Universitat Internacional de Catalunya
Facultat d'Odontologia

Tesi doctoral

Factors affecting the outcomes of root coverage therapy and periodontal plastic surgery

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Factors affecting the outcomes of root coverage therapy and periodontal plastic surgery

Department of Periodontology

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Preface:

This doctoral thesis is based on the following four articles:

Article 1: Blasi G, Monje A, Muñoz-Peñalver J, Oates TW, Avila-Ortiz G, Nart J. Influence of vestibular depth on the outcomes of root coverage therapy: A prospective case series study. J Periodontol. 2022 Dec;93(12):1857-1866. doi: 10.1002/JPER.21-0638. Epub 2022 May 17. PMID: 35482935.

Article 2: Blasi G, Vilarrasa J, Abrahamian L, Monje A, Nart J, Pons R. Influence of immediate postoperative gingival thickness and gingival margin position on the outcomes of root coverage therapy: A 6 months prospective case series study using 3D digital measuring methods. J Esthet Restor Dent. 2023 Apr 6. doi: 10.1111/jerd.13042. Epub ahead of print. PMID: 37021694.

Article 3: Monje A, Blasi G, Amerio E, Sanz-Martin I, Nart J. Dimensional changes in free epithelialized gingival/mucosal grafts at tooth and implant sites: A prospective cohort study. J Periodontol. 2022 Jul;93(7):1014-1023. doi: 10.1002/JPER.21-0521. Epub 2022 Jan 25. PMID: 34970744.

Article 4: Holtzman LP, Blasi G, Rivera E, Herrero F, Downton K, Oates T. Gingival Thickness and Outcome of Periodontal Plastic Surgery Procedures: A Meta-regression Analysis. JDR Clin Trans Res. 2021 Jul;6(3):295-310. doi: 10.1177/2380084420942171. Epub 2020 Jul 27. PMID: 32718265.

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2. INTRODUCTION

2.1 Definition

Gingival recession is a prevalent condition that is characterized by the displacement of the gingival margin in relation to the cementoenamel junction (CEJ) towards the root surface (Cortellini and Bissada 2018). This displacement exposes the root surface to the oral environment, causing various issues, such as aesthetic concerns, excessive dentin hypersensitivity, difficulty in maintaining oral hygiene, and both non-carious and carious cervical lesions. The complications associated with gingival recession extend beyond the physical effects on the teeth and gums and can also have a significant psychological impact on an individual's quality of life, leading to lowered self-esteem, impaired social interactions, and an overall decrease in well-being (Zucchelli and Mounssif 2015).

2.1 Etiology and risk factors:

Gingival recession is a prevalent condition that can be observed in populations with varying levels of oral hygiene, regardless of whether they maintain good or poor oral hygiene practices. When found in individuals with good oral hygiene, the recession is normally located at the vestibular surfaces of the teeth (Serino et al 1994). Nonetheless, individuals with poor oral hygiene may experience gingival recession in interproximal surfaces (Löe et al 1992). Gingival recession can occur in the presence of healthy sulcus and non-diseased interproximal bone levels or may be caused by periodontitis.

One possible cause of gingival recession is a pre-existing lack bone dehiscence at the site, which may be developmental or acquired (Watson 1984).
Gingival recession has been linked to a range of factors, including anatomical, physiological, traumatic, and pathological elements. Anatomically, factors such as fenestration and dehiscence of the alveolar bone, abnormal tooth positioning within the arch, unusual paths of tooth eruption, and variations in individual tooth morphology can potentially contribute to the development of gingival recession. These factors are interrelated and can result in a thinner alveolar osseous plate, making it more susceptible to resorption (Kassab and Cohen 2003). Gingival recession can be influenced by various physiological factors, including orthodontic treatment and the volume of facial soft tissue. Orthodontic movement of teeth outside the alveolar plate can result in the formation of dehiscence, which can act as a "locus minoris resistantiae" for gingival recession development. Furthermore, in cases where plaque-induced inflammation or toothbrushing trauma is present, a thin gingival phenotype may pose a higher risk for the progression of gingival recession. During the post-orthodontic retention phase, toothbrushing trauma can act as an etiological factor for gingival recession, especially in cases where the gingival tissue has been thinned due to tooth malposition (Renkema et al 2013).

Toothbrushing is a significant factor associated with the development of gingival recession. It is often linked to the occurrence of recession and helps explain the observed correlation between low plaque levels and sites with recession. Trauma, which can arise from improper toothbrushing techniques, plays a role in this relationship. Various variables, including pressure applied, duration of brushing, bristle type, and the choice of dentifrice, can potentially confound the impact of toothbrushing on gingival recession (Rajapakse et al 2007). In addition to toothbrushing, incorrect flossing methods can also play a role in tooth abrasion and gingival damage. Improper flossing techniques can result in gingival clefts that extend from the interproximal area to the buccal and lingual gingiva. It is common for individuals who utilize an inadequate flossing technique, characterized by a "sawing" motion as they insert the floss into the gingival sulcus, to exhibit gingival clefts. (Hallmon et al 1986).

Perioral and intraoral piercing has gained popularity as a form of body art. However, it is important to note that tongue and perioral piercings can result in dental and gingival injuries. Tongue piercing, in particular, has been directly linked to injuries to the lingual aspect of the lower front teeth and can lead to gingival injuries. Similarly, individuals with lip studs positioned in a way that causes trauma to the gingiva may experience buccal gingival recession (Campbell et al., 2002; Dibart et al., 2002). It is crucial to distinguish this type of gingival recession, caused by piercing-related trauma, from recession associated with periodontal disease. In cases of periodontal disease, bacterial plaque accumulation on the buccal tooth surface can contribute to connective tissue attachment loss, which may clinically present as gingival recession not only on buccal surfaces but also in the interproximal areas (van Palenstein Helderman et al 1998; Baker et al 1976). Moreover, clinical observations suggest that the placement of restoration margins subgingivally are more prone to alterations in the adjacent gingiva and recession of the soft-tissue margin (Kim and Neiva 2015).

Other conditions that are reported by clinicians and may contribute to gingival recession are: persistent inflammation, shallow vestibular depth and coronal frenum attachment. Further studies are needed to determine the relationship between these conditions and gingival recession (Cortellini and Bissada 2018).

In conclusion, gingival recession is a multifactorial condition that can be caused by several factors. Clinicians should be aware of these factors and educate patients on proper oral hygiene techniques and the potential risks associated with certain behaviors, such as tongue piercing. Early diagnosis and treatment of gingival recession can help prevent further progression and preserve the health of the periodontal tissues.

2.3 Classification:

Numerous classifications have been proposed in the literature for the diagnosis of gingival recessions (Sullivan and Atkins 1968; Miller 1985a). Out of all these classification systems, Miller's Classification has been the most widely used. The classification system categorizes four types of recession defects based on the evaluation of soft and hard periodontal tissues, evaluating the depth, the keratinized tissue, interproximal attachment loss and tooth malposition:

Class I: This involves marginal tissue recession that does not extend to the mucogingival junction. There is no interproximal attachment loss, and 100% root coverage can be expected.

Class II: This involves marginal tissue recession that extends to or beyond the mucogingival junction. There is no interproximal attachment loss, and 100% root coverage can be expected.

Class III: This involves marginal tissue recession that extends to or beyond the mucogingival junction. Bone or soft tissue loss in the inter-dental area is present, or there is a malpositioning of the teeth that prevents the achievement of 100% root coverage. Partial root coverage can be expected.

Class IV: This involves marginal tissue recession that extends to or beyond the mucogingival junction. The bone or soft tissue loss in the inter-dental area and/or malpositioning of teeth is so severe that root coverage cannot be anticipated.

Miller's classification had grown quite popular and was frequently used and cited in the the 90s and 2000s. Some criticisms of this classification were reported, such as the difficult differentiation between Miller classes I and II, the unclear procedures for determining the amount of soft/hard tissue loss in the interproximal area to differentiate class III and IV, and the unclear influence of tooth malpositioning (Pini Prato 2011). For these reasons, a new classification system was developed by Cairo et al based on the interproximal clinical attachment loss measurement (Cairo et al 2011).

Recession Type 1 (RT1): Gingival recession with no loss of interproximal attachment. Interproximal CEJ is clinically not detectable at both mesial and distal aspects of the tooth.

Recession Type 2 (RT2): Gingival recession associated with loss of interproximal attachment. The amount of interproximal attachment loss (measured from the interproximal CEJ to the depth of the interproximal sulcus/pocket) is less than or equal to the buccal attachment loss (measured from the buccal CEJ to the apical end of the buccal sulcus/pocket).

Recession Type 3 (RT3*):* Gingival recession associated with loss of interproximal attachment. The amount of interproximal attachment loss (measured from the interproximal CEJ to the apical end of the sulcus/pocket) is greater than the buccal attachment loss (measured from the buccal CEJ to the apical end of the buccal sulcus/pocket).

This classification solves some of the shortcomings of the widely used Miller classification, such as the difficulty in distinguishing between Class I and Class II, and the use of "bone or soft tissue loss" as an interdental reference to diagnose interproximal attachment loss.

2.4 Prevalence:

According to Romandini et al. (2020), most mild gingival recessions categorized as RT1 tend to affect multiple teeth rather than being limited to a single tooth. However, generalized RT1 gingival recessions are not commonly observed. Several factors have been identified as indicators of the risk of RT1 gingival recessions at both the patient and site level. These include age, gender, ethnicity, and dental care exposure as subject-level risk indicators, and tooth type and mandibular arch as tooth-level risk indicators. These findings indirectly support the role that the periodontal phenotype may serve as a risk indicator for gingival recession, as a thin periodontal phenotype has previously been associated with female gender and mandibular teeth (Eger et al., 1996; Vandana and Savitha, 2005).

In contrast, RT2 and RT3 gingival recessions were predominantly associated with the same risk indicators as those for periodontitis. It was observed that mid-buccal gingival recessions are highly prevalent in the general adult population in the USA, with a prevalence exceeding 90%. However, when specifically considering RT1 gingival recessions, the prevalence is lower at 12.4%. This decline in prevalence can be attributed to the increasing frequency of periodontitis within these subpopulations as age advances, particularly in males, certain ethnic groups, individuals from lower socioeconomic backgrounds, and smokers (Eke et al., 2012). Romandini et al.'s findings are supported by prevalence data from other investigations (Rios et al 2014; Susin et al 2004). While Susin noted a prevalence above 95.7% among patients 30 years of age or older, Rios recorded a prevalence of 93.1%. The few discrepancies that were noticed might be readily explained by the various sampling techniques (such as age restrictions) and the various geographic sources of the samples. As a result of the partial-mouth periodontal assessment used, earlier research on representative samples of the American population, found a lower prevalence of gingival recession (42%–58%) (Albandar and Kingman 1999).

2.5 Progression and Indications for root coverage

When left untreated, gingival recessions do not improve on their own and may progress to greater recession depth. Because of increasing dental hypersensitivity, development of recession depth may result in decreased esthetics and impaired function. (Chambrone et al 2016). Not only that but, the deeper the recession, the lesser the predictability in root coverage procedures (Berlucchi et al 2005). In summary, gingival recession defects should be treated for cosmetic reasons, to lessen root hypersensitivity, and to augment keratinized tissue. Root abrasion/caries and gingival margin inconsistency/disharmony are indications for root coverage procedures as well. (Zucchelli and Mounsiff 2015)

2.6 Surgical approaches, grafts, and substitutes

Several surgical treatments have been presented during the last three decades to treat single and multiple gingival recession defects: The free gingival graft was first introduced by Sullivan and Atkins in 1968 and it can achieve root coverage as well as increase keratinized tissue width and thickness. (Sullivan and Atkins 1968) The free gingival graft was regarded gold standard treatments throughout the 1970s and 1980s. (Caffesse and Guinard 1978, 1980, Espinel & Caffesse 1981) Since then, it has been the most often utilized surgical procedure for augmenting the width of keratinized tissue. (Kim and Neiva 2015) Nonetheless, it has been reported in the literature a limited degree of predictability of beneficial results when using this strategy to cover exposed root surfaces. (Chambrone and Tatakis 2015). It is suggested that the free gingival graft has a lower potential for recession reduction and complete root covering than other techniques (Oates et al 2003; Chambrone et al 2010). This lies in the fact that a section of the graft is placed on the denuded root surface and receives insufficient blood flow, resulting in partial necrosis of the grafted tissue. Despite numerous studies examining the use of free gingival grafts for the treatment of gingival recession defects, the impact of intraoperative variables on the dimensional changes of free gingival grafts at tooth sites remains unclear (Caffesse et al 1979; Mormann et al 1981; Holbrook 1983, Hatipoglu 2007). While some research has been conducted on the effect of surgical techniques and donor site characteristics on the success of free gingival grafts, there is still limited understanding of the role played by intraoperative factors in determining the final outcome of the procedure.

Further investigation into these variables is crucial to fully understand the optimal use of free gingival grafts in clinical practice. By identifying the factors that contribute to successful outcomes, clinicians can tailor their techniques to achieve the best possible results for their patients. Additionally, continued research in this area could lead to the development of more standardized protocols for the use of free gingival grafts, which could improve the predictability and consistency of treatment outcomes.

Because of the limitations with free gingival grafts in terms of root coverage, new treatments, such as bilaminar techniques or regeneration procedures, were presented to achieve the goal of total root coverage between the mid-1980s and the early 2000s. These combined techniques were primarily based on pedicle flaps (laterally or coronally positioned), bilaminar approaches, or regenerative therapies a coronally advanced flap in conjunction with subepithelial connective tissue grafts or a bioresorbable barrier, enamel matrix derivative, or acellular dermal matrix graft.

2.7 Anatomical and Surgical Limitations

Through an examination of 75 RCTs (115 treatment groups) published between 1993 and 2017, Chambrone and Pini Prato found an overall mean root coverage of 83.34% ± 12.46%, with a range of 41.80% to 99.30%. (Chambrone and Pini Prato 2019). While the efficacy of root coverage treatment approaches has been firmly established, it is essential to consider the clinical factors that influence their outcomes, regardless of the surgical approach employed. These differences include surgical variations in flap thickness and design, as well as varied flap positioning strategies. Moreover, differences in suture materials, removal times, and sizes, as well as the use of micro instruments and magnification, have been reported. (Burkhardt and Lang 2005; Baldi et al 1999; Pini Prato et al 2005; Chambrone and Tatakis 2015).

In terms of flap and suturing characteristics, Pini Prato evaluated whether the position of the gingival margin position immediately post-surgically had an impact on recession reduction using coronally advanced flap alone. (Pini Prato et al 2005) It was concluded that the more coronal the position of the gingival margin after suturing the greater the chance of achieving complete root coverage. In conclusion, all cases where a coronal advancement was greater than 2mm, complete root coverage was achieved. This amount of coronal flap displacement, on the other hand, necessitates its relaxation and passive adaptation without tension over the cemento-enamel junction that has been associated post-operative morbidity and swelling. Since its publication in 2005, Pini

Prato's study on coronally advanced flap, has been frequently cited as a reference for achieving complete root coverage in gingival recession treatment. However, it is worth noting that no studies have replicated these findings since then. In addition, there is currently no validation of these results with other surgical approaches, such as the tunnel approach and with the use of autogenous grafts or substitutes. Thus, further research is needed to determine the amount of advancement of the flap needed to achieve complete root coverage.

Other anatomical features such as, keratinized tissue width and thickness, recession depth and width, interproximal attachment loss, vestibular depth, root prominence and frenum pull have been reported as factors that may influence the capacity to achieve complete root coverage. (Pini Prato et al 2012; Gil et al 2018; Aroca et al 2018)

It has been widely recognized that gingival thickness plays a crucial role in the success of root coverage procedures, as thicker tissue is associated with better outcomes (Baldi et al, 1999; Huang et al 2005; Berlucchi et al 2005). However, since the last systematic review on this topic was conducted in 2006 (Hwang and Wang 2006), there has been a significant amount of new research in the field of periodontal plastic surgery that has expanded our understanding of the relationship between gingival thickness and treatment outcomes. Recent studies have increasingly included gingival thickness as an outcome measure, and have also provided longer follow-up periods, which have yielded more information about the long-term effectiveness of root coverage procedures (Barrella et al 2016; Cairo et al 2016; Clementini et al 2018). Moreover, other studies have questioned the importance of initial gingival thickness when a graft is added underneath the flap (Garces-McIntyre et al 2017). Despite these advances, there is still significant variability in outcomes across different gingival defects and treatment procedures (Chambrone et al 2015). Therefore, it is important to further investigate the impact of gingival thickness on the success of root coverage therapy.

In a recent article, Aroca and colleagues noted that there are certain anatomical factors that may have a negative impact on the success of root coverage procedures. (Aroca et al 2018) Specifically, they highlighted the importance of considering both labial muscular pull and vestibular depth when planning such procedures. Labial muscular pull refers to the tension that is exerted by the muscles around the lips and cheeks, which can affect the position of the gingival margin after surgery. Meanwhile, vestibular depth refers to the distance between the gingival margin to the point of greatest concavity of the mucosal fold, which can be shallower in some areas, particularly in the lower jaw.

Although it is well-known that shallow vestibular depth is often associated with gingival recession defects, there is limited evidence on its impact on the outcomes of root coverage procedures. Nonetheless, Aroca and colleagues argue that considering these anatomical factors can help clinicians optimize the results of such procedures, as they may influence the amount of root coverage that can be achieved and the overall esthetic outcome. Hence, further research in this area is warranted to better understand the role of labial muscular pull and vestibular depth in the success of root coverage procedures.

Therefore, considering these distinctions, it is imperative to enhance our understanding of the outcomes of root coverage strategies and increase their effectiveness. By taking into account these clinical aspects, clinicians can develop improved therapeutic approaches and provide better care for patients suffering from gingival recession.

3. HYPOTHESIS:

3.1 General hypothesis

The surgical and anatomical features evaluated in root coverage and soft tissue augmentation procedures will have an impact on mean and complete root coverage, keratinized tissue width and thickness.

3.2 Specific hypothesis

3.2.1 There is a significant influence of vestibular depth on the outcomes of root coverage therapy when evaluated with digital methods when treating gingival recession defects by means of a coronally advanced flap plus an autogenous connective tissue graft.

3.2.2 The immediate post-operative thickness and gingival margin position have an impact on the linear and volumetric changes following the treatment of gingival recession defects using a modified tunnel technique in combination with acellular dermal matrix

3.2.3 The dimensional changes in free epithelialized gingival/mucosal grafts used for keratinized tissue augmentation at tooth and implant sites will significantly vary over a 6-month follow-up period, and this variability will be influenced by various anatomical factors.

3.2.4 The recipient site baseline gingival thickness significantly affects the root coverage achieved in patients with gingival recession, and this effect can be quantified by analyzing the mean and complete root coverage achieved with various types of root coverage procedures.

4. AIMS:

4.1 General goal:

To evaluate the impact of surgical and anatomical features measured with clinical and digital methods in surgical procedures of soft tissue conditioning around teeth and implants.

4.2 Specific goals:

4.2.1 To evaluate the influence of vestibular depth on the outcomes of root coverage therapy consisting of a coronally advanced flap plus an autogenous connective tissue graft.

4.2.2 To evaluate the linear and volumetric changes from the immediate postoperative period to 6 months, following treatment of multiple gingival recession defects using a modified tunnel combined with acellular dermal matrix.

4.2.3 To assess the dynamic dimensional changes over 6 months of follow-up when using free epithelialized gingival grafts simultaneous to apically positioned flaps at tooth and implant sites with the aim of gaining keratinized tissue.

4.2.4 To characterize, for patients with gingival recession, the effect of recipient site baseline gingival thickness on the root coverage achieved with various types of root coverage procedures as identified in prospective clinical trials.

5. MATERIAL AND METHODS/RESULTS:

The detailed description of the materials and methodology used in this research study, along with the findings and outcomes, have been disseminated through three distinct publications in scientific article format. Each publication is identified by the following references, which provide readers with a comprehensive understanding of the research conducted.

Study 1: Blasi G, Monje A, Muñoz-Peñalver J, Oates TW, Avila-Ortiz G, Nart J. Influence of vestibular depth on the outcomes of root coverage therapy: A prospective case series study. J Periodontol. 2022 Dec;93(12):1857-1866. doi: 10.1002/JPER.21-0638. Epub 2022 May 17. PMID: 35482935.

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Abstract

Background: The purpose of this study was to investigate the influence of vestibular depth (VD) on the outcomes of root coverage therapy.

Methods: Patients presenting gingival recession defects (GRD) with a minimum depth of 2 mm underwent root coverage therapy consisting of a coronally advanced flap plus a connective tissue graft (CAF + CTG). Clinical examinations were performed, and intraoral scans were obtained at baseline, 3 and 6 months after surgery to assess changes in probing depth (PD), keratinized tissue width (KTW), recession depth (RD), GRD area, marginal gingival thickness (MGT), and VD. The influence of VD on percentage of root coverage (%RC) and the likelihood of achieving complete root coverage (CRC) were explored.

Results: A total of 20 patients were enrolled, and 44 teeth were treated. RD decreased and MGT increased in all treated sites. At 6 months, mean %RC was 87.47 ± 18.37 and CRC was observed in 61.4% of sites. Mean baseline VD was 7.33 ± 2.67 mm. Mean VD reduction from baseline to 6 months was 1.98 ± 1.27 mm. %RC and CRC were significantly correlated with baseline VD. Each additional 1 mm of baseline VD implied a gain of 6.58% for %RC and increased 2.75 times the probability of achieving CRC.

Narrow baseline KTW and mandibular arch location were associated with inferior treatment outcomes.

Conclusion: Lower %RC and likelihood of achieving CRC can be expected after root coverage therapy via CAF + CTG in sites presenting a shallow vestibulum.

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CASE SERIES

Influence of vestibular depth on the outcomes of root coverage therapy: A prospective case series study

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Abstract

Background: The purpose of this study was to investigate the influence of vestibular depth (VD) on the outcomes of root coverage therapy.

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Conclusion: Lower %RC and likelihood of achieving CRC can be expected after root coverage therapy via CAF + CTG in sites presenting a shallow vestibulum.

KEYWORDS
esthetics, connective tissue graft, coronally advanced flap, gingival recession, root coverage

1 | INTRODUCTION

A gingival recession defect (GRD) is characterized by partial exposure of the root surface to the oral cavity because of apical migration of the gingival margin (GM) respective to the cemento-enamel junction (CEJ). Prevalence and incidence of GRDs are high in the general population.[1,2] The etiology of GRDs is multifactorial, including predisposing and precipitating factors such as traumatic toothbrushing technique and other deleterious habits (e.g., finger picking), irritants (e.g., lip or tongue piercing), local inflammation, and subsequent periodontal breakdown derived from biofilm accumulation, tooth malposition, and high frenal attachment.[3] If left untreated, the probability of progression of GRDs is high.[4] Successful root coverage outcomes can be achieved with different surgical protocols.[5]

Corrective surgical therapy of GRDs primarily aims at shifting the location of the GM to a more coronal location, achieving complete root coverage (CRC) or partial root coverage if CRC is not feasible, with a shallow probing depth and a pleasant soft tissue integration.[6]

Proper planning of root coverage procedures should include a careful analysis and consideration of local factors that may influence the execution of the surgical intervention and the outcomes of therapy. Among these factors, solid evidence supports the importance of interproximal bone and attachment level, marginal gingival thickness (MGT), width of attached gingiva, and recession defect depth (RD) as key elements that can be used to design the surgical plan and even predict the therapeutic result.[7–11] Tooth malpositioning and tooth type (molar versus nonmolar) have also been regarded as relevant predictive factors.[12–14]

In a recent publication, Aroca et al. pointed out that labial muscular pull and a shallow vestibular depth (VD) may negatively influence the results of root coverage procedures.[13] Although, shallow VD is frequently found in association with GRDs, particularly in mandibular sites, evidence regarding its impact on the outcomes of root coverage procedures is scarce. Therefore, the primary objective of this study was to evaluate the influence of VD on the outcomes of root coverage therapy consisting of a coronally advanced flap plus an autogenous connective tissue graft (CAF + CTG).

2 | MATERIALS AND METHODS

2.1 | Experimental design and setting

This clinical investigation was designed as a pre-post case series study and is reported in compliance with the Preferred Reporting of Case Series in Surgery (PROCESS) guidelines.[15] This study was registered in ClinicalTrials.gov under code NCT04813302. The clinical component of the study was conducted in a private practice setting affiliated with the International University of Catalonia (UIC) in Barcelona (Spain). The study took place between September 2019 and March 2021.

2.2 | Ethical approval

The study protocol was reviewed and approved by the Ethical Committee of UIC (PER-ECL-2019-04), and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013.

2.3 | Outcomes of interest

The main outcomes of interest were percentage of root coverage (%RC) and whether CRC was achieved.

2.4 | Sample size calculation

The number of independent teeth that would be required for an estimated linear regression model to reach a power of 80% in detecting $r = 0.5$ as a significant correlation was calculated. This analysis rendered a total of 27 teeth. Assuming that each patient would provide an average of two teeth ($n = 2$), this sample size should be corrected because of intrasubject dependence. A correcting factor D of the sample size was estimated using the formula $D = 1 + (\text{m-1}) \times \text{ICC}$ by Pandis where m is the number of teeth per subject and ICC the intraclass correlation coefficient. Because ICC of RC% could not be extracted from previous studies, we assumed a moderate correlation ($p = 0.5$).[16,17] Therefore, $D = 1.5$ and the sample size for independent teeth should be increased +50%, obtaining an ideal sample size of at least 40 teeth.

2.5 | Eligibility criteria and recruitment

Adult patients (≥18 years) presenting at least one single buccal Cairo RT1 GRD with a minimum of 2 mm of RD on single-rooted teeth with identifiable CEJ were consecutively enrolled. The exclusion criteria were as follows: (1) full-mouth plaque and bleeding score >20%; (2) smoking ≥10 cigarettes a day; (3) systemic contraindications for periodontal surgery; (4) taking medications known to affect gingival homeostasis or interfere with wound healing; (5) pregnancy; (6) active orthodontic therapy; (7) previous periodontal surgery, caries, or restorations in the experimental site(s); and (8) malpositioned/crowded teeth.

Before enrollment, all patients were informed of the purpose and timeline of the study, and were required to read, understand, and sign an informed consent.

2.6 | Clinical procedures

Cause-related periodontal therapy was completed 1 month before surgery. Patients received a presurgical prophylaxis and oral hygiene instructions, including proper toothbrushing, if necessary.

All surgical interventions were performed by the same operator (GB). Briefly, after local anesthesia was achieved,

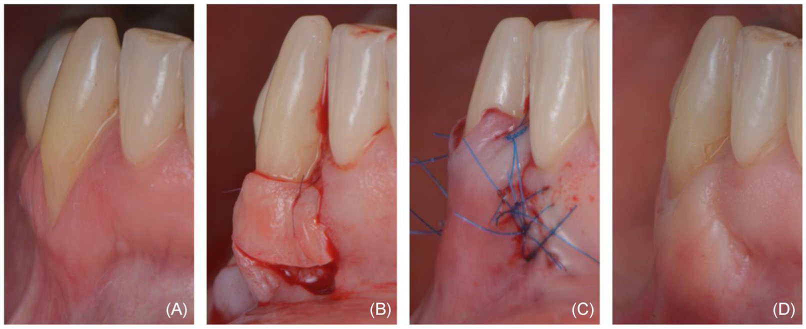

FIGURE 1 Treatment sequence. (**A**) Baseline. (**B**) Flap elevation and positioning of CTG. (**C**) Flap stabilization with sutures and (**D**) 6-month follow-up

one intrasulcular and two vertical releasing incisions lateral to the papillae adjacent to each GRD were made. Subsequently, a split-full-split-thickness flap was elevated beyond the mucogingival junction (MGJ). Periosteal scoring was done and blunt dissection into the vestibular lining mucosa was completed to eliminate muscle tension, so that the mucosal flap margin could be coronally positioned and passively stabilized. The papillae were de-epithelialized and EDTA 24%[1] was applied for 2 min over the exposed root surface for conditioning. A CTG of 1 mm in thickness was harvested from the palatal mucosa by means of extraoral de-epithelization of a free gingival graft.[18] The graft was trimmed to fit the defect area, placed over the root, sutured to the interdental papillae,[2] and subsequently covered with the flap, which was advanced to position its margin at ≈ 1–2 mm coronal to the CEJ with a sling suture, followed by simple interrupted sutures to close both vertical releasing incisions (Figure 1).[3]

Patients were instructed to avoid any mechanical trauma, including toothbrushing in the surgical site, for 2 weeks. Anti-inflammatory medication (Ibuprofen 600 mg oral, three times per day, as required) was prescribed and patients were instructed to rinse with 0.12% Chlorhexidine two times per day for 2 weeks. Sutures were removed after 2 weeks, and patients were allowed to resume their regular oral hygiene routine using a soft toothbrush. Patients were recalled at 1, 3, and 6 months for intraoral evaluation, supragingival plaque control, and data collection.

[1] PrefGel, Straumann, Basel, Switzerland.
[2] 7-0 Polyglactin 910, Vicryl, Ethicon, Johnson & Johnson, New Brunswick, NJ
[3] 6-0 Polypropylene, Prolene, Ethicon, Johnson & Johnson, New Brunswick, NJ

2.7 | Data collection

An interview was conducted during the presurgical visit to obtain information regarding age, sex, medical and dental history (including history of periodontal surgical therapy), current use of medications, and exposure to tobacco.

The following midbuccal clinical measurements were recorded at baseline, 3 and 6 months after surgery using a periodontal probe:[4] probing depth (PD), keratinized tissue width (KTW), and clinical attachment loss. Additionally, a digital dental scan of the whole arch was performed with an intraoral scanner[5] (using a bilateral mouth retractor[6]) to obtain standard tessellation language (STL) files. STL files were transferred into a digital imaging software.[7] Baseline and corresponding follow-up scans of each clinical case were digitally superimposed by using anatomic landmarks as reference points. Digital linear and volumetric measurements to determine soft tissue dimensional changes were performed by a single, calibrated examiner (JM). The examiner was trained using 15 casts with GRDs that were not included in this study. Two sets of assessments were repeated in an interval of 24 h; a difference of ≤0.5 mm in at least 90% of the cases was acceptable.

The following measurements were made:

1. RD was measured from CEJ to the GM in a midbuccal cross section.[19]
2. Recession area was measured by delineating the denuded root surface area between the GM and the CEJ.
3. MGT was measured in an individually defined area at 1 and 2 mm apical to the GM.
4. VD was measured from the GM to the point of greatest concavity of the mucosal fold (Figure 2).

[4] PCP UNC 15, Hu-Friedy, Chicago, IL
[5] 3Shape Trios, Copenhagen, Denmark
[6] Optragate, Ivoclar Vivadent, Schaan, Liechtenstein
[7] Geomagic, 3D Systems, Research Triangle Park, NC

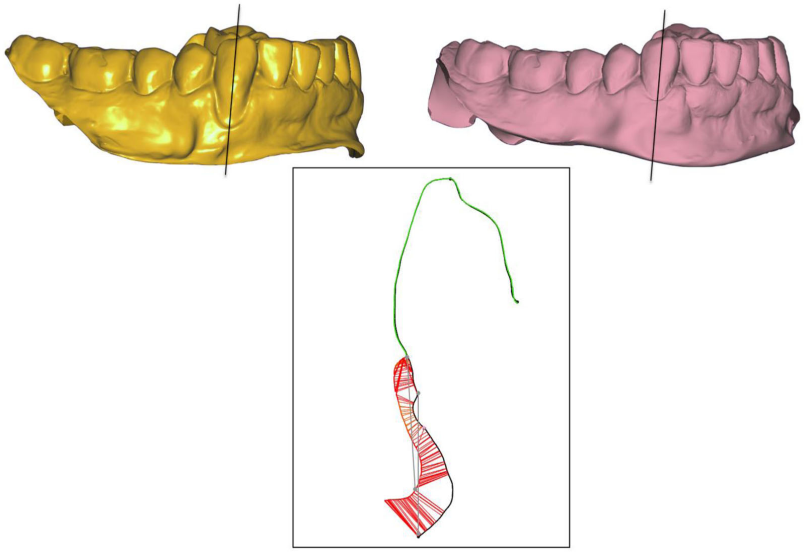

FIGURE 2 Digital superimposition of STL files and linear measurements

2.8 | Statistical analysis

Absolute and relative frequencies for categorical variables, and mean, standard deviation, range, and median for continuous variables were calculated.

Simple binary logistic regression models were estimated using generalized estimation equations (GEE) to assess the probability of CRC at each follow-up time as a function of the outcomes of interest at baseline. Unadjusted estimates of odds ratio (OR) and 95% confidence intervals (CI) were obtained using Wald Chi-squared statistic. Then, a multiple regression model allowed to adjust the results for all the independent variables simultaneously. For the dependent variable %RC, simple linear regression models were applied, also using a GEE approach, in which estimates were obtained for the beta coefficients of the regression with 95% CI, and later adjusted through a multiple regression model. The GEE analysis methodology applied was justified by the intrasubject correlation typical of a multilevel data structure. The level of significance used in the analysis was 5% ($\alpha = 0.05$).

A linear regression model such as the one previously described to evaluate the influence of each variable of interest on CR% would reach a power of 97.9% to detect a correlation of moderate magnitude ($r = 0.5$) as significant with a confidence of 95%. Due to the multilevel structure of the data (several sites per patient), the power had to be corrected so, assuming a moderate intrasubject correlation ($\rho = 0.5$), 80% power could be reached.

TABLE 1 Number of GRD per patient

	No.	%
Total	**20**	**100**
1	4	20.00
2	10	50.00
3	5	25.00
5	1	5.00

3 | RESULTS

The study population consisted of 20 patients (five males and 15 females). All patients were nonsmokers. No patients were lost to follow-up. A total of 44 GRDs were treated, of which 65.9% were mandibular and 34.1% maxillary. Regarding tooth type, 29.5% were incisors, 27.3% were canines, and 43.2% were premolars (Table 1). No postoperative healing complications were observed.

A statistically significant change between baseline, 3 and 6 months was observed for all variables (Table 2). Mean RD was 2.74 ± 0.77 mm at baseline, 0.42 ± 0.64 mm at 3 months, and 0.40 ± 0.62 mm at 6 months. Therefore, from baseline to the 3-month follow-up, mean RD reduction was -2.32 ± 0.73 mm ($p < 0.001$), while this value from baseline to 6 months was -2.35 ± 0.72 mm ($p < 0.001$), which is reflective of GM stability between 3 and 6 months after surgery. Mean %RC was 86.46% ± 19.31% at 3 months and 87.47% ± 18.37% at 6 months ($p < 0.001$).

TABLE 2 Mean ± SD, relative frequencies, and timepoint differences

	Baseline	T1-T0	3 months	T2-T1	6 months	T2-T0
PD	1.14 ± 0.35	0.25 ± 0.49 $p < 0.001$**	1.39 ± 0.49	0.02 ± 0.26 $p = 1.000$	1.41 ± 0.50	0.27 ± 0.54 $p < 0.001$**
RD	2.74 ± 0.77	−2.32 ± 0.73 $p < 0.001$**	0.42 ± 0.64	−0.03 ± 0.08 $p = 0.052$	0.40 ± 0.62	−2.35 ± 0.72 $p < 0.001$**
CAL	3.87 ± 0.85	−2.03 ± 0.98 $p < 0.001$**	1.85 ± 0.77	−0.04 ± 0.29 $p = 1.000$	1.81 ± 0.70	−2.06 ± 0.99 $p < 0.001$**
KTW	2.11 ± 0.78	0.91 ± 0.80 $p < 0.001$**	3.02 ± 1.11	0.07 ± 0.25 $p = 0.167$	3.09 ± 1.05	0.98 ± 0.76 $p < 0.001$**
RA	6.92 ± 3.99	−5.13 ± 3.07 $p < 0.001$**	1.79 ± 2.70	−0.26 ± 0.60 $p = 0.021$*	1.53 ± 2.36	−5.38 ± 3.05 $p < 0.001$**
%RC	–	–	86.5 ± 19.3	1.01 ± 2.87 $p = 1.000$	87.5 ± 18.4	–
CRC	–	–	61.4%	$p = 1.000$	61.4%	–
VD	7.33 ± 2.67	$p < 0.001$**	2.62 ± 1.28	$p < 0.001$**	1.98 ± 1.27	$p < 0.001$**
MGT 1 mm	–	$p < 0.001$**	1.18 ± 0.35	$p < 0.001$**	1.29 ± 0.35	
MGT 2 mm	–	$p < 0.001$**	1.48 ± 0.41	$p < 0.001$**	1.53 ± 0.44	

Multiple comparisons were adjusted using Bonferroni from GEE models (p-values).
Abbreviations: CAL, clinical attachment level; CRC, complete root coverage; KTW, keratinized tissue width; MGT, marginal gingiva thickness; PD, probing depth; RA, recession area; %RC, % root coverage; RD, recession depth; VD, vestibular depth.
*$p < 0.05$.
**$p < 0.001$.

TABLE 3 GEE simple linear regression model for %RC at T2 respective to T0 parameters

	Beta	IC 95%	Significance
VD	6.20	4.78, 7.61	**<0.001***
KTW	8.30	1.66, 14.9	**0.014***
Arch			
Maxilla	0.00		
Mandible	−17.50	−27.74, −7.28	**0.001****
Tooth type			0.988
I	0.00		
C	0.28	−14.3, 14.9	0.970
PM	0.87	−14.1, 15.8	0.910

Abbreviations: C, canines; I, incisors; KTW, keratinized tissue width; PM, premolars; VD, vestibular depth.
Bold indicates statistical significance.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

TABLE 4 GEE multiple linear regression model for %RC at T2 respective to T0 parameters in maxillary sites

	Beta	IC 95%	Significance
VD	3.17	1.67, 4.67	**<0.001****
KTW	0.08	−0.56, 0.72	0.802
Tooth type			**0.024***
I	0.00		
C	4.52	1.04, 8.00	**0.011***
PM	1.15	−0.05, 2.35	0.061

Abbreviations: C, canines; I, incisors; KTW, keratinized tissue width; PM, premolars; VD, vestibular depth.
Bold indicates statistical significance.
*$p < 0.05$.
**$p < 0.001$.

CRC was observed in 61.4% of teeth at 6 months ($p < 0.001$). Mean recession area was 6.92 ± 3.99 mm^2 at baseline, 1.79 ± 2.70 mm^2 after 3 months and 1.53 ± 2.36 mm^2 after 6 months ($p < 0.001$). Mean VD was 7.33 ± 2.67 mm at baseline, was 2.62 ± 1.28 mm at 3 months, and 1.98 ± 1.27 mm at 6 months.

Simple linear regression revealed that %RC after 6 months was significantly correlated with baseline VD ($p < 0.001$) (Table 3). In fact, each additional mm of VD at baseline implied, on average, an increase of 6.58% in %RC (Figure 3A). Furthermore, %RC was correlated with baseline KTW. Mean %RC was 98.8% and 80.1% in maxillary and mandibular sites, respectively ($p < 0.001$). After neutralizing confounding factors with a multiple linear regression model, VD was the only variable retaining statistical significance ($p < 0.01$) (Tables 4 and 5).

Similar correlations were observed for CRC after 6 months. Simple logistic regression revealed that VD is the variable that most influenced the likelihood of achieving CRC (Table 6). The estimate indicated that each additional 1 mm of VD increased 2.75 times the probability of achieving CRC ($p = 0.009$) (Figure 3B). CRC was not

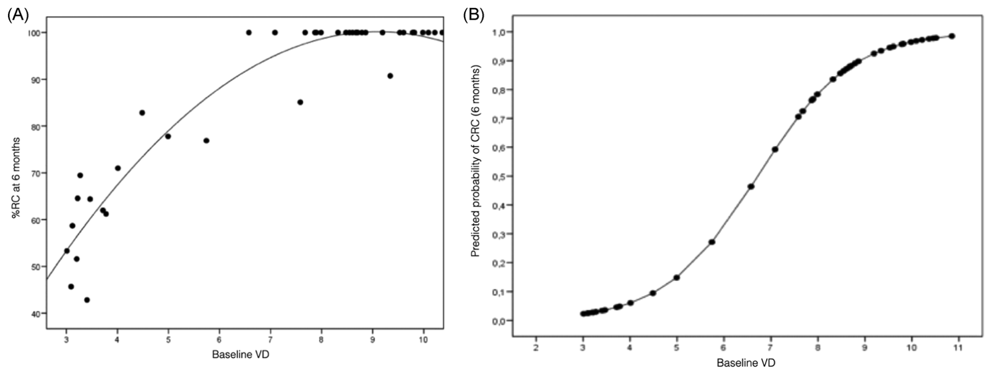

FIGURE 3 (**A**) Correlation between baseline VD and %RC at 6 months. (**B**) Correlation between baseline VD and CRC at 6 months

TABLE 5 GEE multiple linear regression model for %RC at T2 respective to T0 parameters in mandibular sites

	Beta	IC 95%	Significance
VD	7.17	5.44, 8.90	**<0.001****
KTW	−0.43	−3.82, 2.96	0.803
Tooth type			**0.013***
I	0.00		
C	5.78	0.42, 11.1	**0.034***
PM	0.91	−7.65, 9.47	0.835

Abbreviations: C, canines; I, incisors; KTW, keratinized tissue width; PM, premolars; VD, vestibular depth.
Bold indicates statistical significance.
*$p < 0.05$.
**$p < 0.001$.

TABLE 6 GEE simple binary logistic regression for CRC at T2 respective to T0 parameters

	OR	IC 95%	Significance
VD	2.75	1.29, 5.88	**0.009****
KTW	3.08	1.07, 8.82	**0.037***
Arch			
Maxilla	0.00		
Mandible	0.06	0.01, 0.57	**0.014***
Tooth type			0.842
I	0.00		
C	1.71	0.28, 10.4	0.669
PM	1.47	0.25, 8.56	0.669

Abbreviations: C, canines; I, incisors; KTW, keratinized tissue width; PM, premolars; VD, vestibular depth.
Bold indicates statistical significance.
*$p < 0.05$.
**$p < 0.01$.

achieved in any site with a baseline VD < 6 mm. Tooth location was also a determining factor. Moreover, each additional mm of baseline KT multiplied by three the probability of achieving CRC ($p = 0.037$). After neutralizing

TABLE 7 GEE multiple binary logistic regression for CRC at T2 respective to T0 parameters

	OR	IC 95%	Significance
VD	2.73	0.93, 8.02	0.067
KTW	1.13	0.43, 3.00	0.804
Arch			
Maxilla	0.00		
Mandible	0.75	0.03, 21.2	0.866

Abbreviations: KTW, keratinized tissue width; VD, vestibular depth.

confounding factors with a multiple linear regression model, CRC was not statistically correlated with any of the included variables (Table 7). Nevertheless, VD displayed a strong tendency toward significance ($p < 0.067$).

4 | DISCUSSION

To the best of our knowledge, this is the first clinical study designed to evaluate the effect of VD upon the outcomes of a root coverage procedure consisting of CAF + CTG. Digital methods enabled the reliable assessment of variables that have not been frequently reported in the existing literature on root coverage procedures, such as changes in VD, gingival thickness, or recession area. Recently, published studies support the reliability of data collection and analysis of the anatomical baseline features of GRD and subsequent outcomes of therapy using STL files obtained with intraoral scanners.[20–22]

In the present study, mean %RC was 87.47% at 6 months, and CRC was achieved in 27 out of 44 sites. These findings are comparable with those reported by other authors after the treatment of GRDs with CAF + CTG.[23–25] The main purpose of the study was to evaluate whether VD was correlated with %RC and CRC. Our results showed that, among all variables analyzed, VD is the most relevant and influential factor for both %RC and CRC. In both adjusted models, the %RC increases almost 7% and the probability of achieving CRC is multiplied almost three times for each additional mm of VD.

Current evidence indicates that CAF + CTG is the gold standard procedure for the treatment of GRDs.[26–28] Nevertheless, it should be acknowledged that most studies on root coverage therapy via CAF + CTG refer to the treatment of maxillary GRDs and significantly higher %RC and CRC after treating GRDs with CAF + CTG have been observed in the maxilla compared with mandibular sites.[14,26,30] The use of CAF alone or in combination with CTG has rarely been reported in the mandible, while gingival augmentation in mandibular sites using a free gingival graft has been extensively studied.[28,29] Possibly, the difficulty of effectively displacing and stabilizing a flap in a coronal position in mandibular sites influences the clinical decision-making process for many clinicians.[13] A passive flap is of utmost importance to achieve a favorable outcome after a CAF procedure. In fact, it has been demonstrated that higher flap tension generally leads to lower %RC, while lower flap tension is associated with higher recession depth reduction.[31] Likewise, the extent of coronal advancement over the CEJ is of paramount importance.[32] According to Pini Prato et al. passive flap advancement 2 mm coronal to the CEJ results in 100% root coverage.[33] A shallow VD contributes to increase the amount of flap tension and restrains the coronal advancement of a flap, thus limiting the amount of root coverage than can be predictably achieved, which explains the observations hereby reported.

Another relevant finding of our study is that CRC was not observed in any site with a baseline VD < 6 mm. Interestingly, all sites presenting VD < 6 mm were in the mandible. Different techniques have been proposed to overcome the unfavorable anatomical conditions that are frequently found in mandibular sites, particularly in the anterior region, such as thin gingival phenotype, lack of KT and shallow VD.[34–36] However, clinical evidence is scarce. Much of the limited data available on the outcomes of root coverage procedures in the mandible pertains to tunneling techniques.[36–40] Interestingly, all these studies are case series and the mean %RC ranged from 83.25% to 100% in Miller Class I defects.[7] The main advantage of the tunnel approach is that, by leaving the CTG partially exposed or by closing the tunnel laterally, minimal to no coronal advancement is required, and therefore minimal tension is applied to the flap. Additionally, KTW augmentation can be achieved when the CTG is left partially uncovered.[38,41,42] Zucchelli et al. conducted a randomized clinical trial aimed at evaluating the outcomes of CAF with or without removal of labial submucosal tissue (LST) for the treatment of GRDs at mandibular incisors. The addition of LST removal to CAF + CTG resulted in a tension-free flap leading to a significantly higher chance of achieving CRC as compared with CAF + CTG alone (88% versus 48%). Surprisingly, limited postoperative morbidity was reported in both groups.[35] These results are difficult to compare with those obtained in our study, in which maxillary and mandibular sites were included and no LST was performed. Regardless, both studies point out the critical importance of minimal of flap tension to achieve adequate coronal flap mobilization and obtain predictable RC, which is more difficult to achieve in the presence of shallow VD. A recent study that evaluated the influence of VD on RC showed that the addition of LST to CAF not only may improve %RC but also increase VD.[43] One of the shortcomings of this study was the method used to measure VD. This assessment was made intraorally using a periodontal probe while the lip was pulled until the muscles were almost perpendicularly oriented toward the buccal surface of the alveolar bone. As a result of this manual pulling, the VD can change since the position and the force applied with the fingers can vary. In our study the amount of pressure and force applied was standardized by using a bilateral retractor with the teeth in occlusion while taking the intraoral scan.

Our findings revealed that tooth location was a determining factor that influenced %RC. On average, almost 19% less root coverage was observed in mandibular teeth compared with maxillary sites ($P < 0.001$). From these results, it can be inferred that CAF is less predictable in mandibular sites. In accordance with this observation, a recent systematic review evaluating the effectiveness of different approaches to treat GRDs in the anterior mandible showed that laterally positioned flap + CTG and tunnel + CTG achieved a higher mean %RC (91.2% and 89.4%, respectively) compared with CAF + CTG (78.9%).[44] It must be acknowledged that VD is typically lower in mandibular sites compared with maxillary sites. Therefore, it can be argued that the observed effect of arch location in the outcomes of root coverage therapy is directly related to VD.

Another relevant finding from our study is the VD reduction after 3 and 6 months, which was 2.62 ± 1.28 mm and 1.98 ± 1.27 mm, respectively. A reduction in VD can be detrimental for plaque control by impeding proper oral hygiene.[45,46]

Several limitations of the present study should be noted. The low sample size could be a source of bias. Nevertheless, an appropriate statistical power and a strong significance level support drawing sufficiently reliable statements on the influence of VD on treatment outcome. Moreover, preoperative MGT measurements were not recorded and their effect on %RC could not be assessed. A short follow-up period is another potential limitation. Future studies with longer follow-ups are warranted to assess the effect of time on the stability of the clinical outcomes. Although, internal validity is supported by strict eligibility criteria and a single operator executing a specific technique, external validity should be confirmed with multicenter clinical trials including a range of other surgical procedures. Finally, digital assessment of baseline VD involved certain degree of uncertainty due to the absence of reliable anatomical landmarks. An attempt to attenuate the impact of this factor on the quality of the data were made by training and calibrating the examiner to increase the probability of making reproducible measurements.

5 | CONCLUSIONS

The findings of this study indicate that VD is a significant predictor for the outcomes of root coverage therapy via CAF + CTG. Other anatomical factors such as mandibular arch location and reduced KTW negatively affected treatment outcomes, as well. The effect of these factors on the outcomes of other surgical interventions for root coverage should be further explored in future clinical studies.

CONFLICTS OF INTEREST

The authors report no conflicts of interest related to this study. The study was self-funded.

AUTHOR CONTRIBUTIONS

Gonzalo Blasi contributed to conception, design, surgery, and data interpretation and drafted and critically revised the manuscript. Alberto Monje and Jesus Muñoz-Peñalver have been involved in data collection, data interpretation, and data analysis. Thomas W. Oates, Gustavo Avila-Ortiz, and Jose Nart have been involved in data interpretation, drafting the manuscript, and revising it critically and have given final approval of the version to be published. All authors have made substantial contributions to conception and design of the study.

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Abstract

Background: To assess linear and volumetric changes following the treatment of gingival recessions (GRs) by means of a modified coronally advanced tunnel technique combined with acellular dermal matrix (MTUN + ADM).

Materials and methods: Patients presenting GR type 1 (RT1) GRs underwent root coverage surgery consisting of MTUN + ADM. Clinical measurements were made, and intraoral scans were obtained at baseline, postoperatively, and 6 weeks, 3 and 6 months after surgery, to evaluate changes in probing depth (PD), keratinized tissue width (KTW), recession depth (RD), recession area (RA), marginal gingival thickness (MGT), and mucosal volume (MV). The impact of patient-level and surgical-site variables upon percentage root coverage (% RC) and the likelihood of achieving complete root coverage (CRC) were explored.

Results: A total of 20 patients (n = 47 teeth) were treated. After 6 months, RD and RA decreased, while KTW, MGT, and MV increased. The mean % RC was 93% at 6 months and CRC was found on 72.3% of the sites at 6 months. The postoperative MGT changes at 1.5 and 3 mm were significantly correlated to % RC and CRC at 6 months. Each additional mm of postoperative gain of gingival thickness resulted in a 4-fold increase in the probability of achieving CRC. Additionally, gingival margin positioned ≥0.5 mm coronal to the cementoenamel junction immediately after surgery was a strong predictor of CRC.

Conclusions: The MGT gain at 1.5 and 3 mm achieved in the immediate postoperative period is a significant predictor of CRC at 6 months when treating multiple GRs via MTUN + ADM.

Clinical significance: The Scientific rationale for the study relies on the lack of 3D digital measuring tools in the assessment of soft tissue healing dynamics after root coverage therapy. The principal findings of this study can be summarized as follows: tooth type, tooth position, and post-operative gingival margin position and gingival thickness and volume changes are predictors of CRC. Therefore, the practical implications are that the more thickness and more coronal advancement achieved immediately after root coverage surgery, the higher chance of achieving CRC.

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CLINICAL ARTICLE

WILEY

Influence of immediate postoperative gingival thickness and gingival margin position on the outcomes of root coverage therapy: A 6 months prospective case series study using 3D digital measuring methods

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KEYWORDS
acellular dermal matrix, aesthetics, case series, coronally advanced flap, gingival recession, root coverage

1 | INTRODUCTION

Gingival recession (GR) refers to the apical migration of the gingival margin (GM) in relation to the cementoenamel junction (CEJ). It is associated with root surface exposure to the oral environment—thus leading to aesthetic complaints, excessive dentin hypersensitivity, difficulty in oral hygiene measures, and both non-carious and carious cervical lesions (NCCLs).[1]

Various surgical procedures have been developed to achieve complete root coverage (CRC), which is considered the gold standard treatment endpoint.[2–9] However, several anatomical and surgical parameters have been identified as prognostic factors for CRC. Among the anatomical factors, the characteristics and location of GR defects have been described, with deep and wide GRs located in the mandible being less likely to achieve CRC.[10,11] Moreover, the amount of keratinized tissue, interdental tissue loss, buccal depth, and the presence of NCCLs have been assessed as prognostic factors for CRC.[11–13] On the other hand, the success of periodontal plastic procedures also depends on the surgical technique in itself. In fact, microsurgical techniques have shown superior clinical outcomes compared to conventional macrosurgical techniques.[14] Furthermore, flap management, in terms of thickness and tension, has been shown to be of utmost importance.[15–19] Finally, perfect adaptation and suturing of the flap coronal to the CEJ have also been shown to be of paramount importance.[10,20]

The use of an autogenous connective tissue graft is still regarded as the gold standard for the treatment of GRs, in terms of CRC and KTW gain.[21–23] Nevertheless, in order to minimize patient morbidity and reduce chair time and potential complications associated with sub epithelial connective tissue graft harvesting, a number of soft tissue substitutes have been introduced.[24,25] Evidence suggests that acellular dermal matrix (ADM) constitutes the alternative offering clinical results most similar to those achieved with subepithelial connective tissue grafts.[21] Favorable root coverage outcomes were demonstrated using ADM, combined with either the coronally advanced flap (CAF) or the tunnel technique (TUN).[26–28] Regarding the combination CAF + ADM, 13 randomized controlled clinical trials allowed the estimation of a mean root coverage percentage of 79%.[29] This was further confirmed in a recent randomized clinical trial in which the combination of CAF + ADM resulted in root coverage of 70%–80%.[30] In turn, TUN + ADM have shown mean root coverage of 78%, with no statistically significant differences versus CAF + ADM.[31] Similar outcomes were observed by Tavelli et al. in a recent randomized clinical trial in which TUN + ADM resulted in mean root coverage of 89%, and a CRC of 51% at 6 months.[32]

So far, studies evaluating the outcome of periodontal plastic procedures have mainly focused on the assessment of clinically measured parameters. Transgingival piercing approaches, for instance, were traditionally used to measure gingival thickness at different time points.[33,34] Nevertheless, the introduction of three-dimensional (3D) technology and volumetric analysis has revolutionized the investigation of soft tissue healing dynamics, even though research is still needed in the field of root coverage therapy.[35–40]

Thus, the aim of this prospective case series study was to evaluate the linear and volumetric changes from the immediate postoperative period to 6 months, following treatment of multiple GRs using a MTUN combined with ADM.

2 | MATERIALS AND METHODS

2.1 | Experimental design and setting

This study was designed as a prospective case series study and was performed in a private practice setting affiliated with the Universitat Internacional de Catalunya (UIC) in Barcelona (Spain). The study protocol was registered in ClinicalTrials.gov (identifier: NCT04802473), and reported in compliance with the Preferred Reporting of Case Series in Surgery (PROCESS) guidelines.[41] The clinical investigation took place between March 2021 and September 2022.

2.2 | Ethics statement

The study protocol was reviewed and approved by the Ethics Committee of the UIC (Ref.: PER-ECL-2019-06) and was conducted in accordance with the Declaration of Helsinki (1975, revised in 2013).

2.3 | Outcomes of interest

The outcomes of interest were percentage root coverage (% RC) and CRC at different time points (i.e., 6 weeks, 3 months, and 6 months).

2.4 | Sample size calculation

The number of independent teeth that would be required for an estimated linear regression model to reach a statistical power of 80% in detecting $r = 0.5$ as a significant correlation was calculated. This analysis rendered a total of 27 teeth. Assuming that each patient provides an average of two to three teeth ($m = 2.5$), this sample size required correction due to intrasubject dependence. A correcting factor D of the sample size was estimated using the formula $D = 1 + (m-1) \times$ ICC by Pandis, where $m =$ the number of teeth per subject and ICC = the intraclass correlation coefficient.[42,43] Because ICC of RC % could not be extracted from previous studies, we assumed a moderate correlation ($p = 0.5$). Therefore, $D = 1.7$, and the sample size for independent teeth required an increase +70%, obtaining an ideal sample size of at least 45 teeth.

2.5 | Eligibility criteria and recruitment

The inclusion criteria were as follows: adult patients (≥18 years of age) with at least one single buccal Cairo RT1 of ≥2 mm GR (gingival recession with no loss of interproximal attachment) on single-rooted teeth with an identifiable CEJ. On the other hand, the exclusion criteria were: (1) full-mouth plaque and bleeding score >20%; (2) smokers; (3) systemic contraindications for periodontal surgery; (4) medications known to affect the gingiva or interfere with wound healing; (5) pregnancy; (6) active orthodontic therapy; (7) previous periodontal surgery, caries or restorations in the treatment area(s); and (8) malpositioned/crowded teeth. Before enrollment, all patients were informed of the purpose and timeline of the study, and were required to read, understand, and sign an informed consent.

2.6 | Clinical procedure

Initial periodontal therapy was performed 1 month prior to surgery. Patients received presurgical prophylaxis, oral hygiene instructions and modification of tooth brushing technique, if needed. In this sense, they were taught to use a toothbrush of medium hardness applying the Roll brushing technique.

All surgeries were performed by the same operator (GB). After local anesthesia, MTUN + ADM technique was carried out. An initial vertical buccal incision in the mucosal fold was performed to allow access to the surgical area. Tunneling knives were then used to elevate the buccal gingiva by means of a full-thickness tunnel. Flap preparation was extended beyond the mucogingival junction (MGJ). An incision was made in the periosteum, and blunt dissection into the buccal lining mucosa was carried out to remove muscle tension, so that the mucosal flap could be passively positioned beyond the level of the CEJ. The exposed root surfaces were treated with preconditioning EDTA (PrefGel®, Straumann, Basel, Switzerland) for 2 min. In turn, ADM (OrACELL®, LifeNet Health, Virginia Beach, VA, USA) of 1.25–1.75 mm in thickness was trimmed to the exact size of the defect and was positioned into the prepared tunnel (Figure 1A). Sling sutures were then performed to advance the flap coronally and to anchor or stabilize the ADM with 6–0 polypropylene sutures (6-0 Polypropylene, Prolene, Ethicon, Johnson and Johnson, New Brunswick, NJ; Figure 1B).

Patients were instructed to avoid any mechanical trauma or tooth brushing at the surgical sites for 2 weeks. Anti-inflammatory and analgesic medication (ibuprofen 600 mg every 6–8 h) and antibiotics (amoxicillin 500 mg every 8 h) were prescribed, and the patients were instructed to rinse with 0.12% chlorhexidine 2 times a day for 2 weeks. Sutures were removed after 14 days. Two weeks after surgery, the patients restarted mechanical tooth brushing with a soft toothbrush. Finally, the patients were recalled at 6 weeks and at 3 and 6 months for supragingival plaque control.

2.7 | Data collection

An interview was conducted prior to enrollment to obtain information on age, gender, medical history, medication use, smoking, pregnancy, and previous periodontal surgeries.

Probing depth (PD) was recorded clinically using a periodontal probe (PCP UNC 15, Hu-Friedy, Chicago, IL) by (GB). In addition, a digital scan of the arch to be treated was obtained with an intraoral scanner (3Shape Trios, Copenhagen, Denmark), creating Surface Tessellation Language (STL) files. The acquired data were transferred into digital imaging software (3Shape Trios®, Erlangen, Germany). Baseline and corresponding follow-up scans of each clinical case were then virtually superimposed and matched into one common coordinate system (Geomagic, 3D Systems, Research Triangle Park, NC) using the tool Control X. The digital surface model at baseline (T_0) was considered as a reference, and consecutively, the digital surface models at immediate post-surgery (T_1), 6 weeks (T_2), 3 months (T_3), and 6 months (T_4) were imported and aligned using the "initial alignment" and "best-fit alignment" tools. For each tooth presenting with GR, a sagittal plane was traced following the long axis of the tooth, and by using the "2D compare tool," linear changes between the different timepoints were measured through the selection of points of interest, at 1.5 and 3 mm apical to the GM. Furthermore, regions of interest were drawn apically to the CEJ of each treated tooth, and the volumetric changes were calculated using the "3D compare" tool. Linear and volumetric measurements aiming to determine soft tissue dimensional changes were made by a single calibrated examiner (LA; Figure 2).

The following digital measurements were made:

- Recession depth (RD) was measured in mm from the CEJ to the GM in a cross-section at the central buccal site.
- Recession area (RA) was measured in mm^2 by delineating the denuded root surface area between the GM and the CEJ.
- Keratinized tissue width (KTW) was measured in mm from the GM to the mucogingival junction (Figure 2B). This measurement was performed using an orthodontic software (Orthoanalyzer, 3Shape, Erlangen, Germany)
- Marginal gingival thickness change (MGT) changes were measured in mm in individually defined areas at 1.5 and 3 mm apical to GM.

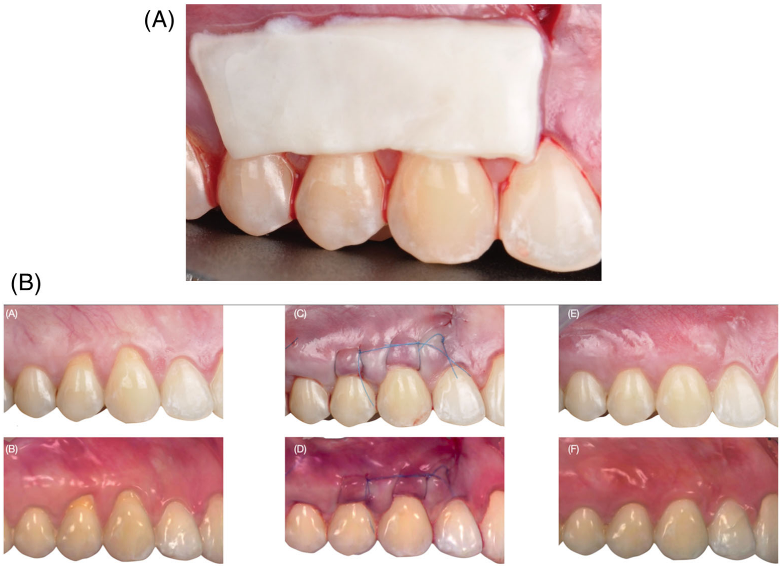

FIGURE 1 (A) Acellular Dermal Matrix trimmed previous to being positioned into the prepared tunnel. (B) Treatment sequence. (a) Clinical baseline; (b) STL baseline; (c) Clinical immediate postsurgery; (d) STL immediate postsurgery; (e) Clinical 6 months follow-up; (f) STL 6 months follow-up.

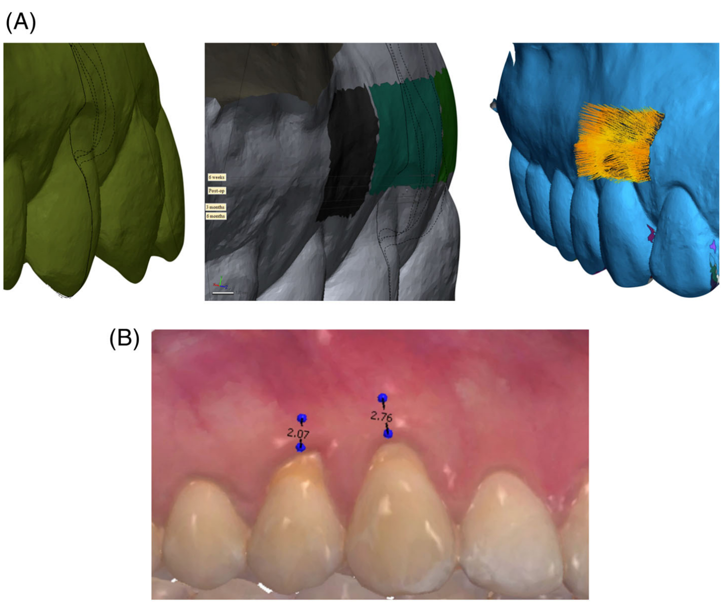

FIGURE 2 (A) Digital superimposition of STL files with linear and volumetric measurements. (B) Digital measurement of KTW.

- Mucosal volume change (MV) was calculated in mm^3 in a selected treated area. In the reference STL model, a rectangular area was delimited, and the volume change of the selected area was calculated between two timepoints using the 3D compare tool.
- Gingival margin position relative to the CEJ immediately postoperatively (GM-CEJ) was measured in mm as the linear distance from the gingival margin to the CEJ. This measurement allowed assessing the amount of coronal advancement of the GM after suturing.

All clinical measurements and gingival volumetric evaluations were performed at baseline and at 6 weeks, 3 months, and 6 months after surgery. Only MV, MGT, and GM-CEJ were measured immediately after surgery.

2.8 | Statistical analysis

For the descriptive analysis, categorical variables were expressed as absolute and relative frequencies, while continuous variables were calculated as the mean, standard deviation (SD), range, and median.

In order to assess the probability of CRC at each follow-up timepoint with regard to the different outcome variables, simple binary logistic regression models were estimated by using generalized estimation equations (GEE). Unadjusted estimates of odds ratio (OR) and 95% confidence intervals (CI) were revealed using Wald's Chi[2] statistic. This was followed by a multiple regression model that permitted adjustment of the results for all the independent variables at the same time. For the dependent variable % RC, simple linear regression models were employed, also using a GEE approach. This led to the obtainment of beta-coefficient estimates with 95% CI, which were eventually adjusted through a multiple regression model. The applied GEE methodology was justified by the intrasubject correlation typical of a multi-level data structure. The level of significance used in the analyses was 5% ($\alpha = 0.05$).

The described linear regression model aimed to assess the influence of each variable of interest upon % RC required to reach a statistical power of 95.7%, in order to detect a correlation of moderate magnitude ($r = 0.5$) as significant with a confidence level of 95%. Due to the multi-level structure of the data (several sites per patient), the power had to be corrected. Thus, assuming a moderate intrasubject correlation ($\rho = 0.5$), a power of 56.1% could be reached.

3 | RESULTS

The description of the relevant patient and surgical site variables is summarized in Table 1. A total of 20 consecutive patients including 47 multiple GRs in all time periods were analyzed. The mean age of the participants was 33.4 years, and the majorities were females (80%). Most of the gingival defects were located in the maxillary arch (80.9%), and more than half of them were in premolar teeth (57.4%). Two patients presented postoperative complications resulting in partial necrosis of the flap and matrix. One patient achieved CRC, while the other achieved 71.24% and 62.26% of RC at both treated sites.

The summary of all the clinical outcomes at baseline (T_0), immediate post-surgery (T_1), 6 weeks (T_2), 3 months (T_3), and 6 months (T_4) is reported in Table 2.

The mean RD amounted to 2.07 ± 0.71 mm at baseline and decreased to 0.15 ± 0.29 mm at 6 months. Thus, the mean RD reduction from baseline to 6 months was −1.92 ± 0.70 mm ($p < 0.001$). The mean % RC was 93.46 ± 14.3% at 6 weeks and 94.64 ± 11.95% at 3 months, remaining stable up to 93.00 ± 12.32% at 6 months. No statistically significant differences were detected in % RC from 6 weeks to 6 months (1.18 ± 10.07; $p = 1.000$) or from 3 to 6 months (−1.64 ± 9.27; $p = 0.635$). Similarly, CRC was observed in 74.5% of the teeth at 6 weeks, 80.9% at 3 months and 72.3% at 6 months. No significant differences were observed in % CRC from 6 weeks to 6 months ($p = 0.001$) or from 3 to 6 months ($p = 0.278$). The mean RA was reduced 5.44 ± 3.11 mm^2 from baseline to 6 months ($p < 0.0001$). Moreover, the mean KTW measured 2.80 ± 0.92 mm at baseline and increased to 3.26 ± 0.95 mm at 6 months. Thus, there was a KTW gain from baseline to 6 months after surgery amounting to 0.45 ± 0.88 mm ($p < 0.001$). The mean change in MGT immediately after surgery was 1.89 ± 0.67 and 1.85 ± 0.72 mm at 1.5 and 3 mm from the GM, respectively. Thereafter, MGT exhibited significant shrinkage at 6 months (0.81 ± 0.47 mm; $p < 0.001$) when measured 1.5 mm from the GM. At 3 mm, a similar tendency was observed, as MGT collapsed significantly at 6 months (0.60 ± 0.51 mm; $p < 0.001$). Likewise, the mean MV change immediately after surgery was 1.73 ± 0.43 mm^3, and was reduced to 0.94 ± 1.12 mm^3 at 6 months ($p < 0.001$).

TABLE 1 Description of baseline (T_0) patient and surgical site variables.

Patient-level variables	Overall ($n = 20$)
Gender	
Male	4 (20%)
Female	16 (80%)
Age (years)	33.4
Treated recessions per patient	2.7 ± 1.7
Surgical site variables	**Overall ($n = 47$)**
Arch	
Maxillary arch	38 (80.9%)
Mandibular arch	9 (19.1%)
Position	
Incisors	7 (14.9%)
Canines	13 (27.7%)
Premolars	27 (57.4%)

Note: Expressed as mean ± standard deviation and *n* (%).

Simple linear regression analysis showed % RC 6 months after surgery to be significantly associated with immediate postsurgical MGT at 3 mm ($\beta = 4.66$; $p = 0.021$), MV ($\beta = 11.1$; $p = 0.031$), and GM-CEJ ($\beta = 12.0$; $p < 0.001$) (Table 3). In other words, each additional mm of immediate postsurgical gingival thickness at 3 mm and coronal to the gingival margin indicated the probability of % RC at 6 months to be 4.66% and 12% higher, respectively. Likewise, one additional mm^3 of immediate postsurgical volume resulted in 11.1% greater % RC at 6 months.

On the other hand, the simple logistic regression analysis showed % CRC at 6 months to be significantly correlated with immediate postsurgical MGT at 1.5 mm (OR = 3.73; $p = 0.016$) and at 3 mm (OR = 2.91; $p = 0.038$; Table 4). Indeed, each additional mm of immediate postsurgical gingival thickness at 1.5 and 3 mm increased the probability of % CRC at 6 months 3.7- and 2.9-fold, respectively. It

TABLE 2 Description of clinical parameters along study periods.

	T_0	T_1	T_2	T_2-T_0	T_3	T_3-T_0	T_4	T_4-T_0
RD	2.07 ± 0.71	–	0.13 ± 0.29	−1.94 ± 0.71, p < 0.001	0.12 ± 0.28	−1.95 ± 0.69	0.15 ± 0.29	−1.92 ± 0.70, p < 0.001
RA	5.77 ± 3.36	–	0.31 ± 0.67	−5.46 ± 3.26, p < 0.001	0.23 ± 0.68	−5.55 ± 3.17	0.33 ± 0.86	−5.44 ± 3.11, p < 0.001
KTW	2.80 ± 0.92	–	3.18 ± 0.87	0.38 ± 0.73, p = 0.001	3.16 ± 0.95	0.36 ± 0.78	3.26 ± 0.95	0.45 ± 0.88, p < 0.001
PD	1.28 ± 0.45	–	1.43 ± 0.50	0.15 ± 0.59, p = 0.293	1.66 ± 0.48	0.38 ± 0.53	1.68 ± 0.47	0.40 ± 0.54, p < 0.001
CAL	3.34 ± 0.90	–	1.55 ± 0.58	−1.80 ± 0.82, p < 0.001	1.78 ± 0.57	−1.56 ± 0.86	1.83 ± 0.54	−1.51 ± 0.88, p < 0.001

	T_0	T_1	T_2	T_2-T_1	T_3	T_3-T_1	T_4	T_4-T_1
MGT 1.5 mm	–	1.89 ± 0.67	1.22 ± 0.53	−0.67 ± 0.57, p < 0.001	0.92 ± 0.52	−0.97 ± 0.52	0.81 ± 0.47	−1.08 ± 0.55, p < 0.001
MGT 3 mm	–	1.85 ± 0.72	1.21 ± 0.54	−0.64 ± 0.69	0.81 ± 0.56	−1.05 ± 0.68	0.60 ± 0.51	−1.26 ± 0.74
MV	–	1.73 ± 0.43	1.47 ± 1.10	−0.26 ± 1.08	1.12 ± 1.18	−0.61 ± 1.14	0.94 ± 1.12	−0.79 ± 1.09

	T_0	T_1	T_2	T_3	T_3-T_2	T_4	T_4-T_2	T_4-T_3
% RC	–	–	93.5 ± 14.3	94.6 ± 11.9	1.18 ± 10.07, p = 1.000	93.0 ± 12.3	−0.46 ± 13.77, p = 1.000	−1.64 ± 9.27, p = 0.635
% CRC	–	–	74.5%	80.9%	p = 1.000	72.3%	p = 1.000	p = 0.278

Note: Expressed as mean ± standard deviation and *n* (%).
Abbreviations: % CRC, percentage of complete root coverage; % RC, percentage of root coverage; CAL, clinical attachment level; KTW, keratinized tissue width; MGT 1.5 mm, marginal gingival thickness change 1.5 mm apical to the gingival margin; MT 3 mm, marginal gingival thickness change 3 mm apical to the gingival margin; MV, mucosal volume change; PD, probing depth; RA, recession area; RD, recession depth.

TABLE 3 Association between baseline clinical parameters and percentage of Root Coverage (% RC) at 6 months.

	Simple binary linear analysis	
Variable	**Beta (95% CI)**	***p*-value**
PD	2.03 (−4.54, 8.60)	0.546
CAL	0.01 (−2.57, 2.58)	0.995
KTW	−0.11 (−2.63, 2.41)	0.932
Arch		
Maxilla	0.00	
Mandible	1.97 (−6.62, 10.6)	0.653
Tooth type		
Incisor/Canine	0.00	
Premolar	−1.03 (−7.00, 4.93)	0.735
Marginal gingival thickness change 1.5 mm T_1	4.20 (−0.48, 8.88)	0.079
Marginal gingival thickness change 3 mm T_1	4.66 (0.71, 8.60)	0.021*
Mucosal volume T_1	11.1 (1.07, 21.2)	0.031*
GM-CEJ T_1	12 (7.53, 16.5)	<0.001**

Note: Results of simple binary linear regression model with generalized estimating equations (GEE).
Abbreviations: CAL, clinical attachment level; GM, gingival marginKTW, keratinized tissue width; PD, probing depth.
*p < 0.05; **p < 0.01.

TABLE 4 Association between baseline clinical parameters and % CRC at 6 months.

	Simple binary logistic analysis	
Variable	**OR (95% CI)**	***p*-value**
KTW	1.13 (0.59, 2.16)	0.707
Arch		
Maxilla	1	
Mandible	0.71 (0.10, 4.94)	0.733
Tooth type		
Incisor/Canine	1	
Premolar	0.79 (0.27, 2.36)	0.675
Marginal gingival thickness change 1.5 mm T_1	3.73 (1.28, 10.9)	0.016*
Marginal gingival thickness change 3 mm T_1	2.91 (1.06, 7.98)	0.038*
Mucosal volume T_1	8.23 (0.74, 92.2)	0.087
GM-CEJ T_1	11.8 × 10^4 (137.6, 10.2 × 10^6)	0.001**

Note: Results of simple binary logistic regression model with generalized estimating equations (GEE).
Abbreviations: CAL, clinical attachment level; GM, gingival margin; KTW, keratinized tissue width; PD, probing depth.
*p < 0.05.**p < 0.0001.

was also observed that the postsurgical gingival margin position in relation to the CEJ was strongly associated with CRC at 6 months (p < 0.0001). As illustrated in Figure 3A, a gingival margin positioned ≥0.5 mm coronal to the CEJ just after surgery predicted almost all the cases of CRC at 6 months. After adjusting multiple logistic models by tooth position, the immediate postsurgical gingival thickness at 1.5 and 3 mm still remained significantly associated with CRC at 6 months (p = 0.039; p = 0.022; Tables 5 and 6). Additionally, it should be noted that mandibular GRs presented a lower probability of CRC at 6 months (p = 0.097; Figure 3B).

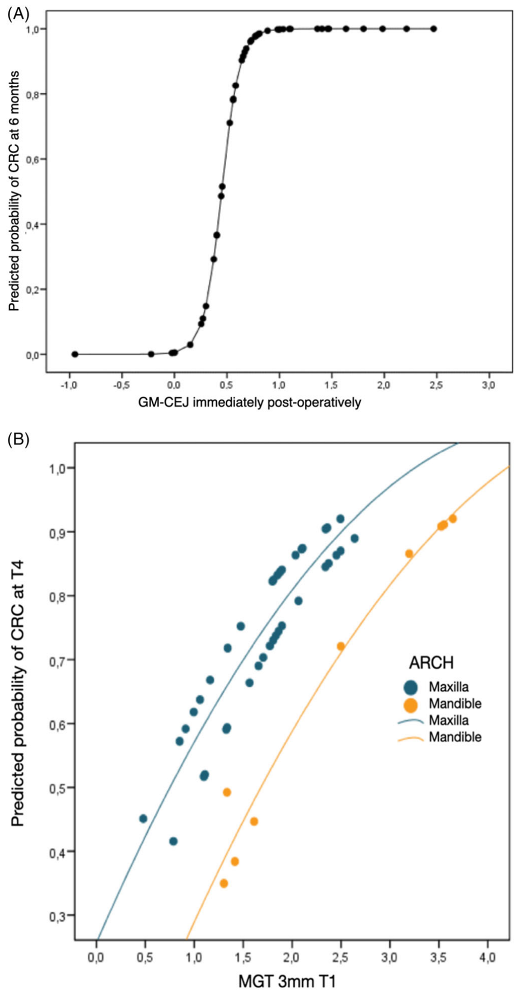

FIGURE 3 (A) Prediction of the probability of CRC at 6 months in relation to the immediate postsurgical gingival marginal position relative to the CEJ. (B) Correlation between immediate postoperative MGT 3 mm and CRC at 6 months.

TABLE 5 Association between tooth position and marginal gingival thickness at 1.5 mm (T_1) and % CRC at 6 months.

Variable	Multiple binary logistic analysis OR (95% CI)	*p*-value
Arch		
Maxilla	1	
Mandible	0.98 (0.25, 3.86)	0.978
Tooth type		
Incisor/Canine	1	
Premolar	0.67 (0.14, 3.10)	0.605
Marginal gingival thickness change 1.5 mm T_1	3.87 (1.07, 13.9)	0.039*

Note: Results of binary multiple logistic regression model with generalized estimating equations (GEE).
*$p < 0.05$.

TABLE 6 Association between tooth position and marginal gingival thickness at 3 mm (T_1) and % CRC at 6 months.

Variable	Multiple binary logistic analysis OR (95% CI)	*p*-value
Arch		
Maxilla	1	
Mandible	0.38 (0.12, 1.19)	0.097
Tooth type		
Incisor/Canine	1	
Premolar	0.58 (0.11, 3.01)	0.515
Marginal gingival thickness change 1.5 mm T_3	3.71 (1.21, 11.4)	0.022*

Note: Results of binary multiple logistic regression model with generalized estimating equations (GEE).
*$p < 0.05$.

4 | DISCUSSION

4.1 | Principal findings

Extensive evidence is available in the literature on the efficacy of ADM in root coverage procedures such as tunneling or CAF techniques at short term.[27,28,44–49]

The present prospective study sought to evaluate the linear and volumetric changes from the immediate postoperative period to 6 months following the treatment of GRs using a MTUN combined with the use of ADM. Although similar research has been previously published and discussed, this is the first study to digitally assess the keratinized tissue over time.[27,44,46] Moreover, to the best of the authors' knowledge, it is the first study to digitally measure GM-CEJ, MGT, and MV, immediately after surgery and throughout the entire healing process.

The application of 3D technology for the analysis of mucogingival surgery outcomes has changed the paradigm of classical measuring systems such as the periodontal probe or transgingival piercing approaches. This shift has allowed more accurate detection of details, such as the change in tissue thickness, coupled with the change in mucogingival line position, during the early stages of healing. In a nutshell, digitization as a method of measurement and monitoring has brought precision and reliability to clinical measurements.

In fact, the use of this innovative methodology in this study has allowed assessment of the changes occurring in the keratinized tissue over time, evidencing an increase of almost 0.5 mm at 6 months. Interestingly, the superimposition of the digital scan models of the different timepoints allowed not only observation of the linear changes in terms of keratinized tissue gain or final gingival margin position, but also evaluation of the dynamics of soft tissue healing in terms of the changes in soft tissue volume. In fact, the study revealed that the MGT is gradually reduced from post-surgery to 6 months, due to shrinkage and collapse of the tissues during the healing and maturation process following root coverage surgery, by 1 to 1.2 mm at 1.5 and 3 mm apical to the GM. Likewise, the final volume also underwent considerable shrinkage over time, decreasing by about 0.80 mm^3 at the end of the observation period. These changes could be due to the resorption that can be expected from the ADM during the healing period.

Regarding the results of the primary clinical endpoint, the % RC and CRC were 93.0% and 72.3%, respectively, 6 months after root coverage surgery with MTUN + ADM. Furthermore, both % RC and CRC remained stable during the follow-up period, as no statistically significant differences were observed between the root coverage achieved at 6 weeks and that recorded at 6 months. Moreover, all research variables showed significant variations throughout the entire observation period.

4.2 | Agreements and disagreements with previous studies

The clinical findings of this study support the view that MTUN + ADM is a reliable and predictable technique for root coverage of single and multiple GRs in both the maxilla and mandible, achieving CRC rates of 74.5% at 6 weeks, 80.9% at 3 months, and 72.3% at 6 months. Specifically, an average root coverage of 93.0% was achieved at 6 months. In addition, GR depth decreased by an average of 1.92 ± 0.70 mm, from an initial depth of 2.07 ± 0.71 to 0.15 ± 0.29 mm 6 months after the procedure.

Several studies on TUN + ADM have reported CRC ranging from 33% to 50%, while mean root coverage was 70%–78%.[31,51] These notable differences could be due to different reasons. On one hand, the inclusion of few GRs located in the mandible in the present study could have favored the increase in root coverage percentages. Second, the type of GR to be treated differed among studies. In the present study, only single/multiple RT1 GRs were considered, whereas in the aforementioned studies single Miller Class I or II GRs were included.[31,51] In fact, GR depth and type, and whether recession is single or multiple, have been widely described as predictive factors of root coverage.[6,52]

On the other hand, several predictive factors have been correlated to the amount of root coverage that can be achieved, as well as to the stability of the results over time. These include the final position of the GM with respect to the CEJ, and gingival thickness.[10,15,18,53] In this study, the GM-CEJ immediately after surgery categorically discriminated between complete and incomplete RC after 6 months. In fact, in the vast majority of cases in which the gingival margin remained 0.5 mm coronal to the CEJ, CRC was reached. These results support the conclusions of previous studies, where greater reductions of the initial recession were observed when more coronal displacement was recorded after surgery.[10,54]

Similarly, a change in MGT at 1.5 and 3 mm from the gingival margin, immediately after surgery, was also found to be a significant predictor of % RC and CRC at 6 months. In other words, for every additional 1 mm thickness change achieved postoperatively, at 1.5 and 3 mm, the probability of achieving CRC increased almost fourfold. This is in agreement with the results of previous studies that found an initial mucosal thickness of 0.8–1.1 mm to be the critical threshold thickness for CRC.[15,18] Moreover, when comparing these results with those of studies using digital methods for analysis, no significant differences in final gingival thicknesses were observed. For instance, the mean thickness at the end of this study was approximately 0.70 mm, while in the study of Zuhr et al., combining TUN + connective tissue graft (CTG), thickness was 0.58 mm, and Ahmedbeyli et al., using CAF + ADM, recorded 0.75 mm.[45,50] As opposed to mucosal gingival thickness, the initial MV after surgery was not a strong predictor of root coverage at 6 months, even though it was so over the shorter term. It is crucial to note that 3D scanners do not provide information at a single timepoint, but rather simply the volume change from two different timepoints. To assess MGT and MV at a single timepoint a Cone Beam Computed Tomography (CBCT) would have been necessary.

As for the changes produced at KTW level, monitoring by means of 3D scanning and the superimposition of scans allowed for study of the changes experienced during the healing process. Specifically, the gain in KTW was approximately 0.45 mm from baseline to 6 months after surgery, which is within the expected range. In other words, the KTW gain shown in other studies also using ADM combined with TUN, CAF or modifications of these techniques, ranged from 0–4 to 1.34 mm.[45,51] However, two randomized clinical trials in which the same TUN + ADM technique was used have shown similar KTW gains of 0.4 and 0.6 mm.[31,51] Nonetheless, this is the first study to evaluate the change in KTW digitally. Contrastingly with other studies, baseline KTW showed no significant correlation with % RC and CRC.[6,52] This could be explained by the fact that the average baseline KTW was more than 2 mm, which is the threshold that has been shown to be necessary to achieve stability of the GM over time.

It should be noted that the tunneling technique has certain clinical limitations. As seen in a randomized clinical trial, when dealing with multiple adjacent defects with different recession heights, the surgical difficulty and risk of exposure are increased when compared to adjacent defects with similar recession heights.[27] Moreover, when tunneling, the limited flap mobility and coronal advancement of the flap caused by the lack of vertical incisions and intact papilla might result in an uncovered graft in these heterogeneous defects. As a consequence, unwanted exposure of the ADM in the early stages of healing does not evolve as favorably as a partially exposed connective tissue graft—the latter even tending to result in a KT increase, when exposed.[55–57] Therefore, exposure of the ADM may lead to erratic healing, in which partial or total resorption of the material will occur.[58]

4.3 | Limitations and recommendations for future research

The present study has a few shortcomings or limitations that should be mentioned. First, the relatively short follow-up period (6 months) could complicate the drawing of conclusions regarding the effectiveness of this surgical approach. In this respect, it must be taken into consideration that a significant relapse of the gingival margin over time has been observed when multiple adjacent GRs was treated with ADM with both TUN and CAF techniques. Therefore, the longer the follow-up period, the more accurate the description of tissue stability and its impact upon the aesthetic outcome of root coverage.[32] Second, the limited number of included sites could constitute a source of bias. However, an appropriate statistical power and strong significance level support the drawing of sufficiently reliable statements on the influence of GM-CEJ and MGT upon the treatment outcomes. Additionally, pre-operative MGT was not evaluated and its effect on % RC and CRC could not be assessed.

Within the limitations of this study, it can be concluded that the MTUN + ADM procedure is a valuable technique that has been shown to be effective in affording root coverage of single or multiple GRs, producing with minimal surgical trauma—particularly when combined with ADM. However, modifications of the technique could improve its efficacy in terms of greater flap advancement and mobility, especially when combined with ADM. On the other hand, it has been possible to demonstrate how monitoring of the results by means of 3D technology systems affords data of great importance for the clinician, and contributes additional value to root coverage studies. Thus, it has been shown that the MGT gain at 1.5 and 3 mm, and GM-CEJ achieved in the immediate postoperative period are significant predictors of CRC at 6 months when GRs are treated with MTUN + ADM.

Finally, the research team encourages further studies involving different flap designs to secure improvements of the technique with a view to securing greater predictability of the results and to offer valuable information for the clinician through digitally monitored healing.

AUTHOR CONTRIBUTIONS

Gonzalo Blasi contributed to study conception, design, surgery and data interpretation, and drafted and critically revised the manuscript. **Lory Abrahamian**, **Javi Vilarrasa** and **Ramón Pons** were involved in data collection, interpretation, and analysis. **Alberto Monje** and **José Nart** were involved in data interpretation, drafting, and critical review of the manuscript, and gave final approval of the version submitted for publication. All authors made substantial contributions to the conception and design of the study.

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DATA AVAILABILITY STATEMENT

Research data are not shared.

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Abstract

Background: A study was made of the dimensional changes in free epithelialized gingival/mucosal grafts (FEGs) used to augment keratinized tissue (KT) at tooth and implant sites, and of the confounders influencing the dynamic changes over 6 months of follow-up.

Methods: A prospective cohort interventional study was made of implant and tooth sites needing KT augmentation by means of an apically positioned flap and FEG. Six intraoperative variables were recorded at baseline (T0). In addition, graft width (GW), graft length (GL), and graft dimension (GD) were assessed at 3 weeks (T1), 3 months (T2), and 6 months of follow-up (T3). Univariate and multivariate analyses were performed to explore associations between the demographic and intraoperative variables and the outcomes over the study period.

Results: Based upon an a priori power sample size calculation, a total of 56 consecutive patients were recruited, of which 52 were available for assessment. A total of 73 graft units were included in 122 sites. At T3, the mean change in GD in FEG was 40.21%. In particular, the mean changes in GL and GW were 12.13% and 33.06%, respectively. Statistically significant changes in GD were recorded from T0 to T1 ($P < 0.0005$) and from T1 to T2 ($P < 0.0005$), but not from T2 to T3 ($P = 0.13$). The change in

GD at T3 was 33.26% at tooth and 43.11% at implant site level (P = 0.01). Age and GW assessed at T0 proved to be related to the changes in GD and GW in the univariate and multivariate analyses. The univariate analysis showed the avascular area (AA) to be related to the changes in GD and GW at the implant sites, whereas graft thickness (GT) was associated to changes in GD and GW at the tooth sites in the univariate and multivariate analyses.

Conclusion: Free epithelialized grafts are exposed to dimensional changes that result in a reduction of approximately 40% of the original graft dimension-the changes being approximately 10% greater at the implant sites than at the tooth sites

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CASE SERIES

Dimensional changes in free epithelialized gingival/mucosal grafts at tooth and implant sites: A prospective cohort study

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Conclusion: Free epithelialized grafts are exposed to dimensional changes that result in a reduction of approximately 40% of the original graft dimension–the changes being approximately 10% greater at the implant sites than at the tooth sites (NCT04410614).

KEYWORDS
connective tissue graft(s), implantology, mucogingival surgery

1 | INTRODUCTION

Soft tissue characteristics at tooth and implant sites were a subject of debate for decades, in particular as regards the significance of keratinized gingiva/mucosa in relation to periodontal/peri-implant health.[1–6] Later findings, however, suggested that the presence of keratinized tissue (KT) at tooth and implant sites affords greater stability of the gingival/mucosal margin, and is associated to less clinical inflammation.[6–8] This was found to be more evident at implant sites compared to the contralateral tooth sites.[9] In turn, clinical studies demonstrated that the proinflammatory profile, defined by inflammatory mediators and cytokines such as prostaglandin E2 (PgE2),[10] tumor necrosis factor-α (TNF-α),[11] and interleukin 1-β (IL-1β),[11] is upregulated at implant sites that exhibit <2 mm of keratinized mucosa (KM). Therefore, interventions seeking to gain KT at tooth and implant sites in areas characterized by a mobile mucosa have been advocated for the prevention and management of periodontal and peri-implant disorders.[12,13]

The use of apically positioned flaps (APFs) combined with free epithelialized gingival/mucosal grafts (FEGs) were suggested to predictably modify the periodontal/peri-implant soft tissue phenotypes with the aim of augmenting KT and promoting long-term health.[13,14] It should be noted that these strategies have shown less favorable outcomes in terms of aesthetics (i.e., color match)[15] when compared to other interventions such as coronally advanced flaps in combination with other grafting approaches such as de-epithelialized grafts.[16] Furthermore, one of the notorious shortcomings associated with this technique is graft dimensional changes, which can eventually compromise the desired final outcome.[17]

Sullivan and Atkins reported that autograft shrinkage occurred at two main timepoints, namely immediately after harvesting and during the healing process.[18] In particular, thicker grafts tend to exhibit greater immediate contraction upon detachment from the donor zone, because of their greater elastic fiber content, though with less secondary contraction during the healing period, and demonstrate greater resistance to functional stresses. Contrarily, thinner grafts can be more easily maintained through diffusion, and neovascularization is easier achieve–though such grafts display greater secondary shrinkage.[19] Furthermore, the nature of the recipient bed,[20] the graft stabilization approach employed,[21] the adjacent gingival phenotype,[22] or smoking habit,[23] among other variables,[20] have been shown to have an impact upon graft stability during healing. Nonetheless, the role played by intraoperative variables in relation to dimensional changes at tooth and implant sites remains unclear. Thus, the purpose of the present prospective cohort study was to assess the dynamic dimensional changes over 6 months of follow-up when using FEGs simultaneous to APFs at tooth and implant sites with the aim of gaining KT.

2 | MATERIALS AND METHODS

A prospective cohort interventional study was carried out from May 2020 to July 2021 in abidance with the principles of the Declaration of Helsinki, and was approved by the Research Ethics Committee of the *Gerencia del Area de Salud de Badajoz* (Badajoz, Spain). The study was carried out in a private practice (CICOM Monje, Badajoz, Spain). All the interventions and records were conducted by a single periodontist (AM), who also supervised the patients during supportive therapy. This study was registered and approved by www.clinicaltrials.gov (NCT04410614). The study was reported following the items checklist of the STROBE statement.[24]

2.1 | Study population

Patients in need of FEG as primary or secondary prevention or management of periodontal and/or peri-implant diseases were recruited. The following inclusion criteria were applied: patients between 18 and 80 years of age, nonsmokers, a lack of, or an insufficient (<2 mm) band of keratinized gingival (KG) or mucosa (KM) at the buccal aspect of teeth/implants, and no presence of systemic diseases or medications known to alter bone or soft tissue metabolism. Patients were further eligible if they exhibited healthy or gingivitis-affected teeth or implants in need of primary prevention (during second stage implant surgery), secondary prevention (because of mucositis defined as profuse bleeding on probing)[25] or anti-infectious therapy (because of peri-implantitis).[25] The exclusion criteria were: pregnant or breastfeeding women, smokers, or individuals with uncontrolled medical conditions or an unwillingness to undergo the free soft tissue grafting intervention or attend the regular check-ups for monitoring the dimensional changes.

2.2 | Surgical intervention at tooth sites

A partial thickness (mucosal) flap was raised following the mucogingival margin. Then, the mucosal flap was apically positioned. Root scaling was performed before the graft was stabilized, using Gracey curettes[*].

[*] Hu-Friedy, Chicago, IL

2.3 | Surgical intervention at implant sites

For procedures seeking to augment KM during second stage implant surgery, no intervention other than placing the healing abutments was carried out simultaneous to APF and FEG. In contrast, for the management of peri-implantitis, APF, implantoplasty[†], and osteoplasty at the crestal aspect (if needed) were carried out as part of anti-infectious therapy.

2.4 | Free epithelialized gingival/mucosal grafting description

The FEG were harvested from the palate. The extent was calculated according to the length and width estimated using a 15C blade[‡]. Graft thickness varied, though attempts were made to secure a thickness of about 1.5 mm (including epithelium and lamina propria). The graft was then soaked in saline solution and sutured using simple interrupted Nylon 5.0 or 6.0[§] and Vycril 5.0[**] sutures upon the recipient bed. If needed, periosteal cross mattress sutures were used. Surgical cyanoacrylate[††] was then applied to protect the donor wound. Resorbable polyglactin 910 4.0 cross sutures[‡‡] were placed on top, and an acrylic suck-down device was customized for each patient.

2.5 | Demographic variables

The recorded demographic variables included age, sex, tooth/implant site (anterior and posterior), and the type of intervention involved (periodontal soft tissue augmentation/peri-implant soft tissue augmentation).

2.6 | Intraoperative variables

The following site-specific variables were recorded at the zenith of the implant/tooth site (Figure 1):

- Avascular area (AA): the area (in mm^2) of the bone dehiscence at the tooth or implant in close contact with the graft. The area was determined examining the width and length of the avascular bed using a North Carolina Probe.
- Recipient bed thickness (RBT): the thickness (in mm) of the vascular recipient bed determined using a North Carolina Probe approximately 3 mm below the mucosal zenith.
- Graft length (GL): the length (in mm) of the graft measured using a North Carolina Probe.
- Graft width (GW): the width (in mm) of the graft measured using a North Carolina Probe.
- Graft dimension (GD): the dimension (in mm^2) of the graft determined examining the graft length and width.
- Graft thickness (GT): the mean thickness (in mm) of the soft tissue graft measured using calipers. The mean value was calculated from three measurements along the graft.

2.7 | Clinical variables during the study period

These data have been included within the text. The following clinical parameters were recorded at the 3-week (T1), 3-month (T2) and 6-month postoperative recall visits (T3): GL, GW, and GD.

In the event the newly-formed gingiva/mucosa could not be identified, Lugol staining was used to outline the area.[26]

2.8 | Postoperative care

The patients were instructed to apply an antimicrobial gel in the area three times a day during 2 weeks (Lacer MucoRepair®, Lacer, Barcelona, Spain), and systemic amoxicillin (750 mg, two tablets per day during 7 days) and antiinflammatory medication (Ibuprofen, 600 mg, one tablet every 6 hours during 5 days) were also prescribed. The sutures were removed after 2 to 3 weeks, and the patients were advised to resume oral hygiene.

2.9 | Statistical analysis

An a priori power analysis was carried out for sample size calculation, based on a study published elsewhere,[23] in order to establish statistical significance ($P < 0.05$). Assuming a SD of 1 mm, a minimum clinical difference of 0.75 mm, a ratio between implant and tooth of two, an alfa error and beta error of 0.05 and 0.20, respectively, and a dropout rate of 15%, a total of 50 and 25 graft units were found to be needed in the implant sites and tooth sites group, respectively. Quantitative

[†] Meisinger LLC, Nauss, Germany
[‡] Swann-Morton, Sheffield, England
[§] Resorba Sutures, Osteogenics Biomedical, Lubbock, TX
[**] Vicryl, Ethicon Inc., Somerville, NJ
[††] Peryacril 90HV, Glustitch Inc., Delta, BC, Canada
[‡‡] Vicryl, Ethicon Inc., Somerville, NJ

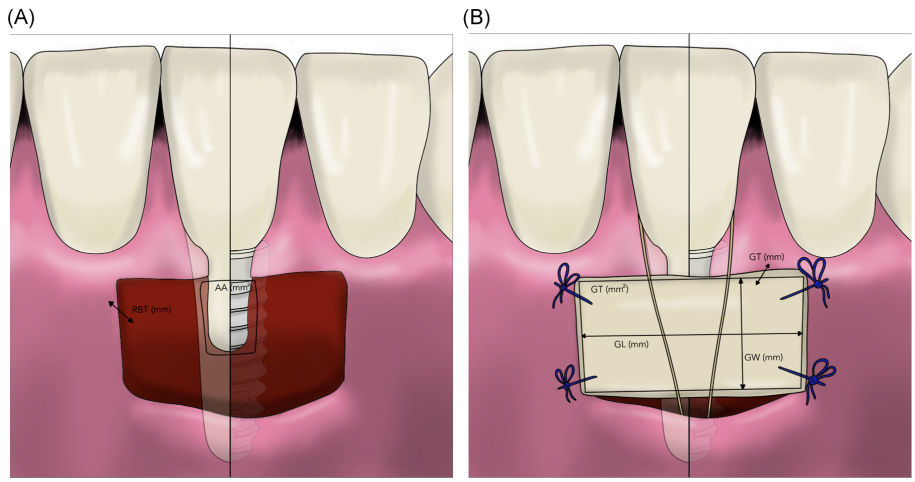

FIGURE 1 Illustrations (**A and B**) depicting the intraoperative variables recorded at T0

variables were reported as the mean and standard deviation (SD), whereas frequencies and percentages were used to describe qualitative variables. Differences between groups were evaluated using the chi-squared test or Fisher's exact test (if at least one cell was ≤ 5) for categorical variables and the student t-test or equivalent nonparametric tests (Mann-Whitney U-test or Wilcoxon test) for quantitative variables, after assessing the normality of data distribution with the Shapiro-Wilk test. In order to test possible predictors of GW reduction, a univariate analysis was performed employing a three-level (patient, graft, implant/tooth) random intercept linear mixed model, using percentage GW reduction as dependent variable and age, sex, intervention, GT, RBT, AA, GL, GW, tooth/implant position and type of site (tooth versus implant) as independent variables. Subsequently, only those variables that exhibited $P < 0.20$ were entered in the multivariate analysis, which was carried out employing a stepwise three-level random intercept linear mixed model. Likewise, univariate and multivariate analyses were conducted for both the tooth and implant subgroups. The SPSS version 26 statistical package (Armonk. New York, USA) was used throughout. Statistical significance was considered for $P < 0.05$.

A Cohen intra-examiner agreement rate was calculated to test the accuracy of the examiner during assessment of the clinical variables during the study period. As part of training, GW and GL were assessed at two different timepoints (before and after supportive maintenance therapy). The study was started when the examiner reached > 85% agreement in a representative sample of 12 patients (20% of the sample size).

3 | RESULTS

3.1 | Demographic data

A total of 56 consecutive patients ($n_{teeth} = 22$; $n_{implants} = 34$) were recruited. Of these, four dropped out during the study period ($n_{teeth} = 1$; $n_{implants} = 3$). Of the patients eligible for analysis, 82.1% were females, and the mean age was 52.4 ± 14.6 year. A total of 73 graft units at 122 sites were included. Anterior mandibular sites predominated over other sites (34.9%). None of the intraoperative variables yielded statistical significance at T0, except AA ($P < 0.0005$) favoring implant compared to tooth sites (see Supplementary Table S1 in online *Journal of Periodontology*). A Cohen intra-examiner agreement rate of 100% and 92% was reached for GW and GL, respectively before the initiation of the study.

3.2 | Free epithelialized gingival/mucosal graft dimensional changes

At the 6-month follow-up assessment (T3), the mean change in GD was 40.21%. In particular, the mean GL and GW reductions were 12.13% and 33.06%, respectively, at T3. Similar dimensional changes were reported at T1 when compared to T0 (16.32%) and at T1 compared to T2 (15.31%). This yielded statistical significance at both timepoints ($P < 0.0005$). Only minor changes occurred from T2 to T3 (1.8%), without reaching statistical significance ($P = 0.13$). The mean difference in GD between the tooth and implant sites was statistically significant at T3 ($P = 0.01$). In particular, the decrease in GD at T3 was 33.26% at the tooth sites and 43.11% at the implant sites. A similar tendency was noted for the tooth and implant sites in the course of the study period, becoming more notorious at T2, because GW and GD at the implant sites yielded greater statistical significance ($P < 0.0005$) compared to the tooth sites ($P = 0.004$) (Table 1, Figures 2, and 3 and Supplementary Table S2 in online *Journal of Periodontology*).

3.3 | Confounders of free epithelialized gingival/mucosal graft dimensional changes

The univariate and multivariate analyses yielded statistical significance between GD and GW and age ($P = 0.002$) and GW assessed at T0 ($P < 0.0005$). Moreover, the type of intervention simultaneous to soft tissue grafting further demonstrated significance in the univariate analysis. In particular, FEG when performed simultaneous to peri-implantitis anti-infectious therapy showed significantly more dimensional changes when compared to other interventions to augment KG/KM at the tooth and implant sites ($P = 0.002$). On evaluating the tooth sites independently, GT furthermore showed significance in the univariate ($P = 0.003$) and multivariate analyses ($P = 0.009$). For the implant sites, AA exhibited statistical significance in the univariate analysis ($P = 0.01$) (Table 2).

4 | DISCUSSION

4.1 | Principal findings

The findings from this prospective cohort study showed that: (1) FEGs are exposed to dimensional changes that result in a reduction of approximately 40% of the original GD; (2) the GD changes are essentially attributable to a decrease in GW, which was approximately 70% compared to GL; (3) the FEG dimensional changes were about 10% greater at the implant sites than at the tooth sites; (4) wider FEGs in older patients are prone to exhibit greater dimensional changes; (5) thicker grafts are more consistent with graft stability at tooth sites; and (6) FEGs stabilized in areas with greater AA are exposed to greater GD and GW changes at implant sites. The later finding may reflect the fact that GD and GW were significantly greater when FEGs were performed simultaneous to anti-infectious therapy, where the AA of the implant is greater.

TABLE 1 Dimensional changes during the study period

	Linear changes Mean ± SD	% Change	P-value	Linear changes Mean ± SD	% Change	P-value	Linear changes Mean ± SD	% Change	P-value	Linear changes Mean ± SD	% Change	P-value
TOOTH SITES	**T0 versus T1 (n = 23)**			**T1 versus T2 (n = 20)**			**T2 versus T3 (n = 20)**			**Overall change (n = 20)**		
GW (mm)	0.96 ± 0.93	13.86%	*<0.0005*	0.85 ± 1.05	14.30%	*0.004*	0.14 ± 0.62	1.92%	*0.315*	1.84 ± 1.35	26.37%	*<0.0005*
GL (mm)	1.13 ± 2.26	7.52%	*0.025*	0.3 ± 1.69	0.15%	*0.437*	0.15 ± 1.31	1.30%	*0.614*	1.35 ± 1.09	9.75%	*<0.0005*
GD (mm^2)	21.09 ± 21.43	20.33%	*<0.0005*	13.33 ± 20.96	13.18%	*0.010*	1.9 ± 10	2.86%	*0.406*	33.88 ± 21.64	33.26%	*<0.0005*
IMPLANT SITES	**T0 versus T1 (n = 50)**			**T1 versus T2 (n = 49)**			**T2 versus T3 (n = 48)**			**Overall change (n = 48)**		
GW (mm)	1.26 ± 1.45	17.45%	*<0.0005*	1.08 ± 15.3	15.72%	*<0.0005*	0.15 ± 0.82	1.17%	*0.253*	2.54 ± 1.92	35.84%	*<0.0005*
GL (mm)	0.92 ± 0.90	5.33%	*<0.0005*	0.92 ± 2.22	5.03%	*<0.0005*	0.54 ± 1.11	3.19%	*0.001*	2.42 ± 2.70	13.12%	*<0.0005*
GD (mm^2)	27.11 ± 27.53	21.92%	*<0.0005*	20.42 ± 28.3	19.00%	*<0.0005*	4.64 ± 14.57	5.07%	*0.032*	53.43 ± 45.45	43.11%	*<0.0005*
TOTAL	**T0 versus T1 (n = 73)**			**T1 versus T2 (n = 69)**			**T2 versus T3 (n = 68)**			**Overall change (n = 68)**		
GW (mm)	1.16 ± 1.31	16.32%	*<0.0005*	1.01 ± 1.4	15.31%	*<0.0005*	0.15 ± 0.76	1.81%	*0.137*	2.33 ± 1.78	33.06%	*<0.0005*
GL (mm)	0.98 ± 1.45	6.02%	*<0.0005*	0,74 ± 2.08	3.61%	*<0.0005*	0.43 ± 1.18	2.64%	*0.004*	2.1 ± 2.38	12.13%	*<0.0005*
GD (mm^2)	25.21 ± 25.77	21.42%	*<0.0005*	18.36 ± 26.43	17.31%	*<0.0005*	3.83 ± 13.37	4.42%	*0.061*	47.67 ± 40.77	40.21%	*<0.0005*

Abbreviations: GW, graft width; GL, graft length; GD, graft dimension.

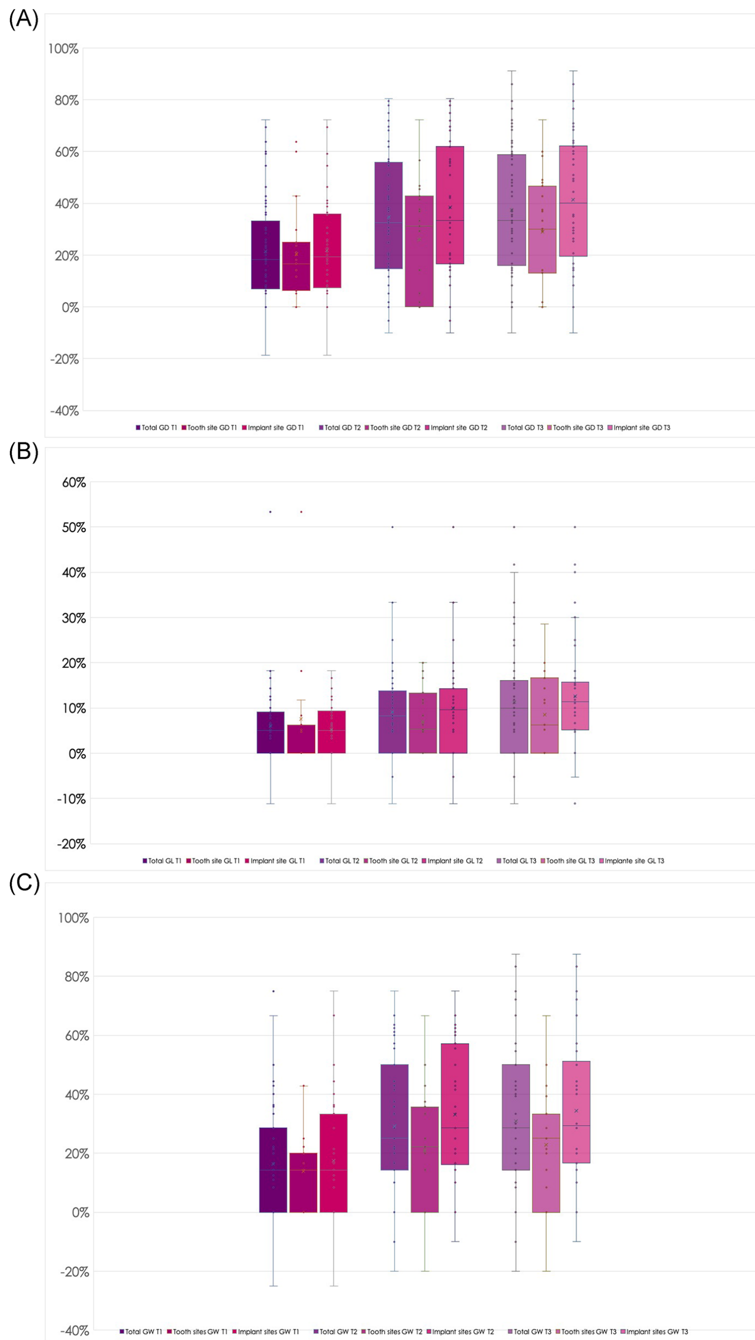

FIGURE 2 Percentage dimensional changes by means of (**A**) total graft dimension (GD), (**B**) total graft length (GL), and (**C**) total graft width (GW)

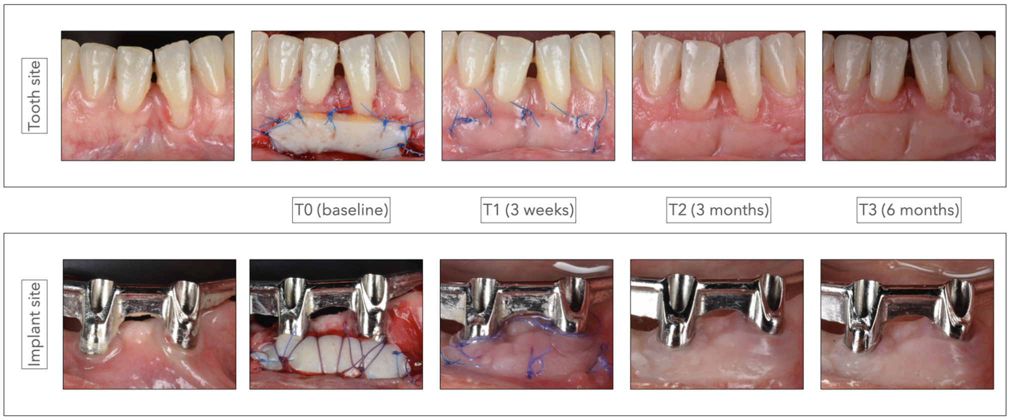

FIGURE 3 Epithelialized soft tissue graft for gaining keratinized tissue at tooth and implant sites

4.2 | Agreements and discrepancies with previous findings

The use of FEGs has been advocated to gain attached tissue,[27] deepening the vestibule,[28] and also to attempt root coverage.[29] The technique was originally described in the 1960s by several authors.[18,30,31] Since then, clinical studies have sought to understand the factors influencing graft integration/success[20,32,33] and dimensional stability.[17,20,22,23] Sullivan and Atkins showed capillary outgrowths to be crucial in the development of granulation tissue and in the vascularization of FEGs.[18] As such, graft areas outlined by a denuded root/implant surface or cortical bone may suffer necrosis.

In addition, the literature has shown the following elements and strategies to be crucial in reducing GD changes: (1) FEGs used to gain KM at implant sites in contrast to grafts used to augment KG at tooth sites;[17] (2) intermediate thickness grafts when compared to very thin grafts;[20] (3) grafts in non-smokers compared to smokers;[23] (4) the presence of a thick gingival phenotype and KT at adjacent sites compared to thin phenotypes;[22] and (5) stabilization using cyanoacrylate compared to suturing up.[21] The present study further contributes to understanding of the variables that dictate graft stability. For instance, it was seen that for tooth and implant sites, GW is pivotal in predicting GD and GW changes. In the light of our findings, it is speculated that wider grafts have been used in scenarios where the vestibule is shallower, and thus more collapse of the mucogingival or alveolar mucosal junction is anticipated rather than "shrinkage" of the graft. In this sense, we feel that this term is inaccurate, considering that GW and GL were not seen to undergo dimensional changes of proportional magnitudes. These changes thus occur as a consequence of vertical collapse, rather than of "shrinkage" attributable to factors inherent to the properties of the FEG or to the nature of the recipient site. This phenomenon has also been described elsewhere.[17,34] Furthermore, it can be speculated that implant sites may have a shallower vestibule because of alveolar ridge atrophy after tooth extraction than that found at tooth sites.[35] This may partially explain the difference in changes in GD and GW.

Not surprisingly, thicker grafts were seen to experience lesser dimensional changes at tooth sites. This agrees with previous studies[20] that reported an average difference of approximately 15% between very thin (GT 0.3 mm) and scalpel-thick grafts (GT 0.9 mm). It has been hypothesized that the stability of thicker grafts is linked to resistance to functional stresses.[18] Interestingly, the univariate analysis showed AA to be associated to dimensional changes at implant sites. This finding was not surprising, given that in avascular zones, there are no capillary outgrowths to promote plasma circulation and organic binding.[36] Hence, it is worth noting that whenever soft tissue grafting is performed at implant sites to increase the KM band–in particular simultaneous to anti-infectious therapy for the management of peri-implantitis–the graft must be secured within the vascular recipient bed, and no attempt should be made to coronally reposition the mucosal margin with the aim of covering the recession, because this may result in partial necrosis of the FEG.

Graft dimensional changes have been more extensively documented at tooth sites than at implant sites. At tooth sites, changes ranging from 25% to 48.3% have been reported.[20,34,37,38] Thus, our findings are in line with the data found in the literature. At implant sites, the reported

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TABLE 2 Univariate and multivariate analysis of the tooth group and implant group

	Univariate analysis				Multivariate analysis			
TOOTH SITE	*Coefficient*	*P-value*	*CI inf*	*CI sup*	*Coefficient*	*P-value*	*CI inf*	*CI sup*
Patient level								
Age	0.002	0.749	−0.009	0.012				
Sex	0.027	0.816	−0.215	0.270				
Graft level								
Intervention								
Primary versus secondary	−0.055	0.795	−0.498	0.387				
Graft thickness	−0.219	0.033	−0.419	−0.020	−0.253	0.009	−0.435	−0.071
Recipient thickness	−0.055	0.593	−0.266	0.157				
Baseline length	−0.002	0.895	−0.032	0.028				
Single/multiple sites	0.224	0.818	−0.180	0.225				
Ratio avascular/baseline graft dimension	0.885	0.943	−2.404	2.581				
Tooth level								
Avascular area	0.003	0.792	−0.020	0.027				
Baseline width	0.059	0.157	−0.025	0.143	0.076	0.037	0.005	0.147
IMPLANT SITE								
Patient level								
Age	0.009	0.008	0.002	0.015	0.006	0.028	0.001	0.012
Sex	0.099	0.378	−0.127	0.326				
Graft level								
Intervention								
Primary versus all	−0.271	0.005	−0.453	−0.089				
Secondary versus all	−0.025	0.838	−0.277	0.226				
Anti-infectious versus all	0.207	0.014	0.045	0.368				
Graft thickness	−0.007	0.932	−0.167	0.153				
Recipient thickness	0.048	0.435	−0.075	0.170				
Baseline length	0.006	0.315	−0.006	0.018				
Mandible versus maxilla	0.029	0.722	−0.134	0.192				
Single/multiple sites	0.066	0.339	−0.071	0.204				
Ratio avascular area/baseline graft area	3.20	0.105	−0.682	7.082				
Implant level								
Avascular area	0.038	0.016	0.007	0.069				
Anterior versus posterior	0.053	0.305	−0.050	0.156				
Baseline width	0.088	<0.0005	0.045	0.130	0.077	0.001	0.035	0.119

Abbreviations: CI inf: Inferior 95% confidence interval; CI sup: Superior 95% confidence interval.
Estimates of multilevel, random-intercept linear mixed models of percentage width changes at 6 months compared to baseline.

mean GD changes range from 33% to 61.8%.[17,26,39,40] In fact, a comparative study showed that after 12 months of follow-up, the mean GD changes were two-fold greater at implant (61%) compared to tooth sites (36%).[17] This is in partial agreement with our own findings. Nevertheless, it must be noted that the difference in terms of GD changes at the tooth and implant sites favored the latter by only about 10%. The differences between outcomes might be attributable to differences in operator expertise, considering that the interventions in the present study were performed by a specialist, in contrast to trainees in a university setting. It is speculated that the grafts were stabilized over the implant/superstructure. That portion of the graft associated with the AA ("dead space")[36] was more likely to slough off–leading to more GD changes. In addition, it should be noted that the residual periodontal ligament may contribute through the formation of granulation tissue, favoring a smoother revascularization phase.[41]

4.3 | Limitations and recommendations for future research

The shortcomings inherent to the study design must be mentioned. Firstly, clinical measurements were carried out with a periodontal probe; errors derived from this approach are therefore likely. To overcome this limitation, it is advisable for future studies to assess GD changes using three-dimensional scanning devices. Furthermore, given that GW experienced substantially more changes than GL over the study period, it is also advisable for future studies to further assess the influence of the vestibular depth upon the GW and GD changes. On the other hand, it should be noted that FEG performed simultaneous to anti-infection therapy for peri-implantitis was associated to significantly more GD changes when compared to other interventions to augment KG/KM at the tooth and implant sites ($P = 0.002$). This finding might have influenced the outcome. Hence, future studies should focus on the determinants of GD changes in FEGs used in standardized interventions at teeth and implant sites.

5 | CONCLUSIONS

Free epithelialized grafts are exposed to dimensional changes that result in a reduction of approximately 40% of the original graft dimension–the decrease moreover being about 10% greater at implant compared to tooth sites. Baseline graft width and thickness, the type of intervention as well as the avascular area of the recipient site all influence the dynamic graft dimensional changes.

CONFLICTS OF INTEREST

The authors have no direct financial interests related to the products and instruments listed in the paper. This study was partially supported by the Department of Periodontology, Universitat Internacional de Catalunya (Barcelona, Spain).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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Abstract

Objective: To evaluate the impact of soft tissue thickness (STT) on root coverage achieved with different periodontal plastic surgery procedures.

Background: Gingival recession has been managed successfully through various surgical approaches, with great variability in outcomes. Anatomic characteristics of the recipient site and selected technique account in part for this variability. Gingival flap thickness is one of the most critical site-related characteristics.

Methods: An electronic search was conducted on the major databases (PubMed, Embase, Web of Science). Human prospective studies with at least 6 mo of follow-up and with a numeric baseline measurement for gingival thickness were eligible. Only studies including nonsmoking patients were considered. Variables included surgical approach, participant characteristics, local anatomic factors, and follow-up time. Primary outcome was mean percentage root coverage (%RC) achieved, and complete root coverage was a secondary outcome.

Results: A total of 42 studies were included (35 randomized controlled trials, 5 case series, 1 prospective cohort study, and 1 controlled clinical trial). Across studies, the pooled %RC was 81.9% (95% CI, 79.1% to 84.7%). The %RC was not significantly associated (*P* = 0.267) with baseline soft tissue thickness; however there was a significant (*P* = 0.031) inverse relationship between STT and %RC after 12-mo follow-up. Subgroup analysis showed that for no graft, there was a significant (*P*= 0.025) positive relationship between STT and %RC with the exclusion of the single outlier study based on STT.

Conclusions: STT plays a limited role in predicting root coverage across all approaches; when flaps are performed with no graft, the effect of STT is most critical. The length of time following surgery appears to influence outcomes, with 12-mo follow-up offering greater insight.

Knowledge transfer statement: The results of this study can suggest to clinicians which periodontal plastic surgery technique to employ when treating challenging cases. In particular, it can be helpful when selecting the treatment approach to treat thin phenotype sites. This study could help clinicians provide a more appropriate treatment decision in such cases.

Factors affecting the outcomes of root coverage therapy and periodontal plastic surgery

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REVIEW

Gingival Thickness and Outcome of Periodontal Plastic Surgery Procedures: A Meta-regression Analysis

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Abstract: ***Objective:*** *To evaluate the impact of soft tissue thickness (STT) on root coverage achieved with different periodontal plastic surgery procedures.*

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Keywords: gingival recession, gingiva, root coverage, gingival phenotype, autologous connective tissue graft, collagen matrix

Introduction

Gingival recession is a common mucogingival deformity. Its prevalence approaches 60% in individuals aged ≥30 y and is >90% for those between

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A supplemental appendix to this article is available online.

the ages of 42 and 65 y (Albandar and Kingman 1999; Kassab and Cohen 2003; Cortellini and Bissada 2018). Root exposure associated with gingival recession may lead to compromised oral hygiene, with caries and periodontal inflammation as well as aesthetic compromises and dentinal hypersensitivity. Predisposing factors to gingival recession include inadequate or traumatic toothbrushing techniques, intracrevicular margins in the presence of minimal or no keratinized tissue, orthodontic tooth movement dislocating the teeth out of the alveolar process, and thin gingival tissues or underlying bone (Cortellini and Bissada 2018).

Gingival recession defects have been managed successfully through various surgical approaches; however, there is a high variability in the success of these procedures. This variability appears directly related to the anatomic characteristics of the recipient site and the treatment approach. One of the recipient site characteristics that seems to influence therapeutic outcomes is gingival flap thickness (Chambrone and Tatakis 2015). Several earlier studies suggested that a gingival flap thickness >1 mm improved the likelihood of optimal root coverage (RC; Baldi et al. 1999; Huang et al. 2005; Cairo et al. 2016). The importance of gingival thickness and its implication on diagnosis, prognosis, and treatment was highlighted in the 2017 World Workshop (Cortellini and Bissada 2018). According to the authors, gingival thickness should be assessed with interdental clinical attachment loss (Cairo et al. 2011) and other clinical features in the diagnosis (i.e., cementoenamel junction and whether it is associated with a step, recession depth, keratinized tissue width; Cortellini and Bissada 2018). Furthermore, the authors recommend different treatment approaches depending on various considerations, including the thickness of the gingival tissues.

The most recent systematic review investigating the role of gingival thickness on treatment outcomes was conducted by Hwang and Wang in 2006. This study discovered a positive association between mean/complete RC (CRC) and flap thickness, examining different RC procedures with a follow-up of at least 3 mo. Interestingly, no correlation between gingival thickness and RC was found when coronally advanced flap (CAF) was analyzed individually. The included studies differed significantly in location and method of tissue thickness measurement, making it impossible to define a critical threshold of thickness above which RC was most likely.

In a recent randomized controlled trial, Clementini et al. (2018) compared RC of single recession defects treated with a trapezoidal CAF with either the split-full-split approach or a partial-thickness elevation alone. The authors found higher complete/mean RC in the split-full-split group. Retention of the periosteum may prove beneficial in the early phases of wound healing and may provide cells and growth factors, crucial to blood clot organization and initial events of the wound-healing cascade. Flap thickness, measured intraoperatively, was significantly associated with improved RC after 12 mo.

While evidence supports a direct relationship between gingival thickness and treatment outcomes, a significant body of evidence has been added in the field of periodontal plastic surgery since the last systematic review in 2006 (Hwang and Wang 2006), and many recent studies have included gingival thickness among their outcomes. Furthermore, observation times have become consistently longer throughout the literature, and there is more information regarding the outcomes over longer periods. Given the reported variabilities in outcomes across gingival defects and procedures, the effect of gingival thickness on the outcomes of RC procedures should be determined. Therefore, the present systematic review with meta-analysis was designed to characterize, for patients with gingival recession, the effect of recipient site baseline gingival thickness on the RC achieved (expressed as mean RC and CRC) with various types of RC procedures as identified in prospective clinical trials.

Materials and Methods

The study was registered on PROSPERO (CRD42017067228). A structured search was developed to identify relevant studies in PubMed (1809–present; Appendix 1). The strategy was adapted for Embase (Elsevier, 1947–present; Appendix 2) and the Cochrane Central Register of Controlled Trials (Cochrane Library; Appendix 3). Search terms incorporated controlled vocabulary and text words. Date, language, and methodology filters were not applied in the initial searches. All references retrieved included at least 1 term from 3 categories: 1) gingival flaps; 2) RC; and 3) therapies, procedures, and materials. Final database searches were run on December 9, 2017, resulting in 1,203 references, and 707 references were reviewed following deduplication in EndNote X7.5 (Clarivate Analytics).

An electronic search was conducted on the major databases (PubMed, Embase, Web of Science). PRISMA guidelines were followed for record management and reporting (Moher et al. 2010). Covidence (Veritas Health Innovation) was accessed to guide record reviews.

Human studies with a prospective design with a minimum observation period of 6 mo were included. The studies had to include either single or multiple recession defects (Miller class I or II, corresponding to RT1 according to the current classification on recession defects) and a baseline measurement for gingival thickness; studies presenting only change in gingival thickness without a baseline value were excluded. Only studies on nonsmoking patients were considered for inclusion. Prospective cohort studies, cross-sectional studies, and retrospective studies were included, as well as randomized controlled trials, while case reports, case series, and systematic reviews and meta-analyses were excluded. Other types of studies not considered for inclusion were narrative reviews and expert opinion publications. Published studies in the following languages were considered: English, Spanish, Italian, and French. The full electronic search strategy for Embase is presented in the Appendix.

Studies were evaluated by 2 independent reviewers (L.P.H. and G.B.), with conflicts resolved by a third reviewer (T.O.). Studies were screened at the title, abstract, and full-text levels. When information was missing or insufficient, an attempt was made to contact the authors. Quality assessment was conducted according to the *Cochrane Handbook for Systematic Review of Interventions*. The criteria considered for evaluation of bias were as follows: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other sources of bias. Each reviewer assessed the study quality independently. Conflicts were resolved by an independent reviewer (T.O.).

For each study, the following information was extracted: sample size, intervention, number of recession defects (single/multiple), arch location, follow-up time, location and method of soft tissue thickness (STT), STT values, %RC, and CRC. Not all studies reported the same parameters: for instance, some studies reported CRC and not %RC and vice versa. Attempts were made to calculate the missing information, but in most cases, insufficient data were provided. The sample was reduced to the studies presenting complete data. The majority of the studies present data (measurements and proportions) on a defect level. Those that present data on a patient level are considered comparable at a defect level. These studies were excluded from the analysis in a later stage only if they introduced significant heterogeneity to the results.

Additionally, the following were reported in detail: inclusion and exclusion criteria; differences among groups at baseline; age range of participants; mandibular/maxillary location of recession defects or both; Miller I/ II or both; number of defects in total and per group; number of participants in total and per group; single or multiple recession defects; all baseline variables reported in the study, including specifically gingival thickness, recession depth and width, and keratinized tissue width; number of smokers, and distribution of the defects per tooth type. The following outcomes were collected: mean RC, CRC, tissue thickness at follow-up, probing depth, recession height, clinical attachment level, keratinized tissue width, and patient-reported outcomes such as aesthetic perception and dentinal hypersensitivity (if applicable).

Statistical Analysis

The principal summary measures were raw mean for percentage RC (%RC) and raw proportion for CRC. Regression coefficients were calculated to assess the effect of moderator variables on primary outcomes.

A meta-analysis was conducted to aggregate studies that provided raw means for %RC. A weighted raw mean was obtained with 95% CIs by means of a random effect model. Heterogeneity was measured by estimating I^2 index and Cochran's Q statistics and corresponding test. Forest plots were obtained to summarize results, while Galbraith plots were obtained to inspect overall consistency. Publication bias was explored by means of funnel plot and Egger's test. Mixed effects models (meta-regression) were used to assess the influence of moderators such as type of material. For secondary outcome (CRC), a weighted proportion was obtained with a meta-analysis under the same previous conditions.

The software used to perform the meta-analysis was R (version 3.5.1; R Foundation for Statistical Computing).

Results

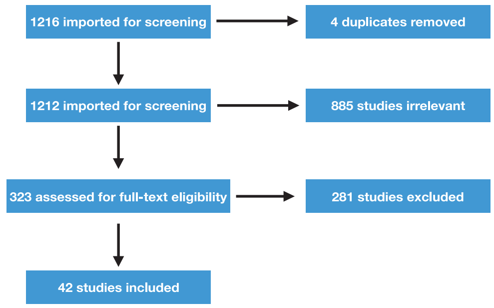
The screening process is shown in Figure 1. Among the 281 studies excluded at full text, reasons for exclusion were the following: 152 lacked a baseline value for gingival thickness measurement; 49 were review articles; 30 lacked a blinded examiner; 14 included Miller class III recession defects; 8 had a sample size <10; 8 were not found and the attempts to retrieve the articles by contacting the authors failed; 5 were published in a language other than English, Spanish, French, or Italian; 4 were excluded because of incorrect study design; 3 were excluded because they focused on dental implants; 2 presented a follow-up <6 mo; 2 included only a qualitative description of gingival thickness (no numeric value); 1 was a book chapter; 1 was a decision-making publication; 1 was a duplicate (not automatically removed through the electronic deduplicating software); and 1 presented insufficient detail regarding inclusion and exclusion criteria.

In total 42 studies were included (Table 1): 40 compared 2 groups (test vs. control); 1 (Hwang and Wang 2006) included 1 group (CAF); and 1 (Lucchesi et al. 2007) compared 2 test groups and 1 control group. In sum, 84 groups of materials were considered relative to mean STT (in millimeters) with mean %RC at follow-up as the primary outcome and with percentage of defects achieving CRC at follow-up as the secondary outcome. The studies included 35 randomized controlled trials, 5 case series, 1 prospective cohort study, and 1 controlled clinical trial. All studies had a minimum follow-up of 6 mo; 17 had a 12-mo follow-up. Two studies had >12 mo of follow-up: 30 mo (Bittencourt et al. 2009) and 60 mo (Gürgan et al. 2004). Studies >12 mo were considered in secondary analyses of follow-up time. The parameter of follow-up time was considered a moderating variable due to high levels of heterogeneity.

Surgical Techniques and Materials

Among the included techniques, 4 studies investigated CAF alone as the surgical technique (Gürgan et al. 2004; Huang et al. 2005; Bittencourt et al.

Figure 1. PRISMA flowchart.



2007; Barrella et al. 2016), although they employed different flap designs, with the main common feature being the coronal advancement of the flap after surgery. However, CAF was a common control intervention: 14 studies compared CAF with various test interventions (Woodyard et al. 2004; Huang et al. 2005; Bittencourt et al. 2006; Lucchesi et al. 2007; Bittencourt et al. 2009; Jagannathachary and Prakash 2010; Nazareth and Cury 2011; Zucchelli et al. 2012; Jepsen et al. 2013; Gupta et al. 2015; Cairo et al. 2016; Moreira et al. 2016; Stefanini et al. 2016). Only 1 study (Zucchelli et al. 2004) investigated the laterally moved, coronally advanced flap (LMCAF). Semilunar advanced flaps (SAFs) were included in 3 studies, all conducted by the same group of authors (Bittencourt et al. 2006; Bittencourt et al. 2007; Bittencourt et al. 2009).

Bilaminar Techniques

Among the studies investigating bilaminar techniques, 13 had a combination of CAF + SCTG (subepithelial connective tissue graft; Muller et al. 1999; Paolantonio et al. 2002; Huang et al. 2005; Bittencourt et al. 2006; Lucchesi et al. 2007; Byun et al. 2009; Zucchelli et al. 2010; Bittencourt et al. 2012; Cardaropoli et al. 2012; Zucchelli et al. 2012; Zucchelli, Marzadori, et al. 2014; Zucchelli, Mounssif, et al. 2014; Eren et al. 2016), while 1 (Aroca et al. 2013) investigated SCTG combined with a coronally advanced tunnel. Various substitutes of autologous connective tissue were employed in combination with CAF. Specifically, 7 studies (Muller et al. 1999; Gürgan et al. 2004; Woodyard et al. 2004; Huang et al. 2005; Felipe et al. 2007; Andrade et al. 2008) included a combination of acellular dermal matrix graft (ADM) with CAF or tunnel (Ozenci et al. 2015). Various authors combined xenogeneic collagen membrane (XCM) with CAF (7 studies: Cardaropoli et al. 2012; Aroca et al. 2013; Jepsen et al. 2013; Ayub et al. 2014; Reino et al. 2015; Moreira et al. 2016; Stefanini et al. 2016). In 1 case, a collagen membrane of unspecified origin was used as a scaffold for seeding autologous gingival fibroblasts (Köseoglu et al. 2013) in the test group, while CAF was combined with the membrane alone in the control group.

Growth Factors and Blood Derivatives

Various adjunctive substances were investigated in combination with flaps only or bilaminar techniques. One study (Berlucchi et al. 2005) tested the combination of enamel matrix derivatives (EMD) with CAF. Various types of blood derivatives were also explored. The following authors tested the addition of blood derivatives prepared with different methods in RC procedures: Huang et al. (2005), Eren et al. (2014), and Keceli et al. (2015). The first 2 combined the blood derivatives to the CAF, while Keceli et al. performed a bilaminar technique (CAF + SCTG) modified by adding platelet-rich fibrin.

Combination Treatment (Growth Factors With Bilaminar)

Alves et al. (2012) compared CAF + ADM with CAF + ADM + EMD in the test group. One study (Ozenci et al. 2015) tested the addition of a bone graft material to CAF with a collagen membrane.

In summary, the most common intervention was the CAF/SAF/LAF (laterally advanced flap)/LMCAF (no-graft group) and the CAF + SCTG, CAF + ADM, and CAF + XCM, with each approach having at least 3 articles.

%RC ranged between 99% (Felipe et al. 2007, test group) and 38.3% (Reino et al. 2015, control group), while CRC frequency ranged between a minimum of 5.26% (Alves et al. 2012, control group) and a maximum of 93.3% (Alves et al. 2012, test group). The values for STT comprised a minimum mean ± SD value of 0.2 ± 0.09 mm (Berlucchi et al. 2005, control group) and a maximum of 1.6 ± 0.25 mm (Barrella et al. 2018, control group).

After removal of studies with incomplete data for %RC (no standard deviation or number of defects), the following 50 groups obtained are reported in Table 2. The mean RC varied between 38.5% (Köseoglu et al. 2013) and 97.5% (Byun et al. 2009). A forest plot showing %RC is presented in Figure 2A. The estimate of the pooled %RC is 81.9% (95% CI, 79.1% to 84.7%). The heterogeneity among studies accounts for 90.5% of the total variability between and within studies ($I^2 = 0.905$; Cochran's $Q = 465.5$, $P < 0.001$).

A sensitivity analysis was performed that excluded the 2 outlier guided tissue regeneration studies (Muller et al. 1999; Köseoglu et al. 2013), and it yielded a new variability estimate of 82.9% (95% CI, 80.3% to 85.4%), without significantly altering the heterogeneity ($I^2 = 88.6\%$; Fig. 2B). This suggested that other sources of heterogeneity must exist. Heterogeneity does not depend on a specific subset of studies; rather, all contribute to the Q statistic.

Table 1.
List of Included Studies.

No.	Author	Year	Type of Study	Follow-up, mo	Technique Used
1	Alves	2012	RCT	6	CAF + ADM + EMD vs. CAF + ADM
2	Andrade	2008	RCT	12	ADM + CAF with vs. without vertical incisions
3	Aroca	2013	RCT	12	MCAT + XCM vs. MCAT + SCTG
4	Ayub	2014	RCT	12	ADM + CAF vs. modified ADM + CAF
5	Barrella	2016	Case series	6	CAF with horizontal incisions vs. CAF for multiple recession defects with no releasing incisions
6	Berlucchi	2005	Controlled clinical study	12	CAF + EMD
7	Bittencourt	2006	RCT	6	CAF + SCTG vs. SAF
8	Bittencourt	2007	RCT	6	SAF + EDTA vs. SAF
9	Bittencourt	2009	RCT	30	SAF vs. CAF + SCTG
10	Bittencourt	2012	RCT	12	CAF + SCTG with or without surgical microscope
11	Byun	2009	RCT	6	CAF + SCTG vs. CAF + SCTG with epithelial collar
12	Cairo	2016	RCT	12	CAF + SCTG vs. CAF
13	Cardaropoli	2012	RCT	12	CAF + SCTG vs. CAF + XCM
14	Dogan	2015	RCT	6	CAF + CGF vs. CAF
15	Duval	2000	RCT	6	GTR with collagen membrane with or without DFDBA
16	Eren	2014	RCT	6	CAF + PRF vs. CAF + CTG
17	Felipe	2007	RCT	6	CAF + ADM vs. CAF + ADM with broad flap
18	Gupta	2015	RCT	6	CAF + PRF vs. CAF alone
19	Gürgan	2004	Case series	60	CAF
20	Huang	2005	Prospective cohort	6	CAF
21	Huang	2005	RCT	6	CAF + PRP vs. CAF
22	Jagannathachary	2010	RCT	6	CAF + ADM vs. CAF
23	Jepsen	2013	RCT	6	CAF + XCM vs. CAF
24	Keceli	2015	RCT	6	CAF + SCTG + PRF vs. CAF + SCTG
25	Köseoglu	2013	RCT	12	CM vs. CM + GF
26	Lucchesi	2007	RCT	6	CAF + glass ionomer vs. CAF + composite vs. CAF (no NCCL)
27	Moreira	2016	RCT	6	CAF + XCM vs. CAF
28	Muller	1999	Case series	6	CAF + SCTG vs. CAF + CM
29	Nazareth	2011	RCT	6	CAF + anorganic bovine-derived hydroxyapatite matrix/cell-binding peptide (P-15) vs. CAF
30	Ozenci	2015	RCT	12	CAF + ADM vs. TUN + ADM

(continued)

Table 1.
(continued)

No.	Author	Year	Type of Study	Follow-up, mo	Technique Used
31	Paolantonio	2002	RCT	12	CAF + ADM vs. CAF + SCTG
32	Peres	2009	Case series	6	CAF + SCTG
33	Reino	2015	RCT	6	CAF + XCM vs. CAF + XCM (extended technique)
34	Skurska	2015	Case series	12	CAF with releasing incisions + SCTG vs. CAF with no releasing incisions (MCAF) + SCTG
35	Stefanini	2016	RCT	12	CAF + XCM vs. CAF
36	Thamaraiselvan	2015	RCT	6	CAF + PRF vs. CAF
37	Wang	2015	RCT	12	CAF + ADM (solvent dehydrated) vs. CAF + ADM (freeze-dried)
38	Woodyard	2004	RCT	6	CAF + ADM vs. CAF
39	Zucchelli	2010	RCT	12	CAF + SCTG (de-epithelialized FGG) vs. CAF + SCTG
40	Zucchelli	2012	RCT	12	LMCAF vs. CAF + SCTG
41	Zucchelli, Marzadori	2014	RCT	12	CAF + SCTG with or without removal of LST
42	Zucchelli, Mounssif	2014	RCT	12	CAF + SCTG (thin) vs. CAF + SCTG (thick)

ADM, acellular dermal matrix graft; CAF, coronally advanced flap; CGF, concentrated growth factors; CM, collagen membrane; CRC, complete root coverage; CTG, connective tissue graft; DFDBA, demineralized freeze-dried bone; EMD, enamel matrix derivatives; FGG, free gingival graft; GF, gingival fibroblasts; GTR, guided tissue regeneration; LMCAF, laterally moved, coronally advanced flap; LST, lingual submucosal tissue; MCAF, modified coronally advanced flap; MCAT, modified coronally advanced tunnel; NCCL, noncarious cervical lesion; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; RC, root coverage; RCT, randomized controlled trial; SAF, semilunar advanced flap; SCTG, subepithelial connective tissue graft; STT, soft tissue thickness; TUN, tunnel; XCM, xenogeneic collagen membrane.

Significant publication bias was identified (Egger's test, $P = 0.018$; Appendix Fig. 1), suggesting that less reliable studies (greater SE) reported lower values of %RC (left side of the plot) while few studies with the same degree of reliability reported opposing results.

Relationship between STT and %RC for All Techniques of RC

The results of the meta-regression exploring the relationship between STT and %RC independent of time points for follow-up found no significant relationship ($P = 0.267$), with large variations in %RC for similar values of STT (Appendix Fig. 2). The scatterplot shows large heterogeneity among the reported studies. For instance, studies reporting an initial low value of baseline STT reported %RC varying between 70% and 100%.

Relationship between STT and %RC at Different Follow-up Times

When follow-up time was analyzed as a predictor, the following time points were taken into consideration: 6 and 12 mo. The relationship shows that the %RC appears to depend on the follow-up time, although this relationship is not significant overall ($P = 0.074$). When studies with a 6-mo follow-up were analyzed ($n = 32$ studies), the relationship between STT at 6 mo and %RC was not statistically significant ($P = 0.890$). However, at 12 mo ($n = 20$), a significant ($P = 0.031$) inverse relationship was present between the STT at this time point and the %RC. Each additional millimeter of STT determines a 28% reduction in %RC at the 12-mo time point ($\beta = -28.5$). The scatterplot depicted in Appendix Figure 3 shows this relationship.

Subgroup analysis between baseline STT and %RC was based on the type of graft material used. For studies that had no graft, including CAF, LAF, LMCAF, and SAF ($n = 17$), there was a nonsignificant ($P = 0.139$) positive relationship ($\beta = 10.9$, SE = 7.34, $R^2 = 5.75\%$). However, with the exclusion of the single outlier study with an unusually high value of baseline STT ≥1.5 mm in the control and test groups (Barrella et al. 2016), a significant relationship ($P < 0.001$) with a strong positive association ($R^2 = 56.7\%$) was evident. For each additional millimeter in STT, the %RC increases by 36.5%. This relationship demonstrates the clinical importance of an adequate thickness of the flap at baseline when any of the aforementioned no-graft procedures are performed.

The SCTG studies ($n = 13$) showed borderline statistical significance ($P = 0.065$) with a positive association

Table 2.
Characteristics of Included Studies.

No.	Author	Group	Material	Sample, *n*	RC, %		STT, mm		CRC, %
					Mean	SD	Mean	SD	
1	Alves 2012	Test	ADM	19	55.4		1.1	0.3	15.79
2	Alves 2012	Control	EMD + ADM	19	44		1.0	0.2	5.26
3	Andrade 2008	Test	ADM	15	74.3		0.5	0.3	40
4	Andrade 2008	Control	ADM	15	83.3		0.6	0.2	53
5	Aroca 2013[a]	Test	XCM	78	71	21	0.8	0.2	22.7
6	Aroca 2013[a]	Control	CTG	78	90	18	0.8	0.3	59.1
7	Ayub 2014[a]	Test	ADM	15	92.2	6.4	0.8	0.3	46.7
8	Ayub 2014[a]	Control	ADM	15	78.8	10.2	0.9	0.3	13.3
9	Barrella 2016[a]	Test	No graft	39	73.2	16.4	1.5	0.1	39.67
10	Barrella 2016[a]	Control	No graft	42	84.4	11.1	1.6	0.3	47.33
11	Berlucchi 2005	Test	EMD	19	85.8		0.5	0.1	36.4
12	Berlucchi 2005	Control	EMD	19	94.7		0.2	0.1	89.5
13	Bittencourt 2006[a]	Test	CTG	17	96.1	7.7	1.0	0.2	76.47
14	Bittencourt 2006[a]	Control	No graft	17	91.0	11.5	1.0	0.3	52.94
15	Bittencourt 2007[a]	Test	No graft	15	70.2	30.5	1.1	0.2	40
16	Bittencourt 2007[a]	Control	No graft	15	90.1	18	1.1	0.3	66.7
17	Bittencourt 2009	Test	No graft	17	91.0		1.0	0.3	58.8
18	Bittencourt 2009	Control	CTG	17	96.3		1.0	0.2	88.24
19	Bittencourt 2012	Test	CTG	24	98		0.9	0.2	87.5
20	Bittencourt 2012	Control	CTG	24	88.3		1.0	0.2	58.3
21	Byun 2009[a]	Test	CTG	10	97.5	7.9	1.1	0.2	90
22	Byun 2009[a]	Control	CTG	10	89.1	25.9	0.9	0.3	70
23	Cairo 2016	Test	CTG	16			0.7	0.1	83
24	Cairo 2016	Control	No graft	16			0.8	0.1	47
25	Cardaropoli 2012[a]	Test	XCM	11	94.3	11.7	0.8	0.3	72
26	Cardaropoli 2012[a]	Control	CTG	11	97.0	6.7	0.9	0.4	81
27	Dogan 2015[a]	Test	CGF	60	86.7	15.6	1.1	0.1	56.7
28	Dogan 2015[a]	Control	No graft	59	82.1	17.5	1.1	0.1	45.8
29	Duval 2000	Test	GTR + DFBA	8	81.6		1.3	0.5	
30	Duval 2000	Control	GTR	9	90.1		1.2	0.4	
31	Eren 2014	Test	PRF	22	92.7				72.7

(continued)

Table 2.
(continued)

No.	Author	Group	Material	Sample, *n*	RC, % Mean	RC, % SD	STT, mm Mean	STT, mm SD	CRC, %
32	Eren 2014	Control	CTG	22	94.2				77.3
33	Felipe 2007	Test	ADM	15	69.0		0.5	0.3	16.7
34	Felipe 2007	Control	ADM	15	84.8		0.6	0.2	30
35	Gupta 2015[a]	Test	PRF	15	91	20.0	1.3	0.2	
36	Gupta 2015[a]	Control	No graft	15	86.6	23.8	1.3	0.2	
37	Gürgan 2004	Test	No graft		44.9	33.9	1.5	0.5	15.38
38	Gürgan 2004	Control	No graft		54.2	36.8	1.3	0.4	26.92
39	Huang 2005	Test	No graft		82.3	24.7	1.1	0.3	60.8
40	Huang 2005(2)[a]	Test	PRP	11	81	28.7	1.1	0.2	63.3
41	Huang 2005(2)[a]	Control	No graft	12	83.5	21.8	1.1	0.4	58.3
42	Jagannathachary 2010	Test	ADM		82.2	28.7	1	0	
43	Jagannathachary 2010	Control	No graft		53	22	1	0.2	
44	Jepsen 2013[a]	Test	XCM	45	75.3	26.7	0.9	0.3	36
45	Jepsen 2013[a]	Control	No graft	45	72.7	26.2	0.9	0.3	31
46	Keceli 2015	Test	PRF + SCTG		89.6		0.9	0.3	55
47	Keceli 2015	Control	SCTG		79.9		0.8	0.3	35
48	Köseoglu 2013[a]	Test	CM + GF	11	69.6	29.3	1.1	0.3	
49	Köseoglu 2013[a]	Control	CM	11	38.3	32.6	1	0.3	
50	Lucchesi 2007–T1[a]	Test	No graft	19	72.0	18.7	0.8	0.4	15
51	Lucchesi 2007–T2[a]	Test	No graft	20	74.2	15.0	0.9	0.3	15.79
52	Lucchesi 2007[a]	Control	No graft	20	80.8	21.1	0.9	0.3	55
53	Moreira 2016[a]	Test	XCM	20	77.2	21.2	1.0	0.1	40
54	Moreira 2016[a]	Control	No graft	20	72.1	14.4	1.0	0.1	35
55	Muller 1999[a]	Test	GTR	13	45	40	0.7	0.2	11
56	Muller 1999	Control	CTG		80	24	0.8	0.4	62
57	Nazareth 2011[a]	Test	Anorganic . . .[b]	15	85.6	21.7	1.2	0.2	66.67
58	Nazareth 2011[a]	Control	No graft	15	90	18.4	1.2	0.2	73.33
59	Ozenci 2015	Test	ADM	27	93.8		0.8	0.1	85
60	Ozenci 2015	Control	ADM	31	75.7		0.8	0.1	37.36
61	Paolantonio 2002[a]	Test	ADM	15	83.3	11.4	0.8	0.4	26.6
62	Paolantonio 2002[a]	Control	CTG	15	88.8	11.7	0.8	0.3	46.6

(continued)

Table 2.
(continued)

No.	Author	Group	Material	Sample, *n*	RC, %		STT, mm		CRC, %
					Mean	SD	Mean	SD	
63	Peres 2009[a]	Test	CTG	40	85.5	23.6	1.0	0.2	62.5
64	Peres 2009[a]	Control	CTG	40	91.4	16.8	0.9	0.2	70
65	Reino 2015[a]	Test	XCM	20	81.9	12.9	1.1	0.2	
66	Reino 2015[a]	Control	XCM	20	62.8	16.6	1.2	0.2	
67	Skurska 2015	Test	CTG		91.8		1.3	0.4	83.33
68	Skurska 2015	Control	CTG		90.5		1.4	0.4	78.43
69	Stefanini 2016[a]	Test	XCM	45	76.3	28.1	0.9	0.3	93.3
70	Stefanini 2016[a]	Control	No graft	45	75.1	26.2	0.9	0.3	84.4
71	Thamaraiselvan 2015[a]	Test	PRF	10	74.2	29.0	1.0	0.1	50
72	Thamaraiselvan 2015[a]	Control	No graft	10	65	44.5	0.9	0.2	50
73	Wang 2015[a]	Test	ADM	38	71.0	32.9	1.3	0.5	
74	Wang 2015[a]	Control	ADM	42	77.2	29.1	1.2	0.6	
75	Woodyard 2004	Test	ADM	12	99		0.8	0.2	
76	Woodyard 2004	Control	No graft	12	67		0.8	0.2	
77	Zucchelli 2010[a]	Test	CTG	25	96.2	8.9	0.8	0.2	84
78	Zucchelli 2010[a]	Control	CTG	25	92.3	13.1	0.7	0.2	72
79	Zucchelli 2012[a]	Test	No graft	25	74.2	8.2	0.8	0.3	4
80	Zucchelli 2012[a]	Control	CTG	25	88.8	11.2	0.8	0.2	48
81	Zucchelli, Mounssif 2014[a]	Test	CTG	30	83.7	11.3	0.8	0.2	83
82	Zucchelli, Mounssif 2014[a]	Control	CTG	30	79.7	11	0.7	0.1	80
83	Zucchelli, Marzadori 2014	Test	CTG	25			0.4	0.1	88
84	Zucchelli, Marzadori 2014	Control	CTG	25			0.4	0.1	48

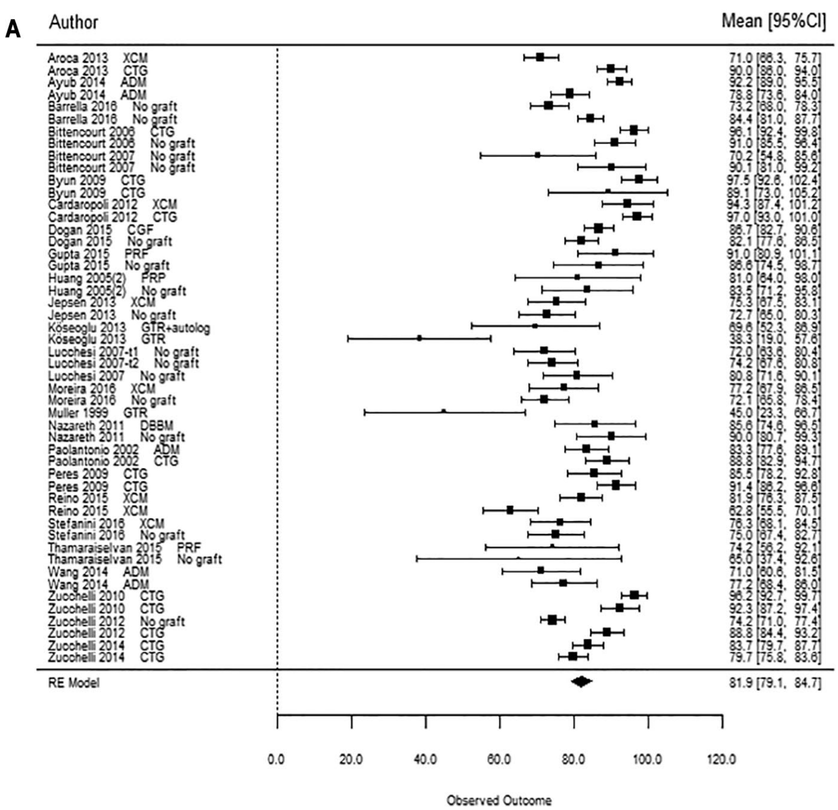
For abbreviations, see Table 1.
[a]Studies that presented complete data for percentage RC.
[b]Anorganic bovine-derived hydroxyapatite matrix/cell-binding peptide (P-15).

(β = 23.7; R^2 = 22.3%). The R^2 implies that 22.3% of the total variability of the outcome can be explained by the mean STT at baseline (see Appendix Fig. 4). For every additional millimeter of baseline STT, %RC increases by 22.3%. Between the no-graft and SCTG groups, if a recession defect with a baseline STT of 1 mm is treated with SCTG, the predicted mean %RC is 93%. If the same defect with an equal STT baseline value is treated with a no-graft technique, the anticipated %RC is 78%.

Evaluation of the ADM studies (n = 5) showed a significant inverse (β = −30.1) relationship (P = 0.010; R^2 = 67.9%). For each increase in baseline STT value, %RC decreased by up to 30%. The scatterplot in Appendix Figure 5 shows the inverse linear relationship between STT and %RC observed for ADM studies. However, a limited number of studies were available for this comparison, and results should be interpreted cautiously.

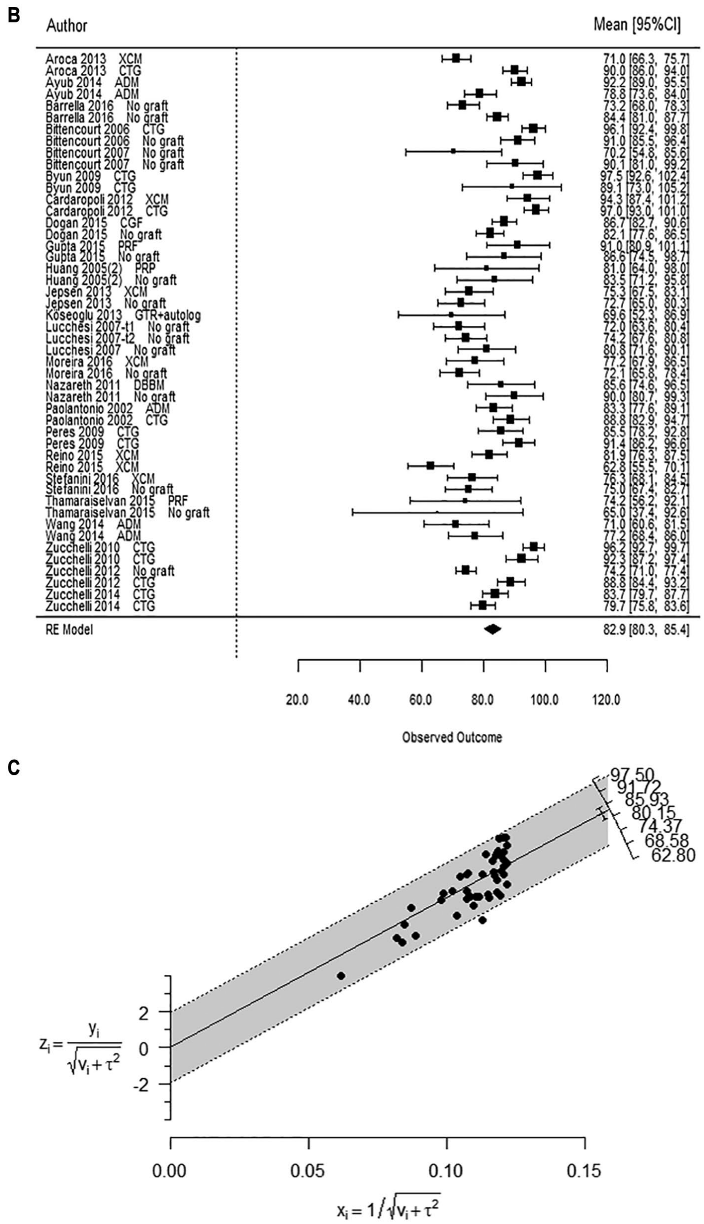
Subgroup analysis of XCM studies (n = 6) found no significant correlation between the variables (P = 0.304).

Figure 2. Forest plots: (**A**) mean root coverage and (**B**) after removal of Köseoglu and Muller studies. (**C**) The Galbraith plot shows each study in terms of the relative weight (sample size and standard error) that it has in comparison with the entire complex of studies. The plot shows that no study lies beyond the confidence interval, which means that the heterogeneity cannot be attributed to a specific study. Rather the entire sample of studies contributes to elevating the heterogeneity. ADM, acellular dermal matrix graft; CGF, concentrated growth factors; CTG, connective tissue graft; DBBM, demineralized bovine bone matrix; GTR, guided tissue regeneration; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; XCM, xenogeneic collagen membrane.



(continued)

Figure 2. (continued)



Relationship between STT and CRC

The effects of baseline STT on CRC were also evaluated, with no significant association ($P = 0.720$). Subgroup analysis between STT and CRC was based on the type of graft material used. For no-graft studies (17 studies after removal of Barrella et al. 2016, which was an outlier), there was a significant relationship ($P < 0.025$), with an R^2 of 24.1%. No significant relationship was found for ADM, SCTG, and XCM between STT and %RC.

A meta-analysis was performed among all studies of RC techniques to explore the effect of baseline STT on CRC rate. A total of 52 groups were included in the meta-analysis (Table 3). The rate of CRC in the SCTG group was up to 31% higher than the no-graft group (the category of reference) for the same value of baseline STT. The forest plot (Appendix Fig. 6) highlights the enhanced values for CRC treated with SCTG relative to other graft treatment option (vs. ADM: $\beta = 0.35$, $P < 0.001$; vs. XCM: $\beta = 0.21$; $P = 0.045$) and no-graft options as well ($P < 0.001$, $\beta = 0.31$), as shown by the fact that all studies with SCTG are shifted to the right-hand side in the graph. The model emphasizes the superiority of SCTG as a grafting material resulting in more frequent CRC in comparison with all other materials analyzed (as demonstrated by the β value; for the same value of STT, the frequency of CRC may be increased by 31% vs. no graft).

Discussion

Thick gingival phenotype has been proposed as a positive predictive factor for RC procedures. Several case series and a systematic review have correlated thicker flaps to improved outcomes for %RC and CRC (Baldi et al. 1999; Huang et al. 2005; Hwang and Wang 2006). Thicker flaps may be easier to manipulate and may maintain greater vascularity than thinner flaps. However, results from the present study suggest great variability in RC for similar values of STT. This is true for %RC and CRC. Moreover, the influence of the flap thickness may depend on the follow-up time and the type of grafting approach taken.

Given the reported differences among the diverse procedures that were analyzed, this study identified 4 surgical interventions for RC: no graft, SCTG, ADM, and XCM. Results for the no-graft group, with exclusion of an outlier study, show a significant relationship between baseline STT and %RC and CRC, in agreement with a previous systematic review on the same topic (Hwang and Wang 2006). While baseline STT ranged from 0.42 to 1.46 mm in the studies included in this systematic review, in Barrella et al. (2016) the mean initial thickness of both groups was 1.5 and 1.6 mm, which seems noteworthy when compared with the overall results of this systematic review . Although in this study the methodology of STT assessment is reported (as performed with an endodontic spreader and a silicon stopper), it is not specified how the measurement was determined once the spreader was removed. This could have been with a digital caliper, manual caliper, a periodontal probe, and so on. Additionally, the height of the measurement varied widely since it depended on the amount of keratinized tissue of each patient, as it was performed at a midpoint location between the gingival margin and the mucogingival junction.

The no-graft group is composed of a variety of approaches and procedures that render the group quite heterogeneous and therefore difficult to compare. The CAF itself can be approached in a variety of ways and with different incision designs and flap elevation approaches (e.g., trapezoidal, triangular, with or without vertical releasing incisions). Furthermore, the location of the defects (maxillary vs. mandibular) and their number (single vs. multiple) can play a role in the observed outcome.

In analysis of the SCTG group, a positive association of borderline significance was observed between STT and %RC. In addition, there was a lack of association between STT and CRC. While these latter findings are in accordance with those of Garces-McIntyre et al. (2017), where no correlation between STT and CRC was found, the current review leaves open a possible role for initial gingival thickness as a consideration for the RC approach taken. According to our meta-analysis, SCTG is the most effective graft material for RC in terms of CRC and can be considered a gold standard regardless of initial STT. The data of the present study suggest that STT plays a marginal role in determining the outcome of RC procedures performed with SCTG, in contrast to the marked influence of flap thickness on RC when no graft is used. Perhaps this suggests that thin tissues may be more successfully treated by adding an autogenous graft (Cairo et al. 2016).

This systematic review revealed that STT negatively affected %RC and had no correlation with CRC with the use of ADM. Regarding the results of %RC, this can be explained by the limited number of studies included in the analysis, since few studies reported %RC. It could also be interpreted as the material's low tolerance to becoming exposed during the healing process as compared with other biomaterials. Nevertheless, when a wider number of studies were analyzed for CRC, no correlation existed with initial STT. The absence of a correlation between STT with XCM and CRC and %RC could be explained by the fact that when biomaterial is added to the flap, it not only increases the thickness and changes the gingival phenotype but also acts as a mechanical barrier that, during the healing phase, avoids a relapse and thus an apical migration of the gingival margin. This theory could also be applied to the ADM and SCTG. In any case, the number of studies available for a comparison for the XCM and ADM groups were rather limited, which suggests interpreting these results with caution.

The main limitation of the present systematic review consisted in the large heterogeneity ($I^2 = 0.905$) among

Table 3.
Studies Included in the Meta-analysis for Relationship between STT at Baseline and Rate of CRC for Different Root Coverage Techniques.

No.	Role	Author	Material	Sample, *n*	*P* Value
1	Test	Alves 2012	ADM	19	0.1579
2	Test	Andrade 2008	ADM	15	0.4
2	Control	Andrade 2008	ADM	15	0.53
3	Test	Aroca 2013	XCM	78	0.277
3	Control	Aroca 2013	SCTG	78	0.591
4	Test	Ayub 2014	ADM	15	0.467
4	Control	Ayub 2014	ADM + EMD	15	0.133
5	Test	Barrella 2016	No graft	39	0.3967
5	Control	Barrella 2016	No graft	42	0.4733
6	Test	Bittencourt 2006	SCTG	17	0.7647
6	Control	Bittencourt 2006	SCTG	17	0.5294
7	Test	Bittencourt 2007	No graft	15	0.4
7	Control	Bittencourt 2007	No graft	15	0.667
8	Test	Bittencourt 2009	No graft	17	0.588
8	Control	Bittencourt 2009	SCTG	17	0.8824
9	Test	Bittencourt 2012	SCTG	24	0.875
9	Control	Bittencourt 2012	SCTG	24	0.583
10	Test	Byun 2009	SCTG	10	0.9
10	Control	Byun 2009	SCTG	10	0.7
11	Test	Cairo 2016	SCTG	16	0.83
11	Control	Cairo 2016	no graft	16	0.47
12	Test	Cardaropoli 2012	XCM	11	0.72
12	Control	Cardaropoli 2012	SCTG	11	0.81
13	Control	Dogan 2015	No graft	59	0.458
14	Test	Felipe 2007	ADM	15	0.167
14	Control	Felipe 2007	ADM	15	0.3
15	Control	Huang 2005	No graft	12	0.583
16	Test	Jepsen 2013	XCM	45	0.36
16	Control	Jepsen 2013	No graft	45	0.31
17	Test	Lucchesi 2007 t1	No graft	19	0.15
17	Test	Lucchesi 2007 t2	No graft	20	0.157
17	Control	Lucchesi 2007	No graft	20	0.55

(continued)

Table 3.
(continued)

No.	Role	Author	Material	Sample, *n*	*P* Value
18	Test	Moreira 2016	XCM	20	0.4
18	Control	Moreira 2016	No graft	20	0.35
19	Control	Nazareth 2011	No graft	15	0.733
20	Test	Ozenci 2015	ADM	27	0.85
20	Control	Ozenci 2015	ADM	31	0.3736
21	Test	Paolantonio 2002	ADM	15	0.266
21	Control	Paolantonio 2002	SCTG	15	0.466
22	Test	Peres 2009	SCTG	40	0.625
22	Control	Peres 2009	SCTG	40	0.7
23	Test	Stefanini 2016	XCM	45	0.933
23	Control	Stefanini 2016	No graft	45	0.844
24	Control	Thamaraiselvan 2015	No graft	10	0.5
25	Test	Zucchelli 2010	SCTG	25	0.84
25	Control	Zucchelli 2010	SCTG	25	0.72
26	Test	Zucchelli 2012	No graft	25	0.04
26	Control	Zucchelli 2012	SCTG	25	0.48
27	Test	Zucchelli, Mounssif 2014	SCTG	30	0.83
27	Control	Zucchelli, Mounssif 2014	SCTG	30	0.8
28	Test	Zucchelli, Marzadori 2014	SCTG	25	0.88
28	Control	Zucchelli, Marzadori 2014	SCTG	25	0.48

For abbreviations, see Table 1.

studies. No specific outlier could be identified as being responsible for this heterogeneity. Rather, all studies made a contribution. Additionally, the methodology (e.g., digital caliper and endodontic file vs. probe) and height of measurement (the precise location of the STT measurement) from the gingival margin were variable, likely leading to some of the heterogeneity identified. Our study divided the interventions by type of graft material used but not by type of surgical technique, another possible limitation. This is obvious especially in the case of CAF, since the variation in flap design or flap elevation can be critical and lead to different results, let alone the fact that our no-graft group includes many techniques that do not involve using a graft material beneath the flap (e.g., LMCAF, LAF, SAF). Also, some commonly used materials (e.g., EMD or guided tissue regeneration) could not be analyzed individually due to the limited number of includable studies. Finally, the exclusion of articles written in languages other than English, Spanish, and Italian could have resulted in publication bias.

In summary, this review focused on the influence of initial STT upon RC. Within the limitations of this systematic review, it can be concluded that STT is a predictor for RC when an RC procedure is performed with no graft and that the effect of STT can be somewhat minimized when opting for an SCTG. In contrast, when nonautogenous graft material is added (XCM/ADM), its influence is diminished.

Author Contributions

L. Paternò Holtzman, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; G. Blasi,

T. Oates, contributed to conception, design, and data analysis, drafted and critically revised the manuscript; E. Rivera, K. Downton, contributed to data analysis, drafted and critically revised the manuscript; F. Herrero, contributed to data analysis, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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6. DISCUSSION:

6.1 Discussion summary of articles

The main goal of the present work was to evaluate the influence of different surgical and anatomical features on the outcomes of root coverage and soft tissue augmentation around teeth and implants using digital and lineal measurements.

From the protocols evaluated, it can be extracted that vestibular depth is a significant predictor for the outcomes of root coverage therapy via coronally advanced flap plus connective tissue graft. Other anatomical factors such as mandibular arch location and reduced keratinized tissue width negatively affected treatment outcomes, as well. Likewise, marginal gingival thickness gain at 1.5 and 3 mm achieved in the immediate postoperative period is a significant predictor of complete root coverage at 6 months when treating multiple gingival recession via modified tunnel technique plus acellular dermal matrix. Additionally, gingival margin positioned ≥0.5 mm coronal to the cementoenamel junction immediately after surgery was a strong predictor of complete root coverage. Besides, free epithelialized grafts are exposed to dimensional changes that result in a reduction of approximately 40% of the original graft dimension–the changes being approximately 10% greater at the implant sites than at the tooth sites. Finally, it can be concluded that soft tissue thickness is a predictor for root coverage when a root coverage procedure is performed with no graft and that the effect of soft tissue thickness can be somewhat minimized when opting for an subepithelial connective tissue graft. In contrast, when non-autogenous graft material is added (xenogeneic collagen matrix/acellular dermal matrix), its influence is diminished.

6.2 Discussion summary Article 1: Influence of vestibular depth on the outcomes of root coverage therapy: A prospective case series study.

The purpose of this study was to investigate the relationship between vestibular depth and the effectiveness of root coverage procedures using a coronally advanced flap plus connective tissue graft. The researchers found that the mean percentage of root coverage at 6 months was 87.47%, and complete root coverage was achieved in 27 out of 44 sites. These results were consistent with previous conducted studies which also reported comparable outcomes for gingival recession treatment using similar techniques (Roman et al 2013; Keceli et al 2015; Neves et al 2019).

One of the main findings of this study was that vestibular depth was the most influential factor in determining the mean percentage of root coverage and the likelihood of achieving complete root coverage. The analysis showed that for each additional millimeter of vestibular depth, there was an almost 7% increase in the mean percentage of root coverage and a nearly threefold increase in the probability of achieving complete root coverage. This highlights the importance of considering vestibular depth when planning and performing root coverage procedures.

The use of a coronally advanced flap plus connective tissue graft is considered the gold standard treatment for gingival recession defects, as supported by several systematic reviews (Cairo et al 2008; Cairo et al 2014; Chambrone et al 2012; Buti et al 2013). However, this technique has been less frequently reported in the mandible compared to the maxilla. This discrepancy may be due to the challenges of effectively displacing and stabilizing a flap in the coronal position in mandibular sites, which influences clinicians' decision-making processes. Achieving a passive flap is crucial for successful outcomes after a coronally advanced flap procedure. Higher flap tension is generally associated with lower mean percentage of root coverage, while lower flap tension is linked to greater reduction in recession depth. Furthermore, the extent of coronal advancement over the cemento-enamel junction plays a significant role in the outcome. Passive flap advancement 2mm coronal to the cemento-enamel junction has been shown to result in 100% root coverage (Pini-Prato et al 2000). Shallow vestibular depth contributes to increased flap tension and limits the predictability of achieving substantial root coverage, as observed in this study.

Another noteworthy finding was that complete root coverage was not achieved in any site with a baseline vestibular depth less than 6mm, and all sites with vestibular depth less than 6mm were in the mandible. Overcoming the anatomical challenges commonly found in mandibular sites, such as thin gingival phenotype, lack of keratinized tissue width, and shallow vestibular depth, has been a subject of study (Aroca et al 2018). Tunneling techniques have been proposed as an alternative for mandibular root coverage, with case series reporting mean percentages of root coverage ranging from 83.25% to 100% in Miller Class I defects Thalmair et al 2016; Nart and Valles 2016; Nuñez et al 2018, Sculean and Allen 2018; Sculean et al 2021). One advantage of the tunnel approach is that minimal to no coronal advancement is required, reducing flap tension. Another study by Zucchelli et al 2014 investigated the outcomes of adding labial submucosal tissue removal to coronally advanced flap plus connective tissue graft in mandibular incisors and found significantly higher rates of complete root coverage compared to the coronally advanced flap plus connective tissue graft alone (Zucchelli et al 2014). Additionally, a recent study that evaluated the influence of vestibular depth on root coverage showed that the addition of labial submucosal tissue to coronally advanced flap not only may improve mean percentage of root coverage but also increase vestibular depth (Stefanini et al 2021). The importance of minimizing flap tension to achieve adequate coronal flap mobilization and predictable root coverage is emphasized in both studies.

Tooth location was identified as another factor influencing the mean percentage of root coverage, with mandibular teeth showing nearly 19% less root coverage compared to maxillary sites. This difference can be attributed to the typically lower vestibular depth in mandibular sites. Therefore, the effect of arch location on root coverage outcomes is directly related to vestibular depth.

The study also observed a reduction in vestibular depth after 3 and 6 months, which can hinder effective plaque control and oral hygiene maintenance. This highlights the importance of long-term follow-up studies to assess the stability of clinical outcomes over time (Halperin-Sternfeld 2016; Monje and Blasi 2019).

Several limitations should be acknowledged, including the small sample size, short follow-up period, and the need for multicenter trials to confirm external validity. Additionally, the assessment of baseline vestibular depth using digital methods had some degree of uncertainty due to the absence of reliable anatomical landmarks.

In conclusion, this study demonstrated that vestibular depth is a critical factor influencing the outcomes of root coverage procedures using a coronally advanced flap plus connective tissue graft. Shallow vestibular depth limits the predictability of achieving root coverage and should be carefully considered in treatment planning.

6.3 Discussion summary Article 2: Influence of immediate postoperative gingival thickness and gingival margin position on the outcomes of root coverage therapy: A 6 month prospective case series study using 3D digital measuring methods

The present prospective study aimed to assess the changes in linear and volumetric measurements over time following the treatment of gingival recessions using a modified tunnel technique in combination with acellular dermal matrix. This study utilized digital assessment methods, which had not been previously employed for evaluating keratinized tissue changes (Ahmedbeyli et al., 2014; Ozenci et al., 2015; Zuhr et al., 2021). The application of 3D technology in analyzing mucogingival surgery outcomes has revolutionized traditional measuring techniques such as periodontal probes or transgingival piercing approaches. By utilizing this innovative methodology, the study demonstrated an increase of approximately 0.5 mm in keratinized tissue width at the 6-month follow-up. The study revealed a gradual reduction in marginal gingival thickness from post-surgery to 6 months, with a decrease of 1 to 1.2 mm at 1.5 and 3 mm apical to the gingival margin. Additionally, the final volume underwent significant shrinkage, decreasing by about 0.80 mm^3 by the end of the observation period. These changes could be attributed to the expected resorption of the acellular dermal matrix during the healing process.

Regarding the primary clinical endpoint, the study reported mean percentage root coverage of 93.0% and complete root coverage of 72.3% at 6 months following root coverage surgery with the modified tunnel plus acellular dermal matrix. These percentages remained stable throughout the follow-up period, with no statistically significant differences between the root coverage achieved at 6 weeks and that recorded at 6 months. Moreover, all research variables exhibited significant variations during the observation period. The clinical findings support the view that the modified tunnel plus acellular dermal matrix is a reliable and predictable approach for achieving root coverage of gingival recessions in both the maxilla and mandible. The technique achieved complete root coverage rates of 74.5% at 6 weeks, 80.9% at 3 months, and 72.3% at 6 months, with an average root coverage of 93.0% at 6 months. Furthermore, there was a significant reduction in gingival recession depth, from an initial depth of 2.07 ± 0.71 mm to 0.15 ± 0.29 mm at 6 months. Previous studies on the tunnel plus acellular dermal matrix approach have reported complete root coverage ranging from 33-50%, with mean root coverage ranging from 70-78% (Papageorgakopoulos et al., 2008b; Shepherd et al., 2009). The variations in results could be attributed to different factors, such as the inclusion of gingival recessions in specific locations or the type of recession being treated. In the present study, only single/multiple RT1 gingival recessions were considered, whereas previous studies included single Miller Class I or II gingival recessions (Papageorgakopoulos et al., 2008b; Shepherd et al., 2009).

Several predictive factors have been associated with the amount of root coverage and its stability over time. These factors include the final position of the gingival margin relative to the cemento-enamel junction and gingival thickness. In this study, the distance between the gingival margin and the cemento-enamel junction immediately after surgery was a significant predictor of complete root coverage at 6 months. Complete root coverage was more likely when the gingival margin was 0.5 mm coronal to the cemento-enamel junction. These findings support previous studies where greater reductions in recession depth were observed when more coronal displacement was achieved (Pini Prato et al., 2005; Pini-Prato et al., 1999). Similarly, a change in marginal gingival thickness at 1.5 mm and 3 mm from the gingival margin immediately after surgery was found to be a significant predictor of mean root coverage and complete root coverage at 6 months. Previous studies have also identified an initial mucosal thickness of 0.8-1.1 mm as a critical threshold for complete root coverage (Baldi et al., 1999; Hwang & Wang, 2006). When comparing these results with studies using digital methods, no significant differences in final gingival thickness were observed. For instance, the mean thickness at the end of this study was approximately 0.70 mm, while studies by Zuhr et al. and Ahmedbeyli et al. reported thicknesses of 0.58 mm and 0.75 mm, respectively (Ahmedbeyli et al., 2014; Zuhr et al., 2021).

It is important to acknowledge the limitations of this study. The relatively short follow-up period of 6 months may hinder drawing conclusions regarding the long-term effectiveness of the surgical approach. Additionally, the limited number of sites included could introduce bias. Nonetheless, the study had sufficient statistical power and a strong significance level to provide reliable insights into the influence of gingival margin distance to the cemento-enamel junction and marginal gingival thickness on treatment outcomes.

In conclusion, the modified tunnel plus acellular dermal matrix procedure is an effective technique for achieving root coverage in single or multiple gingival recessions, with minimal surgical trauma. The technique demonstrated high success rates and a decrease in gingival recession depth. Further long-term studies are warranted to evaluate tissue stability and the aesthetic outcome of root coverage.

6.4 Discussion summary Article 3: Dimensional changes in free epithelialized gingival/mucosal grafts at tooth and implant sites: A prospective cohort study

The findings of this prospective cohort study revealed several important insights regarding free epithelialized gingival grafts. Firstly, the study demonstrated that these grafts undergo dimensional changes, resulting in a reduction of approximately 40% of the original graft dimension. This reduction is primarily attributed to a decrease in graft width, which is approximately 70% compared to graft length. Interestingly, the study found that the dimensional changes of these grafts were about 10% greater at implant sites compared to tooth sites. Additionally, wider grafts in older patients were more prone to exhibit greater dimensional changes. Thicker grafts were associated with greater stability at tooth sites. Moreover, grafts stabilized in areas with greater avascular area experienced more significant changes in graft dimension and width at implant sites.

The use of free epithelialized gingival grafts has been advocated for various purposes such as gaining attached tissue, deepening the vestibule, and attempting root coverage (Ochsenbein et al., 1974; Nabers et al., 1966; Holbrook et al., 1983). The technique was originally described in the 1960s by several authors (Sullivan and Atkins 1968; Pennel et al 1969; Nabers et al 1966). Since then, researchers have conducted clinical studies to understand the factors influencing graft integration/success and dimensional stability (Mormann et al., 1981; Caffesse et al., 1979; Golmayo et al., 2021; Karakis et al., 2019; Silva et al., 2010). Sullivan and Atkins (1969) emphasized the importance of capillary outgrowths in the development of granulation tissue and vascularization of free epithelialized gingival grafts, highlighting the risk of necrosis in graft areas lacking adequate vascularization. Literature has identified several crucial factors and strategies for reducing graft dimension changes. These include using free epithelialized gingival grafts to gain keratinized mucosa at implant sites, employing intermediate thickness grafts instead of very thin grafts, selecting non-smokers as graft recipients, ensuring the presence of a thick gingival phenotype and keratinized tissue at adjacent sites, and stabilizing grafts using cyanoacrylate instead of suturing (Golmayo et al., 2021; Mormann et al., 1981; Silva et al., 2010; Karakis et al., 2019; Gumus et al., 2014). The authors speculate that wider grafts may be used in cases where the vestibule is shallower, leading to the collapse of the mucogingival or alveolar mucosal junction rather than "shrinkage" of the graft. They also suggest that implant sites may have shallower vestibules due to alveolar ridge atrophy after tooth extraction, potentially explaining the observed differences in graft dimension changes (Schmitt et al., 2013). Consistent with previous research, the study found that thicker grafts exhibited less dimensional change at tooth sites, likely due to their increased resistance to functional stresses (Mormann et al., 1981; Sullivan and Atkins, 1968). Furthermore, the analysis revealed a significant association between avascular area and dimensional changes at implant sites, indicating the importance of capillary outgrowths in promoting graft stability (Miller, 1987).

Notably, graft dimensional changes have been more extensively documented at tooth sites compared to implant sites (Mormann et al., 1981; Hatipoglu et al., 2007; Rateitschak et al., 1979; James et al., 1978). The current findings align with the existing literature, showing that mean graft dimension changes at implant sites are generally greater than those at tooth sites (Golmayo et al., 2021; Monje et al., 2020; Schmitt et al., 2016; Parvini et al., 2021). However, the difference in graft dimension changes between tooth and implant sites observed in this study was only about 10%, possibly influenced by operator expertise.

The study has a few limitations worth mentioning. Clinical measurements were conducted using a periodontal probe, introducing potential errors. Future studies should consider using three-dimensional scanning devices to assess graft dimension changes more accurately. Additionally, given that graft width experienced more significant changes than graft length during the study period, the influence of vestibular depth on graft width and dimension changes should be further investigated. Moreover, the study noted that simultaneous anti-infection therapy for peri-implantitis was associated with significantly more graft dimension changes compared to other interventions at tooth and implant sites. Future investigations should focus on understanding the determinants of graft dimension changes in free epithelialized gingival grafts used in standardized interventions at teeth and implant sites.

In conclusion, this prospective cohort study sheds light on the dimensional changes of free epithelialized gingival grafts. It provides valuable insights into the factors influencing graft stability, including graft width, thickness, avascular area, and the characteristics of the recipient site. The findings contribute to the existing knowledge and highlight the importance of careful consideration when performing these grafting procedures. Further research using advanced measurement techniques and standardized interventions is warranted to deepen our understanding of graft dimension changes and optimize clinical outcomes.

6.5 Discussion summary Article 4: Gingival Thickness and Outcome of Periodontal Plastic Surgery Procedures: A Meta-regression Analysis

Thick gingival phenotype has been suggested as a positive predictive factor for root coverage procedures (Baldi et al., 1999; Huang et al., 2005; Hwang and Wang, 2006). Previous studies have correlated thicker flaps with improved outcomes in terms of mean percentage of root coverage and complete root coverage. Thicker flaps are believed to be easier to manipulate and maintain better vascularity. However, the present study suggests that there is great variability in root coverage outcomes even for similar values of soft tissue thickness. This variability is observed for both mean percentage of root coverage and complete root coverage. Additionally, the influence of flap thickness may depend on the follow-up time and the type of grafting approach used. In this study, four surgical interventions for root coverage were identified: no graft, connective tissue graft, acellular dermal matrix, and xenogeneic collagen matrix. The results for the no-graft group, excluding an outlier study, showed a significant relationship between baseline soft tissue thickness and mean root coverage as well as complete root coverage, consistent with a previous systematic review (Hwang and Wang, 2006). However, it should be noted that the baseline soft tissue thickness in Barrella et al. (2016) was notably higher compared to the overall results of this systematic review. The measurement of soft tissue thickness was performed using an endodontic spreader and a silicon stopper, but the exact method of measurement after the spreader was removed was not specified.

The connective tissue graft group showed a positive association, although borderline significant, between soft tissue thickness and mean percentage of root coverage. However, no correlation was found between soft tissue thickness and complete root coverage. Despite these findings, connective tissue graft was determined to be the most effective graft material for root coverage in terms of complete root coverage, regardless of initial soft tissue thickness. The study suggests that adding an autogenous graft may be beneficial for treating thin tissues (Cairo et al., 2016). The systematic review revealed that soft tissue thickness had a negative impact on the percentage of root coverage when acellular dermal matrix was used, but there was no correlation with complete root coverage. The absence of a correlation between soft tissue thickness and complete root coverage or mean percentage of root coverage in the xenogeneic collagen matrix group could be attributed to the additional thickness and mechanical barrier provided by the biomaterial during the healing phase. The study acknowledges limitations such as the heterogeneity among studies, variable methodology for measuring soft tissue thickness (e.g., digital caliper, endodontic file, probe), and the exclusion of certain surgical techniques and materials due to limited data. These limitations should be considered when interpreting the results.

In summary, this systematic review emphasizes the significance of initial soft tissue thickness in predicting the outcomes of root coverage procedures. Soft tissue thickness appears to be a predictor for root coverage when no graft is used, but its influence is somewhat minimized when a graft is employed. The addition of non-autogenous graft materials reduces the impact of soft tissue thickness on root coverage outcomes.

7. FUTURE PERSPECTIVES

Despite the advancements in the field of root coverage therapy and soft tissue augmentation, there are still several areas that require further investigation and improvement.

1. Long-term Stability: Although the studies discussed in this thesis provide valuable insights into the short-term outcomes of root coverage and periodontal plastic surgery procedures, long-term stability remains a crucial aspect that requires investigation. Future studies should focus on evaluating the maintenance of root coverage and soft tissue stability over extended periods.

2. Comparative Studies: While individual studies have provided valuable information on specific techniques, comparative studies are needed to establish the superiority of one technique over another. Direct comparisons between different surgical approaches, graft materials, and measurement methods would help clinicians make evidence-based decisions regarding treatment selection and improve the predictability of outcomes.

3. Patient-Centered Outcomes: In addition to clinical parameters, it is important to evaluate patient-centered outcomes, such as patient satisfaction, morbidity, esthetics, and quality of life. Incorporating patient-reported outcomes into future research will provide a more comprehensive understanding of the impact of root coverage procedures on patients' well-being and treatment success.

4. Standardization of Measurement Techniques: There is a need for standardized and validated measurement techniques for evaluating root coverage and soft tissue changes. Consistent and reliable methods for measuring parameters such as vestibular depth, gingival thickness, and keratinized tissue width will enhance the comparability and reproducibility of research findings.

5. Digital Technology: The integration of digital technology, such as three-dimensional imaging, holds great potential in enhancing treatment planning and outcome prediction. Future research should explore the application of digital tools in root coverage therapy for outcome assessment.

8. CONCLUSIONS

8.1 Vestibular depth is a critical factor influencing the outcomes of root coverage procedures using a coronally advanced flap plus connective tissue graft. Shallow vestibular depth limits the predictability of achieving root coverage and should be carefully considered in treatment planning.

8.2 Gingival margin positioned ≥0.5 mm coronal to the cementoenamel junction immediately after surgery was a strong predictor of complete root coverage. The marginal gingival thickness gain at 1.5 and 3 mm achieved in the immediate postoperative period is a significant predictor of complete root coverage

8.3 Free epithelialized grafts are exposed to dimensional changes that result in a reduction of approximately 40% of the original graft dimension-the changes being approximately 10% greater at the implant sites than at the tooth sites

8.4 Soft tissue thickness plays a limited role in predicting root coverage across all root coverage approaches; when flaps are performed with no graft, the effect of soft tissue thickness is most critical.

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