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VISEU

THE USE OF OSSIFYING COLLAGEN MEMBRANES IN THE HORIZONTAL ALVEOLAR DEFFECTS TREATMENT AFTER DENTAL IMPLANT PLACEMENT: 1-YEAR RESULTS FROM A PROSPECTIVE CLINICAL TRIAL

Dissertação apresentada à Universidade Católica Portuguesa
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Por:
Nasser Matala Alvarez

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Orientador: Professor Doutor Tiago Borges
Co-orientador: Professor Doutor Bruno Leitão Almeida

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Obrigado aos meus pais, aos meus irmãos, à minha namorada Sara, ao meu colega Noval e ao professor Tiago Borges e ao professor Bruno Leitão por me terem orientado na minha tese e por me motivarem a aprender sempre mais e a melhorar como médico dentista e como pessoa.

Resumo

Introdução: A reabilitação parcial ou total de pacientes edêntulos com implantes dentários está relacionado com uma alta taxa de sucesso na reabilitação oral. Fatores que podem alterar a perda de volume ósseo são as doenças sistêmicas, extração dentária, tumores, traumas e doenças periodontais e, que irá limitar o posicionamento dos implantes nas áreas edêntulas alveolares.

Objetivo: O objetivo deste estudo é avaliar os resultados clínicos e radiográficos na colocação implantes dentários em cristas edêntulas com pequenos defeitos horizontais alveolares, tratadas com uma membrana de colagénio com propriedades ossificantes para o aumento do volume alveolar perdido.

Materiais e Métodos: Foram estudados pacientes tratados com implantes dentários em simultâneo com colocação de uma membrana de colagénio OSSIX Volumax™ em locais edêntulos mandibulares, diagnosticados com um defeito ósseo horizontal não crítico para a colocação dos mesmos. Os dados foram recolhidos em três momentos: T0 (*baseline* ou momento da colocação dos implantes), T1 (6 meses após a colocação dos implantes) e T2 (12 meses após a colocação dos implantes. Para a medição das alterações volumétricas a nível vestibular através da sobreposição de impressões digitais, foram estudadas as variáveis *Buccal Volume variation (BVv)* e *Mean Buccal variation (MBV)*. Em termos de alterações ósseas marginais foram caracterizadas em duas variáveis *mesial marginal bone changes (mMBC)* e *distal marginal bone changes (dMBC)*.

Resultados: A utilização da membrana de colagénio reticulada mostrou um aumento médio de 28.70+-15.81% em termos de alterações volumétricas (BVv) aos 12 meses , 0.81+-0.50mm nas medidas lineares da superfície alveolar (MBV) de T0 para T2 (12 meses) e uma perda óssea de -0.71mm nos implantes anteriores e -0.29mm nos implantes posteriores em termos de alterações ósseas marginais. Os resultados para o MBC não foram estatisticamente significativos.Conclusão: Existe uma forte associação entre a utilização de uma membrana de colagénio ossificante e um ganho de volume bucal, em relação à manutenção do osso marginal não se verificou uma melhoria em relação à literatura.

Palavras-chave:Implante , Aumento de volume , defeito ósseo , membrana de colagénio , perda de osso marginal , regeneração óssea guiada.

Abstract

Introduction: The partial or total rehabilitation of edentulous patients with dental implants is related to a high success rate in oral rehabilitation. Factors that can alter the loss of bone volume are systemic diseases, tooth extraction, tumors, trauma, and periodontal diseases, which will limit implant positioning in the alveolar edentulous areas.

Objective: The aim of this study is to evaluate the clinical and radiographic results of placing dental implants in edentulous ridges with small horizontal alveolar defects, treated with a collagen membrane with ossifying properties to increase the lost alveolar volume.

Materials and Methods: Patients treated with dental implants simultaneously with placement of an OSSIX collagen membrane Volumax in mandibular edentulous sites, diagnosed with a non-critical horizontal bone defect for implant placement, were studied. Data were collected at three time points: T0 (baseline or time of implant placement), T1 (6 months after implant placement) and T2 (12 months after implant placement. The Buccal Volume variation (BVv) and Mean Buccal variation (MBV) variables were studied for measuring volumetric changes at the buccal level by superimposing fingerprints. In terms of marginal bone changes were characterized in two variables mesial marginal bone changes (mMBC) and distal marginal bone changes (dMBC).

Results: The use of the cross-linked collagenium membrane showed an average increase of 28.70+-15.81% in terms of volumetric changes (BVv) at 12 months, 0.81+-0.50 mm in the alveolar surface linear measurements (MBV) from T0 to T2 (12 months) and a bone loss of -0.71 mm in the anterior implants and -0.29 mm in the posterior implants in terms of marginal bone changes. The results for the MBC were not statistically significant.

Conclusion: There is a strong association between the use of an ossifying collagen membrane and a gain of buccal volume , in relation to the maintenance of marginal bone there was not an improvement comparing with the literature.

Keywords: Implant, Bone volume, Bone defect, Marginal bone loss, Guided bone regeneration, Collagen membrane.

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List of Acronyms

dMBC- distal Marginal Bone Changes

GBR- Guided bone regeneration

e-PTFE- Expanded polytetrafluoroethylene

MBC- Marginal Bone Changes

mMBC- mesial Marginal Bone Changes

MBV- Mean Buccal Variation

BVv- Buccal Volume variation

ROI- Region of interest

1. INTRODUCTION

Total or partial edentulism remains a global oral health problem. Worldwide, epidemiological data document a wide variation in the prevalence of edentulism, which may reach 70% in population groups aged 60 years or more. Some studies show a reduction in prevalence in developed countries as a result of preventive oral health measures. However, the increase in the average life expectancy has been balancing this trend and promoting the need for rehabilitation with dental implants (1).

Rehabilitation with dental implants is a well-documented treatment for partially and totally edentulous patients, which translates into improved quality of life provided by the restoration of aesthetic needs and dental function(2). For this to be possible, it is indispensable that there is a sufficient amount of bone for the correct positioning of the implant. When this is not confirmed, bone re-absorption occurs, implying the need for surgical procedures in order to increase the bone volume of the alveolar ridge and achieve the desired rehabilitation (3). Thus, if correctly performed, it achieves a high survival and success rate, but not all patients are recommended for the placement of implants, mainly due to the occurrence of bone deficiencies. (2, 3)

The loss of alveolar bone can be caused by periapical pathology , peridontitis , facial trauma and aggressive tooth extraction technique. The consequence is usually the loss of the contours of the alveolar ridge, which results in aesthetic issues and makes the ideal placement of an implant unfeasible, caused by the tooth extraction that initiates a sequence of inflammation, epithelialisation, fibroplasia and remodelling, culminating in the alveolar repair process (4).

After tooth extraction, the alveolar ridge undergoes a remodelling process. The alveolar bone resorbs and horizontal bone loss may occur in the first six months after tooth extraction, which reduces the bone volume indispensable for the correct positioning of the implant (5, 6). The level to which the ridge resorbs results from the bone level at the extraction site, as opposed to the bone level of the adjacent teeth, i.e. tooth alveolus with horizontal bone loss remodels faster, as the reduced level of the alveolar ridge results in a lower need for bone filling. This resorption process leads to a narrower and shorter ridge, the effect of which is to shift the ridge to a more palatal/lingual position (6).

Tooth extraction is a clinical procedure indicated in situations where a tooth cannot be rehabilitated or maintained in an acceptable functional or aesthetic condition. After the extraction procedure, there follows a process of bone remodelling and resorption that often ends in a decrease in the volume of local hard and soft tissues. Therefore, there may be phenomena of bone resorption that make rehabilitation unfeasible, especially if the planning involves their rehabilitation with osseointegrated implants, which implies that the time for their placement should be considered (7, 8).

Nowadays, in advanced dentistry, there are several factors to be taken into account in restorative, aesthetic and surgical processes. One of the most important is the regulation of bone remodelling after tooth loss, as a failure of this process leads to the compromise of implant placement and subsequent rehabilitation. Alveolar bone remodelling after tooth loss was first described by Greenstein, Ashman and Bruins in 1985 (8).

After extraction or loss of teeth, the main processes of the mandible and maxilla remain relatively stable; however, the changes in the shape of the alveolar process are extremely significant both in the vertical and horizontal axis. Such changes follow a predictable pattern. As such, an ideal classification system for the alveolar bone consists of a simplified descriptive model of the residual ridge, providing an objective baseline to evaluate and compare different treatment options and assist in the selection of appropriate surgical techniques. On the other hand, knowledge of the resorption and remodelling pattern that occurs in various parts of the edentulous mandible enables the dentist to decide about the interception techniques in order to the residual alveolar process (9).

The alveolar bone is a critical component of the support apparatus for teeth in the maxillofacial skeleton. A healthy alveolar process including the alveolar bone, periodontal ligament and cementum is indispensable for maintaining healthy bone .Unlike other connective tissues, bone is a special connective, rigid and resilient tissue, primarily responsible for supporting the soft tissue integument and protecting internal organs. The rigidity and resilience of bone are aided by the mineralisation of collagen fibres and non-collagenous proteins within the bone matrix. Although alveolar bone is similar in microstructure and bone cellularity in other parts of the body, the physiological and functional needs of the dental apparatus make it unique among all bone tissues (9).

The alveolar processes consist of fractions of the maxilla and mandible that support the tooth roots, formed by the alveolar bone and compact corticals ofthe external surfaces of the alveolar processes. At the anatomical level, intrinsically related to the presence of the teeth, being conditioned by the positioning of the roots, axis of the impant and clinical implications, varying from patient to patient (10).

1.1 Clinical classification of bone defects concerning the placement of dental implants.

1.1.1-Fenestrations

Regarding the morphology of the buccal and lingual bone plates, fenestrations are root areas of partially uncovered bone and present the intact marginal bone, which forms a band or bone bridge between the interproximal ridges. These areas are covered only by periosteum (tissue that covers the external surface of the bone) and gum. The defect is called dehiscence in cases where the denuded areas are distended until the marginal bone, without the preservation of the bone band (10).

In the alveolar process, the position of the teeth, as to the buccolingual or buccolingual-palatal dimension, influences the thickness of the alveolar bone which is established around the tooth and, consequently, the thickness of the gingiva. If the tooth roots are very prominent, there may even be an absence of alveolar bone in certain areas, giving rise to fenestrations. Consequently, the root surfaces are only covered by soft tissue(11). For example, in the case of a proclined tooth, the soft and hard tissues in the buccal aspect of this tooth expose a thinner morphology and are more prone to the occurrence of gingival recession defects in comparison to the adjacent teeth which are in their physiological position(11).

A fenestration is a defect caused by deficient bone thickness which can be buccal, lingual or palatal and where there is a window of exposure of an implant totally surrounded by bone (10, 11).

1.1.2-Dehiscences

Gingival recession is defined as the displacement of marginal tissues apical to the cementoenamel junction with exposure of the root surface (12, 13). The etiology of gingival recession can be divided into predisposing and triggering factors. The former comprise cortical bone and thin gingival biotypes or absence of adherent gingiva, bone dehiscences and fenestrations, age, among other factors. It is likely that one of the first factors related to its occurrence is the morphological and anatomical situation of the tooth, namely in cases where the buccal bone plate is very thin, which favours the appearance of bone dehiscences. The absence of stability and the development of bone dehiscences are factors considered as collateral results after buccal displacement of the mandibular incisors, especially when they are outside the buccal alveolar bone (13, 14). Hard tissue defects arising from tooth loss can usually result in an adverse anatomy to the maxillary and mandibular alveolar processes that become unsuitable for implant placement without bone grafting (15). A dehiscence consists of a defect resulting from deficient bone thickness that can be buccal, lingual or palatal from the implant neck to a more apical region (16).

1.1.3-Horizontal ridge deficiencies and vertical ridge deficiencies

Irregularities in the height and contour of the gingiva and alveolar bone ridge cause aesthetic problems for some patients. Alveolar ridge deformities are classified according to their morphology and severity. Therefore, the bone augmentation technique used to reconstruct these different ridge defects depends on the horizontal and vertical extent of the defect(17). Studer et al., and, 1987, proposed a semi-quantitative classification of ridge defects according to their severity (mild, moderate or severe) in vertical and horizontal dimensions, as well as in accordance with their extent (one, two, three or four teeth). This classification completed the qualitative classification and allowed a preoperative prognosis of tissue augmentation procedures (18). Alveolar bone defects can be classified according to their horizontal and vertical component: Class I Thickening defect (bucco-lingual) with normal height (apico-coronal); Class II Height defect

(apico-coronal) with normal thickness (bucco-lingual); Class III Combined defect (thickness and height loss) (Seibert, 1983).(19)

1.2. Bone regeneration

Oral rehabilitation with dental implants in partially or totally edentulous patients is becoming increasingly common. Successful rehabilitation with implants requires bone volume which is essential for fixing the implant and promoting aesthetic and functional quality (20). To achieve a successful rehabilitation and an esthetic outcome on all levels, it is indispensable to be sure about the bone volume (vertical and horizontal) and about the soft tissue that is available in order to guarantee a perfect 3D placement of the implant, resulting in the desirable esthetic outcome (21). If the bone is insufficient, it is essential to restore the appropriate bone volume before or during implant placement. In this sense, "guided bone regeneration combined with bone graft and membrane, compared to the use of membrane or bone graft alone", consists of the "most predictable way to achieve better results in terms of quantity and quality of regenerated bone" (21, p. 14).

The rehabilitation of partial or total edentulism using osseointegrated implants contributes significantly to improving the quality of life of patients. However, bone loss or insufficiency, as a characteristic of several systems and periodontal diseases, trauma and tumours, remains a major challenge for osseointegration (22). The structural, functional and aesthetic results of implant placement are compromised by alveolar bone resorption, however, guided bone regeneration has been documented as the most predictable and successful in cases of horizontal defect treatment (23). Bone regeneration is thus an effective procedure in reducing the exposed implant surface. The complete resolution of these defects, regardless of the process used, is, however, not predictable.

Evidence shows that the percentage of successful implants with fenestrations and dehiscences, performed simultaneously with the bone regeneration process, is high (23).

1.2.1-Bone grafts

A bone graft has three fundamental functions: "to restore the integrity of the defect, to provide mechanical support and to promote bone healing" (24, p. 5). Grafts may be classified according to several parameters, among which are the mechanisms promoting bone neoformation, the origin and the degree of resorption of the material. Regarding their origin, they can be divided into four categories: autogenous, allografts, xenografts and alloplastics (24).

1.2.1.1-Autogenous

Autogenous or autografts (from the patient's own) are considered the ideal type of graft because they are the only ones with viable cells and have the capacity of osteoconduction, osteogenes and and osteoinduction, accelerating bone formation. They can be taken from intra or extra-oral sites according to the quantity and quality of bone desired (24, 25, 26). In cases in which there is a need for bone augmentation, the autogenous bone graft is the most chosen, given that it is the most predictable graft for the regeneration of bone tissue (25). These grafts do not originate an immune response, suppress the risk of disease transmission and allow the penetration of blood vessels and migration of osteoprogenitor cells. The major disadvantages of autografts are donor site-related morbidity, unpredictable resorption rate and limited quantity. Autogenous bone graft is typically harvested. From the chin , jaw , lower leg bone , hip or the skull. (26).

1.2.1.2-Allogenic

Allografts or homografts are bones from the same species and are usually in one of two forms: freeze-dried bone allograft (FDBA) or demineralized freeze-dried bone allograft (DFDBA). Their preparation follows very strict protocols so that there is no immunological reaction at the recipient site and that the risk of disease transmission is practically null, this type of bone graft typically harvested during other surgeries, such as hip surgeries. The bone is cleaned, sanitized, and meticulously prepared for donation. (27).

The main advantages of this type of graft are the availability of different sizes and shapes and the fact that there is no need for a second surgery. The disadvantages refer to the complex preparation necessary, with the non acceptance by the patient and with the possibility of a risk of transmission of diseases, although very low,(27,28).

1.2.1.3-Xenogenic

Xenografts consist of materials originating from different species. The various sources of xenogenic raw material, after processing, provide a morphologically and chemically identical and biologically compatible matrix to the bone matrix (29). The main advantages of xenografts are that they are available in large quantities, avoid a second surgery, morbidity and complications related to the donor site (30). The risk of disease transmission is almost null, and they can be produced in large scale with well defined and constant characteristics taking into account standardized manufacturing protocols. In terms of disadvantages, the risk of disease transmission stands out, which, although practically null, may always exist, an example of xenogenic boen graft is a graft obtained mainly from bovine bone, where only the mineral part is extracted (30, 31).

1.2.1.4-Aloplastic

The attempt to fill bone defects using completely synthetic materials has been carried out for many years. The major advantage of such materials is that the architecture of the graft can be completely controlled, they are free of immunological reactions and do not transmit any diseases (32).Most of them are manufactured from calcium carbonate, calcium sulfate, bioactive glass, synthetic hydroxyapatite or beta tricalcium phosphate. (32)

1.3-Membranes

The use of membranes serves as a barrier to block the migration of connective and epithelial tissue into the lost bone cavities, to enable the reproduction of osteoblasts and bone regeneration (33).

Commercially there are several types, however, the most used are the non-resorbable membranes of expanded polytetrafluoroethylene (PTFE-e) and the resorbable ones which are made of collagen, having, in the first instance, as their main purpose to block the proliferation of non-osteogenic tissues to the cavitated area or by exodontias or in bone fenestrations after surgical procedures (33, 34). Guided bone regeneration, a terminology proposed by Nevins and Mellonig, 1998, consists of the technique used for the reconstruction of bone tissue defects before or simultaneously with the rehabilitation with osseointegrated implants (32). In order to obtain guided bone regeneration, a membrane must avoid the action of fibroblast, cells from the periosteum, avoid solubility factors and allow concentration of growth factors (33, 34). The function of the membrane thus consists in the formation of a favourable environment to enhance functional regeneration, which can be achieved through the natural biological potential that comprises factors such as the prevention of inflammation resulting from bacterial presence, the mechanical stability of the clot, the creation and maintenance of the space filled by it, in addition to the isolation of undesirable tissues from the site of regeneration (35).

The membrane, resorbable or not, is a mechanical barrier and protects the grafted tissue and the blood clot, provides the exclusion of other cells from the periodontal tissues, and promotes bone formation and local healing (33, 34, 35). In summary, guided bone regeneration is the best documented method of bone augmentation and has made it possible to place implants in areas where there was insufficient bone for the correct positioning of implants, requiring the use of barrier membranes in order to re-establish the ideal bone volume of the alveolar ridge (35, 36, 37).

1.3.1-Collagen membranes

The collagen membrane with slow resorption is used for protection and allows a filling with blood and osteogenic cells in the bone defect, thus excluding any epithelial/soft tissue infiltration in the grafted area (36). Its advantages consist of homeostasis, chemotaxis for fibroblasts of the periodontal ligament and gingival, ease of manipulation and adaptation, ability to increase soft tissue thickness. It is also noteworthy that it can be kept exposed to the oral cavity, since scientific evidence documents its effectiveness in guided bone regeneration, even in the absence of primary wound closure, especially with the use of resorbable collagen membranes (36, 37). Early degradation of the barrier membrane may result in decreased bone formation in guided bone regeneration procedures (37). In their systematic literature review study, the same authors found that among cross-linked membranes, the Ossix® membrane (dentsply sirona), was the most commonly used in 53.18% of patients, while the others were a prototype from Geistlich Biomaterials, virtually identical to Bio-Gide® except for its chemical cross-linking designated 10806 or VN, in 38.15% of patients and a type I collagen membrane derived from porcine pericardium in 8,67% (37).Collagen membranes, derived from animals, are commonly used as reabsorption membranes. Collagen is one of the major structural proteins of the extracellular matrix and supports the growth of various tissues, in addition to having the advantage of being less inflammatory and non-cytotoxic (37). However, the rapid degradation caused by the enzymatic activity o fpolymorphonuclear leukocytes and macrophages, as well as the low stability, may affect the ability of these membranes to protect new bone, and as such, the membranes can morestable physical, chemical and enzymatic properties have been developed using different cross-linking techniques (38). The same authorsreported that crosslinked collagen membranes had a slower degradation rate than non-crosslinked membranes. When evaluating the bone regeneration ability of cross-linked and non-crosslinked collagen membranes made from the same collagen.The same authors found new bone regenerations of 27±15mm and 36±9mm for the non-cross-linked and cross-linked collagen membranes, respectively (38).

1.3.2-PTFE membranes

Non-resorbable membranes include polytetrafluoroethylene (PTFE) membranes, which can be divided according to their structure: expanded polytetrafluoroethylene (PTFE-e) and high density polytetrafluoroethylene (PTFE-d) and also include titanium meshes (39). The main disadvantage of these membranes is the necessity of a second surgical procedure for their removal. However, it presents criteria which may cover up this disadvantage, namely: the capacity of maintaining space for a sufficient period of time (40). Since the beginning of guided bone regeneration, PTFE-e membranes have been considered the "Gold Standard", which is due to their good structural integrity and biocompatibility, having been the first membranes used in guided bone regeneration (41, 42). Exposure of PTFE-e membranes is very frequent and should be kept covered over the conveniently sutured flap throughout the bone regeneration procedure, so that exposure of the membrane is avoided, as bacterial infection of the membrane, due to its porosity, will result in lower bone gains. Thus, the literature recommends that it be removed after exposure to the oral cavity (42). With regard to PTFE-d membranes, due to their small porosity, scientific evidence shows that if membrane exposure occurs, they can remain exposed without the need for a second surgical intervention, unlike PTFE-e membranes (42). However, the limited porosity may result in potential problems for initial clot formation, wound stabilization and membrane stability (41, 42).

1.4-Objectives

The main objective of this study is to access both clinical and radiographical results of the soft tissue and peri-implant bone marginal level in areas with little horizontal bone defect, treated with dental implants and a high-volume glycose cross-linked collagen membrane.

2. MATERIALS AND METHODS

2.1-Study design

This study is a retrospective study, comprising adult patients treated with dental implants and a glycose cross-linked collagen membrane in edentulous class 0 mandibular alveolar crests. Patient´s recruitment was executed independently of the investigation, accordingly with the inclusion criteria listed below. All patients were treated in a private clinic and all the surgical procedures were executed by a specialist in Oral Surgery (TB). The study protocol was approved in January 2022 by CES-UCP under register number 183/2022. This study was started in the year 2022, evaluating the first six months of follow-up of the treated patients.

2.2- Inclusion and exclusion criteria

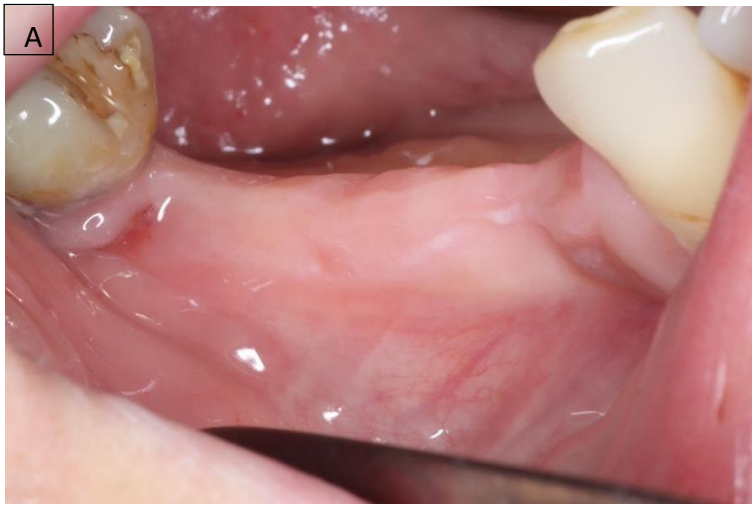
The inclusion criteria included patients (>18 years old) with a mandibular edentulous area, American Society of Anaesthesiologists (ASA) status I (healthy patient), whit just contour deficit or when there is no need of bone augmentation, patients with a moderate horizontal defect were included too and who personally signed and agreed with the informed consent declaration and with the treatment plan that was previously delivered.

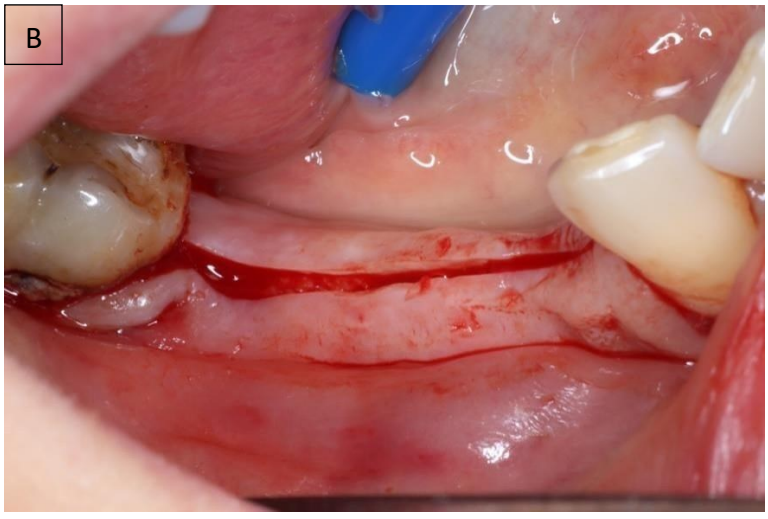
The patients with systemic bone diseases capable of influencing bone healing, smokers, patients under pregnancy and who declared to be under treatment with drugs that potentially alter the bone metabolism were excluded.

2.3- Surgical procedure

The surgical procedure is described in Figure 1 and included: local anesthesia of the edentulous area using articaine with epinephrine 1/80000; linear muco-periosteal incision of the alveolar crest and muco-periosteal flap elevation; insertion of the dental implants (Astra Tech EV, Dentsply Implants, Dentsply Sirona, USA) at the edentulous area in accordance with the manufacturer surgical protocol; placement of a collagen membrane (Ossix Volumax™, Datum Dental Ltd, Bat Sheva, Israel) between the muco-periosteal

flap and the buccal bone wall, after implant insertion; immediate placement of a final prosthetic abutment (with 2 mm height); and the flap was sutured with a 5/0 polyamide suture (Seralon™, Serag-Wiessner, Nalia, Germany). Postoperative instructions were given to the patients, which included oral hygiene procedures, chlorhexidine 0.12% rising and medication (Paracetamol 1000mg, , and amoxicillin 1g twice a day for seven days). The sutures were removed after 8 days.This surgical procedure was made by professor doutor Tiago Borges.





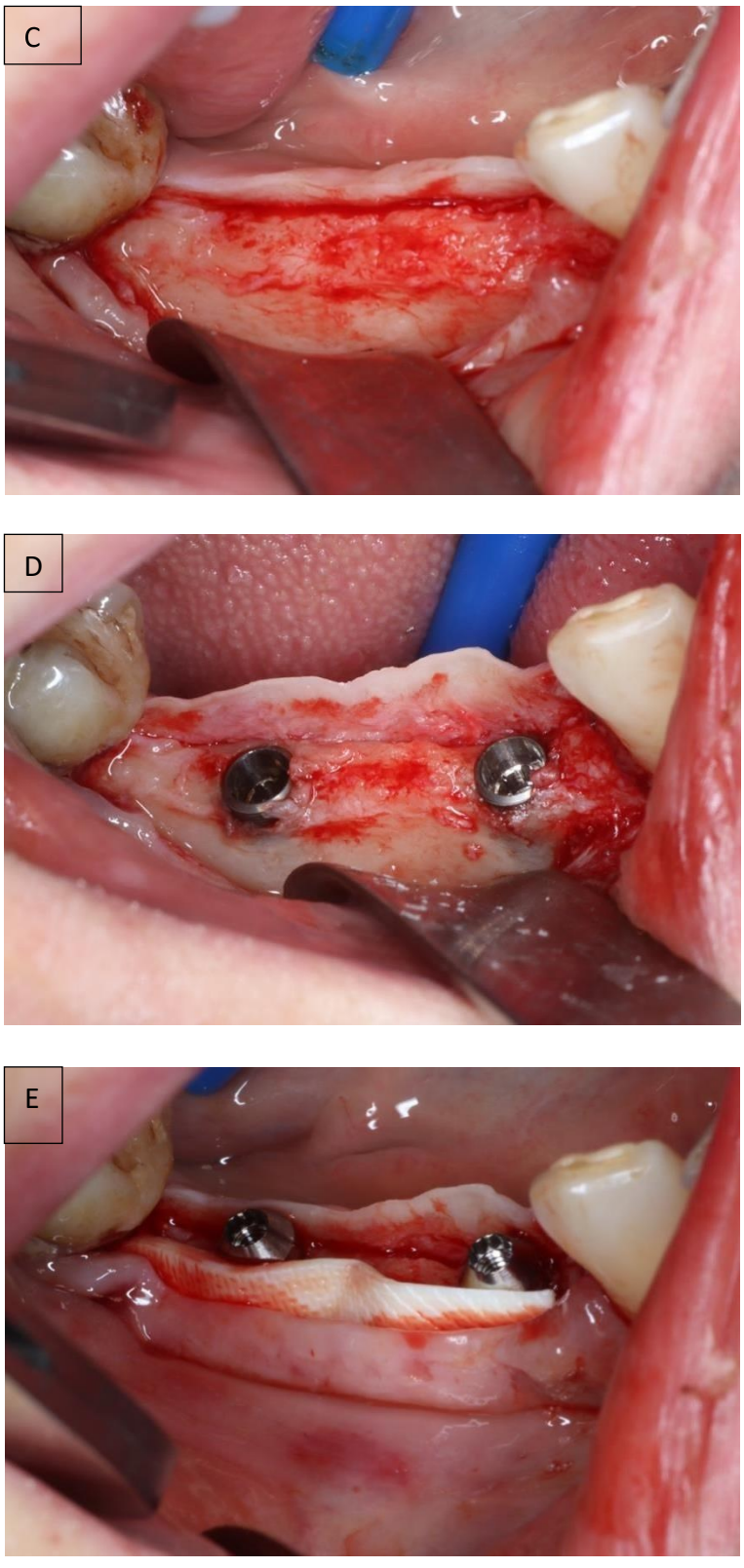


Figure 1- Membrane insertion between the facial area of the muco-periosteal flap and the buccal bone wall (Surgical procedure and image by Professor Tiago Borges) A-Edentulous area; B-Incision; C-muco-periosteal flap; D-Implant placement; E-Membrane insertion

2.4-Outcome Assessment

2.4.1 Matching digital models

Digital impressions were taken before the implant placement (T0), six months after implant insertion (T1) and 12 months after implant placement (T2) using an intraoral optical scanner (IOS) (Primescan®, Dentsply Sirona, USA). To quantify the tissue changes that occoured in all the treated sites a digital assessement model, described by Borges et al. 2020, was used in this investigation (49). The totality of digital models were exported in STL format from the IOS (Figure 2A) and were visualized with Geomagic Control X® (Geomagic, Inc., North Carolina, USA), allowing to superpose the digital files and to see the volumetric changes between different time points at peri-implant tissue areas like Buccal Volume Variation (BVv) and mean buccal variation (MBV) .The digital assessment protocol was adapted from Borges et al (2020) and Fernandes et al (2021) and consisted in two different measurements methods: one linear analysis of the alveolar surface next to the treated area and a volumetric assessment of the alveolar volumetric changes that occurred at the peri-implant tissues.

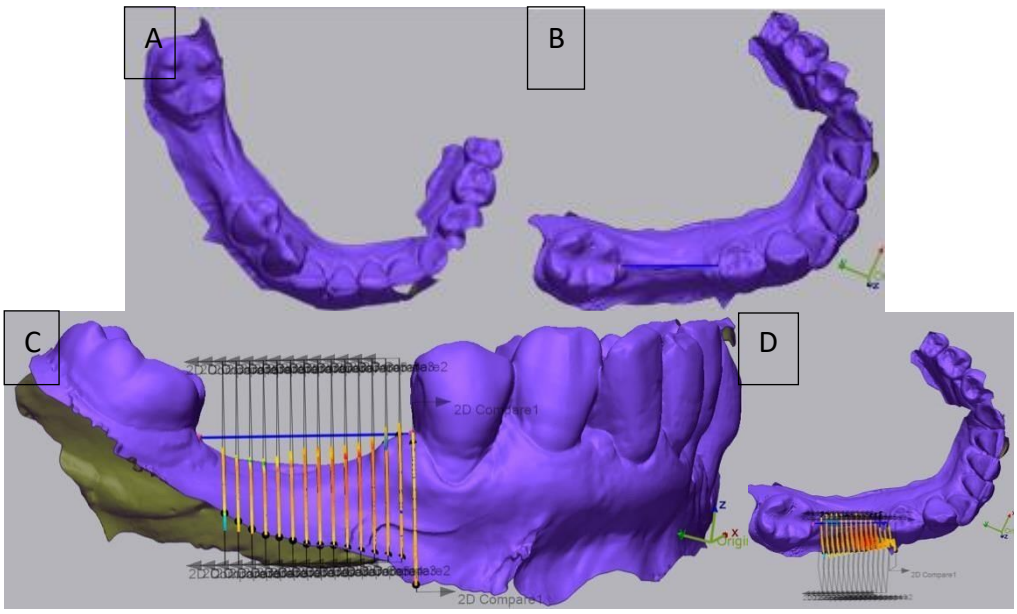


Figure 2- A- STL file use for digital analysis; B- horizontal reference line for linear analysis; C-Region of interest (ROI) creation; D- comparison of the different files at the ROI, using the color map.

2.4.2-Linear surface measurements

With the "3D Compare" tool, changes in thickness in T1 were compared to T0 and changes in T2 will be compared with T0. Color maps were created by overlapping the models, where the change in color meant the variation in thickness at that area.

To assess thickness alterations in all models, it was necessary to ensure that the measurements were computed from the same place (“Align Between Measured Data Autoguess”, “local Based On Auto Guess” and “Best Fit Alignment). For this, an horizontal line was defined along the alveolar crest that served as a reference (Figure 2B).

Subsequently, a rectangular area of interest was adjusted around this line, based on the free gingival margin of the adjacent tooth, and limited 5 mm apical; A line passing in a mesio-distal direction through the interproximal zone restricted this area. It was divided into perpendicular lines with a separation of 0,5mm between them. This area was the study patronized region for each patient and was repeatedly used to determine the regions of interest (ROI) of the peri-implanttissue at the buccal and palatal surface (Figure 2C and 2D).

The division of the area of interest in the models already superimposed, helped to calculate the buccal linear changes (MBC).

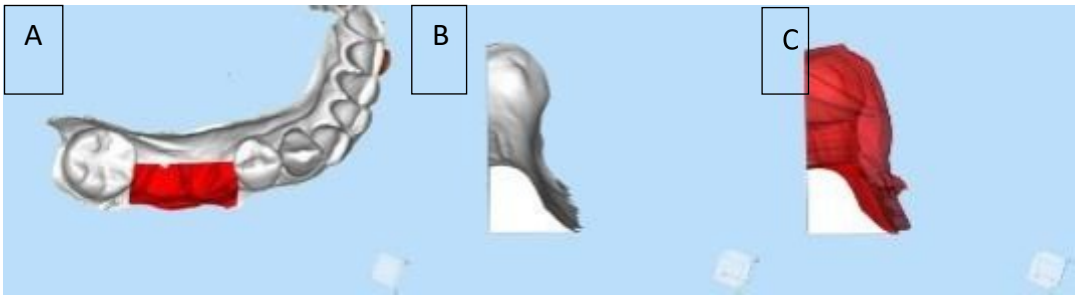


Figure 3: A- 3D volumetric ROI; B- volumetric ROI at T0; C-Volumetric ROI at T1.

2.4.3-Volumetric dimensional measurements

STL models obtained at T0, T1 and T2 were imported to the Materialise Magics® (Materialise, Leuven, Belgium) computer program, where the function

"Surface to Solid" allowed to give volume to our models. A 3D volumetric ROI was manually chosen with "Cut or Punch" function taking into consideration interproximal areas as mesio-distal boundaries (Figure 3). All cuts were made in the same regions in every digital models making sure that all the measurements are executed in the same regions. With the help of the "Boolean" section, the models will be superimposed making it possible to calculate the volume in the area of initial interest and compare it with the models in the post-operative follow-ups. In order to analyze the changes in the peri-implant volume, the variable Buccal Volume variation (BVv), will be computed in mm3 and expressed in percentage (%) of volume change.

2.5- Marginal bone changes

Peri-apical X-rays were executed immediately after implant placement (baseline), six months after implant insertion (T1) and twelve months after implant placement (T2) using a silicone customized bite block to asure the parallel position of the x-ray sensor and, consequently the reliability of the radiographic measurements at the different time points . The crestal bone changes at the peri-apical x-ray were evaluate by an examiner (NA) that was not involved in the surgical procedure, using software for radiographic analysis (SIDEXISTM, Sirona Dental Systems Inc., NY, USA). The framework chosen to calibrate the measurement system was the distance between the implant neck and the most apical part of each fixture, along an ideal line running parallel to the long fixture axis.

Final MBC values were present as the mean measurements obtained at the mesial (mMBC) and distal (dMBC) aspect of each implant from the implant platform uppermost point of the micro threaded part to the adjacent crestal bone.

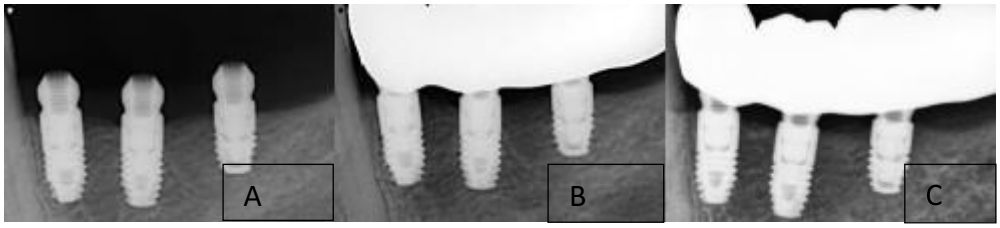


Figure 4- Peri-apical radiograph at T0(A), T1(B) and T2(C)

2.6-Statistical analysis

After data collection, values were grouped in the Excel software, version 16,6 (Microsoft Corporation, Redmond, USA) to be statistically accessed.

Statistical analyses were caried out with the “Statistical Package for the Social Sciences (SPSS), version 26.0 for Windows (IBM Corporation, Armonk, NY, USA). Variables related to patient`s demographic characterization like age, gender and implant site (incisive/premolar) were computed. Clinical and radiographic variables such as MBV, BVv, mMBC, dMBC and MBL were also evaluated and treated by statistical methods. The outcomes measurements were presented as mean values, standard deviation, minimum, maximum and 95% confidence interval.

The assumption of normality for these variables was computed using the Shapiro-Wilk test. Finally, a Pearson´s correlation test was conduct in order to study the influence between variables and their outcomes. The hypothesis tests will contemplate at the 5% level of significance.

3. RESULTS

The sample is composed of 7 females and 1 male with a mean age of 54.13 years and a standard deviation of 8.08 years.

Table 1 --Demographic data of the sample of the study

Patient	Gender	Implant site	Age	Implant
#1	F	46; 45	59	3.6x6mm; 3.6x6mm
#2	F	47; 45	57	3.6x6mm; 3.6x8mm
#3	F	47; 46	59	3.6x8mm; 3.6x8mm
#4	F	37; 35	60	3.6x8mm; 3.6x8mm
#5	M	47; 46	65	3.6x6mm; 3.6x8mm
#6	F	46; 45	45	3.6x6mm; 3.6x9mm
#7	F	37; 35; 34	55	3.6x6mm; 3.6x8mm; 3.6x8mm
#8	F	47; 46	41	3.6x6mm; 3.6x8mm
N=8	7F/1M	N=17	54,13 ± 8.08	

Table 2 shows the characterization of the variables in variation at T0_T1, T1_T2 and T0_T2: MBV, BVv, mMBC for mesial sites in anterior and posterior implants and dMBC for distal sites in anterior and posterior implants. It should be noted that all variables under study, with the exception of ΔT1_T2MBV, are from populations with normal distributions by the Shapiro Wilk test, as shown in the appendix.

Table 2 --Characterization of variables

Variável	Mínimum	Máximum	Mean	Standard deviation	CI (95%)
ΔT0_T1 MBV (mm)	0.40	1.68	0.97	0.465	[0.584; 1.361]
ΔT1_T2 MBV (mm)	-1.34	0.22	-0.22	0.562	[-0.806;0.373]
ΔT0_T2 MBV (mm)	0.34	1.54	0.81	0.508	[0.273;1.340]
ΔT0_T1 BVv (%)	6.34	77.15	32.06	24.427	[11.639; 52.483]
ΔT1_T2 BVv (%)	-40.72	1.21	-9.64	15.659	[-26.070;6.797]
ΔT0_T2 BVv (%)	5.74	53.71	28.70	15.812	[12.108;45.295]
ΔT0_T1 mMBC (mm) anterior	-2.64	-0.03	-1.06	0.858	[-1.778; -0.342]
ΔT1_T2 mMBC (mm) anterior	-0.19	1.05	0.48	0.637	[-0.193; 1.143]
ΔT0_T2 mMBC (mm) anterior	-1.44	-0.02	-0.69	0.663	[-1.387; 0.004]
ΔT0_T1 mMBC (mm) posterior	-1.04	0.07	-0.43	0.361	[-0.733; -0.130]
ΔT1_T2 mMBC (mm) posterior	-0.70	0.97	0.15	0.587	[-0.462; 0.769]
ΔT0_T2 mMBC (mm) posterior	-1.35	1.04	-0.25	0.809	[-1.097;0.601]
ΔT0_T1 dMBC (mm) anterior	-2.30	0.00	-0.89	0.737	[-1.506; - 0.274]
ΔT1_T2 dMBC (mm) anterior	-0.40	0.81	0.11	0.485	[-0.399; 0.619]
ΔT0_T2 dMBC (mm) anterior	-1.64	-0.06	-0.74	0.687	[-1.460; -0.018]
ΔT0_T1 dMBC (mm) posterior	-1.89	0.11	-0.70	0.733	[-1.308; -0.082]
ΔT1_T2 dMBC (mm) posterior	-0.19	1.05	0.29	0.480	[-0.211; 0.797]
ΔT0_T2 dMBC (mm) posterior	-1.13	0.44	-0.34	0.667	[-1.044; 0.357]

mMBC: mesial marginal bone changes; dMBC: distal marginal bone changes; N: number of implants; Implant 1: anterior: anterior implants posterior: posterior implants ; SD: standard deviation; CI: confidence interval.

It is observed that MBV at T0_T1 ranges from a minimum of 0.40mm to a maximum of 1.68mm, and the CI (95%) for the mean is [0.584; 1.361]. On the other hand, BVv at T0_T1 presents a mean value of 32.06% with a standard deviation of 24.427%, which reveals a high dispersion hence the CI (95%) for the mean [11.639; 52.483]. For mMBC at T0_T1 the mean for anterior implant was -1.06±0.858 mm and for posterior implant was -0.43±0.361 mm. However, given the 95% confidence intervals, [-1.778; -0.342] and [-0.733; -0.130] anterior and posterior implant, respectively, it can be stated that the values remain significantly below zero. The mean dMBC T0_T1 for anterior implant was -0.89±0.737 mm, and to posterior implant -0.70±0.733 mm. However, given the 95% confidence intervals, [-1.506; -0.274] and [-1.308; -0.082], respectively, anterior and posterior implantats it can be stated that the values remain significantly below zero.

Considering the variables with the variation T0_T2, MBV has a mean of 0.81±0.508 and the CI (95%) is [0.273;1.340]. i.e., the value of MBV increased significantly between T0 and T2. Regarding BVv we observe the mean of 28.70% with standard deviation of 15.812%, which reveals a high dispersion hence the CI (95%) for the mean [12.108; 45.295]. The mean for anterior implant was -0.69±0.663 mm and the posterior implant mean -0.25±0.809 mm were observed for mMBC. However, given the 95% confidence intervals, [-1.387; 0.004] and [-1.097; 0.601] anterior and posterior implant , respectively, it can be stated that the T0_T2 variation values for posterior and anterior implants are approximatelyzero. The mean dMBC for anterior implants was -0.74±0.687 mm, and it increased for posterior implants by -0.34±0.667 mm. However, given the 95% confidence intervals, [-1.460; -0.018] and [-1.044; 0.357] anterior and posterior implants respectively, it can be stated that the values remain significantly below zero in dMBC in anterior implants and approximately zero in posterior implants.

Since the variables are approximately normal, we used the parametric t test for paired samples to compare the anterior and posterior implants results of mMBC and dMBC at T0_T1. Thus, for mMBC anterior and posterior we obtained T=-1.920; p=0.096, i.e., the differences observed in the results of mMBC are not statistically significant with the application of the implant. Similarly for dMBC T=-0.634; p=0.546, i.e., the differences observed in dMBC results are not statistically significant with the application of the implant. Considering the results at T0_T2 for mMBC anterior and posterior implants , we obtained T=-1.042; p=0.345, i.e., the differences observed in the mMBC results are not statistically significant with the application of the implant. Similarly, for dMBC for anterior and posterior implants n, we obtained T=-1.025, p=0.352, i.e., the differences observed in dMBC results are not statistically significant with the application of the implant.

3.1. Correlation between variables

Pearson's correlation coefficients are shown in table 3. It is observed that considering the variables related to T0_T1 MBV presents a direct statistically significant correlation of strong intensity with BVv (r=0.934) and also with BVv at T0_T2 (r=0.871). mMBC anterior implants presents a direct significant correlation of strong intensity with dMBC anterior at T0_T1 (r=0.878). The

variable mMBC post at T0_T1 shows significant, direct and strong correlation with dMBC post T0_T1 (r=0.713) and with mMBC post at T0_T2 (r=0.890). The variables dMBC post T0_T1 and mMBC post T0_T2 are significantly correlated (r=0.813).

Table 3 --Pearsons correlation coefficients

	MBV(mm) T0-T1	BVv(%) T0-T1	mMBC(anterior) T0-T1	mMBC(posterior) T0-T1	dMBC(anterior) T0-T1	dMBC(posterior) T0-T1	MBV(mm) T0-T2	BVv(%) T0-T2	mMBC(anterior) T0-T2	mMBC(posterior) T0-T2	dMBC(anterior) T0-T2	dMBC(posterior) T0-T2
MBV(mm) T0-T1	1	0.934**	-0.381	0.449	-0.135	0.186	0.351	0.871*	0.116	0.228	0.275	-0.162
BVv(%) T0-T1		1	0.015	0.289	-0.257	0.069	0.039	0.807	0.240	0.028	0.007	-0.009
mMBC(anterior) T0-T1			1	0.015	0.878**	0.218	0.174	0.089	0.771	0.259	0.400	0.768
mMBC(posterior) T0-T1				1	0.108	0.713*	0.577	0.554	0.048	0.890*	0.135	0.304
dMBC(anterior) T0-T1					1	0.300	0.552	0.286	0.628	0.498	0.732	0.666
dMBC(posterior) T0-T1						1	0.096	0.048	-0.133	0.813*	-0.068	0.776
MBV(mmr) T0-T1							1	0.565	0.203	0.591	0.839*	-0.054
BVv(%) T0-T2								1	0.526	0.371	0.498	0.072
dMBC(anterior) T0-T2									1	0.007	0.416	0.430
mMBC(posterior) T0-T2										1	0.280	0.556
dMBC(anterior) T0-T2											1	0.026
dMBC(posterior) T0-T2												1

*-significativo a 5%; **-significativo a 1%

Table 4 . Normality tests

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
MBV_mmT0_T1	,167	6	,200*	,963	6	,845
MBV_mmT1_T2	,402	6	,003	,681	6	,004
MBV_mmT0_T2	,280	6	,153	,848	6	,151
BVv_percT0_T1	,192	6	,200*	,972	6	,904
BVv_percT1_T2	,340	6	,029	,711	6	,008
BVv_percT0_T2	,218	6	,200*	,954	6	,770
mMBCimp_post_mmT0_T1	,226	6	,200*	,879	6	,265
mMBCimp_post_mmT1_T2	,219	6	,200*	,972	6	,909
mMBCimp_post_mmT0_T2	,148	6	,200*	,985	6	,975
dMBCimp_post_mmT0_T1	,192	6	,200*	,913	6	,453
dMBCimp_post_mmT1_T2	,244	6	,200*	,888	6	,307
dMBCimp_post_mmT0_T2	,272	6	,189	,862	6	,196
mMBCimp_ant_mmT0_T1	,190	6	,200*	,950	6	,743
mMBCimp_ant_mmT1_T2	,182	6	,200*	,921	6	,511
mMBCimp_ant_mmT0_T2	,262	6	,200*	,820	6	,088
dMBCimp_ant_mm_T0_T1	,198	6	,200*	,901	6	,379
dMBCimp_ant_mm_T1_T2	,190	6	,200*	,912	6	,447
dMBCimp_ant_mm_T0_T2	,199	6	,200*	,873	6	,237

4.DISCUSSION

Evidence shows that dental implants now provide a better quality of life due to high esthetics, durability and predictability, and are considered the standard of oral health care in preventing negative functional and esthetic outcomes associated with missing teeth, with high success and survival rates (6,8). In their longitudinal study with a 5-year follow-up by Beschnidt et al. (43), in a sample of 185 patients with 271 implants, a 98.6% survival rate was recorded, with more than 99% of patients reporting satisfaction with the restoration and a mean marginal bone loss of -0.28 ± 0.60 mm.

The GBR procedure, by applying cell occlusive membranes that mechanically exclude non-osteogenic cell populations from the surrounding soft tissues, has become a well-documented and highly successful procedure for increasing the height and width of the atrophic jaw prior to implant placement(44). There are a lot of treatments for regeneration after bone loss , in all of them ,membranes are really important but there are diferences between them. Collagen membranes are biocompatible and have the abilitiy to induce healing so they became an important option for GBR (44, 45). In their study, Sbricoli et al. (45) found that GBR represents a well-established procedure for bone augmentation and can be performed using various types of membranes and grafts. The membranes should be chosen for each clinical case according to the desired biodegradation characteristics. Resorbable and non-resorbable membranes differ in terms of clinical and technical handling, complication rate and expected long-term results. Among the different resorbable membranes available, collagen membranes can be considered to have a very sound scientificbasis and widely validated clinical use. They offer advantages in terms of not having to remove the membrane in the second stage of surgery, favorable biological attributes, and similar long-term performance in dehiscence-type defects. However, longer degradation times and resistance of the membrane to resorption are also associated with significantly higher exposure rates for cross- linked collagen membranes and sometimes a foreign body reaction during resorption. Although these limitations, the same authors point out thatpolytetrafluoroethylene membranes show clinical evidence of success in the treatment of vertical and horizontal bone defects (45). In a systematic review of the literature, Tay et al. (46) evaluated the incidence and types of complications that occur after horizontal GBR and proposed management strategies to deal

with these clinical situations, with the secondary objective of histomorphometric validation of the healing process in areas where postoperative complications occurred after GBR. Site-level analysis showed a weightedaverage incidence rate of low-grade injury and low-grade infection. Analyzes at the patient level showed that minor and major complications were 16.1% and 1.6%, respectively, whileneurosensory changes in the donor were 7.0%. Subgroup analysis also showed that the GBR staging procedure increased the proportion of major and minor postoperative complications. Although barrier membrane exposure is often associated with decreased bone regeneration and graft resorption, the type of membrane used (resorbable or nonresorbable) had nostatistically significant effect on any postoperative complications (46).Histologically, it is common to observe a layer of fibrous connective tissue rather than bone at the interface between the native bone at the recipient site and the regenerated bone in cases with membrane exposure after the GBR procedure (46). The same study further evidences that minor wound dehiscence was the highest incidence proportion of post-surgical complications. To manage these post-surgical complications, methods ranging from daily application of antiseptics, the use of systemic antimicrobials, regular revisions and the complete removal of non-integrated biomaterials are commonly prescribed in an attempt to minimize tissue loss at the surgical site (46). In a previous study, cross-linked collagen membranes were shown to have greater resistance to degradation compared to non-cross-linked barriers (47). A randomized clinical trial, in which the efficiency of ribose-cross-linked collagen membranes and non-cross-linked membranes was evaluated, documented that both membranes resulted in improved bone volume at the regenerated sites, and were predictable in GBR of dehiscence and fenestration defects, with better results in lateral augmentation when using the ribose-cross-linked membrane, especially in soft tissue healing (47).

To analyze the results on the use of the Ossix Volumax membrane in the treatment of patients with non-critical previous alveolar defects, we used the following variables as a basis: mean buccal variation (MBV), buccal volume variation (BVv), mesial marginal bone changes (mMBC) and distal marginal bone changes (dMBC) before implant insertion, six months after implant placement, twelve months after implant placement and the period between six months (T1) and twelve months (T2). The results obtained in the mean buccal variation (MBV)

express a growth in the linear width of the tissue between T0 and T1, of 0.97+-0.46mm between T1 and T2 the results express a decrease of -0.22+-0.56 mm and between T0 and T2 a mean growth of 0.81+-0.50 mm. This means that a significant growth was observed in the first 6 months, a stabilization between six months and twelve months and a significant growth during the first year of follow-up .Regarding buccal volume variation (BVv) from T0 to T1 we can observ a mean increase of 32.06+-24.42%, between T1 and T2 we can see a mean increase of -9.64+-15.65 % and between T0 to T2 we can see a mean increase of 28.70+-15.81 %. These findings show an improvement in terms of percentage of volume variation 6 months after implant insertion, a period of normal stabilization between T1 and T2 and a growth of volume percentage from T0 to T2 in conjunction with the use of OSSIX Volumax membrane.

When we compared the results with the literature, there is an agreement regarding the volumetric improvement after guided bone regeneration. In a study conducted by Scheneider et al (48) that evaluated peri-implant changes in 6 and 12 months after implant installation and bone augmentation, the result was an increase in the amount of bone in the buccal alveolar ridge of 0.72+- 0.47 mm. The mean increase between 6 months and 12 months was 0.55 +- 0.53 and mean increase in 12 months follow-up was 1.27 +- 0.67 mm on average. Authors concluded that GBR had a greater contribution to volume increase compared to a no graft procedure (49). Smidt et al. found a successful result when using ribose cross-linked membrane to restore poor buccal tissue volume concluding that it had a positive impact on the buccal volume of the restoration when using OSSIX Volumax in placing dental implants in reduced alveolar ridges (50).

The linear and volumetric variables variations were assessed throughout a fully digital protocol using a computer software to superimpose STL files as described by Borges et al. This method allowed to objectively observe dimensional changes in the alveolar ridge avoiding an observer-dependent analysis like periodontal probe measurements or the pink esthetic score(51).

The mean marginal bone changes (mMBC) mesial marginal bone changes (mMBC) and distal marginal bone changes (dMBC) are the measurements obtained by measuring the distal and mesial sites of the marginal bone around the implants using a periapical radiograph. This type of measurements have been used in several studies being a good indicator of success or failure in what refers

to osseous maintenance around the implant (52,53). Borges et al. in an investigation regarding posterior placed implant in the mandible, report MBC -0,44 +-0.59 mm after 12 months follow up in a group of patients treated with two mandibular implants and immediate abutments. Comparing the results of the two studies we see a similarity on bone loss (54). In another study by Borges et al about periimplant bone changes in different abutment heights and insertion timing in posterior mandibular areas using the same implantation protocol they obtained -0.72+-0.36mm of bone loss at 12 months follow-up (55). Another study about the effect of one-time abutment placement on interproximal bone levels and peri-implant soft tissues done by Molina et al (56) reported -0.60+-0.40mm of bone loss at 12 months follow up. We can see a similiarity between our results and the results published in the literature.

Among the limitations of this study we foundd the small number of patients, which limits the statistical study, a larger sample is needed to find more significance in the results. Another limitation is the method of volumetric measurement used, which is not specific for the type of tissue since the measurement is made at the surface without differentiation the layers and type of tissue that suffers changes over time. More clinical research will be necessaryto confirm or reject the benefits of the use of ossifying collagen membranes in the horizontal alveolar deffects treatment.

5. CONCLUSION

There is a strong association between the use of an ossifying collagen membrane and a gain of buccal volume, in relation to the maintenance ofmarginal bone there was not an improvement comparing with the literature.

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