جـامعة بيروت العربية
BEIRUT ARAB UNIVERSITY

COMPARATIVE EVALUATION OF RESORBABLE (PERICARDIUM) VERSUS NON RESORBABLE MENBRANE (POLYTETRAFLUOROETHYLENE) FOR HORIZONTAL BONE AUGMENTAITON OF POSTERIOR ATROPHIC MANDIBLE.

(Randomized Controlled Trial)

تقييم مقارن للغشاء القابل للامتصاص (التامور) مقابل للغشاء غير القابل للامتصاص (بولي تترافلورو إيثيلين) لزيادة العظام افقيا للفك السفلي الخلفي.

(دراسة سريرية عشوائية محكمة)

By

Hiba Abdelkarim AlRifaii

Thesis

Submitted in Partial Fulfillment of the Requirements for the Degree

of Master in Periodontology

Department of Periodontology

Faculty of Dentistry

2024

Abstract

Background: Deficient bony ridges often complicate the implant treatment plan. Several treatment modalities are used to regenerate bone, including guided bone regeneration (GBR). The purpose of this study is to compare the effect of two types of membrane, resorbable and non- resorbable used in GBR for horizontal bone augmentation in atrophic posterior mandible.

Aim of the study: the aim is to compare the outcome of the resorbable pericardium membrane and the non-resorbable PTFE membrane in GBR in staged approaches, in terms of clinical outcome, new bone quality and quantity radiographically and histologically.

Material and methods: A randomized controlled clinical trial was designed,20 patients with mandibular atrophic ridge will be randomly divided into 2 groups. Both groups will be treated with a staged approach. 10 patients will be treated with GBR by means of non-resorbable d-PTFE titanium reinforced membrane (Group A). and the other 10 patients, by means of pericardium membrane (Group B). Both groups will be grafted by a mixture of xenograft and autograft. All the clinical and radiographic evaluation will be recorded. After 6 months in the second stage, a CBCT radiograph will be taken, and implants will be placed after taking a bone specimen for histological studies.

Results: data will be collected, tabulated, and statistically analyzed using appropriate tests

Keywords: GBR, pericardium membrane, PTFE membrane, alveolar ridge reconstruction, atrophy.

Introduction

Lack of adequate bone for implant placement due to a previous history of periodontal disease, traumatic tooth extraction, or bone loss from prolonged use of a removable prothesis, is a common challenge in implant dentistry (Soldatos NK et al ,2017). Bone loss after tooth extraction has been reported to range between 40% and 60% during the first 3 years, and thereafter it is estimated to range between 0.25% and 0.5% annually (Helmi MF,et al,2019).

Alveolar atrophy refers to the pathological condition where there is moderate to severe resorption of alveolar bone due to tooth loss (Tsuchida Set al 2023). When teeth are lost, the functional stimulus for the alveolar bone is also lost, leading to predictable bone resorption (Jonasson G et al ,2018). The pattern of resorption varies based on location, where in the mandible, alveolar bone resorption is primarily horizontal, while in the interforaminal regions, it tends to be centripetal and in retroforaminal areas, the resorption is vertical and centrifugal. (Tsuchida Set al 2023). The presence of the inferior alveolar nerve (IAN) further complicates treatment in the posterior regions of the mandible when using Osseo integrated implants. These challenges necessitate careful planning and consideration during implant placement to achieve successful outcomes. (Tsuchida Set al 2023)

Various methods are employed to regenerate bone in areas with deficiencies, including using autogenous or allogeneic block grafts (cortical, cancellous, or cortico-cancellous), ridge splitting techniques, distraction osteogenesis, orthodontic tooth movement, and guided bone regeneration (GBR) with or without additional filler materials. (Toscano N, et al 2010).

Numerous materials have been utilized for bone regeneration, with ongoing research in this field to address bone defects. Particularly in the context of widespread implant usage, various options such as autogenous bone, allogeneic bone, and synthetic bone have been employed to treat oral and maxillofacial bone defects (Ferraz MP et al ,2023). Although fresh autogenous bone yields optimal regeneration results due to its osteoinductive and osteoconductive properties, it comes with drawbacks like pain and edema from donor site injury, limited harvest volume, and high graft resorption rates. Consequently, allogeneic bone graft materials, lacking inherent bone regenerative capacity but obviating the need for an additional donor site, have gained significant use. However, due to their source from other individuals, these tissues may provoke an immune response in recipient tissues, posing a potential antigenic challenge. (Tang G, Liu Z, Liu Y, et al,2021)

Barrier membranes play a crucial role in guided bone regeneration (GBR), with various types being utilized resorbable (pericardium collagen …) and non-resorbable membrane. (e-PTFE,d-PTFE….).

Polytetrafluoroethylene (PTFE) serves as the foundational material for the most prominent and earliest non-absorbable membranes used clinically. This substance is derived from an unbranched, linear, semi-crystalline polymer comprising a combination of fluorine and carbon. PTFE falls under the category of polyhaloolefins and is classified as a thermoplastic material. Additionally, it is widely regarded for its high inertness. Titanium-reinforced membranes have been created to overcome this deficiency. A titanium skeleton with high strength and stiffness is inserted into the PTFE membrane to give it excellent plasticity and volume stability. (Kameda T, Ohkuma K, Oka S, 2018)

Several types of PTFE membrane have been introduced (e-PTFE and D-PTTFE). The e-PTFE membrane promotes tissue cell attachment and stabilizes wounds by having small pores that limit the migration of connective tissue and epithelial cells (Qiang Guo et al 2022). However, its exposure to the oral cavity increases the risk of bacterial penetration and often requires premature removal, which can negatively impact outcomes (Ghensi P et al ,2017). Resorbable membranes have a higher rate of resorption after exposure, leading to potential adverse effects. The ability of the e-PTFE membrane to attach to tissue often necessitates a second surgery for removal. Consequently, non-resorbable membranes are now widely used instead of e-PTFE membranes (Sasaki JI et al 2021). The use of d-PTFE in dentistry is gaining acceptance due to its smaller pore size, reducing the risk of bacterial contamination when left exposed in the oral cavity. d-PTFE membranes effectively maintain space, stabilize wounds, and allow sufficient time for bone regeneration. Their non-attachment to tissue enables removal through the mucosal flap without causing trauma. Nevertheless, due to limited porosity, adequate blood supply to the area relies on marrow space and cortical perforations for successful bone regeneration (Ghensi P et al ,2017).

At present, titanium-reinforced membranes have become a well-established foundational material for creating stable volumes conducive to osteogenic space, thereby facilitating bone tissue regeneration in clinical settings (Windisch P et al 2021). According to a recent meta-analysis, titanium-reinforced d-PTFE emerged as the optimal choice for guided bone regeneration (GBR) or guided tissue regeneration (GTR), as it demonstrated the highest vertical bone regeneration potential coupled with a low incidence of complications (Windisch P et al 2021).

Hence, absorbable membranes that can mimic the effects of nonabsorbable ones have gained recent attention. For instance, we opted for pericardium, an absorbable membrane derived from human pericardial tissue (Ren Y et al 2022).

The pericardium is a sac made of fibrous and serous tissues that envelops the heart in mammals. It has been extensively utilized in cardiac surgery for tasks such as reconstruction, repairing valves, and closing the pericardial layer. Pericardial tissue is renowned for its excellent handling properties and consistent ability to retain sutures (Waleed, Mohamed, Abbas., D., A., Khalik,2023). Furthermore, it possesses innate qualities that make it resistant to thrombosis and infection. Xenogeneic pericardium, sourced mainly from bovine and porcine origins, and occasionally from equine sources, is commonly used. These tissues are available in large patches, allowing for customized shaping to suit various cardiovascular procedures. Predominantly composed of collagen fibers, xenogeneic pericardium possesses elastic properties, enabling it to adapt to intricate anatomical structures. (Tristan, 2020)

The selection of an appropriate tissue barrier involves considering various properties of the pericardium membrane. These include its physical characteristics, biocompatibility, biodegradability, immunogenicity, capacity to attract and stimulate periodontal ligament fibroblast cells, as well as its ability to promote adherence and proliferation of regenerative cells. Additionally, the membrane's potential to effectively seal the underlying defect is crucial for its success. Pericardium membranes have demonstrated strong crosslinking, suggesting a longer duration for resorption. (Jéssica, Suzuki etal 2022).

Additionally, the pericardium membrane provides a scaffold for attachment, migration, and proliferation of periodontal ligament fibroblasts, thereby promoting regeneration of soft tissues. As part of guided bone regeneration, the pericardium membrane facilitates the release of growth factors and preserves blood supply to the affected area, thereby promoting growth of bone and soft tissue and enabling regeneration of periodontal tissues. (Ernie et al ,2020).

Pericardium has found widespread use in regenerating bone defects around implants or serving as a barrier membrane for maxillary sinus perforations. However, there remains a scarcity of clinical studies assessing these procedures. (Tsuchida Set al 2023).

In this context, the purpose of this study is to compare the efficiency of non-resorbable membrane versus resorbable membrane in guided bone regeneration in atrophic posterior mandible.

Null hypothesis is that there is no significant difference between the pericardium and the d-PTFE membrane.

Aim of the study:

The primary objective of this study is to evaluate and compare clinically, radiographically, and histologically the efficiency of native pericardium porcine collagen membrane (Botiss Jason®) versus d-PTFE non resorbable membrane for horizontal augmentation of alveolar ridge for patients with posterior mandibular atrophy.

Plan of the study:

Study design: This study will be carried out as a randomized controlled clinical trial following CONSORT guidelines.

Study setting:

Eligibility criteria

Twenty partially edentulous patients with horizontal bone deficiency in the posterior mandibular ridge requiring bone augmentation and implant-supported restoration who will be referred to the Periodontal department in the faculty of dentistry at Beirut Arab university, Lebanon, will be included in the protocol. Subjects will be randomly assigned to one of 2 groups: controls (group A:10) who will receive GBRB using d-PTFE barrier, and experimental (group B:10) who will receive GBR using native pericardium collagen membrane. Subjects from both groups will be treated with the selected barrier and the underlying space-making composite graft of xenograft plus autogenous bone to help support the overlying membrane.

Inclusion criteria:

1. Both males and females of age 18 years or older
2. Mandibular posterior atrophic alveolar ridge Required horizontal bone augmentation procedures prior to implant placement.
3. Alveolar bone height suitable for implant placement.
4. Systemically healthy.
5. The capacity to understand and accept the conditions of the study.
6. Continuing participation over at least 1 year of follow-up.

Exclusion criteria

1. Heavy smokers (i.e., 2 or more packs of cigarettes per day);
2. Insufficient oral hygiene
3. Acute local or systemic infection
4. Systemic conditions such as diabetes, hyperparathyroidism, osteoporosis, severe liver or kidney condition, active sinusitis, cancer, and use of immunosuppressive agents or corticosteroids, any autoimmune disorder, and/or bisphosphonate therapy.
5. Pregnancy or the possibility of becoming pregnant during the study; and
6. Addiction to drugs or alcohol

Patients who meet the inclusion criteria will be informed about the objectives and conditions of the study. Each patient will receive written information and provide written informed consent before participation in any study-related procedure. After enrollment, each patient will receive a unique identification number, according to which all data will be recorded. Patients will be blinded and will not know the assigned study group.

Material and methods

Material

- Xenograft*
- Pericardium membrane*
- d-PTFE membrane*
- PGA suture 4-0
- PTFE sutures 4-0

Methods

All the patients will be subjected to the pre surgical phase which include:

1. **Patient history:**
    a. Personal history
    b. Past medical and dental history

2. **Clinical and radiographic examination**
    a. Both extra and intra oral examination will be done
    b. A routine panoramic x-ray for patient selection
    c. A CBCT x-ray for preoperative implant site assessment

3. **Phase 1 therapy:**
    a. Plaque control education:
        i. Diet control (in patient with rampant caries)
        ii. Removal of calculus and root planning
        iii. Correction of restorative and prosthetic irritation factors

---

*

* Jason® Collagen Membrane
* Cytoplast™ Ti-Reinforced Membrane

iv. Excavation of caries and restoration (temporary or final, depending on whether a definitive prognosis for the tooth has been determined and location of caries)

v. Antimicrobial therapy (local or systemic if needed)

b. Each patient will undergo oral hygiene measures such as electronic scaling, polishing and mouthwash usage for a couple days.

4. <u>Surgical phase</u>

a. Patient preparation:

- Extraoral scrubbing with 5% povidone-iodine solution.
- The patient's mouth will be rinsed with a solution of chlorhexidine digluconate 0.2% for 2 minutes.

b. Surgical procedures

STAGE 1

- A local anesthetic will be administered using 4%lidocaine hydrochloride.
- A mid-crestal horizontal incision within the keratinized tissue of the edentulous ridge.
- A vertical incision will be made to coronally advance the flap.
- A periosteal release of the flap will be performed.
- A dissection will be made to remove the tension and muscle fibers in the flap in order to have a tension free and a coronally advanced flap.
- Cortical perforations will be made with #8 round bur.
- 8-mm tenting screws will be placed with 3 mm incorporated into the bone.
- Bone harvesting using a bone scraper.
- Creation of 50:50 bone mixtures of xenograft and autogenous bone placement
- Lingual fixation of ti-reinforced d-PTFE membranes (cytoplast ti-250xl; osteogenics biomedical) in group A or fixation of pericardium native collagen membrane (jason membrane) in group B.
- Filling and adaptation of the biomaterial mixture under the membrane.
- Buccal-side fixation using two or three mini-screws (pro-fix membrane fixation screws)

- Free-tension primary closure using double-line suturing by PTFE (4-0) sutures, and PGA sutures (4-0 and 6-0)
- Written postoperative instructions and medications will be given to the patients. These include amoxicillin 500 mg tablets, hydrocodone/APAP 10/325, 0.12% chlorhexidine solution, and ibuprofen 600 mg, chlorhexidine gluconate mouth rinse (0.12% t.i.d.), and topical chlorhexidine 4 times per day applied to the surgical site.

CLINICAL EVALUATION

1. Swelling will be rated on a 0–3 scale (0, none; 1, minor; 2, moderate; 3, severe)
2. Healing of tissues: will be evaluated by the presence or absence of pus, color of overlying mucosa, and presence or absence of dehiscence within the flaps.
3. Pain was evaluated according to the Visual Analogue Scale (VAS), on the 2nd, 7th and 14th postoperative days (Coulthard, et al., 2014)
4. Paresthesia was evaluated according to the Two Point Discrimination Test (TPD) (Meshram, et al., 2013) on the 4th, 7th and 14th postoperative days

RADIOGRAPHIC ASSESSMENT:

- CBCT will be done preoperatively, immediate postoperative and 6 months postoperative.
- The buccolingual dimension will be recorded.

STAGE 2

- After 6 months, all treated sites will be reopened for barrier removal in group A and screw removal in group B and implant placement.
- Bony tissue biopsies were taken using a 3-mm-diameter trephine bur at the sites of implant placement.
- A unique identification number will be assigned to each biopsy specimen to blind the single operator who performed all histological and histomorphometric analyses.

- After two to three more months, the stage-two surgery will be performed, and the case will be referred to the restorative dentist for the final restoration.

HISTOLOGICAL AND HISTOMORPHOMETRIC ANALYSES

- Bone biopsies will be fixed in 10% (v/v) phosphate-buffered formalin followed by decalcification.
- After decalcification, the samples will be dehydrated in a graded series of alcohol baths and embedded in paraffin.
- Histological sections 5-µm-thick will be prepared using the microtome (Microm International GmbH, Heidelberg, Germany) and stained with hematoxylin/eosin to display cytoplasmic, nuclear, and extracellular matrix features.
- The ImageJ software (U.S. National Institutes of Health, Bethesda, Maryland) will be used to perform histomorphometric analyses.
- To this end, careful microscopic evaluation of each entire biopsy will be measured:
    - bone tissue area (B.Ar)
    - graft material area (Mat. Ar),
    - soft tissue area (St.Ar),
    - All variables will be expressed relative to the total area (Tot.Ar) as percentage.

Ethical guidelines:

Ethical research committee approval

Approval of the ethical committee of the faculty of dentistry, Beirut Arab university, Lebanon. Must be obtained prior to the study.

Informed consent:

The objectives, risks and benefits of the study are to be explained to the patient s and a signed informed consent is to be required before the treatment can commence.

Participants safety

Biosafety principles are mandatory during the entire treatment procedures. Patients are informed about all the possible clinical and or adverse outcomes and they will be required to be reported if any of them occur on spot.

References:

- Ernie, Maduratna, Setyawati., Nahdhiya, Amalia, Puspita, Klana. Concise review: Periodontal tissue regeneration using pericardium membrane as guided bone regeneration.. (2020). doi: 10.1063/5.0036635

- Ferraz MP. Bone Grafts in Dental Medicine: An Overview of Autografts, Allografts, and Synthetic Materials. Materials. 2023 May 31;16(11):4117 .

- Ghensi P, Stablum W, Bettio E, Soldini MC, Tripi TR, Soldini C. Management of the exposure of a dense PTFE (d-PTFE) membrane in guided bone regeneration (GBR): a case report. Oral Implantol (Rome). 2017;10(3):335-342. Published 2017 Nov 30. doi:10.11138/orl/2017.10.3.335.

- Helmi MF, Huang H, Goodson JM, Hasturk H, Tavares M, Natto ZS. Prevalence of periodontitis and alveolar bone loss in a patient population at Harvard School of Dental Medicine. BMC Oral Health. 2019 Dec;19:1-1 1.

- Jonasson G, Skoglund I, Rythén M. The rise and fall of the alveolar process: Dependency of teeth and metabolic aspects. Archives of oral biology. 2018 Dec 1;96:195-200 2.

- Jéssica, Suzuki, Yamanaka., Ana, Clara, Oliveira., Ana, Raquel, Fernandes, Bastos., Emanuel, M., Fernandes., Rui, L., Reis., Vitor, M., Correlo., Antonio, Carlos, Shimano. Collagen membrane from bovine pericardium for treatment of long bone defect.. Journal of Biomedical Materials Research Part B, (2022). doi: 10.1002/jbm.b.35148.

- Kameda T, Ohkuma K, Oka S. Polytetrafluoroethylene (PTFE): A resin material for possible use in dental prostheses and devices. Dent Mater J. 2019 Feb 8;38(1):136-142 .

- Qiang Guo, Yan Huang, Mengdi Xu, Qinglin Huang, Jinxue Cheng, Shiwen Yu, Yuxin Zhang, Changfa Xiao. PTFE porous membrane technology: A comprehensive review. Journal of Membrane Science. Volume 664, 2022, 121115, ISSN 0376-7388 .

- Ren Y, Fan L, Alkildani S, et al. Barrier Membranes for Guided Bone Regeneration (GBR): A Focus on Recent Advances in Collagen Membranes. Int J Mol Sci. 2022;23(23):14987. Published 2022 Nov 29. doi:10.3390/ijms232314987

- Soldatos NK, Stylianou P, Koidou VP, Angelov N, Yukna R, Romanos GE. Limitations and options using resorbable versus nonresorbable membranes for successful guided bone regeneration. Quintessence International. 2017 Feb 1;48(2) 3.

- Sasaki JI, Abe GL, Li A, et al. Barrier membranes for tissue regeneration in dentistry. Biomater Investig Dent. 2021;8(1):54-63. Published 2021 May 20. doi:10.1080/26415275.2021.1925556

- Tang G, Liu Z, Liu Y, et al. Recent Trends in the Development of Bone Regenerative Biomaterials. Front Cell Dev Biol. 2021;9:665813 .

- Toscano N, Shumaker N, Holtzclaw D. The art of block grafting, a review of the surgical protocol for reconstruction of alveolar ridge deficiency. J Implant Adv Clin Dent 2010;2:45–66 .

- Tristan, Gueldenpfennig., Alireza, Houshmand., Stevo, Najman., Sanja, Stojanović., Tadas, Korzinskas., Ralf, Smeets., Martin, Gosau., Jens, Pissarek., Steffen, Emmert., Ole, Jung., Ole, Jung., Mike, Barbeck. The Condensation of Collagen Leads to an Extended Standing Time and a Decreased Pro-inflammatory Tissue Response to a Newly Developed Pericardium-based Barrier Membrane for Guided Bone Regeneration.. in Vivo, (2020). doi: 10.21873/INVIVO.11867

- Tsuchida S, Nakayama T. Recent Clinical Treatment and Basic Research on the Alveolar Bone. Biomedicines. 2023 Mar 10;11(3):843 4.

- Waleed, Mohamed, Abbas., D., A., Khalik. Horizontal Ridge Augmentation of the Atrophic Maxilla Using Pericardium Membrane Versus Titanium Mesh: A Clinical and Histologic Randomized Comparative Study.. International Journal of Oral & Maxillofacial Implants, (2023). doi: 10.11607/jomi.9715

- Windisch P, Orban K, Salvi GE, Sculean A, Molnar B. Vertical-guided bone regeneration with a titanium-reinforced d-PTFE membrane utilizing a novel split-thickness flap design: a prospective case series. Clin Oral Investig. 2021 May;25(5):2969-2980. doi: 10.1007/s00784-020-03617-6. Epub 2020 Oct 10. PMID: 33040203; PMCID: PMC8060182.