

How to Cite:

Helal, M. E.-D., Ibrahim, R. O., El-Refaie, M. I. F., & Kenawy, S. M. (2022). Clinical and radiographic evaluation of non-incised papilla surgical approach (NIPSA) versus modified minimally invasive surgical technique (M-MIST) in treatment of intraosseous defects in patients with stage III periodontitis: A randomized clinical trial. *International Journal of Health Sciences*, 6(S6), 2270–2283. <https://doi.org/10.53730/ijhs.v6nS6.10482>

Clinical and radiographic evaluation of non-incised papilla surgical approach (NIPSA) versus modified minimally invasive surgical technique (M-MIST) in treatment of intraosseous defects in patients with stage III periodontitis: A randomized clinical trial

Marwa EL-Desouky Helal BDS, MSC*

Assistant Lecturer, Department of Oral Medicine, Oral Diagnosis, Periodontology, Modern University for Technology and Information (MTI University), Faculty of Dentistry, Cairo, Egypt.

*Corresponding author email: Marwa.helal@dentistry.cu.edu.eg

Riham Omar Ibrahim MSC, PhD

Professor of Periodontology, Faculty of Dentistry, Cairo University, Egypt

Mahmoud Ibrahim Fahmy El-Refaie MSC, PhD

Professor of Oral Medicine, Oral Diagnosis, Periodontology, Faculty of Dentistry, Cairo University, Egypt | Dean faculty of Dentistry, Modern University for Technology and Information (MTI University), Cairo, Egypt.

Sarah Mohammed Kenawy MSC, PhD

Lecturer of Oral and Maxillofacial Radiology Department, Faculty of Dentistry, Cairo University, Egypt

Abstract---Background: Minimally invasive surgical (MIS) procedure" in multiple and isolated intra-osseous defects maintained the entire interdental papilla with significant improvement in clinical and radiographic outcomes compared to traditional periodontal surgeries. Methods: Thirty-two intra-osseous defects in 15 patients were enrolled for this study and were randomly allocated to both groups i.e. (16 defects) per group. Patients in group I (test group) went for Non-Incised Papilla Surgical Approach (NIPSA), while, in group II (control group), patients received Modified Minimally Invasive Surgical Technique (M-MIST). All clinical and radiographic periodontal parameters were measured at baseline, six months and twelve months. Results: Patients in both groups showed significant

improvements in clinical and radiographic outcomes after twelve months of follow-up including reductions in CAL, potential effect in post-surgical patients' satisfaction and intra-osseous defect fill. Absence of significant difference regarding intergroup comparisons. The minimal surgical flap design plays a very important role in the success of the therapy, creating and maintaining a stable space for the clot. Conclusions: NIPSA is viewed as a promising minimally invasive technique even in hopeless teeth with severe periodontal bone loss, clinical attachment loss to the apex and minimal keratinized tissue.

Keywords---non-incised papilla surgical approach, surgical flaps, alveolar bone loss, periodontitis, intra-osseous defects.

Introduction

The concept "minimally invasive surgical (MIS) procedure" in periodontal regeneration was introduced for the treatment of multiple and isolated intra-osseous defects, utilizing an intra-sulcular incision, maintaining the entire interdental papilla and elevating minimal flaps to have access to the intra-osseous defects. MIS procedure yield significant reduction in probing pocket depth, improvement in clinical attachment level, little increase in post-operative recession, significant postsurgical comfort, less chair time, faster wound healing and lower morbidity compared with traditional periodontal surgeries [1]. There is an increasing interest in the scientific community for the investigation of different flap designs to reduce the negative outcomes of interdental wound failure. Thus, the concept of minimal invasive surgical techniques was developed with gentle tissue manipulation under high magnification and minimal surgical trauma [2].

The "minimally invasive surgical technique" (MIST) was proposed in 2007 [3]. In the MIST approach, the defect associated interdental papilla was accessed either with the modified papilla preservation technique (MPPT) in large interdental spaces [4], or the simplified papilla preservation flap (SPPF) in narrow interdental spaces [5]. Later, the concept of space provision for regeneration with the modified minimal invasive surgical technique (M-MIST) was introduced. The surgical approach consists of only buccal horizontal incision at the base of papilla and connected with a tiny interdental access through small mesial and distal intra-sulcular incisions. [6]. A 3-armed randomized controlled clinical trial was published to compare the efficacy of "modified minimally invasive surgical technique" alone versus modified-minimally invasive surgical technique combined with amelogenin and amelogenin plus bone mineral-derived xenograft, in the treatment of isolated interdental intra-osseous defects. They concluded that, modified minimally invasive surgical technique with or without regenerative materials was efficacious in the treatment of intra-osseous defects [7].

It was found that modified minimally invasive surgical technique alone or with recombinant Human Platelet Derived Growth Factor gel showed no statistical difference in CAL gain, PD reduction between the two groups. Mishra et al. published a human study showing that significant pocket reductions, clinical

attachment gains were obtained at 3 and 6 months in both groups only [8]. Thus Clinicians should be trained enough for minimal invasive surgical techniques as flap design represented a very important parameter in any surgical procedure in which the stability of the marginal tissue and good revascularization during early wound healing were essential to promote stable wound closure, the success of the therapy, creating and maintaining a stable space for the clot. [9].

Moreno-Rodríguez and Caffesse (2017) introduced the non-incised papilla surgical approach (NIPSA) to gain access to periodontal defects from its apical aspect with the aim of achieving clinical improvements compared with marginal access techniques. NIPSA allowed the structure of the interproximal tissue to be maintained without affecting or detaching the marginal tissues. In this way, the interproximal tissue represented as a “dome” to preserve the stability of the clot in the underlying defects and anticipated the collapse of marginal soft tissues. So, NIPSA had great potential effect in treatment deep isolated deep inter- proximal with buccal intra-osseous defects especially when there is deep interdental gingival recession [10]. However, M-MIST suggested to be used to treat deep interproximal with intact lingual intra-osseous defects especially when there is wide area of keratinized tissue and thick phenotype in order to preserve the interdental papilla after surgery [11].

Most studies that investigated the different flap design on the blood clot stability indicated a positive effect of faster periodontal wound healing [12]. A recent systemic review with meta- analysis carried by Clementini et al. showed that that the use of biomaterials or membranes does not seem to contribute to the improvement of clinical periodontal parameters after a minimally invasive periodontal surgery. However, this was not true for the traditional periodontal surgery, since the absence of a regenerative material has a significant impact on the effectiveness of these surgical procedures [13].

Aim of the study

The aim of this randomized clinical trial was to evaluate the clinical and radiographic effectiveness of Non-Incised Papilla Surgical Approach (NIPSA) compared to Modified Minimally invasive surgical technique (M-MIST) in the treatment of periodontal intraosseous defects in stage III periodontitis patients.

Materials and Methods

Study design and patient population

The present study is a randomized, controlled, parallel-grouped clinical trial that included thirty- two intra-osseous defects in 15 patients aged between 20 and 60 years old with stage III periodontitis presenting intraosseous defects. Patients were randomly assigned into two equal groups: (Test Group) in which NIPSA was done, while in (Control Group) the M-MIST was done. Subjects were selected from the outpatient clinic. Department of Oral Medicine and Periodontology, Faculty of Dentistry, Cairo University between August 2019 to August 2020 patient's screening was continued until the target sample was achieved, identifying, and recruiting potential subjects were achieved through patients' database.

Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Age: 20-60.	Systemic disease that contraindicates the surgical procedures.
Patients with Stage III periodontitis (clinical attachment level (CAL) $\geq$ 5mm and pocket depth (PD) $\geq$ 6 mm).	Poor patient's compliance
Patients having at least one tooth with Two walls or combined 2- to 3-walls intraosseous defects $\geq$ 3 mm deep.	Presence of an orthodontic appliance.
Patients with defect not extended to a root furcation area.	Pregnancy or breast feeding.
Non- smoker patients	
Patients consent approval and signing.	

Surgical techniques

The study groups were carried out as follows:

- Test group: Patients received Non-Incised Papilla Surgical Approach (NIPSA).
- Control group: Patients received Modified-Minimally Invasive Surgical technique (M-MIST).

In NIPSA group, an apical horizontal incision on the buccal mucosa, as far as possible from the interdental papillae and marginal KT was performed. Soft tissue was reflected apico-coronally by a full-thickness flap showing the granulation tissue filling the osseous defect after exposing the coronal limit of the intra-osseous component of the defect, while the marginal tissue was kept unaltered. In M-MIST group, access to the defect was gained through the tiny buccal triangular flap: from the buccal 'window' the soft tissue filling the defect (i.e. the so-called granulation tissue) that was sharply dissected from the papillary supra-crestal connective tissue and from the bony walls with a micro-blade and removed with a mini-curette (the soft tissue was sharply dissected from the osseous defect). In both groups, a digital periapical radiograph using long cone paralleling techniques with the aid of Digora software pre-operatively (baseline), 6 months and 1- year post-surgically was carried- out to evaluate for the effectiveness of the surgical procedure in the treatment of the intra-osseous defect. Following surgery Augmentin (gsk Glaxo-smith Kline) 1gm tablet twice daily for five days and Ibuprofen 600mg tablets twice daily for three days.

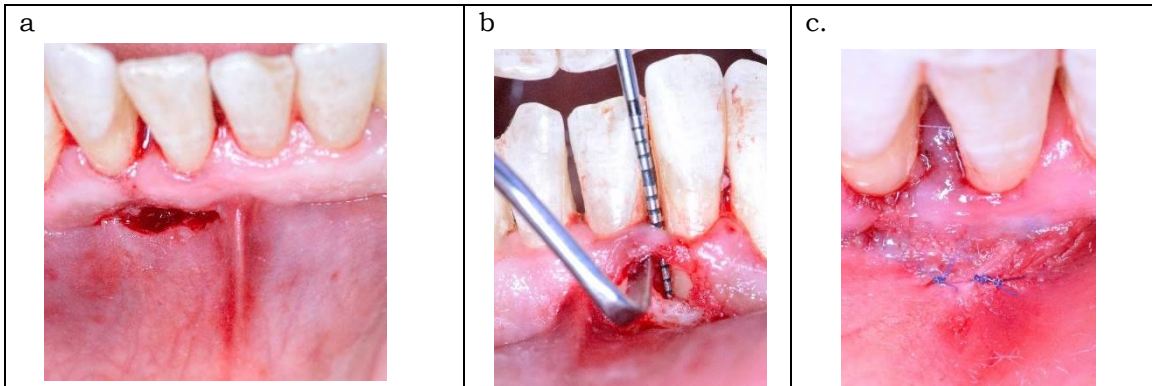
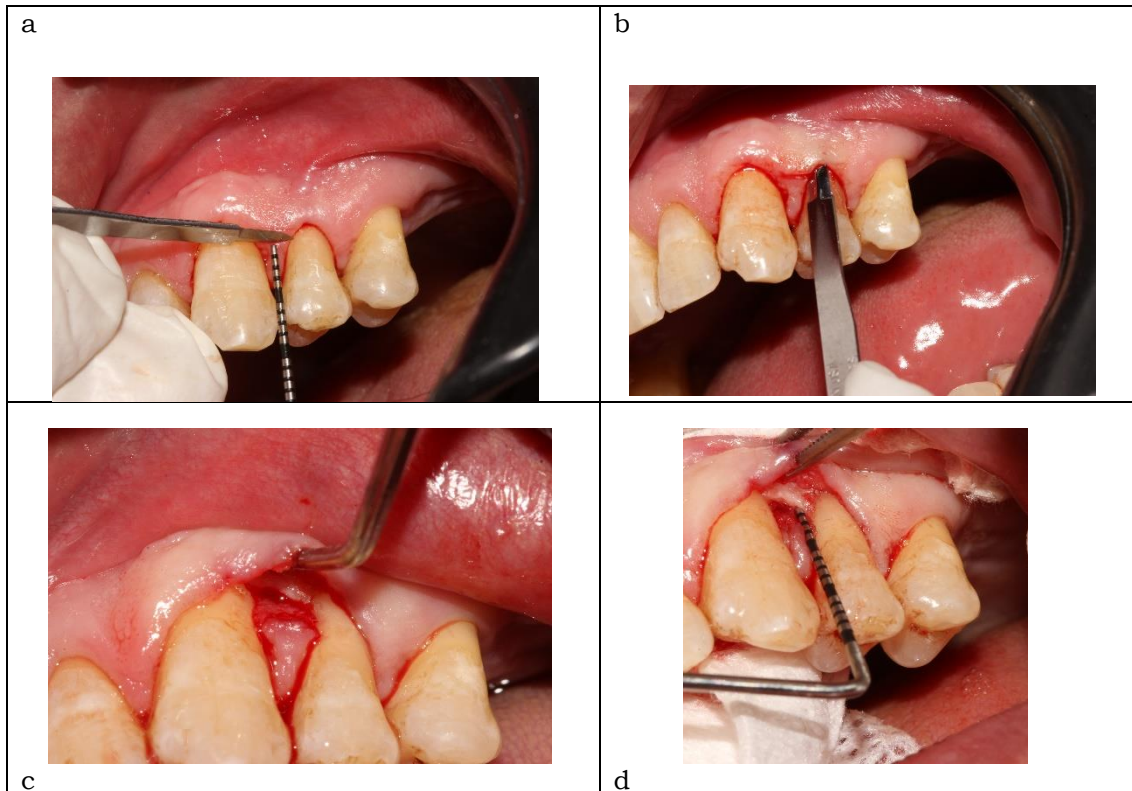
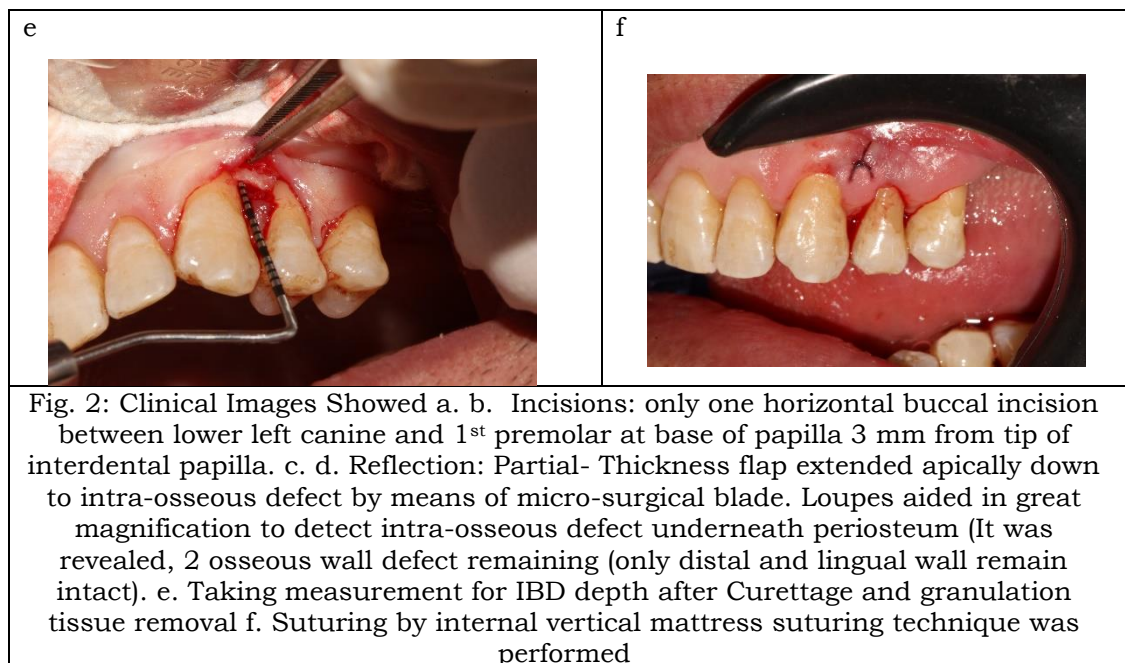
NIPSA Group

Fig. 1: Clinical Images Showed a. Incisions: only one horizontal incision in lower right lateral and central incisor with intra-osseous defect down to MGJ apical to interdental papilla b. Reflection: Full- Thickness flap extended laterally (Mesial and distal) from area of intra-osseous defect underneath interdental papilla by means of micro-surgical mucoperiosteal elevator. c. Suturing by (internal horizontal mattress suture with internal vertical mattress suture) was performed

M-MIST Group:



Data collection and follow-up

Patients were followed up for twelve months after both surgical procedures. Clinical assessment was recorded at baseline (2- months after phase I therapy), 3,6,12 months after surgery including (CAL- PD- GR- GB score), while radiographic assessment for intra-osseous defect fill was recorded using standard digital radiography. Post-surgical patient satisfaction using questionnaire of three questions.

Radiographic evaluation

Standardized periapical radiographs were obtained preoperatively and at follow-up appointments using the long cone paralleling technique. All radiographs were obtained using the same x-ray machine (Minary, SOREDEX, Tuusula- Finland) with exposure parameters (70 KVp, 7 mA and 0.08 seconds exposure time). For radiographic standardization, construction of radiographic stents was done in order to perform an individualized Extension Cone Paralleling (XCP) index for each patient [14]. Then, radiographic images were calibrated on Digora software for measurement the changes in the depth of the intra-osseous defect.

Patient centered outcome

Post- surgical patient satisfaction was evaluated using a questionnaire of three questions that were asked to determine patient's satisfaction with the outcome of surgery. These questions could all be answered by the patient using a 7- point response scale Where: Very Satisfied = 7; Not Satisfied = 1 [15].

Results

Demographic data

Age, Gender

A total of 15 participants with 32- intra-osseous defects i.e. (16 defects) per group were enrolled in this study and all of them attended the 12-months follow-up period. The mean, standard deviation (SD), frequencies (n), percentages (%), and P-value for demographic data of all participants are presented in (Table 1). The mean age of patients in the group of NIPSA (test group) was 35.31 years (± 6.78) and for the M-MIST, the control group was 35.13 (± 5.11) years. As for gender distribution, the NIPSA group included 3 males (18.8%) and 13 females (81.3%), for the M-MIST group 6 males (37.5%) and 10 females (62.5%). Results of the current study showed that there was no statistically significant difference between mean age values in the two groups. In addition, there was no statistically significant difference between gender in the two groups.

Table 1
Mean, standard deviation (SD), percentages and results of Student's t-test and Chi-square test for comparisons of demographic in the two groups

	Test (n = 16)	Control (n = 16)	P-value
Age (Years)			
Mean (SD)	35.31 (6.78)	35.13 (5.11)	0.930
Gender [n (%)]			
Male	3 (18.8%)	6 (37.5%)	0.246
Female	13 (81.3%)	10 (62.5%)	

*: Significant at $P \leq 0.05$

Clinical assessment

Clinical attachment level (CAL)

Comparison between the two groups

The mean, standard deviation (SD), P-value data for clinical attachment level (CAL) are presented in (Table 2). At baseline (2 months after phase I therapy) as well as after twelve months; there was no statistically significant difference between CAL in the two groups (P -value = 0.050, Effect size = 0.06) and (P -value = 0.260, Effect size = -0.38), respectively.

Table 2
Descriptive statistics and results of Mann-Whitney U test for comparison between CAL in the two groups

Time	Test Group (n = 16)	Control Group (n = 16)	P-value	Effect size (d)
	Mean (SD)	Mean (SD)		
Baseline	7.06 (1.65)	7.00 (1.37)	0.050	0.06
12 months	2.94 (1.00)	1.31 (1.49)	0.260	-0.38

*: Significant at $P \leq 0.05$

Changes within each group

In both groups; there was a statistically significant decrease in Mean CAL after twelve months (P -value = 0.001, Effect size = 3.69) and (P -value = 0.001, Effect size = 4.13), respectively.

Radiographic assessment Radiographic defect fill

The mean, standard deviation (SD) and P -value data for Radiographic defect fill are presented in (Tables 3).

Table 3
Descriptive statistics and results of repeated measures ANOVA test for comparison between Radiographic defect fill (mm) in the two groups

Time	Test Group (n = 16)		Control Group (n = 16)		P -value	Effect size (Mean difference)
	Mean	SD	Mean	SD		
Bl- 6 m	1.10	0.56	1.47	0.42	0.050	-0.371
Bl- 12 m	1.98	1.02	2.67	0.63	0.072	-0.692
6 m -12 m	0.88	0.53	1.20	0.34	0.051	-0.321

*: Significant at $P < 0.05$

Comparison between the two groups

In the three different time periods; there was no statistically significant difference between mean radiographic defect fill in the two groups (P -value = 0.050, Effect size = -0.371), (P -value = 0.072, Effect size = -0.692) and (P -value = 0.051, Effect size = -0.321) respectively. While there was a statistical significant increase in mean of radiographic defect fill for each group in different time periods from Bl-6m; Bl- 12m and 6m- 12m (P -value <0.001, Effect size = -2.588), (P -value < 0.001, Effect size = -5.263) and (P -value < 0.001, Effect size = -6.935).

Patient- reported outcome data Post- surgical patient satisfaction

At baseline time and after 12 months, all cases in the two groups had no statistical significant difference (P -value = 0.448; 0.169) respectively. However, from Bl- 12 months, there was a statistically significant difference between post-surgical patient satisfaction in the two groups (P -value = 0.001, Effect size = 0.500) and (P -value = 0.004, Effect size = 0.688), respectively.

Discussion

It was believed that the important critical key features for successful outcome in the treatment of periodontal defects is; creating and maintaining space to retain the clot and promote regeneration, maintaining primary closure and the third is minimizing the post-operative soft tissue shrinkage of the marginal tissues [16]. Rethman et al. concluded that using conventional periodontal surgery resulted in

flap dehiscence and recorded the absence of primary closure of interdental area in 70% to 80% of the treated sites ^[17]. From that point, the philosophy of minimal invasive surgical procedures was developed to have minimal tissue trauma, less cell damage and necrosis, primary passive wound closure was achieved by micro suturing to eliminate gaps and dead spaces. Thus, reduce morbidity, closer the wound apposition, reduce hemorrhage and reduce trauma at the surgical site with anastomosis of microsurgical wounds within 48 hours under high power of magnification with better surgical performance ^[18].

This randomized clinical trial was designed to evaluate the clinical and radiographic effectiveness of Non-Incised Papilla Surgical Approach (NIPSA) compared to Modified Minimally invasive surgical technique (M-MIST) in the treatment of periodontal inter-proximal intraosseous defects in stage III periodontitis patients. Patients suffering from systemic diseases that contraindicate periodontal surgical procedures, Poor patient's compliance, psychological problems, Pathology at the site of intervention were excluded from this study. This was according to a study performed by Gomez de Diego et al. ^[19]. Regarding the surgical procedures, all included patients were given careful instructions on proper oral hygiene measures including tooth brushing (modified stillman brushing technique) twice daily with a soft- bristled toothbrush after initial periodontal therapy (Non- Surgical) that was performed 2 months prior to any surgical procedures. Then, immediate (baseline) periapical digital radiographic system was obtained using Digital x-ray machine with the fixed pre-mentioned exposure parameters. Images were captured using standardized paralleling technique by the (XCP) alignment system with the radiographic stent and the large 3x4 cm phosphor storage plates (PSPs) imaging plate. The vista scanner scanned imaging plates automatically, and then, radiograph served as a baseline radiograph for future comparisons.

In Group A patients received NIPSA technique ^[20], while for Group B the patients received M-MIST technique ^[21]. Both techniques were able to achieve the planned goal for minimal invasive surgical techniques with best clinical success and no major complications were found. Non-incised papillae surgical approach (NIPSA) emphasized the preservation of the papillae and marginal tissues which allow space for the blood clot, primary healing, and wound stabilization. This surgical approach had been specifically indicated as periodontal reconstructive procedure for interproximal intra-bony defects requiring a buccal aspect of the tooth extension to allow correct visualization of the defect's boundaries and provide access through a minimal incision ^[22]. To the best of our knowledge, no RCT compared between marginal approach (modified minimal invasive surgical technique (M-MIST)) and apical approach (non- incised papilla surgical approach (NIPSA)). For NIPSA, a few preliminary studies describe the apical approach for periodontal reconstructive surgery, although apical approach techniques have been widely developed with good results ^[23].

Moreno -Rodrguez and Caffesse reported the importance of changing the flap design from traditional technique to minimal invasive surgical techniques as flap design represented a very important parameter in any surgical procedure regarding the stability of the marginal tissue, creating and maintaining a stable space for the clot and good revascularization during early wound healing that

were essential to promote stable wound closure. Thus, NIPSA represents a new surgical approach for the management of soft tissues in periodontal surgery, maintaining the papillae and marginal tissues intact [24]. The results of the present study showed that periodontal reconstructive surgery in teeth with advanced periodontal loss and deep periodontal pockets associated with deep intraosseous defects can be achieved by both techniques with a reduction in the periodontal pocket depth, a significant gain in clinical attachment and bone fill at 1 year follow up.

Concerning NIPSA group, there was a statistical significant difference from baseline to 1- year follow- up and between (BL- 3m), (BL- 6m), (BL- 12m), time periods concerning CAL. In addition, a statistically significant difference was found also between (Bl-3m) and each of (Bl-6m) and (Bl-12m). However, there was no statistically significant difference between the (Bl-6m) and (6m-12m). In addition, there was no statistical significant difference observed between both groups. For M-MIST group, a statistical significant difference was observed regarding CAL from baseline to 1- year follow- up and between baseline and each of 3, 6 months. Furthermore, there was statistically significant difference between (Bl-3m) and each of the (Bl-6m) and (Bl-12m). However, there was no statistically significant difference between (6m-12m) and each of the (Bl-3m) and (Bl-6m) groups.

Accordingly, approximately similar findings were observed in retrospective cohort study conducted by Moreno- Rodriguez et al. that compared the NIPSA and MIST with EMD. It was reported that there was a statistical significant clinical attachment gain (CAG) ($P < 0.001$), PD reduction (5.53 ± 2.56 mm) at one-year post-surgery with a lower postoperative gingival recession of NIPSA than MIST. The higher value in CAL gain and PD reduction less GR might be attributed to longer follow- up period 1- year or due to the use of a regenerative biomaterial of EMD [25]. Moreno Rodriguez and Caffesse conducted a study of case series of 10 treated patients with deep intra- bony defects treated with NIPSA in conjunction with HA graft and EMD procedure. The postoperative healing period ranging from 6-18 months with a mean of CAL gain (7.3 mm) and mean PPD reduction of (7.3 mm) were observed with no variation in REC. They suggested that the adoption of biologic products/ compounds is based on their ability to induce or accelerate the process of matrix formation and cell differentiation. These products enforce the healing process but lack the mechanical properties to help in the provision of space and blood clot stabilization [26].

Furthermore, Xiyan Pei conducted case series and cohort studies that compared three novel approaches (entire papilla preservations (EPP), non-incised papillae surgical approach (NIPSA) and modified vestibular incision sub-periosteal tunnel access (M-VISTA)). The resultant findings are in accordance to the present study that EPP and NIPSA seemed to have advanced results of CAL gain ranged from (5.3 to 6.3 mm), PD reduction ranged from (5.5 to 6.5 mm). it was attributed to the presence of a great volume of intact supra-crestal soft tissue, better preservation of the blood supply in the interdental area. [27]. In addition, a meta-analysis that was conducted by Cortellini et al. reported similar findings to current study, where it included ten studies (1 retrospective, 5 cohorts and 4 RCTs) for treatment of periodontal defects with at least 6 months of follow-up. All

the studies consistently support the efficacy of minimally invasive surgery for treatment periodontal defects in groups of M-MIST, M-MIST + EMD and M-MIST + bone mineral derived xenograft (BMDX) with significant probing pocket depth reduction with mean (4.4 ± 1.6), (4.4 ± 1.2) and (4.0 ± 1.3) respectively, CAL gain with mean (4.1 ± 1.4 mm), (4.1 ± 1.2 mm) and (3.7 ± 1.3 mm). and thus the regenerative potentiality of biomaterials was increased [28]. While Cortellini and Tonetti focused on the intrinsic healing potential of the surgical approach and reported that M - MIST was designed to optimize wound and blood clot stability, flap margin blood perfusion and provided a stable space for regeneration [29].

The evaluation of radiographic changes in the present study revealed that there was a statistical significant difference in bone level treated by (NIPSA) between baseline and after 1- year follow up with percent mean change (68.93 %). While in M-MIST there was a statistical significant difference between the baseline and after 1- year follow up with (74.19%) percent mean change. However, there is no statistical significant was observed between both groups. And this similar to what reported in systematic review and meta- analysis by Clementini et al. that showed high mean change in radiographic bone fill of (58.25%) for all studies with small differences were also observed (59.29% for RCTs and 53% for case series) in favoring to (MIPS), when comparing minimal invasive periodontal surgeries (MIPS) to traditional flap approaches [30], Chambrone and Tatakis highlighted the importance of paying attention to patient- reported outcomes, being a topic that needs additional research and should be considered in the decision- making process. In the current study, there was a statistical significant increased with mean of post-surgical patient satisfaction after 2 months (3.88 ± 1.67) and after 12 months become (5.44 ± 1.36) in control group. But for test group, there was a statistical significant increased with mean after 2 months (4.38 ± 1.09) and after 12 months become (6.13 ± 0.96). However, there was no statistical significant difference was observed between both groups [31].

Finally, the present study suggested that NIPSA have to be used to treat deep inter- proximal with buccal intra-osseous defects especially when there is deep interdental gingival recession and the clinician to have improvements in bone fill, preserving the remaining intact free gingival from further recession post-operative. However, M-MIST suggested also to be used to treat deep interproximal with intact lingual intra-osseous defects especially when there is wide area of keratinized tissue and thick phenotype in order to preserve the interdental papilla after surgery. Case selection for specific morphology, depth of intra- osseous defect and soft tissue overlying that defect is a must to be suitable for each minimal invasive surgical technique in order to get significant CAL gain, PD reduction, bone fill and minimal post- operative gingival recession with preserving interdental papilla.

Conclusions

Within the limitations of this randomized clinical trial, there was no significant difference between buccal approach “M-MIST” and apical approach “NIPSA” in stage III periodontitis patients with inter-proximal intra-osseous defects. Both were closely effective in improving the clinical parameters including clinical

attachment gain, probing depth reduction post- operative patients' satisfactions and radiographic defect fill.

Recommendations

Further RCT and systematic reviews should be performed to compare different techniques of minimal invasive surgeries together and/or with conventional techniques to assess their effectiveness on improving clinical, radiological and patient- centered outcomes.

Funding

"This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors."

Conflict of Interest: None

References

1. Harrel, S. K., Nunn, M. E. and Belling, C. M. (1999): "Long-Term Results of A Minimally Invasive Surgical Approach for Bone Grafting". *J. Periodontol.* Dec; 70 (12): 1558-63.
2. Shanelec, D. A., Tibbetts L. S. A. (1996): "Perspective on the Future of Periodontal Microsurgery". *Periodontol.* 2000; 11: 58-64.
3. Cortellini, P. and Tonetti, M. S. (2007): "A Minimally Invasive Surgical Technique with an Enamel Matrix Derivative in the Regenerative Treatment of Intra Bony Defects, A Novel Approach to Limit Morbidity". *J. Clin. Periodontol*; 34 :87 9.
4. Cortellini, P., Prato, G. P., Tonetti, M. S. (1999): "The simplified Papilla Preservation Flap. A Novel Surgical Approach for the Management of Soft Tissues in Regenerative Procedures." *Int. J. Periodontics. Restorative Dent.*; 19: 589 99.
5. Cortellini, P., Prato, G. P., Tonetti, M. S. (1995): "The Modified Papilla Preservation Technique. A New Surgical Approach for Interproximal Regenerative Procedures". *J. Periodontol.*; 66: 261 6.
6. Cortellini, P. and Tonetti, M. S. (2009): "Improved Wound Stability with a Modified Minimally Invasive Surgical Technique in the Regenerative Treatment of Isolated Interdental Intra-Bony Defects". *J. Clin. Periodontol.* ;36(2): 157-163.
7. Cortellini, P. and Tonetti, M. S. (2011): "Clinical and Radiographic Outcomes of the Modified Minimally Invasive Surgical Technique with and without Regenerative Materials: A Randomized-Controlled Trial in Intra-Bony Defects". *J. Clin. Periodontol.* Apr; 38(4): 365-73.
8. Mishra, A., Avula, H., Pathakota, K. R. and Avula, J. (2013): "Efficacy of Modified Minimally Invasive Surgical Technique in the Treatment of Human Intra-Bony Defects with or without Use of rhPDGF-BB Gel: A Randomized Controlled Trial". *J. Clin. Periodontol.*; 40(2): 172-9.
9. Harrel, S. and Rees, T. (1995): "Granulation Tissue Removal in Routine and Minimally Invasive Surgical Procedures". *Compendium of Continuing Education Dentistry*; 16: 960–967.

10. Moreno-Rodríguez, J. A. and Caffesse R. G. (2017): "A New Papilla Preservation Technique for Periodontal Regeneration of Severely Compromised Teeth." *Clinical Advances in Periodontics*; 1–16.
11. Cortellini, P. and Tonetti, M. S. (2009): "Improved Wound Stability with a Modified Minimally Invasive Surgical Technique in the Regenerative Treatment of Isolated Interdental Intra-Bony Defects". *J. Clin. Periodontol.*;36(2): 157-163.
12. Moreno-Rodríguez, J. A. and Caffesse R. G. (2017): "A New Papilla Preservation Technique for Periodontal Regeneration of Severely Compromised Teeth." *Clinical Advances in Periodontics*; 1–16.
13. Clementini, Marco, Ambrosi, A., Ciccirelli, V., De Risi, V. and Sanctis, M. (2021): "Clinical Performance of Minimally Invasive Periodontal Surgery in the Treatment of infra-bony Defects: Systematic Review and Meta- analysis." *Journal of Clinical Periodontology*; 46 (12): 1326- 53.
14. Pradeep, A R. 2012 "Platelet-Rich Fibrin Combined With a Porous Hydroxyapatite Graft for the Treatment of Three-Wall Intrabony Defects in Chronic Periodontitis: A Randomized Controlled Clinical Trial." *Journal of Periodontology*; 1–8.
15. Kiyak, H. A., Hohl, T., West, R. A. and McNeill, R. W. (1984): "Psychologic Changes in Orthognatic Surgery Patients: A 24-Month Follow Up." *Journal of Oral and Maxillofacial Surgery*; 42 (8): 506–12.
16. Moreno- Rodríguez, J.A. and Caffesse, R.G. (2018): Non-Incised Papillae Surgical Approach (NIPSA) in Periodontal Regeneration: Preliminary Results of a Case Series". *Int. J. Periodontics. Resto. Dent.*; 38: 105–111.
17. Rethman, Michael, P., Stephen, K. and Harrel. (2010): "Commentary Minimally Invasive Periodontal Therapy: Will Periodontal Therapy Remain a Technologic Laggard?". *J. Periodontol.* 81: 1390–95.
18. Shanelec, D. A., Tibbetts L. S. A. (1996): "Perspective on the Future of Periodontal Microsurgery". *Periodontol.* 2000; 11: 58-64.
19. Gómez-de Diego R, Mang-de la Rosa Mdel R, Romero-Pérez MJ, Cutando-Soriano A, López-Valverde-Centeno A. Indications and contraindications of dental implants in medically compromised patients: update. *Med Oral Patol Oral Cir Bucal.* 2014;19(5): e483-e489.
20. Moreno-Rodríguez, J. A. and Caffesse R. G. (2017): "A New Papilla Preservation Technique for Periodontal Regeneration of Severely Compromised Teeth." *Clinical Advances in Periodontics*; 1–16.
21. Cortellini, P. and Tonetti, M. S. (2009): "Improved Wound Stability with a Modified Minimally Invasive Surgical Technique in the Regenerative Treatment of Isolated Interdental Intra-Bony Defects". *J. Clin. Periodontol.*;36(2): 157-163.
22. Moreno-Rodríguez, J. A. and Caffesse R. G. (2017): "A New Papilla Preservation Technique for Periodontal Regeneration of Severely Compromised Teeth." *Clinical Advances in Periodontics*; 1–16.
23. Moreno- Rodríguez, J.A. and Caffesse, R.G. (2018): Non-Incised Papillae Surgical Approach (NIPSA) in Periodontal Regeneration: Preliminary Results of a Case Series". *Int. J. Periodontics. Resto. Dent.*; 38: 105–111.
24. Moreno- Rodríguez, J.A. and Caffesse, R.G. (2018): Non-Incised Papillae Surgical Approach (NIPSA) in Periodontal Regeneration: Preliminary Results of a Case Series". *Int. J. Periodontics. Resto. Dent.*; 38: 105–111.

25. Moreno Rodríguez, Antonio, J., Ortiz Ruiz and Caffesse, R. G. (2019): "Periodontal Reconstructive Surgery of Deep Intraosseous Defects Using an Apical Approach. Non-Incised Papillae Surgical Approach (NIPSA): A Retrospective Cohort Study. *Journal of periodontology* 90(5): 454–64."
26. Moreno- Rodriguez, J.A. and Caffesse, R.G. (2018): Non-Incised Papillae Surgical Approach (NIPSA) in Periodontal Regeneration: Preliminary Results of a Case Series". *Int. J. Periodontics. Resto. Dent.*; 38: 105–111.
27. Xiyang, Pei. (2021): "New Surgery Approaches Preserving Entire Papilla to Treat Isolated Interdental Intra-Bony Defects: A narrative review". *Clin. Exp. Dent. Res.* 1–7.
28. Cortellini, P., Stalpers, G., Mollo, A., Tonetti, M. S. (2011): "Periodontal Regeneration Versus Extraction and Prosthetic Replacement of Teeth Severely Compromised by Attachment Loss to the Apex: 5-Year Results of an Ongoing Randomized Clinical Trial". *J. Clin. Periodontol.*; 38: 915-924.
29. Cortellini, P. and Tonetti, M. S. (2009): "Improved Wound Stability with a Modified Minimally Invasive Surgical Technique in the Regenerative Treatment of Isolated Interdental Intra-Bony Defects". *J. Clin. Periodontol.*; 36(2): 157-163.
30. Clementini, Marco, Ambrosi, A., Ciccirelli, V., De Risi, V. and Sanctis, M. (2021): "Clinical Performance of Minimally Invasive Periodontal Surgery in the Treatment of infra-bony Defects: Systematic Review and Meta- analysis." *Journal of Clinical Periodontology*; 46 (12): 1326- 53.
31. Chambrone L, Tatakis DN. Long-Term Outcomes of Untreated Buccal Gingival Recessions: A Systematic Review and Meta-Analysis. *J Periodontol.* 2016 Jul;87(7):796-808. doi: 10.1902/jop.2016.150625. Epub 2016 Feb 15. PMID: 26878749.
32. Suryasa, W. (2019). Historical Religion Dynamics: Phenomenon in Bali Island. *Journal of Advanced Research in Dynamical and Control Systems*, 11(6), 1679-1685.
33. Suryasa, W., Sudipa, I. N., Puspani, I. A. M., & Netra, I. (2019). Towards a Change of Emotion in Translation of Kṛṣṇa Text. *Journal of Advanced Research in Dynamical and Control Systems*, 11(2), 1221-1231.
34. Khikmatullaeva, Khaydarov, N. K., Abdullaeva, M. B., & Aktamova, M. U. (2021). Cognitive disorders in stroke. *International Journal of Health & Medical Sciences*, 4(2), 202-207. <https://doi.org/10.31295/ijhms.v4n2.1700>