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REVIEW ARTICLE

Minimal invasiveness in the reconstructive treatment of peri-implantitis defects

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1 | INTRODUCTION

Peri-implantitis was defined at the 2018 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions as a biofilm-mediated pathologic condition occurring in the tissues surrounding dental implants, characterized by peri-implant mucosal inflammation and progressive bone loss.[1] Different treatments have been proposed for peri-implantitis, including non-surgical and surgical approaches, with mechanical and/or chemical surface decontamination, the use of antimicrobial products and various surgical techniques (ie, access flaps, resective or reconstructive procedures).[2] While nonsurgical treatment seems to provide modest and nonpredictable outcomes,[3,4] different surgical approaches have proven to be more effective in terms of disease resolution.[5,6]

In the treatment of peri-implantitis, the classical surgical approach entails a mucoperiosteal flap, the removal of the granulation tissue, and the detoxification of the contaminated implant surface. However, while nonreconstructive surgical approaches (ie, access flaps or resective surgery) aim to arrest further progression of the disease, reconstructive procedures aim to regenerate the intrabony component of the osseous defect. Nowadays, the decision-making process in the selection of the surgical technique in the treatment of peri-implantitis is based on the configuration of the peri-implant bone defect. As most peri-implantitis lesions feature a combined defect configuration including a supracrestal (class II) as well as an intra-bony component (classes Ia-e),[7] a surgical procedure combining implantoplasty at the supracrestal and buccally exposed implant surfaces (ie, class Ib and Ic defects), concomitant to the application of bone substitute materials (or other regenerative approaches) at the intrabony defect component, has been proposed, yielding positive results.[8]

A recent systematic review with meta-analyses, on the efficacy of the reconstructive surgical treatment in peri-implantitis-related bone defects, showed that these techniques may lead to larger improvements in marginal bone levels and defect fill over open-flap debridement.[9] However, no statistically significant differences could be observed for clinical parameters, such as probing depth or bleeding on probing. Nevertheless, subset meta-analyses could not be conducted to analyze confounders of the outcomes. Hence, it could be hypothesized that, similar to what occurs in regenerative procedures around teeth, diagnostic/preoperative considerations, flap design, the choice of biomaterials/adjuncts, and suturing techniques, may influence the short- and long-term outcomes, including patient perception of the treatment, the incidence of complications and the morbidity/invasiveness of the intervention[10-14] in the reconstructive therapy of peri-implantitis lesions.

It is, therefore, the aim of the present review to describe the factors and techniques that may contribute to minimal invasiveness in the reconstructive treatment of peri-implantitis defects. To fulfill this objective, a systematic search, to comprehensively evaluate the

available scientific literature, on minimally invasive reconstructive approaches in the surgical treatment of peri-implantitis lesions, has been performed.

2 | ELECTRONIC SEARCH

A systematic search strategy was conducted to evaluate the existing body of evidence on minimal invasive strategies used in reconstructive therapy for the management of peri-implantitis.

2.1 | Eligibility criteria

The eligibility criteria were as follows: (a) clinical studies on reconstructive therapy of peri-implantitis, including "combined" approaches (ie, resective/implantoplasty plus reconstructive); and (b) randomized clinical trials, controlled clinical trials, or prospective/retrospective case series, with a minimum of 10 patients (five per group in controlled studies).

2.2 | Screening strategy

The electronic search was performed in Medline via PubMed. The search was limited to human subjects and to studies reported in English. The search strategy was an update of the one prepared for the European Workshop of Periodontology on Bone Regeneration,[9] adding the term "minimal invasiveness" [i.e. (((((((peri implantitis) OR peri-implantitis) OR periimplantitis)) AND ((((((surgical treatment) OR surgery) OR surgical) OR reconstructive) OR regenerative) OR regeneration))) NOT (((review) NOT in vitro) NOT animal))) AND ((minimal*) OR invasive*)].

2.3 | Results of the systematic screening

The initial electronic search identified 808 records in PubMed. However, after screening for titles and abstracts, only two recently published manuscripts focusing on reconstructive therapy of peri-implantitis were identified.[15,16] Therefore, it was decided to remove the term "minimal invasiveness" from the search strategy and update the search from February 2018 to July 2021. This search yielded 305 articles published since February 2018. After abstract screening and full-text evaluation, 19 manuscripts corresponding to 18 investigations fulfilled the inclusion criteria. The hand search identified six additional manuscripts. However, it should be noted that most of these manuscripts did not describe any particular techniques that could be considered "minimally invasive" or evaluate patient-reported outcome measures. Therefore, it was decided that, for the present review, only those manuscripts resulting from the described search and the ones identified for the XV European Workshop on Periodontology[9] were considered. Thus, studies included were those that presented reconstructive approaches, that may be considered minimally invasive, or that proposed innovative techniques, devices, or adjuncts that may result in less morbidity for the patient, independently of whether properly evaluated or not. Further considerations related to the diagnostic examinations, the incidence of complications, and the factors influencing the long-term results were also considered for inclusion in the current review.

3 | MINIMAL INVASIVENESS IN RECONSTRUCTIVE THERAPY OF PERI-IMPLANTITIS: MYTHS AND REALITIES

By definition, "minimal invasiveness" refers to diagnostic or therapeutic techniques that limit the invasiveness while increasing treatment predictability along with accuracy. A minimal invasive therapy should therefore lead to an uneven and smooth healing process resulting in reduced/minimal sequalae compared with conventional approaches. In the arena of periodontal regeneration, this term has been used for more than 3 decades to describe procedures that pursued less invasion by means of minimal flap elevation.[17-19] These strategies frequently include "papilla preservation" techniques and have claimed the use of microsurgical instruments and magnification to enhance access and visibility. These modalities have certainly led to effective outcomes in terms of clinical attachment level and radiographic bone gains while reducing marginal recession and papilla collapse.[11] Therefore, their implementation in the management of peri-implantitis lesions might be suitable to reduce soft tissue changes that are frequently exhibited after disease resolution.[20] Nonetheless, it is important to note a few drawbacks that may limit "minimal invasion" in the therapy of peri-implantitis: (a) comprehensive mechanical and/or chemical and/or pharmacological and/or electrolytic implant surface detoxification is key to succeeding and, therefore, access is demanded[21]; (b) peri-implantitis bone lesions are two times larger in size than periodontal lesions[22]; and (c) peri-implantitis is often associated with local potentially predisposing factors such as the lack of keratinized mucosa[23] or inadequate implant position, and peri-implantitis bone lesions rarely present a pure circumferential infraosseous defect configuration.[24,25] Hence, the clinician must be aware that any attempt to pursue minimal invasiveness may conflict with long-term disease resolution.

As stated in the XV European Workshop on Periodontology, the evidence on the efficacy of reconstructive therapy at peri-implantitis–related defects is limited, because of the large variability in the results, even if it seems that a greater improvement in marginal bone level and in radiographic defect fill is expected.[9] Results from the present systematic review did not yield enhanced methods that might be considered of minimal invasiveness. Moreover, the search did not identify studies that addressed patient-reported outcome measures. To provide a more detailed view of the different aspects that may lead to minimal invasive procedures, the studies have been grouped according to: (a) surgical (eg, new flap designs, suturing techniques) and prosthodontic factors (eg, prostheses modifications), (b)

the use of products or devices that may impact upon invasiveness and morbidity (eg, growth factors, lasers, electrolytic cleaning), and (c) the use of antimicrobial adjuncts to grafting materials (eg, vancomycin, doxycycline).

3.1 | Surgical and prosthodontic factors

Only one manuscript presents a "minimally invasive" surgical technique and fulfills the inclusion criteria of the present electronic search (Table 1). [26] This pilot study included 10 patients with 10 implants diagnosed with peri-implantitis and presenting a contained peri-implant defect, as determined clinically and radiographically. The proposed mini-invasive surgical approach consists of the elevation of a flap to access the peri-implantitis defect only from one side (commonly the palatal/lingual), leaving the other side intact and limiting as much as possible the mesio-distal extension of the flap, avoiding vertical incisions and preserving the interdental papillae. According to the authors, healing was uneventful, and no relevant pain, hematoma, or edema were noted. However, even if mean probing depth was reduced after 1 year, treatment success, expressed as a composite outcome, was not presented, and the mean maximum probing depth at the studied implants was 7.9 mm at the end of follow-up.

TABLE 1 Scientific papers proposing minimally invasive surgical techniques in the reconstructive treatment of peri-implantitis considered for this review

Study	Intervention	Number of patients (number of implants)	Outcomes
Iorio-Siciliano et al.[26]	MISA consisting of the elevation of a flap only on one side (palatal aspect)	10 (10)	Significant PD reduction and radiographic bone gain were noted, with minimal mucosa al recession and limiting patient morbidity
Fletcher and Tarnow[27]	COAP, a flapless surgical technique designed to access the contaminated implant surface through the removal of a collar of soft tissue adjacent to the implant	3 (4)	Bone fill and absence of bleeding on probing were observed 8-24 mo after therapy. Minimal postoperative pain and swelling were reported
Wilson[28]	Videoscope-assisted minimally invasive surgical approach	1 (1)	No pain was reported after the procedure. No further bone loss but apparent bone fill was observed after 1 y, together with absence of deep pockets
Trombelli et, al.[29]	SPAL. In this technique a split-thickness flap is elevated leaving a periosteal layer creating a pouch to stabilize the xenograft. In case of insufficient keratinized mucosa, a connective tissue graft was placed on the buccal aspect	3 (3)	Treatment resulted into significant reconstruction of the peri-implant support in absence of deep pockets or inflammation
Noelken and Al-Nawas[32]	LAPIDER. Horizontal mucosal incision 5 mm apical to the marginal mucosa, subperiosteal coronal flap elevation, debridement of the implant surface with Er:YAG laser, grafting with particulated autogenous bone + connective tissue.	1 (1)	MBLs improved interproximally, buccally and orally at the 1-y examination. PDs and recession decreased significantly, while the facial mucosa thickness improved
Lee et al.[30]	PEAS. After the disconnection of the prostheses, the granulation tissue was removed through a peri-implant circular incision in a similar manner to the ENAP	1 (1)	The surgical intervention was effective in arresting peri-implantitis as no further bone loss but bone fill was observed over a 2-y period
Cortellini et al.[31]	Reconstructive approaches for the treatment of peri-implantitis lesions using PPF and MIST (ie, exposing just 1-2 mm of the defect-associated residual bone crest, avoiding "passing" the papilla and releasing incisions if possible)	21 (21)	Primary wound closure was obtained in 100% of the sites. Significant reduction in BOP and PD was observed. Significant radiographic bone fill was observed and maintained throughout the 5 y of follow-up (~2.5 mm). No discomfort or problem with daily activities was reported by the patients. Postoperative pain was of low intensity (ranging 10-24 on a 0-100 visual analog scale)

Abbreviations: BOP, bleeding on probing; COAP, circumferential occlusal access procedure; ENAP, excisional new attachment procedure; Er:YAG, erbium-doped yttrium aluminium garnet; LAPIDER, laser-assisted peri-implant defect regeneration; MBLs, marginal bone levels; MISA, mini-invasive surgical approach; MIST, minimally invasive surgery; PD, probing depth; PEAS, peri-implant excisional procedure and access surgery; PPF, papilla preservation flap; SPAL, subperiosteal peri-implant augmented layer.

Although they do not fulfill the preestablished inclusion criteria related to the sample size (10 patients), it is worthwhile presenting some case reports describing innovative techniques.[27-30,32]

The circumferential occlusal access procedure aims to solve some of the difficulties that may appear during regenerative procedures, such as a shallow vestibule, a thin mucosa, or sites without keratinized tissue.[27] These features may increase the risk for membrane exposure, in cases of barrier membrane use, with the consequent contamination and eventual loss of the graft.[33] In this technique, both the decontamination of the implant surface and the bone grafting, if indicated, are performed through the peri-implant sulcus. First, a collar of soft tissue surrounding the implant is removed using a curette/scalpel circularly around the implant, down to the base of the bone, to remove the inflamed tissue. In a second phase, if bone grafting is indicated, an interproximal knife is used to lift the inner part of the soft tissue surrounding the implant to create a pouch, the bone substitute is placed in the defect, and a collagen membrane, with a punch hole in the center, is placed over the head of the implant and into the pouch, covering the bone-grafting material without the need of any suture. As, in contrast to periodontal lesions, peri-implantitis lesions may frequently present bacterial invasion within the connective tissue,[34] the proposed approach, which includes peri-implant mucosa curettage and also favors clot stability, may somehow improve the results of nonsurgical therapy that has proven to be ineffective in most of the studies.[35] A conceptually very similar technique was proposed in 2021,[30] with the name of peri-implant excisional procedure and access surgery. This technique proposes the removal of the granulation tissue through a peri-implant circular incision, together with a chemical (hydrogen peroxide) and mechanical decontamination (with a titanium brush). However, two prerequisites are needed: (i) presence of enough keratinized tissue to avoid leaving the implant site without keratinized mucosa; and (ii) the possibility to remove the prostheses.

Other minimally invasive surgical approaches have been proposed, including the use of a videoscope to remove foreign bodies (eg, cement, titanium particles),[28] and the so-called subperiosteal peri-implant augmented layer technique, in which a periosteal pouch is created after performing a partial-thickness flap to stabilize a xenograft.[29] This technique was previously presented for the horizontal augmentation of the ridge at the time of implant placement in cases of the presence of dehiscence-type defects.[36] The rationale for the technique relies upon the stabilization of the graft particles and the clot by the periosteal layer, which may also act as a source of osteogenic cells.[37] However, further clinical and preclinical research is needed to determine the beneficial effects of this approach. The subperiosteal peri-implant augmented layer technique is described in detail in section 6 of the current work (Figure 1).

Apical accesses have been proposed in periodontal regenerative procedures to avoid placing incisions directly on top of the bone defects, following the nonincised papilla surgical approach.[38,39] Similarly, a modified surgical approach using the erbium-doped yttrium aluminium garnet laser has been proposed to overcome the soft tissue recession that may appear after peri-implantitis defects regeneration (laser-assisted peri-implant defect regeneration).[32] In this technique, a horizontal mucosal incision, 4-5 mm apically from the marginal mucosa, is made to gain access to the implant apex, and, after mucoperiosteal coronal flap elevation, the implant surface is debrided with the erbium-doped yttrium aluminium garnet laser, followed by grafting with particulate autogenous bone and a connective tissue graft. Conceptually, this approach avoids cutting the interdental papilla complex and the mucosal margin recession that may occur if incisions are made on top of the bone defect (Figure 2). However, long-term results are missing and definitive evidence in favor of this technique should be derived from properly conducted randomized clinical trials.

Finally, as inappropriate prosthetic designs may hamper adequate oral hygiene practices and have proven to be associated with peri-implantitis prevalence,[40] it is likely that prosthetic modifications allowing access to oral hygiene could be helpful to obtain the best results for peri-implantitis therapy. Even if it was performed in patients with peri-implant mucositis, a recently published randomized clinical trial clearly demonstrated that modifying the prostheses to allow better access for biofilm control resulted in a higher percentage of disease resolution at 6 months (66%) than in those cases in which only mechanical instrumentation was performed (9.6%).[41]

3.2 | Use of products or devices that may impact on invasiveness and morbidity

Historically, the decision-making process for reconstructive procedures of peri-implantitis defects has been influenced by classical periodontal and dental implant surgery. Specifically, the principles of guided tissue regeneration using a barrier membrane on top of the surgically treated area with the aim of stabilizing the graft and excluding the epithelium ingrowth have been widely used (Table 2).[42] One of the first proposals was published by Khoury et al[33] treating 41 deep peri-implant defects with either autogenous bone grafts alone or in combination with resorbable or nonresorbable membranes using a submerged healing approach. The reported clinical and radiographic data showed comparable results with no additional benefits for the sites that received a barrier membrane.[33] One aspect of the proposed technique that has to be emphasized is that the bone block harvesting procedure requires a second surgical site, with consequently increased patient morbidity. Furthermore, the application of an e-PTFE (Expanded Polytetrafluoroethylene) membrane may increase the risk of membrane exposure. Therefore, it is clear from the authors' perspective that such an intervention cannot be considered minimally invasive and should be avoided to minimize patient discomfort and limit the risk of postoperative complications. Similar conclusions were drawn by Roos-Jansäkeret al[43] in a 5-year randomized clinical trial where the adjunct benefit of a resorbable membrane use (test group) was investigated compared with a regenerative procedure without membrane (control group): the obtained results displayed a significant improvement in terms of clinical and radiographic outcomes without detecting a statistically

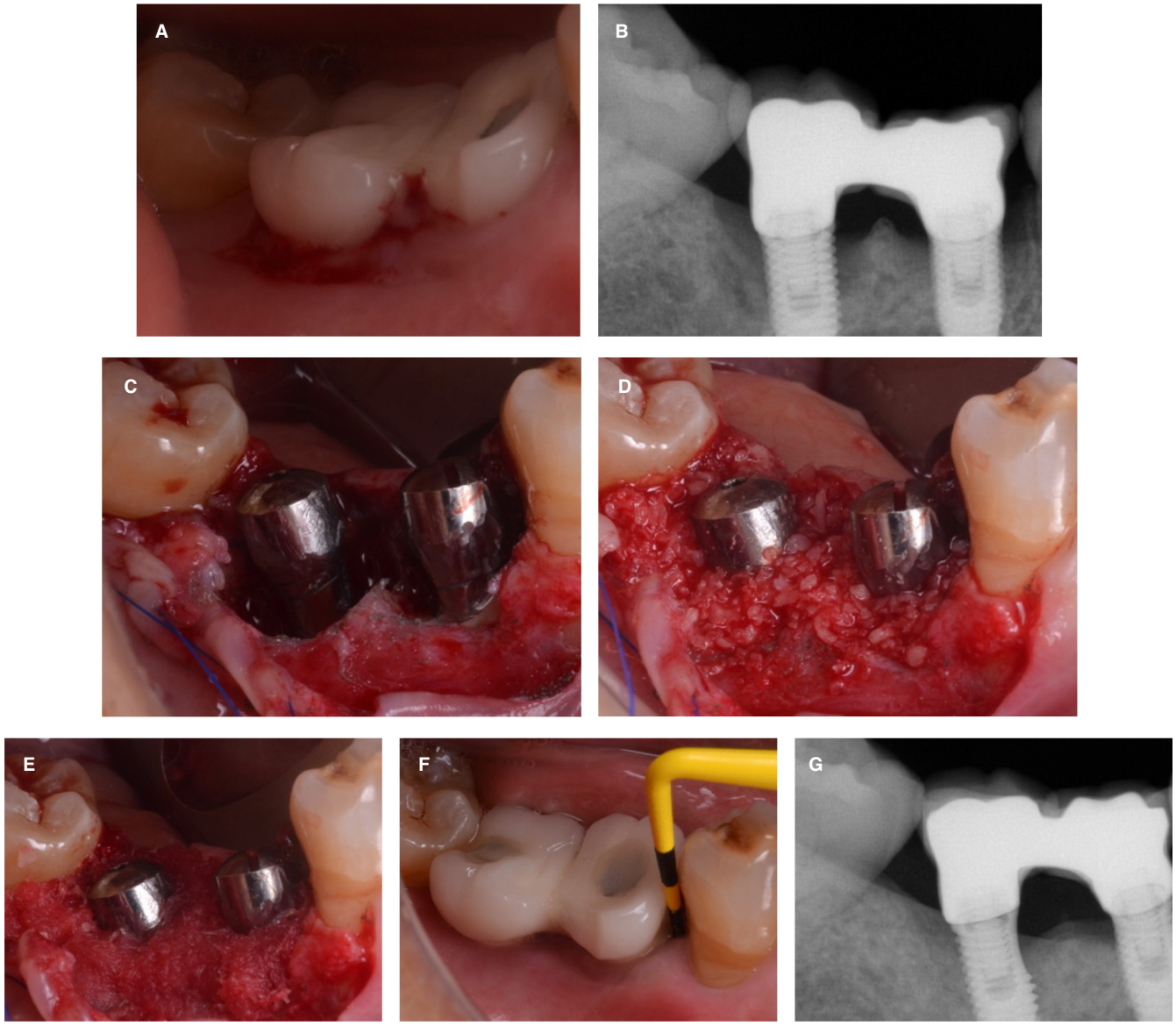


FIGURE 1 Advanced peri-implantitis lesion exceeding 50% of the implant length. A, Clinical presentation. Note profuse bleeding and suppuration. B, Periapical x-ray displays advanced bone loss with angular defects in the interproximal aspects. C, Upon surgical access a three-wall defect (class Ib) is noted. Implantoplasty was used as adjunct method to detoxify the implant surface. The SPAL technique is performed, where the periosteum is attached to the alveolar bone and outlining the lesion to promote enhanced stability of bone. D-E, Mineralized and demineralized bone allograft. F, Clinical disease resolution was demonstrated at 12-month follow-up. G, Radiographic bone gain was evident. SPAL, subperiosteal peri-implant augmented layer

significant difference between the two groups.[43] Consequently, despite the lack of solid evidence, the routine use of a barrier membrane as a pivotal step in the surgical reconstructive treatment of peri-implantitis might not be recommended. Nevertheless, in cases of deep noncontained defects, to stabilize the grafting material, its application might be taken into consideration.

Another controversial aspect that should be considered is the ideal grafting material. Historically, intra-orally harvested autogenous bone has been proposed because of its excellent characteristics.[44] Nevertheless, increased patient morbidity, a limited quantity of available material, and a high pattern of resorption have been described as major disadvantages.[45] Consequently, clinicians have searched for alternative materials with good clinical results, with the aim of reconstructing the lost peri-implant hard tissue and ideally promoting re-osseointegration.[46]

Growth factors, such as enamel matrix derivative or platelet-rich fibrin, have been proposed to improve the outcomes of reconstructive procedures around peri-implantitis defects. Scaffolds with platelet-rich fibrin contain several bioactive molecules, such as platelet-derived growth factor, transforming growth factor beta, and insulin-like growth factor, which may be progressively released during matrix fibrin remodeling in early healing stages. This ability has been demonstrated as capable of improving the outcomes of access flaps in the surgical treatment of peri-implantitis, in terms

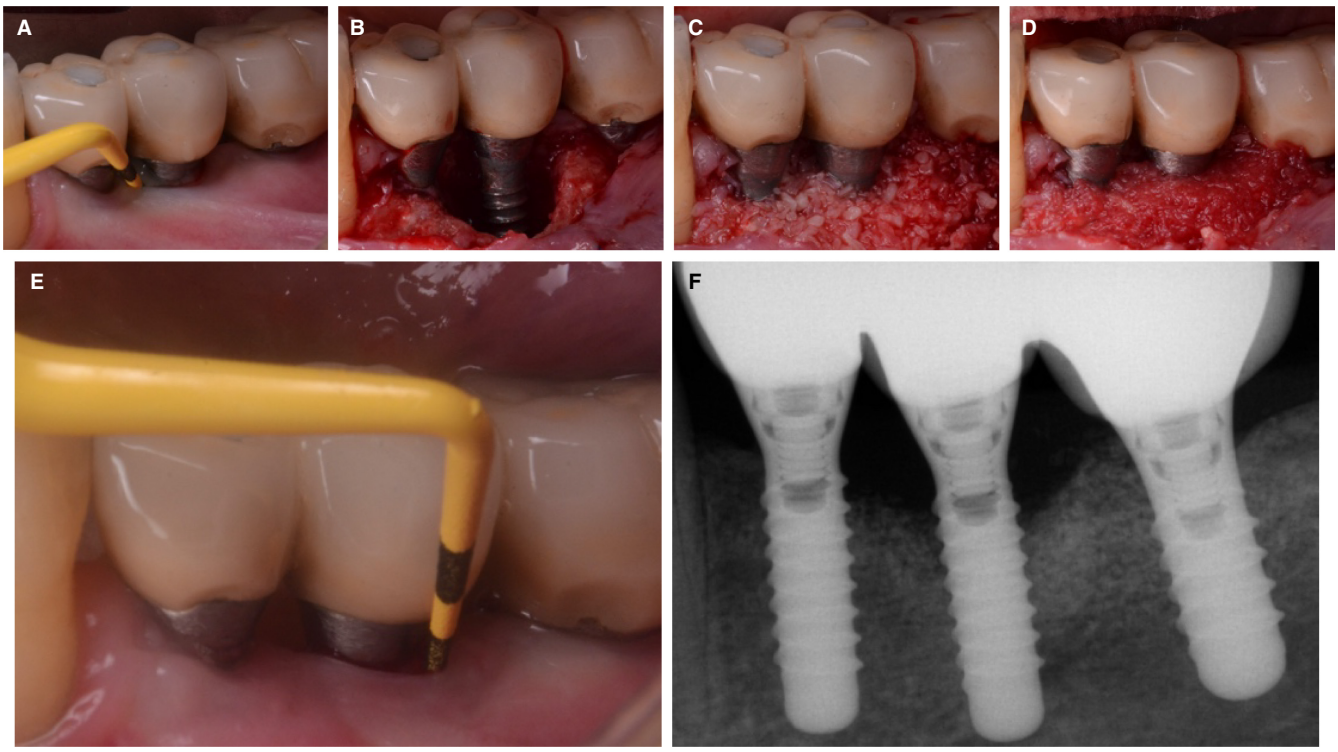


FIGURE 2 Peri-implantitis case scenario. A, Clinical examination unveiled suppuration and increased pocket depth from baseline. B, Upon clinical access a three-wall (class Ib) defect configuration is noted. Note the papilla preservation approach. A combination of C, Mineralized and D, Demineralized allograft was used for grafting after comprehensive surface detoxification by means of Ni-Ti brush and H_2O_2 for 2 minutes. E, Disease was resolved at 15-month follow-up with minimal soft tissue alterations. F, Note the bone gain to flatten bone architecture

of probing depth reduction and gains in clinical attachment level.[47] Particularly interesting is a prospective study evaluating the clinical effect of platelet-rich fibrin combined with guided bone regeneration in the reconstruction of peri-implantitis defects in 80 patients.[48] Patients were randomly allocated to the control group, treated with a bone substitute following guided bone regeneration principles, or to a test group, which received a mixture of platelet-rich fibrin and a bone substitute covered with platelet-rich fibrin membranes. Interestingly, levels of pain, 24 hours after the surgery, were significantly lower in the test group, indicating that the addition of platelet-rich fibrin may influence postoperative patient-reported outcome measures. Better results were also provided in terms of probing depth reduction and regenerated bone density. However, another investigation performed in Turkey, using demineralized bovine bone mineral, together with a different fibrin clot membrane (the so-called concentrated growth factors obtained by separation from centrifuged venous blood, using a different centrifuge machine, and presenting different mechanical characteristics in terms of stiffness), failed to provide any further improvement in the regenerative treatment of peri-implantitis defects when compared with demineralized bovine bone mineral plus a native collagen membrane.[49] No evaluation of the patient´s perspective of treatment was carried out in this study. If the morbidity associated with venous blood collection is overcome by the theoretically better postoperative perception by the patient, this needs to be properly evaluated in future clinical trials evaluating patient-reported outcome measures[50] more thoroughly.

Finally, amelogenins (enamel matrix derivative) could also accelerate wound healing by osteopromotive and antibacterial effects.[51] Specifically, enamel matrix derivative have proven to be able to promote blood vessels formation and expression of transforming growth factor beta, vascular endothelial growth factor, and fibronectin.[52] The first report of the possible use of enamel matrix derivative for the treatment of peri-implantitis was a case series of 51 patients with a 3.0-7.5 year follow-up.[53] Encouraging results after application of enamel matrix derivative to the decontaminated implant surface, followed by defect-filling with either a xenograft or an allograft previously hydrated with a platelet-derived growth factor and covered with a collagen membrane or a connective tissue graft, were observed. Probing depth reductions were approximately 5 mm, while radiographic bone level gains were approximately 3 mm. Similar results were presented in another case series of 30 patients with peri-implantitis, performed in Australia,[54] in which, after surgical access and debridement, defects were filled with a mixture of demineralized bovine bone mineral, enamel matrix derivative, and doxycycline powder. After a 3-year period, results were considered successful for 56.6% of the implants (probing depth < 5 mm, no further bone loss > 10%, no bleeding on probing/suppuration, no recession > 0.5 mm in anterior implants, or > 1.5 mm for posterior implants).

TABLE 2 Studies evaluating products or devices that may impact upon the invasiveness and morbidity of reconstructive procedures in the treatment of peri-implantitis lesions: interventions, number of patients/implants, and summary of main outcomes

Study	Intervention	N patients (implants)	Outcomes
Froum et al.[53]	Regenerative approach including surface decontamination, EMD, a combination of PDGF with DBBM or MFDBA, and coverage with a collagen membrane or a subepithelial connective tissue graft	38 (51)	No implant was lost during the follow-up (3-7.5 y). PD reduction ranged 3-10 mm. Radiographic bone gain was 3.8 mm in those implants presenting a visible interproximal defect at the baseline examination. Bone sounding was performed in those cases in which the greatest bone loss was on the facial or oral aspect of the implant, accounting for a 3.0 mm bone gain
Hamzacebi et al.[47]	Conventional access flap surgery adding the application of PRF	19 (38)	PRF group demonstrated higher mean PD reduction and more CAL gain after 6 mo
Isehed et al.[55,56]	EMD in access flap surgery (RCT)	29 (29)	At the 3-y follow-up visit, 100% of the implants survived in the EMD group, while in the control group survival was 83%. At the 5-y follow-up appointment, survival rates were 85% of the implants in the EMD group vs 75% in the control group.
Isler et al.[49]	Regenerative approach using DBBM covered either with a CM or CGF (RCT)	52 (52)	Treatment resulted in significant reductions of BOP and PD in both groups at 6 and 12 mo without significant differences among groups. Mean defect fill was also not statistically significant different between groups.
Mercado et al.[54]	Surgical access and debridement, defects filled with a combined mixture of DBBM, EMD, and doxycycline powder	30 (30)	56.6% of the implants were considered successfully treated according to a composite outcome (PD < 5 mm, no further bone loss > 10%, no BOP/suppuration, no recession > 0.5 mm for anterior implants and > 1.5 mm for posterior implants) after 36 mo
Schlee et al.[60,61]	Regenerative approach with DBBM plus autogenous covered with a CM after decontamination with EC or combination of an EC and a powder spray (RCT)	24 (24)	Mean PD and BOP were significantly reduced, while significant radiographic bone fill was observed 18 mo after therapy. No significant differences between groups were observed
Sun et al.[48]	Effect of adjunctive PRF to GBR with DBBM and a CM (RCT)	80 (80)	Pain and bleeding were significantly lower 24 h and 7 d after surgery in the PRF group. Compared with the control group, the PRF group revealed significantly higher regenerated bone density 60 and 120 d after surgery
Wang et al.[64]	Effect of adjunctive of Er:YAG laser in the surface decontamination prior to a reconstructive procedure with a mixture of DBBM plus allograft and covered with an acellular dermal matrix membrane (RCT)	24 (NR)	Laser irradiation led to a significantly higher PD reduction 6 mo after surgery. No differences were observed for CAL gain or radiographic linear bone gain

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; CGF, concentrated growth factor; CM, collagen membrane; DBBM, demineralized bovine bone mineral; EC, decontamination with an electrolytic method; EMD, enamel matrix derivative; Er:YAG, erbium-doped yttrium aluminium garnet; GBR, guided bone regeneration; MFDBA, mineralized freeze-dried bone allograft; NR, not reported; PD, probing depth; PDGF, platelet-derived growth factor; PRF, platelet-rich fibrin; RCT, randomized clinical trial.

Also testing enamel matrix derivative, a randomized clinical trial on the regenerative treatment of peri-implantitis, with or without adjunctive enamel matrix derivative, including 29 patients, was conducted in Sweden, providing results after 5 years of follow-up.[55,56] The primary outcome variable was implant survival, which was significantly superior in the enamel matrix derivative group than in the nonenamel matrix derivative group after 3 years (100% vs 83%), but not after 5 years (85% vs 75%).[56] However, the multivariate modeling identified the use of enamel matrix derivative, together with bone level changes, as positively associated with implant survival, while suppuration, smoking habit, or the presence of residual pockets after treatment, were negatively associated. It seems clear that larger studies are needed before reaching any conclusion regarding the potential beneficial effects of enamel matrix derivative in the treatment of peri-implantitis, and if the use of this biologic contributes to reduce the invasiveness of these procedures.

If re-osseointegration is considered a requirement for successful reconstructive treatment of peri-implantitis, it is compulsory to effectively eliminate the biofilm from the implant surface, as well as achieve a proper decontamination. Several mechanical and/or chemical methods for implant surface decontamination have been used in clinical studies focused on the reconstructive therapy of peri-implantitis defects, showing radiographic bone fill. However, re-osseointegration rates in animal studies range from 39% to 46%.[57]

Therefore, even if it is doubtful that re-osseointegration is mandatory to achieve stable peri-implant tissues, ideally it should be the aim of regenerative procedures.

Electrolytic cleaning is one of the approaches that has been proposed to decontaminate the implant surface with the objective of favoring re-osseointegration.[58] The mode of action of this approach consists of the application of an electrolyte solution (ie, sodium formiate) pumped by a device through a platinized ring acting as an anode and sprayed on the implant surface. The electrolysis produces hydrogen cations (H^+) that penetrate and break up the biofilm.[59] The clinical outcomes of electrolytic cleaning vs electrolytic cleaning plus a powder-spray system using erythritol were investigated by Schlee et al[60,61] in a randomized clinical trial. In brief, 24 patients (34 implants) with peri-implantitis were surgically treated with these decontamination devices, followed by an augmentation procedure using autogenous bone mixed with demineralized bovine bone mineral, in a 50:50 ratio, covered with a native collagen membrane and using a submerged healing approach. Six out of 34 implants had to be extracted because of reinfection throughout the 18-month follow-up. Significant radiographic bone fill and probing depth reduction were observed in the remaining implants in both groups, without significant differences among them.

Another device that has been proposed as an effective tool for implant surface decontamination is erbium-doped yttrium aluminium garnet laser.[62,63] Specifically, a recent pilot randomized clinical trial evaluated the adjunctive benefit of erbium-doped yttrium aluminium garnet laser in the regenerative surgical therapy of peri-implantitis, using a mixture of human allograft with demineralized bovine bone mineral and covered with an acellular dermal matrix membrane.[64] In this 6-month study, using the laser led to significantly higher probing depth reduction, but the other parameters were not significantly affected (ie, clinical attachment level gain and marginal bone level). Lasers may be useful, not just in the decontamination of the implant surface because of their bactericidal capacity, but also to attenuate the inflammation of the peri-implant tissues,[65] although as it occurs with nonsurgical periodontal therapy, the increased costs may hamper its effectiveness.[66]

3.3 | Use of antimicrobial adjuncts to grafting materials

Despite mechanical instrumentation, it is difficult to completely remove biofilms from implant surfaces. Therefore, local and/or systemically delivered antimicrobials have been evaluated, to understand if their adjunctive use may improve the results of both the nonsurgical and surgical treatment of peri-implantitis (Table 3).[6,67-71] Specifically, local antimicrobials may provide added value, because they may solve some of the problems related with the prescription of systemic antimicrobials, such as the development of antibiotic resistances or the limited penetration into bone tissue,[72,73] and they may be useful in the chemical decontamination of the exposed implant surfaces. However, none of these reports evaluated the impact of the antimicrobial adjuncts on the invasiveness of these interventions, and therefore, randomized clinical trials are needed to confirm if the notable results observed in some cases when arresting peri-implant inflammation also correlate with a lower invasiveness.

Recently, a randomized clinical trial evaluating the effect of systemic metronidazole as an adjunct to nonsurgical treatment of peri-implantitis was published.[71] Even if this approach may not be considered a reconstructive procedure, the results showed significant radiographic bone fill as a consequence of the treatment provided. While previous reports on nonsurgical therapy of peri-implantitis tended to show more modest results,[35] the mean radiographic bone gain attained in the test group of this study (consisting of a mechanical nonsurgical debridement session,

TABLE 3 Studies proposing the use of antimicrobial adjuncts to grafting materials in the reconstructive treatment of peri-implantitis: intervention, number of patients/implants, and summary of main outcomes

Study	Intervention	N patients (implants)	Outcomes
Nart et al.[69]	After mechanical and chemical decontamination, a vancomycin and tobramycin impregnated allograft was placed in the defect and covered with a collagen membrane allowing a nonsubmerged healing	13 (17)	No implant was lost. Significant reductions in BOP and PD. Mean radiographical intrabony defect filling was 86.7% ± 18.2%
La Monaca et al.[109]	After mechanical debridement, chemical decontamination using hydrogen peroxide (3%), chlorhexidine (0.2%) and a tetracycline hydrochloride solution was performed before defect filling with mineralized dehydrated bone allograft and a resorbable membrane	34 (34)	At 1 y, no implant showed peri-implant bone loss ≥ 1.0 mm and 91% of the implants presented absence of PD ≥ 5 mm and absence of BOP. However, this percentage was 59% at the 5-y examination and 23% of the implants presented bone loss ≥ 1.0 mm
Gonzalez Regueiro et al.[6]	Combined approach with implantoplasty of the supraosseous component together with the reconstruction of the intrabony defect using a bone substitute hydrated with a piperacillin/tazobactam 100/12.5 mg solution	43 (43)	After 12 mo, 86% of the implants presented disease resolution according to a composite outcome (absence of BOP/suppuration, further bone loss ≤ 0.5 mm)

Abbreviations: BOP, bleeding on probing; PD, probing depth.

including mucosal curettage, and prescription of metronidazole 500 mg, three times a day, for 7 days) accounted for 2.3 mm after 12 months, exceeding by far the one observed in other studies, where an average of approximately 0.5 mm was observed after nonsurgical therapy used with adjunctive metronidazole plus amoxicillin.[74,75] Indeed, the radiographic bone gain in the study of Blanco et al[71] is comparable with the 1.9 mm reported after surgical reconstructive treatment[9] (Figure 3). This could be explained by the baseline severity of the peri-implantitis lesions, the type of implants treated, and the stability of clot formation after nonsurgical debridement. Unfortunately, patient-reported outcome measures were not reported, although it seems plausible that the invasiveness of this nonsurgical treatment should be lower than that of classic reconstructive procedures following a guided bone regeneration approach. Therefore, leaving aside relevant considerations on the use of adjunctive systemic antibiotics, such as the increase in antibiotic resistance, the adjunctive use of systemic metronidazole as an adjunct to nonsurgical treatment of advanced peri-implantitis lesions resulted in promising results after 12 months, although larger studies with a longer follow-up and a more comprehensive evaluation of each patient's perspective are needed.

4 | HOW COULD THE NEED FOR AND NUMBER OF INVASIVE PREOPERATIVE DIAGNOSTIC EXAMINATIONS BE MINIMIZED?

It is expected that the incidence of peri-implant biologic complications will tend to increase in the near future as the number of dental implants placed increases year by year.[76,77] In this sense, it is important to emphasize that one of the tasks for clinicians is to develop a long-term effective supportive periodontal/peri-implant therapy program to intercept peri-implantitis at an early stage, when reconstructive treatment could still be feasible with a higher percentage of expected success. In particular, because the morphology of the peri-implantitis defects may potentially influence the reconstructive outcomes, it seems reasonable to assume that assessing the configuration of the bone lesions once they are developed may optimize the surgical approach and, therefore, reduce the invasiveness.

As stated by the 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions, recording peri-implant probing depth on a regular basis has a clear prognostic value without any drawback, as it has been demonstrated that gentle probing produces no harm to the supracrestal connective tissue.[78] On the other hand, even although radiographic imaging is an essential component of treatment planning, exposure to ionizing radiation must always be justified and result in a net benefit to the patient[79] (Figure 4).

According to Jacobs et al,[79] the use of cone beam computed tomography after the insertion of dental implants should be limited to specific postoperative complications that require implant retrieval (eg, neurovascular trauma), and should not be indicated for regular follow-up to obtain a three-dimensional view of the peri-implant tissues. During supportive periodontal/peri-implant therapy, clinicians are encouraged to use peri-implant bi-dimensional bone level measures "on correctly taken periapical radiographs, even if has had no true prognostic value and considering that only the proverbial tip of the iceberg of the actual size and morphology of a defect seen". Whether radiographic images should be requested even with no signs of augmented peri-implant probing, and the frequency of radiographic examinations, are still matters of controversy.

Cone beam computed tomography is frequently considered a useful tool for peri-implantitis diagnosis and treatment planning, although the underestimation of defect severity may affect the prognosis and clinical decision-making.[80] Clinicians need to be cautious in establishing prognoses and treatment based on cone beam computed tomography assessment, as it has been reported to offer modest performance in the characterization of peri-implantitis defects, because of poor resolution and/or the presence of artifacts. Indeed, beam-hardening is the phenomenon that occurs when an x-ray beam passes through an object, resulting in selective attenuation of lower energy photons. In cone beam computed tomography, beam hardening from a very dense target, namely the implant and the prosthetic reconstruction, may result in characteristic artifacts that render the precise determination of bone difficult. However, even if cone beam computed tomography was found to be less accurate when interpreting the severity of bone loss, it was perfectly accurate identifying peri-implant bone morphology, potentially justifying the request for a three-dimensional examination before a surgical approach to a peri-implantitis defect (Figure 5). In a recent 5-year prospective study, Roccuzzo et al[81] found that the reconstructive treatment of single peri-implantitis intrabony defects resulted in a high implant survival rate in patients who fully adhered to supportive

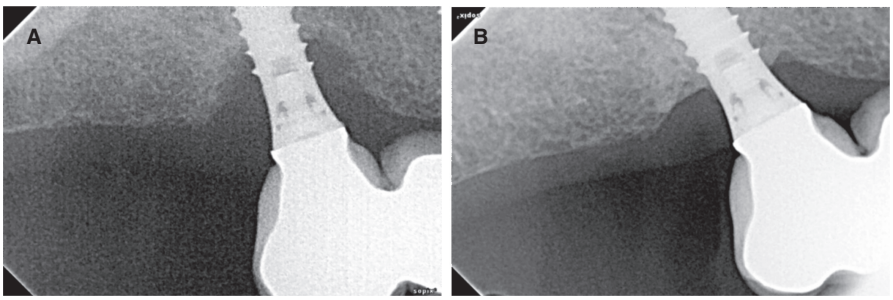


FIGURE 3 Peri-implantitis case treated by means of nonsurgical treatment with systemic metronidazole (500 mg every 8 hours for 7 days). A, Baseline periapical radiograph (December 2015). B, Radiographic bone gain (June 2021)

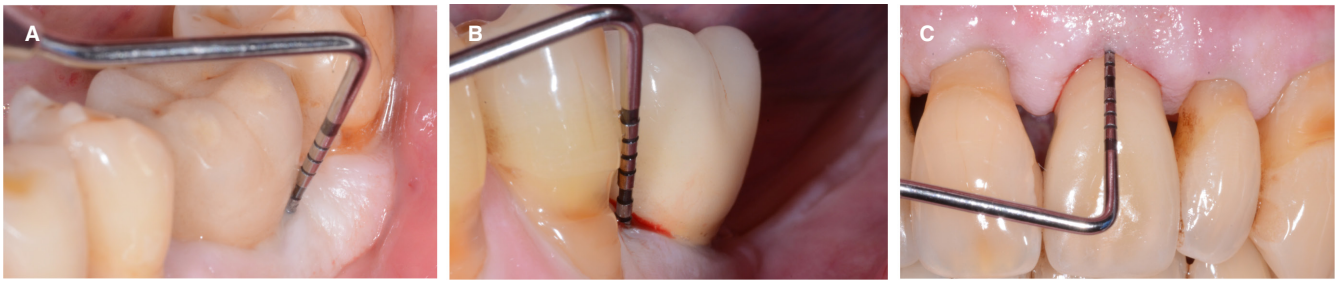


FIGURE 4 Several clinical scenarios characterized by increased peri-implant probing depth, bleeding, and/or suppuration on probing that require additional radiographic two-dimensional evaluation

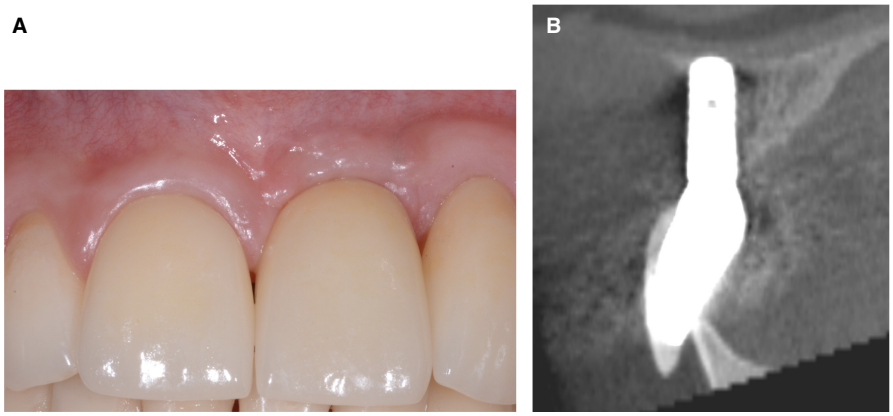


FIGURE 5 Patient erroneously referred for the treatment of peri-implantitis on implant 21. A, Note the absence of marginal clinical signs of peri-implant infection (bleeding on probing and pus) despite B, Complete resorption of the buccal bone wall. This clinical scenario did not require any treatment

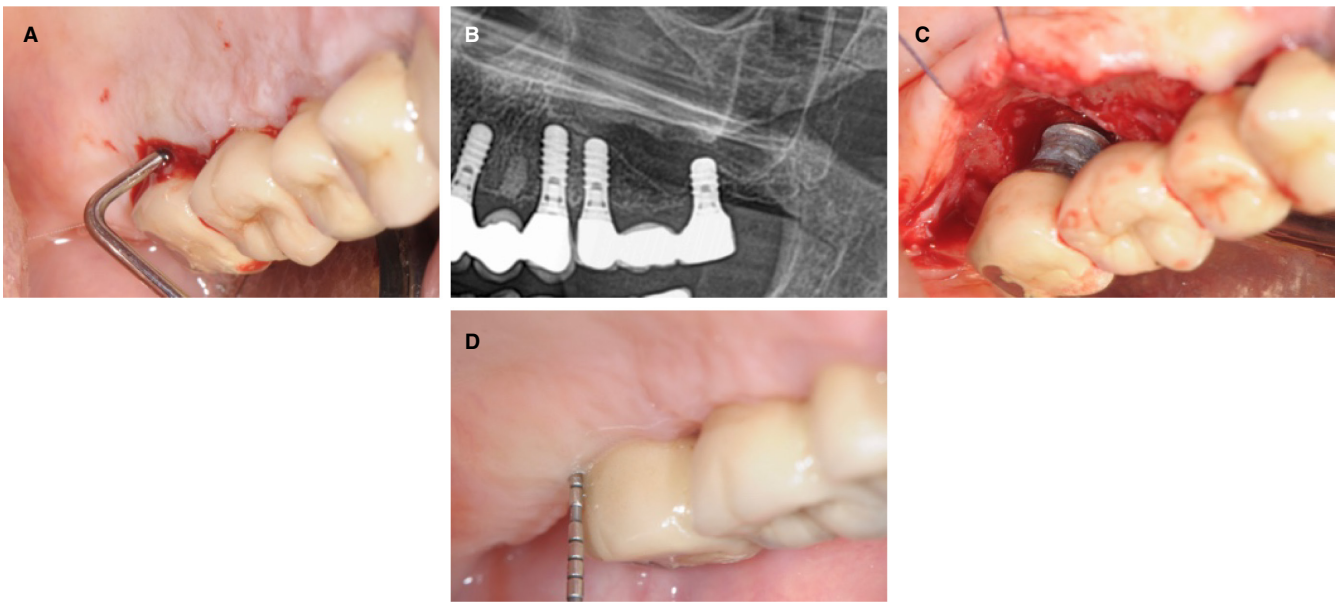


FIGURE 6 A, Case of a patient presenting peri-implantitis. B, Even although the conventional radiographic image does not show the infrabony defect, which is mainly on the palatal side of the implant, C, It became visible at the time of regenerative surgery; careful probing under anesthesia eliminated the absolute need for a three-dimensional image. D, Three years after surgical treatment, peri-implant tissues are healthy with minimal probing depth and no bleeding. There is no indication for a further radiographic examination

periodontal/peri-implant therapy visits, but the resolution of the lesions did not seem to be significantly associated with the defect configuration.

Taking all these factors into account, and to minimize the invasiveness of diagnostic examinations, a tailored supportive periodontal/peri-implant therapy program should be adapted to each patient's need and risk profile, and include routine peri-implant probing, but not necessarily radiographic images.[82] In case of augmented probing depths, with the concomitant presence of bleeding and/or suppuration, a conventional periapical radiograph can be performed to establish a more accurate diagnosis of defect morphology and to plan the most indicated surgical approach[24] (Figure 6).

5 | COMPLICATIONS, SEQUELAE, AND MORBIDITY IN THE RECONSTRUCTIVE TREATMENT OF PERI-IMPLANTITIS

The use of a bone graft with or without the combination of barrier membranes or other regenerative technologies (eg, enamel matrix derivative) is the most common approach in the reconstructive treatment of peri-implant defects. Autologous bone is the gold standard for regenerative purposes because of its properties; however, it has certain limitations such as the limited availability and the increased intrasurgical morbidity associated with the donor site. The use of a xenograft may overcome both limitations and reduce surgical time, thus reducing intraoperative morbidity. Several studies have compared the use of autologous grafts with xenografts, reporting statistically significant better results in radiographic bone fill, mean probing depth reduction, and mean suppuration reduction with the use of a xenograft.[83] However, its impact on patient morbidity or surgical time has not been adequately studied. The combination of platelet-rich fibrin with a xenograft has been reported to significantly reduce a patient's pain 24 hours after surgery compared with flap curettage and granulation tissue removal alone, as well as to obtain higher reductions in plaque index, sulcus bleeding index, and probing depth 7 days postsurgery, and greater defect fill 60 days after surgery.[48] These results suggest that platelet-rich fibrin combined with a bone graft may have a positive effect in terms of short-term recovery and healing compared with access flap alone. However, further studies with longer follow-up periods are needed to confirm the superiority of this approach.

The reconstructive treatment of peri-implant defects is not exempt from intra- and postsurgical complications. The most frequent complications reported in the literature are soft tissue dehiscences, membrane exposures, infection, and sequester formation.[49,84] The placement of barrier membranes increases the risk of postsurgical complications, especially nonresorbable[33] and acellular dermal matrix membranes.[64] To date, we have not identified in the literature a minimally invasive surgical approach for the reconstructive therapy of peri-implantitis that has demonstrated a capability to reduce the occurrence of such complications when compared with conventional approaches.

6 | PATIENT-REPORTED OUTCOME MEASURES AND CLINICAL SEQUELAE IN THE RECONSTRUCTIVE TREATMENT OF PERI-IMPLANTITIS

The reconstructive treatment of peri-implant defects has proven to induce favorable results in terms of radiographic bone levels and defect fill.[9] However, changes in mucosal margin are scarcely reported.[9,84] Mucosal recession after peri-implantitis surgery seems to be of greater magnitude when resective[85] or combined (resective plus reconstructive) surgical approaches are performed, when compared with reconstructive approaches.[86] In fact, there are reports of mucosal margin level gain after peri-implant reconstructive procedures.[86-89] However, these results do not seem to be predictable, and they are also not consistent among studies. A recent systematic review with meta-analysis on the efficacy of the reconstructive treatment of peri-implantitis estimated a statistically significant weighted mean recession of −0.65 mm (95% confidence interval: [−0.97; −0.33]), 12 months after treatment,[9] while a previous systematic review reported a nonstatistically significant weighted mean mucosal gain of 0.22 mm (95% confidence interval: [−0.07; 0.51]) after 36 months of follow-up. Nevertheless, and independently of the surgical approach chosen for the treatment of peri-implantitis, the occurrence of mucosal recession after surgery should be avoided to the best of our capabilities, because the unveiling of the grayish metallic cervical portion of the implant to the oral cavity, independently of its size, may compromise patients' esthetics and satisfaction, especially when it occurs on implants located in the anterior region.[16]

The use of minimally invasive flaps could minimize the apical migration of the peri-implant mucosal margin after surgery. In 2018, Fletcher and Tarnow[27] proposed a flapless approach called the circumferential occlusal access procedure as an alternative to conventional flaps,[27] as already explained in section 3.1. This surgical approach aims to reduce the risk of mucosal recession and membrane exposure caused by soft tissue dehiscences by accessing the implant through a circumferential pouch surrounding the implant.

The subperiosteal peri-implant augmented layer technique has recently been proposed by Trombelli et al[29] for the regenerative treatment of peri-implant defects. This technique consists of raising a partial thickness flap in the buccal aspect of the implant, leaving the periosteal layer on top of the implant and the surrounding peri-implant bone crest. After this, a full thickness pouch is created by tunneling the periosteal layer to expose the peri-implant defect. Careful debridement of the granulation tissue and implant surface decontamination is performed before filling the intrabony component of the defect with a bone xenograft. To stabilize the graft, the periosteal layer is sutured to the palatal flap. In those cases where there is a lack of adequate keratinized mucosa or the graft cannot be covered completely with the periosteal layer, a connective tissue graft is added on top of the periosteal flap. Last, the mucosal layer is coronally advanced and sutured covering the whole area. This technique has been presented in a proof-of-principle case report of three subjects and four implants with peri-implant defects (class Ib/Ic) and a follow-up of 6 months, reporting favorable results in both radiographic and clinical variables, including an improvement in the mucosal margin levels for all implants, with reductions in mucosal recession, when compared with baseline, and increments in the band of keratinized tissue. Even if the technique deserves further evaluation in long-term clinical trials to evaluate its invasiveness, it seems that it may be reduced, as the split-thickness flap allows for a smaller access when compared with traditional flaps used for guided bone regeneration (ie, including releasing incisions). What is more, it seems to provide favorable results without using a membrane, which may impact surgical time, costs, and the incidence of complications.

The surgical approach called laser-assisted peri-implant defect regeneration proposes a novel technique aiming at reconstructing both hard and soft tissues around dental implants.[32] It consists of a horizontal mucosal incision, 5 mm apical to the marginal mucosa, combined with a supraperiosteal preparation in the apical direction and a subperiosteal full-thickness flap in the coronal direction, which allows access to the implant surface. The peri-implant defect is debrided and detoxified with erbium-doped yttrium aluminium garnet laser. Afterwards, the bone defect is filled with an autogenous graft from the mandibular ramus, and a connective tissue graft is placed underneath the subperiosteal layer to increase mucosal thickness. A bilayer suturing technique is performed in the periosteum and the mucosa. A case report, with a follow-up of 12 months, is presented in the paper, with favorable results in both clinical and radiographic variables, and a noticeable improvement in keratinized mucosa thickness, width, and marginal level.

Nevertheless, these techniques should be further evaluated in properly designed clinical trials, with a sufficient sample size and follow-up period, to adequately evaluate their effectiveness.

Regarding patient satisfaction with the treatment provided, there is a noteworthy absence of data on patient-reported outcome measures in the literature regarding the regenerative treatment of peri-implantitis lesions.[9] One randomized clinical trial,[90] comparing the use of a nanocrystalline hydroxyapatite vs the use of a natural bone mineral graft in combination with a collagen membrane for the reconstructive treatment of peri-implantitis lesions, reported a high degree of satisfaction among participants, related to the fact that the treatment provided allowed them to maintain their implants for a longer period of time. Another multicenter randomized clinical trial,[91] comparing the use of a xenograft and a resorbable collagen membrane vs open flap debridement of peri-implantitis lesions, also reported high and comparable levels of satisfaction with the treatment provided in both groups, after 6 weeks and 12 months of follow-up. Furthermore, no differences in pain medication intake or pain scores were found among subjects from test and control groups. Even although the use of minimally invasive surgical approaches has been claimed to reduce patient morbidity and improve postoperative healing, these aspects are frequently overlooked and neither registered nor reported in the literature. Therefore, strong conclusions cannot be made with regard to patient-reported outcome measures in the minimally invasive reconstructive therapy of peri-implantitis.

7 | FACTORS INFLUENCING THE INVASIVENESS AND OUTCOMES OF THE RECONSTRUCTIVE THERAPY OF PERI-IMPLANT DEFECTS

The outcomes of reconstructive therapy have been proven to be influenced by multiple factors, including the surgical approach, the implant characteristics, site-specific features, and the bone defect configuration. The management of peri-implantitis is based upon the empiric knowledge derived from the therapy of periodontitis-related defects. It is understood that supracrestal defect configurations lack reparative potential, and, therefore, the therapy may be unsuccessful, independent of the reconstructive strategy. On the other hand, infra-osseous defect configurations are prone to exhibit favorable outcomes whenever reconstructive measures are applied.[24] In fact, Schwarz et al[92] explored the impact of infra-osseous defect configuration upon the reconstructive outcomes of peri-implantitis lesions using deproteinized bovine bone mineral in combination with a collagen membrane. Interestingly, it was demonstrated that circumferential-like defects (class Ie) yielded more favorable outcomes when compared with dehiscence or crater-like defects.[92] Later on, Aghazadeh et al[93] tested the association of defect configuration and depth upon the clinical and radiographic outcomes of reconstructive therapy using either autogenous bone or deproteinized bovine bone mineral combined with a resorbable barrier membrane. It was shown that defect fill was significantly correlated with initial defect depth and that bone fill was significantly enhanced in circumferential-like defects when compared with two- or three-wall defects.[93] Therefore, well-contained defects are potential candidates for minimal invasiveness by means of a less invasive surgical approach (simplifying access and the number of incisions) or the application of reconstructive therapy not necessarily fulfilling the principle of guided bone regeneration in terms of using a barrier membrane. On the other hand, Roccuzzo et al,[81] in a long-term cohort study using deproteinized bovine bone mineral with 10% collagen, did not find an association between defect configuration and implant survival. This could be explained by the stable nature of the bone filler, in contrast to traditional bone substitutes that are presented in particles and may be less prone to reach stability within the defect. Thus, based upon existing evidence, it seems that defect configuration may affect, to a certain extent, the invasiveness and the reconstructive outcomes of peri-implantitis (Figures 7 and 8).

Another site-specific feature speculated to influence the reconstructive outcome in the management of peri-implantitis is soft tissue characteristics. It seems reasonable that, given that implants lacking keratinized and attached mucosa are more exposed to peri-implantitis, soft tissues may play a role in disease resolution.[23,94,95] Nonetheless, evidence to date is conflicting. Ravidà et al,[96] in a retrospective study, showed that the presence of keratinized mucosa had a negligible influence on either the clinical resolution or bone levels in peri-implantitis implants after surgical therapy. It must be disclosed that this study was conducted in a university setting and also that nonreconstructive strategies to manage peri-implantitis were included, which may have influenced the results. However, other trials have shown favorable outcomes in the surgical nonreconstructive management of peri-implantitis when the soft tissues were simultaneously conditioned by means of free epithelialized mucosal grafts in scenarios associated with a lack of keratinized mucosa.[97,98] Therefore, inconclusive statements can be drawn based upon existing evidence; nevertheless, it seems reasonable that those cases where the lack of keratinized mucosa played a role in the onset and progression may lead to further recurrence if the soft tissues are not conditioned simultaneously or staged to the anti-infective therapy (Figure 9).

Debate has been further evoked by the suitability of the approach in terms of submerging the reconstructive compartment to promote an aseptic healing. Schwarz et al,[99] in a preclinical experimental induced peri-implantitis model, showed that submerged healing improved the surgical treatment outcome, in particular concerning the radiographic and histomorphometric findings. In line with this, Roos-Jansaker et al,[100] in a 3-year prospective clinical study, tested the influence of submerging the implant for 6 months after reconstructive therapy. It was demonstrated that less optimal outcomes were shown when a transmucosal vs submerged healing approach was applied. More recently, Monje et al,[101] in a prospective 1-year case series, reported favorable outcomes in terms of disease resolution and radiographic bone gain in 85% of the cases that initially exhibited three-wall defect configurations and that underwent submerged healing for 8-10 weeks.[101] By contrast, Astolfi et al,[15] in a retrospective case series, observed no benefit of a submerged healing approach for 8-10 weeks when compared with transmucosal healing. Hence, although evidence seems to favor submerged healing protocols, this must not be recommended on a daily basis for all cases, given that (1) removing the prosthesis may alter patient satisfaction, (2) the achievement of a tension-free primary closure may lead to a distortion of the mucosal margin, which may lead to a loss of

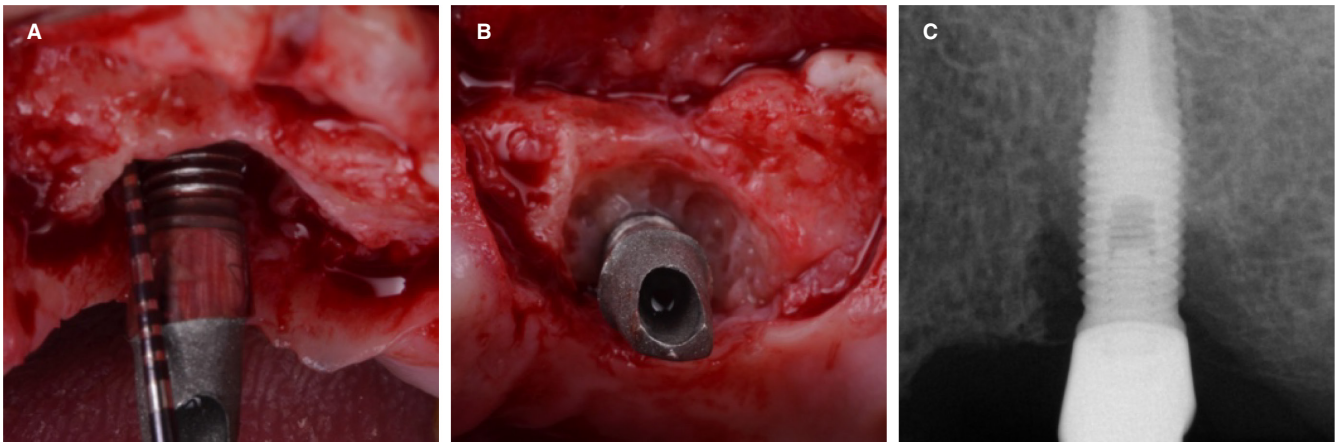
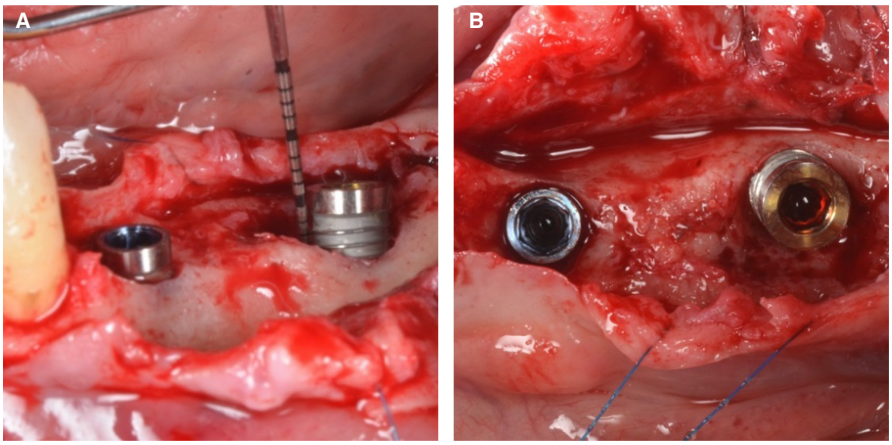


FIGURE 7 Circumferential-like defects are indicated to reconstructive therapy because of the stability that the residual bony walls may provide for the grafting material. A, Frontal and B, Occlusal views of class I defect configuration and C, The periapical radiographic image

FIGURE 8 Class Ib peri-implantitis-related bone defects are the most frequent defect configuration. They are often associated with implants placed too buccally. This feature impacts the reconstructive procedure as bone regeneration in the buccal aspect of these implants is often compromised. A, Frontal view. B, Occlusal view



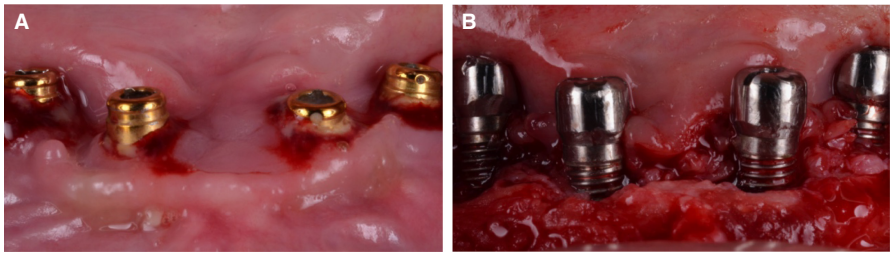


FIGURE 9 In scenarios exhibiting minimal keratinized mucosa and slight crater-like defects, it may be preferable to select a nonreconstructive procedure aiming to achieve a flat bone architecture by means of osteoplasty. A, Frontal image during diagnosis and B, Intraoperative frontal image

the buccal band of keratinized mucosa, and (3) in combined defects it might be challenging to achieve primary closure and may also lead to residual pockets. It is the authors' opinion that, whenever possible, the prosthetic supra-structure must be temporally removed to attain better access for an efficient surface detoxification prior to grafting. Moreover, prosthesis that somehow predisposed the onset of the disease by an inadequate emergence design, must be modified or replaced to promote adequate access for self-performed oral hygiene measures.[41] It is worth noting that the association of peri-implantitis and the inadequate design of prosthetic supra-structures has been reported as being high.[24,40,102]

Another element that has been demonstrated as relevant in the reconstructive outcomes of peri-implantitis relates to the implant surface topographic characteristics. Wetzel et al,[103] in a preclinical study, aimed at analyzing the influence of the implant surface (titanium plasma spray vs sandblasted, large grit, acid-etched vs smooth surface) on reconstructive and nonreconstructive procedures to manage experimental peri-implantitis in dogs. Interestingly, it was found that implant surface characteristics did not significantly influence bone gain during a 6-month follow-up study period.[103] Shibli et al[104] compared four different surface characteristics (commercially pure titanium surface, titanium plasma spray, acid-etched, and surface oxide sandblasted) in reconstructive therapy carried out after experimental peri-implantitis in dogs. It was demonstrated in a 5-month follow-up histologic examination that bone gain and re-osseointegration were independent of surface characteristics but relied upon surface detoxification by means of photosensitization therapy using a diode laser.[104] Almohandes et al[105] aimed at investigating the influence of surface characteristics (TiO-blasting/acid-etched vs smooth/acid-etched) on the reconstructive outcomes of experimental peri-implantitis in dogs using a variety of bone-grafting substitutes with or without a barrier membrane. Compared with moderately rough surface implants, it was shown that smooth surface implants performed better in terms of radiographic bone gain, level of re-osseointegration, and resolution of disease. Rodriguez et al[106] compared the resolution of experimental peri-implantitis in dogs of two different implant surface characteristics (resorbable blast texture vs laser microtextured) by means of reconstructive therapy using bovine bone and a barrier membrane. It was found that laser microtextured implants led to a difference of 0.4 mm in bone gain compared with resorbable blast textured-surface implants. This is aligned with the clinical findings from Roccuzzo et al,[107,108] who, in a clinical study evaluating reconstructive therapy of peri-implantitis defects using deproteinized bovine bone mineral with 10% collagen, observed that both implant survival and disease resolution were influenced by implant surface characteristics. In particular, disease resolution was found in 42% of the sandblasted, large grit, acid-etched implants and in 29% of the titanium plasma spray implants. Furthermore, sandblasted, large grit, acid-etched implants outperformed titanium plasma spray implants in terms of implant survival by 25%.[107,108] Therefore, existing evidence indicates the significance of implant surface characteristics on the expected outcomes in the reconstructive treatment of peri-implant defects.

8 | LONG-TERM OUTCOMES OF THE RECONSTRUCTIVE THERAPY OF PERI-IMPLANT DEFECTS

Despite the large body of evidence recently published, very few studies have reported long-term outcomes of the reconstructive therapy of peri-implantitis defects. More specifically, Roos-Jansaker et al[100] showed, in a 3-year case-control study, a mean bone fill of 1.3 or 1.6 mm if treatment consisted of bone grafting alone or of bone grafting combined with a barrier membrane, respectively. The authors noted that the key to maintaining long-term outcomes was adherence to a strict supportive peri-implant maintenance program. In fact, the plaque index decreased from 40% to 10% during the first year and remained stable during the following 2 years.[100] Froum et al,[53] in a 3- to 7.5-year follow-up case series using a combination of enamel matrix derivative and platelet-derived growth factor mixed with mineralized allografts or deproteinized bovine bone mineral and a barrier membrane or a connective tissue graft, reported that bone level gain ranged from 3 to 3.75 mm with no implant loss during the study period. The authors stated that all the patients adhered to a strict supportive peri-implant maintenance program.[53] Schwarz et al,[88] in a 4-year randomized clinical trial, showed a mean 1.4 mm of clinical attachment level gain using two different surface detoxification strategies grafted using deproteinized bovine bone mineral and a collagen membrane. The authors demonstrated that the method of surface detoxification (ie, erbium-doped yttrium aluminium garnet laser or plastic curettes plus cotton pellets plus sterile saline) did not influence the resolution of peri-implantitis.[88]

In a 5-year case series study, La Monaca et al[109] evaluated the maintenance of reconstructive outcomes achieved by means of mineralized allograft and a resorbable membrane. It was demonstrated that at 1-year follow-up, disease resolution was 91%. Nonetheless, at 5-year assessment, only bleeding on probing reduction was statistically significant compared with baseline, and no difference was found in probing pocket depth or peri-implant bone level compared with baseline records. Thus, it could be hypothesized that there is a progressive decrease in bone filling after the reconstructive treatment of peri-implant defects.[109] More recently, Roccuzzo et al,[108] in an up-to-date clinical study with the longest follow-up, demonstrated that the reconstructive outcomes after using deproteinized bovine bone mineral with 10% collagen can be maintained over a 10-year basis if periodic supportive peri-implant maintenance is provided. Implant survival was 80% and 55% for sandblasted, large grit, acid-etched and titanium plasma spray implants, respectively. In light of the findings, the authors concluded that the decision-making in managing peri-implantitis should be further based upon implant surface topographic features.[108] Irrespective of the intervention applied, the available evidence emphasizes the need to adhere to strict supportive periodontal/peri-implant therapy to sustain long-term outcomes.[110] In fact, minimally invasive strategies for supportive periodontal/peri-implant therapy are valid and effective, aiming at reducing pain/discomfort while enhancing the effectiveness of supportive periodontal/peri-implant therapy. For instance, the use of

glycine powder air polishing devices during supportive periodontal/peri-implant therapy has demonstrated higher efficiency in removing biofilm and achieving higher patient satisfaction with implant-supported prosthesis compared with traditional methods. This finding may indicate the time is reduced, and the comfort achieved during supportive periodontal/peri-implant therapy is higher using this strategy, as it might be unnecessary for a prosthesis to be removed during supportive periodontal/peri-implant therapy to reach a plaque-free environment.[111]

9 | SUMMARY AND CONCLUSIONS

The primary goal of the treatment of peri-implantitis is to arrest the progression of peri-implant bone loss. In particular, reconstructive therapies are more ambitious, attempting the reconstruction of the hard and/or soft tissues lost as a result of the disease. The concepts of minimal invasiveness evaluated in the reconstructive treatment of peri-implantitis lesions include specific flap designs[27,29,32] with the aim to minimize the surgical trauma, preserving the interproximal tissue and the position of the peri-implant mucosal margin, in an analogous manner to the different "papilla preservation" and apical accesses techniques that have been shown to minimize the surgical trauma in regenerative periodontal treatment.[12,38] However, most of these techniques have been presented as case reports, and no controlled clinical trials or randomized clinical trials have been performed to show the superiority of these techniques over conventional surgical access. In any case, it has to be acknowledged that so long as implant position, defect configuration, and/or soft tissue characteristics may impact the flap design, it is difficult to conduct randomized clinical trials including comparable lesions.

Classically, the reconstructive treatment of peri-implant defects has followed the principles of guided bone regeneration, that is, the use of barrier membranes that prevent the migration of epithelial cells in the defect. However, although there may be controversy from the biologic point of view that the isolated use of bone substitutes can favor re-osseointegration, the truth is that different clinical trials have not been able to determine the clinical advantages of the use of barrier membranes.[43] What is more, the use of barrier membranes probably requires more experience and also impacts upon the morbidity of these procedures, as long as surgical sites need to be wider for the adequate placement of the membrane. Other products that may potentially influence invasiveness and morbidity are the use of several bioactive molecules or growth factors (eg, enamel matrix derivative, platelet-rich fibrin)[52] that may promote neovascular events. Nevertheless, the effect of growth factors or other devices that may be helpful in implant decontamination has not been studied properly and no recommendations for their use could currently be performed.

Similarly, antimicrobial adjuncts may be useful in the treatment of peri-implantitis, although it remains questionable if their use should be exclusively restricted to machined implants.[68] Interestingly, recent studies report positive results after the use of systemic metronidazole concomitant to the nonsurgical therapy of peri-implantitis,[71] with increased radiographic bone gain in the longest follow-up, suggesting that, in opposition to previous knowledge, nonsurgical treatment may be a minimally invasive method to solve a relevant percentage of peri-implantitis cases (~50%) and that time is an important factor to consider before moving into surgery.

Surprisingly, no information could be retrieved from the studies considered in this review regarding patient-reported outcome measures or esthetic parameters, which may be relevant so long as the surgical treatment of peri-implantitis results in buccal soft tissue dehiscences. Therefore, it is unclear if minimally invasive reconstructive procedures may diminish the incidence of buccal soft tissue dehiscences.

In conclusion, the invasiveness of the reconstructive procedures for peri-implantitis lesions has not been properly evaluated, so it is difficult for these authors to provide guidelines on this topic. However, it is reasonable to believe that minimizing the trauma on the peri-implant soft tissues may provide some benefits from the patient's perspective, although this always has to be balanced with proper access for implant surface decontamination.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to this study.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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