Minimally invasive surgical techniques for the treatment of different types of isolated intrabony defects: A narrative review

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
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Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online) *Dent Med Probl.* 2022;59(2):309–318

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Funding sources
None declared

Conflict of interest
None declared

Acknowledgements
None declared

Received on November 25, 2021
Reviewed on January 26, 2022
Accepted on February 8, 2022

Published online on June 30, 2022

Abstract

The aim of this literature review was to present minimally invasive surgical techniques (MISTs) for the regeneration of intrabony defects and the impact of these surgical procedures on clinical outcomes. Less invasive surgical procedures lead to a more uneventful postoperative healing and reduce patient morbidity. The introduction of these techniques together with the use of magnification tools enables gentle tissue manipulation with performing minimal incisions and flap elevations in the field of surgical treatment of intrabony defects. Minimally invasive surgical techniques induce minor surgical trauma and improve the wound stability with favorable results in terms of clinical outcomes and the patient's comfort. The defect anatomy, patient-centered factors and the various biomaterials applied are considered. Recent evidence concludes that the adjunctive use of regenerative materials seems to have a less determinant effect on the clinical performance of minimally invasive surgical techniques. In addition, more studies are required to investigate the clinical efficacy of these surgical techniques in the treatment of intrabony defects in comparison with the conventional papilla preservation flap techniques.

Keywords: review, surgical treatment, periodontal, attachment loss, intraosseous defects

Cite as
Kaddas C, Dereka X. Minimally invasive surgical techniques for the treatment of different types of isolated intrabony defects: A narrative review. *Dent Med Probl.* 2022;59(2):309–318
doi:10.17219/dmp/146540

DOI
10.17219/dmp/146540

Introduction

Over the last decades, less invasive surgical procedures that could lead to a more uneventful postoperative healing and reduce patient morbidity has been one of the most important objectives of the clinicians. The introduction of the operating microscope in surgery served this purpose and gave the surgeons the chance to follow the principles of the conventional surgical procedures in a less extensive and more precise way.[1,2] The potential of gentle tissue manipulation under magnification was called minimally invasive surgery (MIS)[3] and gradually, the concept of minimal surgical trauma was applied in the field of periodontal surgery.[4]

A periodontal lesion extends apically toward the tooth root, causing the loss of the periodontal support and the destruction of the alveolar bone. As a result, osseous defects occur. Their morphology depends mainly on the presence of the microbial plaque and local anatomical factors. Infrabony lesions represent vertical defects, in which the base of the pocket is detected apical to the level of the alveolar crest.[5] Periodontitis is an infectious disease that may also be correlated with systemic illnesses, such as cardiovascular diseases[6] and preeclampsia.[7] The conservative non-surgical periodontal therapy with scaling and root planing alone or in combination with topical and/or systemic adjuncts, like subantimicrobial-dose doxycycline, antimicrobials, chlorhexidine chips, and melatonin, leads to favorable clinical outcomes in terms of the clinical attachment level (CAL) gain.[8,9] However, infrabony lesions may be related to a higher risk of progression of periodontal disease, as they tend to present deeper residual pocket depth (PD) after non-surgical periodontal therapy.[5] Thus, a variety of surgical approaches and regenerative materials have been developed in order to treat the residual defects.[10] The conventional flap surgery in combination with regenerative materials, such as membrane barriers, bone grafts and enamel matrix derivatives (EMDs), has proven to be very effective in the regeneration of intrabony defects.[11–13]

Recently, progress in the field of magnification has led to the development of new less invasive periodontal surgery techniques. Minimally invasive surgerical techniques (MISTs) are characterized by small incisions, limited flap reflection and suturing for primary wound healing. Based on the principle of the papilla preservation techniques,[14] which is to maintain the interdental papilla tissue as intact as possible, researchers have introduced and improved new surgical approaches for periodontal regeneration.[15–19] Less invasive surgical procedures demonstrated favorable clinical outcomes in the treatment of intrabony defects, even in esthetic areas.[16,20] In addition, the minimal surgical trauma and the reduced chair time made them better accepted by patients, and improved patient perception over surgical procedures.[20] These new perspectives has led more clinicians to apply MISTs in the treatment of intrabony lesions, when it was indicated.

The aim of this literature review was to present MISTs for the regeneration of intrabony defects and the impact of these surgical procedures on clinical outcomes.

Literature search

A literature search was performed in MEDLINE via the PubMed database for articles published until August 2021. The database was searched using search terms and free text terms, in different combinations.

To be included in the review, studies had to be written in the English language, be published in an international peer-reviewed journal, and present (MISTs) and periodontal regeneration for the treatment of intrabony defects.

The assessment of the titles, abstracts and full texts of the papers was performed by the 2 authors. Finally, in the present review, 6 randomized clinical trials (RCTs), 10 case series studies and 1 prospective cohort study were included. All studies applied MISTs and presented a minimum of 6 months of follow-up. Clinical attachment level, PD and recession (REC) were reported as clinical outcomes (Table 1).

Minimally invasive surgical techniques

Minimally invasive surgical (MIS) approach

The minimally invasive surgical (MIS) approach was first introduced by Harrel.[15,16] The initial incision is made intrasulcularly around the teeth adjacent to the osseous defect, with the blade parallel to the long axis of the root. Subsequently, an incision is performed, usually on the lingual aspect, to connect the 2 intrasulcular incisions. The interdental papilla is sharply dissected from the underlying bone and small flaps are reflected buccally and lingually. Flap reflection is followed by the removal of the connective and granulation tissue within the osseous defect. This is performed with the use of a blade and small curettes as well as an ultrasonic scaler, which is also used for the initial root debridement. The remaining granulation tissue is shredded and removed with a mechanical instrument, and root planing is refined with finishing burs. In order to obtain the primary closure of the wound, a vertical mattress suture is used to close the flaps.[15,16,20]

Minimally invasive surgical technique (MIST)

In 2007, Cortellini and Tonetti proposed the minimally invasive surgical technique (MIST)[18] based on the MIS approach combined with the modified papilla preservation flap technique (MPPT)[21] or the simplified papilla preservation flap technique (SPPT).[22] The width of the interdental space determines the choice of the surgical approach; if it is ≤2 mm, SPPT is used, whereas if it is >2 mm, MPPT is per-

Table 1. Characteristics of the selected studies

Authors, year	Study design	Treatment	Follow-up	Parameters	Results
Harrel et al. 2005[29]	case series	MIS + EMD	11 months	PD CAL REC	ΔPD: −3.56 ±1.31 CAL gain: 3.57 ±1.75 ΔREC: −0.01
Cortellini and Tonetti 2007[18]	case series	MIST + EMD	12 months	PD CAL REC defect resolution	ΔPD: −4.8 ±1.8 CAL gain: 4.8 ±1.9 ΔREC: −0.1 ±0.9 bone fill: 88.7 ±20.7
Cortellini and Tonetti 2007[23]	case series	MIST + EMD	12 months	PD CAL REC defect resolution VAS	ΔPD: −5.2 ±1.7 CAL gain: 4.9 ±1.7 ΔREC: 0.4 ±0.7 bone fill: 77.6 ±21.9 VAS: pain 19 ±10 discomfort 28 ±11
Cortellini et al. 2008[34]	case series	MIST + EMD	12 months	PD CAL REC defect resolution VAS	ΔPD: −4.6 ±1.3 CAL gain: 4.4 ±1.4 ΔREC: 0.2 ±0.6 bone fill: 83 ±20 VAS: pain 19 ±9 perception of the hardship of the surgical procedure 24 ±12 discomfort 21 ±10
Cortellini and Tonetti 2009[19]	case series	M-MIST	12 months	PD CAL REC	ΔPD: −4.6 ±1.5 CAL gain: 4.5 ±1.5 ΔREC: 0.1 ±0.3
Trombelli et al. 2009[24]	case series	SFA + HA + collagen	10 ±3 months	PD CAL REC	ΔPD: −5.2 ±2.6 CAL gain: 4.8 ±2.7 ΔREC: 0.4 ±1.5
Harrel et al. 2010[33]	case series	MIS	6 years	PD CAL REC	ΔPD: −3.78 ±2.12 CAL gain: 3.70 ±1.15 ΔREC: 0.004 ± 0.56
Trombelli et al. 2010[41]	RCT	test: SFA + HA/GTR control: SFA	6 months	PD CAL REC	test: ΔPD: −5.3 ± 2.4 CAL gain: 4.7 ±2.5 ΔREC: 0.4 ±1.4 control: ΔPD: −5.3 ±1.5 CAL gain: 4.4 ±1.5 ΔREC: 0.8 ±0.8
Cortellini et al. 2011[36]	RCT	group 1: M-MIST group 2: M-MIST + EMD group 3: M-MIST + EMD +BMDX	12 months	PD CAL REC defect resolution	group 1: ΔPD: −4.4 ±1.6 CAL gain: 4.1 ±1.4 ΔREC: 0.3 ±0.6 bone fill: 77 ±17 group 2: ΔPD: −4.4 ±1.2 CAL gain: 4.1 ±1.2 ΔREC: 0.3 ±0.5 bone fill: 71 ±18 group 3: ΔPD: −4.0 ±1.3 CAL gain: 3.7 ±1.3 ΔREC: 0.3 ±0.7 bone fill: 78 ±27
Ribeiro et al. 2011[37]	RCT	test: MIST + EMD control: MIST	6 months	PD CAL REC	test: ΔPD: −3.56 ±2.07 CAL gain: 3.02 ±1.94 ΔREC: 0.46 ±0.87 control: ΔPD: −3.50 ±0.88 CAL gain: 2.82 ±1.19 ΔREC: 0.54 ±0.58

Authors, year	Study design	Treatment	Follow-up	Parameters	Results
Mishra et al. 2013[30]	RCT	test: M-MIST + rhPDGF-BB control: M-MIST	6 months	PD CAL REC defect resolution	test: ΔPD: –4.18 ±0.60 CAL gain: 3.00 ±0.89 ΔREC: 0.82 ±0.60 bone fill: 36 ±18 control: ΔPD: –3.82 ±0.87 CAL gain: 2.64 ±0.67 ΔREC: 0.55 ±0.52 bone fill: 35 ±11
Harrel et al. 2014[17]	case series	V-MIS	6 months	PD CAL REC	ΔPD: –3.88 ±1.02 CAL gain: 4.04 ±1.38 ΔREC: –0.13 ±0.61
Harrel et al. 2016[40]	case series	V-MIS	12 months	PD CAL REC	ΔPD: –4.11 ±0.98 CAL gain: 4.58 ±1.19 ΔREC: –0.48 ±0.65
Harrel et al. 2017[39]	case series	V-MIS	36 months	PD CAL REC	ΔPD: –3.80 ±1.18 CAL gain: 4.16 ±1.18 ΔREC: –0.36 ±0.64
Ahmad et al. 2019[31]	RCT	test: M-MIST + PRF control: M-MIST	6 months	PD CAL REC defect resolution	test: ΔPD: –4.12 ±0.95 CAL gain: 4.00 ±1.06 ΔREC: 0.06 ±0.25 bone fill: 37.4 ±10.0 control: ΔPD: –4.18 ±0.98 CAL gain: 4.00 ±1.09 ΔREC: 0.06 ±0.25 bone fill: 33.8 ±11.1
Mizutani et al. 2021[35]	prospective cohort study	DM group: MIST/M-MIST + EMD non-DM group: MIST/M-MIST + EMD	3 years	PD CAL REC defect resolution	DM group: ΔPD: –4.5 ±1.4 CAL gain: 3.8 ±1.1 ΔREC: 1.1 ±0.9 bone fill: 58.3 ±10.4 non-DM group: ΔPD: –4.7 ±1.4 CAL gain: 4.1 ±1.1 ΔREC: 0.6 ±1.0 bone fill: 65.5 ±18.8
Liu et al. 2022[38]	RCT	test: MIST + DBBM + collagen control: MIST	12 months	PD CAL REC defect resolution	test: ΔPD: –2.31 ±1.47 CAL gain: 2.00 ±1.38 ΔREC: 0.31 ±0.93 bone gain: 3.85 ±1.69 control: ΔPD: 2.50 ±1.22 CAL gain: 2.53 ±1.80 ΔREC: –0.03 ±1.19 bone gain: 3.00 ±1.56

RCT – randomized clinical trial; MIS – minimally invasive surgery; EMD – enamel matrix derivative; MIST – minimally invasive surgical technique; M-MIST – modified minimally invasive surgical technique; SFA – single-flap approach; HA – hydroxyapatite; GTR – guided tissue regeneration; BMDX – bone mineral-derived xenograft; rhPDGF-BB – recombinant human platelet-derived growth factor BB; V-MIS – videoscope-assisted minimally invasive surgery; PRF – platelet-rich fibrin; DM – diabetes mellitus; DBBM – deproteinized bovine bone mineral; PD – pocket depth; CAL – clinical attachment level; REC – recession; VAS – visual analog scale. The PD, CAL and REC values are provided in millimeters [mm], bone fill as percentage [%], and bone gain also in millimeters [mm].

formed. The simplified papilla preservation flap technique consists in an oblique incision close to the buccal side of the interdental papilla col, while in MPPT, a horizontal incision at the buccal side of the papilla is performed. Two intrasulcular incisions extended buccally and lingually to the 2 teeth neighboring the defect are made. The mesiodistal extension of the intrasulcular incisions is as limited as possible, and 2 small full-thickness flaps are reflected to expose 1–2 mm of the bone crest. Vertical releasing incisions are made when better reflection of the flaps is demanded. The defect debridement and root planing follow with the use of small curettes and power-driven instruments. Finally, the suturing of the flaps is achieved with a single modified internal mattress suture, while the vertical incisions, if performed, are sutured with simple passing sutures. The surgical procedures are performed with the use of an operative microscope.[18,20,23]

Modified minimally invasive surgical technique (M-MIST)

In order to further reduce surgical trauma, Cortellini and Tonetti described the modified minimally invasive surgical technique (M-MIST) in 2009.[19] This technique is an improved and less invasive version of MIST. As in MIST, MPPT or SPPT is used to access the defect adjacent to the interdental papilla. The interdental incision is extended intrasulcularly at the buccal aspect of the involved teeth. A very small triangular flap is reflected to expose the coronal part of the bone crest. The granulation tissue filling the defect is moved away with the use of a micro-blade to split it from the interdental tissues. The incisions are not extended to the palatal tissues. After the removal of the granulation tissue underneath the papilla, the defect debridement and root planing are performed with the use of micro-curettes and power-driven instruments. Access is achieved through a buccal window to thoroughly debride the defect and the roots, with respect to the papillary fibrous attachment. Afterward, a single modified internal mattress is performed to close the flap. All the surgical procedures are carried out with the aid of an operative microscope.[19,20]

Single-flap approach (SFA)

In the same year when M-MIST was introduced by Cortellini and Tonetti (2009), a similar surgical technique was proposed by Trombelli et al.[24] This technique consists in the limited elevation of a mucoperiosteal flap buccally or lingually, depending on the extension of the defect. Using a periodontal probe, the extension and the morphology of the defect are evaluated. Subsequently, sulcular incisions are performed, following the gingival margin of the teeth neighboring the surgical area. Following the contour of the underlying bone crest, a diagonal or horizontal butt-joint incision is made. The spot of this incision depends on the height of the interdental tissues. Taking this into account, the higher the interdental papilla is, the more apically the incision is performed, but always at least 1 mm coronal to the bone crest. In this way, an envelope flap, without the releasing incisions, is elevated and the supracrestal soft tissues as well as the rest of the papilla remain undetached. After the reflection of the flap, the debridement of the defect and the instrumentation of the roots follow, using curettes and mechanical instruments. For the reposition of the flap, firstly, a horizontal internal mattress suture is placed, and then a second vertical or horizontal internal mattress suture, in a more coronal spot of the flap and the papilla, is performed to achieve primary closure. The surgical procedures are carried out with the aid of ×2.5 magnifying loupes.[24]

Videoscope-assisted minimally invasive surgery (V-MIS)

The principal features of MISTs are small incisions and tiny flaps. Although these techniques limit surgical trauma, clinicians need to deal with a smaller surgical area than the one created in the conventional flap access. For this reason, Harrel in 1995 performed MIS with the aid of surgical telescopes (loupes),[15] and later Cortellini and Tonetti introduced MIST with the use of the surgical microscope.[18] Nevertheless, the inadequate magnification of the loops and the impractical use of the surgical microscope in clinical practice made MISTs less acceptable to the clinicians. To overcome this issue, Harrel in 2013 suggested the use of a videoscope flexible insertion tube with a digital camera to better visualize the surgical site.[25] A flow of gas over the end of the videoscope keeps away blood and debris, and prevents the lens from being blurred through the surgical procedure, providing a clear image of the surgical area on the monitor. In addition, a carbon fiber retractor makes the management of the soft tissues easier. Access to the defect is achieved with MIS, but only a tiny buccal or lingual split-thickness flap is performed, without the use of blunt dissection. The videoscope is placed at the defect and the removal of the granulation tissue as well as the root debridement follow. These procedures are meticulously performed, as the videoscope allows better visualization of the area. Finally, a single modified vertical mattress suture is positioned at the base of the papilla, while the tip of the papilla is approximated with the use of a wet gauze and finger pressure.[17,25]

Minimally invasive surgical techniques (MISTs) and periodontal regeneration of intrabony defects

The successful regeneration of intrabony defects depends mainly on 2 factors – the surgical technique and the selected biomaterials.[13] Since MISTs were introduced in the periodontal regenerative surgery, they have been combined with a variety of biomaterials, such as EMDs, bone grafts (demineralized freeze-dried bone allografts (DFDBA), xenografts) alone or with barrier membranes, as well as with growth factors and platelet-rich fibrin (PRF).[18,24,26–31] Several clinical studies have been conducted aiming to evaluate the efficacy of MISTs with or without the adjunctive use of biomaterials, and define the best treatment modality for intrabony defects (Table 1).

The enamel matrix derivative Emdogain® has been widely used for the regeneration of intrabony defects alone or in combination with other biomaterials and different surgical techniques, leading to various clinical outcomes.[32] Harrel et al. in 2 studies with an 11-month and

a 6-year follow-up, evaluated the use of enamel matrix proteins in conjunction with the MIS approach.[29,33] A total of 160 sites of intrabony defects in 16 patients were treated and the results showed significant improvement in PD and CAL as compared to baseline. Specifically, at 11 months, changes in PD, CAL and REC were 3.56 mm, 3.57 mm and 0.01 mm, respectively, while at 6 years, the differences were not statistically significant. The authors concluded that clinical outcomes remained stable over the 6-year period and underlined favorable effects for the patient's esthetics, as they observed minimal gingival recession.[29,33]

In a series of studies, Cortellini and Tonetti evaluated the clinical efficacy and the patient perception of MISTs in conjunction with the application of EMD in the treatment of isolated and multiple adjacent deep intrabony defects.[18,23,34] Clinical outcomes were assessed at a 1-year follow-up, the single defects resulted in CAL gain of 4.9 ±1.7 mm, associated with 3.0 ± 0.6 mm of residual PD and an increase in REC of 0.4 ±0.7 mm,[18,23] whilst the multiple defects resulted in CAL gain of 4.4 ±1.4 mm, associated with 2.5 ±0.6 mm of residual PD and an increase in REC of 0.2 ±0.6 mm.[34] The authors concluded that MISTs combined with EMD could be applied successfully for these defects, and that it was an advantageous procedure in terms of patient morbidity.[18,23,34] In a recent prospective cohort study, the clinical results of MISTs combined with EMD were also evaluated for the treatment of isolated intrabony defects in 10 patients with diabetes mellitus (DM) type 2, who completed a 3-year follow-up.[35] The mean PD reduction, CAL gain and REC increase were similar to those of the non-DM group and statistically different as compared to baseline after 3-year observation. Improvement in the radiographic defect depth and the radiographic bone fill were also comparable between the 2 groups. Thus, the application of MISTs combined with EMD could lead to favorable clinical results regardless of the presence of DM, although a larger number of cases would be preferable to validate this conclusion.[35] On the other hand, in an RCT where MISTs alone were compared to MISTs + EMD and MISTs + EMD + bone mineral-derived xenograph (BMDX) for the treatment of isolated interdental intrabony defects, it was shown that the additional application of regenerative materials did not improve the results, although, as it was emphasized, the power of the study was limited to detect a difference of 0.96 mm.[36]

In a randomized, prospective, controlled clinical study, Ribeiro et al. compared MISTs + EMD and MISTs alone for the treatment of intrabony defects in a group of 14 patients.[37] Similar and significant results in terms of changes in PD, CAL, REC, and the radiographic parameters were demonstrated in the 2 groups at 3 and 6 months of follow-up. Thus, it was shown that in this type of bony defects, EMD did not offer an additional benefit to MISTs.[37] In another more recent RCT, Liu et al. compared the efficacy of MISTs alone and MISTs + deproteinized bovine bone mineral (DBBM) + collagen membrane in the treatment of isolated 1-, 2- and 3-walled defects in 2 groups of 15 and 16 patients, respectively, who attended a 1-year follow-up.[38] Both groups noted significant CAL gain and bone fill after 1-year evaluation. Nevertheless, the authors failed to find any significant differences in terms of PD reduction and CAL gain as well as in radiographic bone gain between the 2 groups. These results indicate that the use of DBBM + collagen membrane does not have any additional effect on 1-year outcomes.

Videoscope-assisted minimally invasive surgery (V-MIS) in combination with EMD and DFDBA was also performed for the regenerative treatment of 1-, 2- and 3-walled defects.[17,39,40] These studies demonstrated statistically significant improvement of the clinical measures as compared to baseline at 6 months, 12 months and 36 months postoperatively.[17,39,40] It is worth reporting that V-MIS led to minimal REC and, in some cases, the soft tissue height increased as compared to baseline. These results could be explained by the fact that with the use of the videoscope, tiny incisions and more effective root debridement can be insured.[17]

Moreover, MISTs were applied in conjunction with guided tissue regeneration (GTR) and a hydroxyapatite (HA)-based biomaterial.[24,41] Twenty-four intraosseous defects were treated with MISTs + HA/GTR or MISTs alone, and clinical outcomes in terms of PD reduction, CAL gain and REC increase were assessed at 6 months. It was concluded that MIST with and without HA/GTR should be considered as a valuable minimally invasive approach in the treatment of deep intraosseous periodontal defects.[41]

Minimally invasive surgical techniques have also been evaluated with growth factors. In a randomized, controlled, two-armed study, Mishra et al. assessed the impact of the addition of the recombinant human platelet-derived growth factor BB (rhPDGF-BB) gel on the efficacy of MISTs.[30] The results of the study showed significant PD reduction and CAL gain as compared to baseline in both groups – MISTs alone and MISTs + rhPDGF-BB – but no statistically significant intergroup differences were observed at 6 months postoperatively. Thus, improvement in the clinical and radiographic parameters was attributed to the performed surgical technique.[30] Recently, another RCT conducted to investigate the outcomes of MISTs with or without PRF for the treatment of isolated intrabony defects led to similar results with regard to the additional use of growth factors.[31] Although the 36 defects treated in 36 patients showed comparable improvement in the clinical and radiographic parameters at a 6-month follow-up, the authors concluded that, due to the limitations of the study design, such as a small sample size and a short observation period, the effect of PRF could not be excluded.[31]

Discussion

Minimally invasive surgical techniques gave a new perspective with regard to the periodontal regeneration of isolated and multiple intrabony defects, aiming to reduce the invasiveness of the surgery and patient morbidity as well as chair time. The use of microsurgical instruments and high magnification[42] as well as the introduction of the videoscope[25] made the single-flap MIST a feasible treatment modality in isolated 1-, 2- and 3-wall interproximal defects, which can be accessed and effectively debrided through a buccal or lingual flap window.[17,19,24] Nevertheless, even with the aid of magnification, the tiny unilateral flap elevation often enough is not adequate to access defects that extend to the opposite side of the buccal or lingual flap.[19,24] In such cases, the flap design has to be modified to the double-flap MIST with the elevation of the interdental papilla, and even vertical incisions for the adequate exposure of the defect.[18,20,23] The double-flap MIST was considered suitable for the treatment of intrabony defects with pure 3-wall, or shallow 2- and/or 1-wall subcomponents.[23] Though, in cases when severe defects are extended in almost all the sides of the tooth and/or a deep buccal or lingual bone dehiscence is present, a larger flap reflection, and possibly vertical or periosteal incisions are demanded for the complete exposure of the defect and the application of the selected regenerative biomaterials.[10,20] Thus, it seems that the extension of the defect determines the choice between the single- or double-flap MIST, and their limitations over deeper and more extensive defects.

The least possible increase in REC after the periodontal surgery of intraosseous defects is a great challenge for the operators aiming to fulfil the patients' demands with regard to esthetics, especially when the defect concerns the anterior esthetic zone. In the analyzed studies, the limited surgical trauma and the gentle manipulation of the soft tissues with MISTs led to the minimal,[18,23] and even not significant recession of the gingival margin as compared to the baseline values.[17,19,24] This is in accordance with the results of a meta-analysis by Clementini et al., demonstrating a mere and not statistically significant REC increase, using the MIST principles.[43] In a case series, in order to maintain the gingival margin stable after the surgical treatment of vertical defects, the authors applied atraumatic cause-related therapy, and subsequently the papilla preservation flap (PPF) technique in combination with the coronally advanced envelope-type buccal flap.[44] After 1 year, the shift of the gingival margin was nor statistically neither clinically significant.[44] Therefore, both MISTs and the conventional PPF techniques can be considered as less impairing the patient's esthetics, and thus should be preferred over the traditional flap designs.[45] Nevertheless, there is a need to clarify if MISTs could demonstrate the same esthetic outcomes in all types of defects. Some studies indicated that neither the morphology of the defect[17,19,46] nor the gingival biotype[46] could be considered as predictors for increased recession, whenever MISTs were performed. In their study, Farina et al. concluded that the apical shift of the gingival margin after the periodontal surgery depended on the presurgical interproximal PD and suggested the additive use of biomaterials in deep defects located in esthetic areas.[46] In contrast, Cosyn et al. claimed that non-supportive defects and a thin-scalloped gingival biotype were related to a greater post-surgical increase in REC.[28] Thus, more studies are necessary to determine the risk factors that may compromise the patient's esthetics after periodontal surgical treatment.

It has been reported that the application of MISTs in the treatment of intrabony defects induces subtle postoperative pain and decreases patient morbidity.[43] The lesser invasiveness and the minimal surgical trauma caused by MISTs reduces the patient's discomfort and need for painkiller consumption, irrespective of the type of regenerative materials applied.[10] Moreover, the perception of the post-surgical pain and the amount of analgesics taken by patients as well as the overall chair time have been found to be significantly lower for the MIST procedures as compared to the conventional surgical techniques.[10,46] In addition to favorable patient-centered outcomes, a low percentage of postoperative adverse effects has been documented during the healing period.[23,40,47] The primary wound closure was achieved in all cases examined, after the surgical procedure with MIST for the treatment of both single and multiple sites of defects. One week later, the rate of wound closure remained high at 95% and 100%, respectively.[23,34] In their study, Trombelli et al. noted the absence of membrane exposure in the patients treated with bioresorbable membranes and bone graft, although 2 smokers were included.[24] This was another benefit of MISTs, which increased their efficacy in the treatment of intrabony defects, as membrane exposure has been proven to jeopardize the clinical outcomes of regenerative therapy.[24,48] Mild postoperative pain and low patient morbidity rendered MIS a patient-friendly procedure and improved patient perception over surgical treatment.

The successful application of MISTs requires the use of magnification instruments for the adequate visualization of the surgical field.[16,18,25] Although the operative microscope and the videoscope can serve this purpose better than loupes, their cost could be a major consideration for the clinicians.[17,25] Moreover, since MISTs involve the surgical procedures performed under high magnification and the delicate manipulation of the soft tissues, they are regarded as clinically sensitive techniques, and require the clinicians' clinical skills and experience.

The defect anatomy is another factor that has to be further investigated in terms of its effect on the clinical efficacy of MISTs. In particular, intrabony defects with more residual bony walls are associated with a greater CAL gain and a decreased percentage of failure in clinical outcomes in case when MISTs are performed.[28,49] Contrarily, in their study, Harrel et al. used MISTs with the aid of the videoscope and concluded that the number of residual bony walls

did not have a significant impact on CAL gain.[17] Concerning the influence of the depth and the angle of the defect on the efficacy of MISTs, findings are also contradictory. Specifically, Cortellini et al. claimed that defects with a wider radiographic angle at baseline demonstrated less CAL gain, while the depth of the 3-wall subcomponent did not seem to affect clinical outcomes.[34] On the contrary, in another study by the same authors, the relation between the angle of the defect and CAL gain was found to be insignificant, while deeper 2- and 3-wall subcomponents showed more favorable clinical outcomes in terms of CAL gain.[49] Differences in the results of the abovementioned studies can be attributed to the small number of the participants. Thus, more studies with greater sample sizez are needed to clarify whether the defect anatomy can play a role as a determinant in the treatment of intrabony defects with MISTs.

Patient-centered factors, like poor oral hygiene and smoking, have been established to have a negative impact on the clinical outcomes of periodontal regeneration procedures.[50,51] Although most of the studies in which MISTs were applied included patients with well-controlled full-mouth plaque and bleeding scores; the presence of plaque was related with a reduced CAL gain after the periodontal surgery treatment. In addition, the occurrence of postoperative complications and non-compliance with the scheduled recall sessions were also predictors for failure in CAL gain and vertical radiographic bone gain.[27,28] It remains questionable if smoking can influence the clinical efficacy of MISTs. Trombelli et al. observed similar outcomes in terms of residual PD, CAL gain and REC increase between smokers and non-smokers, but significantly better early wound healing for the non-smokers group.[52] Nevertheless, these clinical results seem to be inferior for heavy smokers (>10 cigarettes per day). The inclusion of light smokers and a small sample size can be considered as limitations of that study, and more investigations are needed for firm conclusions.

Over the last decades, the conventional surgical techniques in conjunction with various biomaterials have been widely used for the regeneration of bone defects that remain after the cause-related therapy, with significant benefits in terms of defect filling and periodontal attachment gain.[13,53,54] Minimally invasive surgical techniques have been successfully combined with biologically active materials, such as amelogenins[18,23,29,33–35,37] and growth factors,[30,46] bone replacement grafts,[27,28] and PRF,[31] or in conjunction with two[17,24,36,38,39,41] or more[36] different biomaterials for the periodontal regeneration of intrabony defects. Cortellini in 2012 proposed various regenerative strategies with MISTs depending on the defect morphology.[20] Thus, the single-flap MISTs can be applied in the case of any defect anatomy, either alone or combined with EMD. In addition, the double-flap MIST is suggested to be performed in conjunction with EMD for the treatment of self-supporting defects, and with EMD and graft for non-contained defects. Nevertheless, the additional use of regenerative materials does not seem to significantly improve the clinical outcomes of MISTs, as reported in the available RCTs.[30,31,36–38,41] In a meta-analysis of 4 RCTs, the mean differences between the MISTs + biomaterials and MISTs alone groups in terms of PD reduction, CAL gain and REC increase were 0.20 mm (95% confidence interval (*CI*): –0.26–0.66; $p = 0.40$), 0.24 mm (95% *CI*: –0.32–0.71; $p = 0.32$), and 0.03 mm (95% *CI*: –0.22–0.28; $p = 0.81$), respectively.[55] None of these differences was found to be statistically significant, confirming the fact that extra additives to MISTs do not provide further clinical benefits. On the contrary, the impact of biomaterials is important when they are combined with the conventional surgical techniques.[13] Although, the PPF techniques improved the clinical efficacy of the conservative surgery in the treatment of intrabony defects,[45] periodontal regenerative therapy still leads to significantly superior clinical outcomes.[13] The regenerative potential of MISTs as a standalone protocol in the treatment of intrabony defects may be a consequence of the primary wound closure, and the optimal wound and blood clot stability.[18,23,24] In addition, the integrity of the interdental tissues can insure the necessary blood supply and space for the formation of the blood clot.[19,24] These factors have been documented in experimental studies to be determinants for periodontal regeneration and the clinical efficacy of MISTs can be attributed to them.[56–58] Though, the small sample sizes and the short follow-up periods of the available RCTs do not allow the extrapolation of definitive conclusions.

A practical question would be if the evolved flap design of MISTs could be considered more conducive in the surgical treatment of intrabony defects in comparison with the conventional PPF techniques. This was the main objective of 2 RCTs comparing the efficacy of the single-flap MISTs and of the double-flap PPF technique with or without the use of regenerative materials.[46,59] In 2 groups of 14 patients, Trombelli et al. compared buccal MISTs and SPPT/MPPT for the treatment of intrabony defects.[59] Although the MISTs group demonstrated significantly greater PD reduction and CAL gain than the PPF group at a 6-month follow-up, these values were not statistically significantly different, when the comparison was adjusted to the pre-surgical PD and CAL values of the 2 groups. Both PD reduction and CAL gain were significantly different for the 2 groups as compared to baseline. An increase in REC was similar for the 2 groups at 6 months, but statistically significantly greater only for the MISTs group as compared to baseline. The authors had to take into account that the 2 groups were different in terms of age, number of smokers, PD, and bleeding score positive sites, though it was considered to have a significant impact only on PD reduction.[59] In another RCT, Schincaglia et al. assessed clinically and radiographically the efficacy of a single buccal or oral flap elevation MIST and the double-flap papilla preservation technique (SPPT, MPPT) combined with rhPDGF-BB and β-tricalcium phosphate (β-TCP) in

the treatment of 1-,2- and 3-wall defects.[60] The 2 groups demonstrated significant changes in PD, CAL, REC, and the radiographic parameters at a 6-month follow-up, but the parameters were not significantly different between the 2 groups. Although PD reduction and CAL gain were slightly greater for the MISTs group, it included significantly fewer 1-wall defects than the PPF group. Nevertheless, patients from the MISTs group reported significantly lesser postoperative pain and painkiller consumption, while the early wound healing was better.[60] This was attributed to the lesser invasiveness and the limited flap extension of MISTs, which provide minimal trauma and better wound stability.[46] In a more recent RCT, Windisch et al. compared the clinical outcomes of MISTs + EMD with the more extended flap design of MPPT or SPPT + EMD for the treatment of 23 and 24 subjects, respectively.[61] As in the previous two RCTs, no significant differences were observed in the clinical parameters between the 2 groups.[61] It can be concluded that MISTs are at least as effective as the conventional PPF techniques, though this conclusion has to be further examined in more studies that will directly compare these techniques.

Conclusions

Minimally invasive surgical techniques significantly decreased surgical trauma in the soft tissues and the rates of wound failure after the periodontal surgery. As a consequence, many favorable clinical outcomes were observed in the studies in which MISTs were applied, while the patient perception of the periodontal surgery was improved. The adjunctive use of regenerative materials seems to have a less determinant effect on the clinical performance of MISTs. It is critical for the clinicians to estimate adequately the defect morphology in order to apply the most suitable surgical technique. Finally, more studies are required to evaluate the potential superiority of MISTs over the conventional techniques.

Ethics approval and consent to participate

Not applicable.

Data availability

All data analyzed during this study is included in this published article.

Consent for publication

Not applicable.

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