clinically, the bone defect was investigated measuring the clinical attachment loss as sum of recession and PD usually from the implant shoulder to the bottom of the pocket, all measurements were done in millimetres [22]. Periapical radiographs were studied in relation to an implant reference point, usually the shoulder, all measurements had the implant thread as a reference and differences from baseline Mbls to Mbl at follow-up was easy [22]. Reconstructive techniques, as reported in Table 1, produce greater defect fill than conventional surgery alone [2,17–24].

From the results shown in Forest plot 1, the pooled OR for the nine studies points to a greater defect fill for the test group (WMD = 1.01 mm; 95% CI: 0.55/1.46; n = 9, p = .0001) (Figure 2).

**Bleeding on probing**

Four of the included studies reported meticulously on the measurement process of BoP [17,18,23,24]. BoP was evaluated 30 s after probing [17,18] or 15 s after probing [24]. None of the treatments had a significant impact on BoP and any significant difference among the test and control groups was reported after 12 months [2,17–24].

There were no statistically significant findings, indicating no greater reduction in BoP in either the test or the control group in the nine analysed studies, Forest plot 3 (Figure 3).

**Probing pocket depth**

Eight of the included studies reported on PPD as an outcome [2,17–20,22–24]. One study did not report on PPD as an additional outcome for years 3 and 5 of the follow-up period [21]. Andersen et al. reported PPD as an additional outcome for year 7 of follow-up [20]. PPD was recorded at baseline and 12 months after surgery at six sites around each implant [17,18,20] and at four sites per each implant [2,19,21,23,24]. Measurements were made to the nearest millimetre [2,18,23,24]. The PPD was reported for both the test and the control group. Both interventions had promoted a marked decrease in PPD at 12 months, but no significant difference was reported between groups [17,18,20,22–24]. Measurements were made to the nearest millimetre [2,18,23,24]. The PPD was reported for both the test and the control group. Both interventions had promoted a marked decrease in PPD at 12 months, but no significant difference was reported between groups [17,18,20,22–24]. One study showed a greater decrease in PPD in the test group than in the control group [2]. The analysis failed to identify a significant difference in terms of PD reduction between the test and the control groups in the seven analysed studies, Forest plot 2 (Figure 4).
**Discussion**

This systematic review aimed to compare the different outcomes of conventional surgical techniques and reconstructive surgical techniques as treatments for peri-implant osseous defects.

The latest systematic review addressing this field was conceived with a limited focus on reconstructive techniques employing radiopaque bone graft or bone substitute materials; meta-analysis was calculated exclusively on studies related to such materials [14]. In this review, we included all types of applied materials such as amelogenins and titanium granules with the aim to increase the spectrum of knowledge.

The population in the study was chosen from studies conducted on patients diagnosed with peri-implantitis. The examined interventions were reconstructive and conventional surgical techniques that were compared to determine the outcome in the treatment of peri-implant osseous defects. The examined outcomes were absence of BoP or suppuration, PD reduction and radiographic assessment of the Mbl. The most significant result shown by the meta-analysis was a greater gain in clinical attachment for the test group's patients (standardized mean difference = 0.6 mm). The reported Mbl differed between studies [2,17–19,21,23,24]. However, the meta-analysis failed to prove statistically significant differences in PD and BoP between conventional and reconstructive surgical techniques.

Contrary to the nine studies that fulfilled the criteria for this systematic review, most of the studies found were observational and non-randomized studies. An additional parameter that reduced the number of included studies dramatically was the length of the follow-up, with the most common period being six months, i.e. too short to determine the outcome of the examined techniques as we see it. A longer follow-up period with a minimum of 12 months was motivated by the need to provide information on the stability over time of the outcomes after surgery [21].

There is insufficient evidence to allow definition of a single superior treatment in terms of effect and predictability among the reconstructive techniques [11]. Bone filling materials dominate the reconstructive techniques [2,17–19,21,23,24].

The small number of available RCTs and the use of different materials in different studies lead to data disturbance interpretation difficulties when it comes to defining clinical recommendations [27]. There is, on the other hand, clear evidence that patients observing strict supportive therapy programs sustain positive long-term outcomes after reconstructive techniques independently of the technique chosen [28].

The studies reported a wide range of results (+0.7–3.6 mm) on defect fill [2,17–19,21,23] and one study [24], reported no defect fill when reconstructive surgery was compared with conventional surgery [24].

One possible reason for the multitude of outcomes is the difficult comparison of different implant systems included in the analysis [29]. The same length implants of the same or a different brand may differ in pitch thread, causing an overestimation or underestimation of the degree of pathology when the thread exposure is the grading instrument [29]. Moreover, different implant surface features could be a reason for different remission grades from peri-implantitis, an aspect not yet fully understood or investigated [18,21].

The surgical technique used in all the studies involved elevating a full thickness mucoperiosteal flap around the affected implants and removing granulation tissue and dental calculus [2,17–19,21,23,24]. When combined, the great variation in surgical techniques, reconstructive materials and bone defect morphology results in a plethora of different outcome values [24].

The fact that different materials for bone augmentation were used is worth considering [2,17–19,21,23,24]. The PTGs and Endobon were radiopaque [2,17,18,20,23], while the presence of EMD per se cannot be observed radiographically [19,21]. The choice between different grafting materials might affect the treatment outcome, which cannot be ignored in this review [24]. Although the implant surface decontamination procedures differ [2,17–19,21,23,24], there is no evidence of a specific chemo-mechanical decontamination procedure that improves the postsurgical outcome. Two studies presented a minor defect fill difference between the test and the control group, but neither a peri-surgery, nor a post-surgery antibiotic regime was prescribed in these two studies [19,21]. The remaining seven studies applied an antibiotic regime [2,17–19,21,23,24,30] suggested in a recent review [30] that the reason for the differences in defect fill seen after peri-implant surgery is related to the magnitude and morphology of the bone defect, with the deepest ones being better candidates for reconstructive techniques than for conventional surgical techniques [30].

In a recent systematic review [31], it is suggested that the adjunctive use of antibiotics in the surgical treatment of peri-implantitis has a beneficial effect [31]. A reduction of up
to one mm in PPD and radiographic defect fill was reported in the groups treated with antibiotics after a follow-up period of 12 months [31]. The long-term effects are of course of interest. A study on adjunctive use of antibiotics in non-reconstructive peri-implant surgery showed that this beneficial effect was not notable after three years of follow-up [31,32]. Isehed et al. [19,21] did not add an antibiotic regime to the surgical treatment of peri-implantitis but still achieved improvements in the outcomes of PPD and BoP [19,21]. For this reason, it is unclear and impossible to determine whether adherence to an antibiotic regime alone has impacted the outcomes in the considered studies. Moreover, Carcucu et al. [33] suggest that despite that antibiotic regimes have certain positive effects on the outcomes of peri-implant surgery, their administration should be restricted to carefully assessed peri-implant surgeries [33]. Antibiotic resistance is another growing phenomenon pointing at the necessity to limit the administration of local and systemic antibiotics [34].

Although BoP, suppuration on probing and PPD decreased in all seven RCT studies after surgical treatment of the peri-implantitis, the parameters did not differ in a statistically significant way from those in the control groups [21,17–19,21,23,24]. Persisting BoP is a pattern already observed in several studies and it has been suggested that it is due to the extreme difficulty of performing daily peri-implant home care [24].

The removal of superstructures was not mentioned in three of the studies [2,18,23]. There is consensus about the importance of removing the superstructures before probing the peri-implantitis defects to increase measurement reliability [35]. Discrepancies between measurements of peri-implantitis defects have been reported when the same defect was probed with and without connected superstructures.

In addition to improving clinical parameters and enabling superior defect fill, reconstructive techniques play a role in sustaining soft tissue height [24,25].

A strong positive factor of this systematic review is that all the studies selected were RCTs. A limiting factor is the different bone substitute materials used as well as different preoperative and surgical protocols. Future research should aim to carry out RCTs with longer follow-up periods in order to better examine the superiority of reconstructive surgery over conventional surgical techniques.

Conclusions

Given the limitations of this study and the sparse literature, the evidence may suggest that reconstructive techniques and conventional surgical techniques have a similar clinical outcome. Reconstructive techniques may potentially be more suitable than open flap debridement alone in aesthetic areas, given a certain degree of support for the soft tissues; however, more longitudinal RCTs comparing conventional surgical techniques with reconstructive techniques are suggested.

Acknowledgements

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Author contributions

MR and SS provided substantial contributions to the conception and design of the study and in the acquisition, analysis and interpretation of data, however MR under supervision. HA contributed to the conception and design of the study and interpretation of data for the work. SS, MR and HA drafted the work and revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved. All authors contributed to the article and approved the submitted version.

Disclosure statement

The authors declare no conflict of interest.

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