CORPUS PUBLISHERS

Open Access Journal of Dental and Oral Surgery (OAJDOS)

ISSN: 2833-0994

Volume 4 Issue 1, 2023

Article Information

Received date : December 26, 2022

Published date: January 09, 2023

*Corresponding author

Ricardo Lillo E, Universidad Mayor, School of Dentistry, Santiago de Chile, Email: ricardo.lillo@umayor.cl

DOI: 10.54026/OAJDOS/1050

Keywords

Peri-implantitis, peri-implant bone regeneration, peri-implant defect, peri-implant surgical treatment, bone graft, bone substitute, barrier membranes



Research Article

# Current Regenerative Surgical Approaches for the Treatment of Peri-implantitis: A Systematic Review

**Francisca C Rivera Cornejo, Loreto B Torres Sánchez, Ricardo Lillo E* and Felipe Marti C**

*Buco Maxillofacial Implantology, Mayor University, Santiago 2022, Chile*

## Abstract

The treatment of peri-implantitis is a significant challenge due to the various strategies proposed in the literature, involving different types of grafts and membranes in the regenerative surgical technique.

**Purpose:** The objective of this review is to describe the different regenerative surgical techniques currently used to treat peri-implant defects and their efficacy.

**Materials and Methods:** Literature in the Pubmed and Scopus databases was evaluated to rescue ECCAs that described regenerative surgical treatment for peri-implantitis. The inclusion criteria included patients with at least one osseointegrated implant affected by a pathological condition compatible with the definition of peri-implantitis, describing a clinical intervention aimed at regenerative surgical treatment of the condition, with a minimum follow-up period of 6 months. . The Cochrane Collaboration tool for risk of bias assessment was used and the synthesis of the results was done by means of a tabulation.

**Results:** A total of 11 RCTs were included, taking into account clinical and radiographic parameters to later evaluate the efficacy of regenerative surgical therapy for peri-implant bone defects.

**Conclusion:** It was shown that regenerative surgical therapies for the treatment of peri-implantitis were effective, achieving an improvement in clinical and radiographic parameters. Results were determined against the background of varying definitions of peri-implantitis and study heterogeneity. For future RCTs, it is necessary to unify the definition and the initial clinical and radiographic parameters of peri-implant disease to achieve homogeneity of the studies.

## Introduction

Dental implants are considered one of the treatments of choice to replace missing teeth in edentulous patients. Its efficacy has been demonstrated based on high survival rates, predictable long-term results, and decreased complication rates [1]. However, the incidence of aesthetic, biological and technical complications continues to be high [1-2]. Biological complications that affect osseointegrated implants are of great clinical interest, including mucositis and peri-implantitis. Although both are caused by bacteria and present an inflammatory lesion, mucositis only affects soft tissues, while peri-implantitis also affects peri-implant bone, causing its progressive loss [3]. Various studies indicate that the success rate of dental implants in Chile is calculated to be between 91% and 98%. It should be noted that these studies had an observation period of between 2 and 5 years, which we can classify as short-term follow-up. medium term [4-6]. This correlates with reported worldwide success rates that vary from 89% to 99% [7,8]. Peri-implantitis is defined as a pathological condition associated with bacterial plaque that occurs around peri-implant tissues, characterized by inflammation of the peri-implant mucosa and progressive loss of supporting bone tissue. These signs are detected through clinical and radiographic parameters, which are finally those necessary for the diagnosis of the disease. Commonly, clinical parameters include gingival inflammation, bleeding on probing; with or without suppuration, increased probing depth, and radiographic bone loss [9]. However, despite the fact that this is widely described in the literature, in the different studies there are certain discrepancies based on the specific diagnostic criteria to define peri-implantitis as such, which is also linked to the wide range of prevalence of the disease. which according to Derks and Tomasi ranges from 1 to 47% [10]. Based on the above, the Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions 2018, proposes the diagnosis of peri-implantitis in situations in which there are no data from previous explorations, based on the presence of bleeding and/or suppuration on probing. careful, PS greater than or equal to 6mm, bone level greater than or equal to 3mm apical to the most coronal portion of the intraosseous component of the implant or to the smooth rough interface of the implant [11,12].

There are numerous factors that contribute to the etiology of peri-implantitis, including: residual subgingival cement, incorrect implant placement, and the absence of attached gingiva. As well as a previous history of peri-implantitis, poor plaque control and smoking [13-16]. The keratinized mucosa is considered a fundamental structure for the stability of peri-implant tissues, as supported by studies that show that increasing keratinized tissues improves peri-implant health, reduces mucosal inflammation and results in less marginal bone loss around the implants [17]. There are consistent scientific bases that support that there is a greater risk of generating peri-implantitis in patients with a history of chronic periodontitis, poor plaque control and without regular maintenance care after implant treatment. This is indicated by Schwarz et al. in a bibliographic review carried out in 2017, which also indicates that smoking and the presence of diabetes in patients undergoing implant therapy, as risk factors or indicators for peri-implantitis, are not conclusive [9]. Delving into the bone morphology of peri-implant defects, they can be classified as infrabony, suprabony, and a combination of both. Monje et al., 2019 proposes the following classification based on the morphology and severity of peri-implant bone defects [12]:

a. **Class I:** Infrabony defects (Class Ia: Buccal (vestibular) dehiscence, Class Ib: 2-3 wall defect, Class Ic: Circumferential defect),
b. **Class II:** Supracrestal/horizontal defect)
c. **Class III:** Combined defects (Class IIIa: Buccal dehiscence + horizontal bone loss, Class IIIb: 2-3 wall defect + horizontal bone loss, Class IIIc: Defect circumferential + horizontal bone loss (Figure 1).

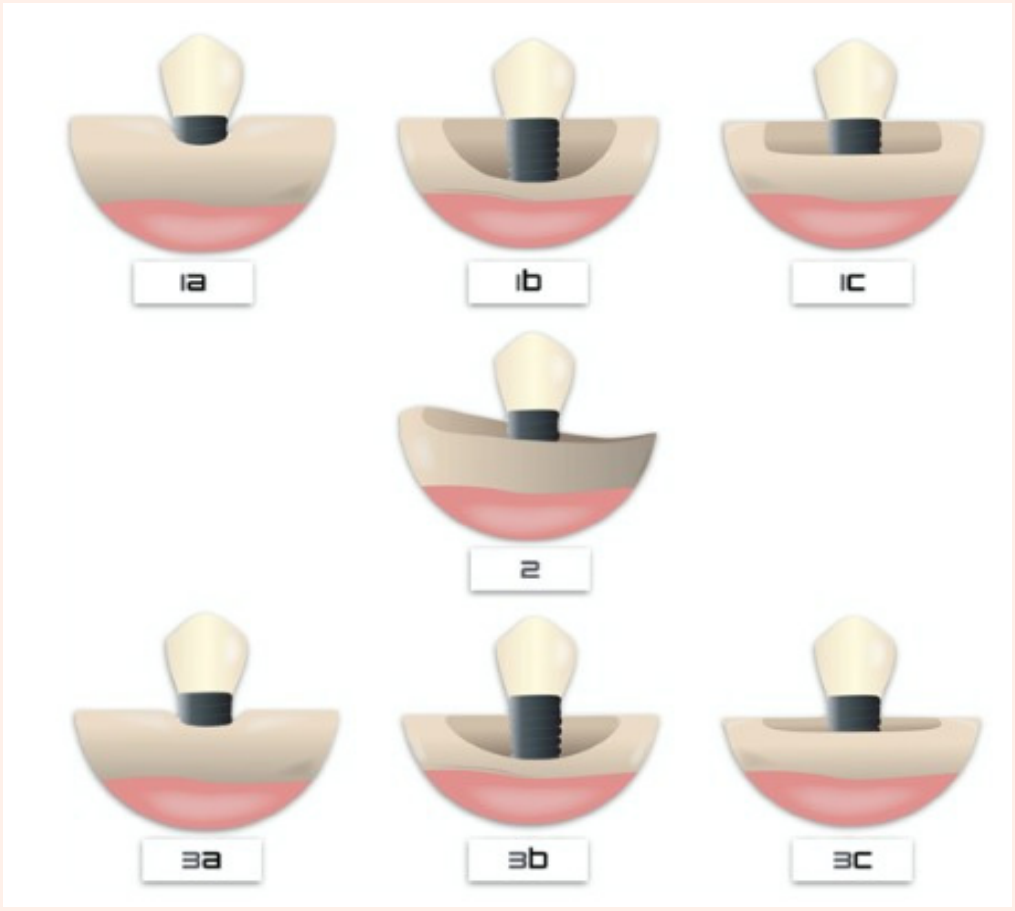


**Figure 1:** Combined defects of horizontal bone loss by Monje A. et al. (2019)

It is important to highlight that the most prevalent defect is the infrabony, which generally presents with a vestibular dehiscence, and both at the patient level and at the implant level, type Ib is the most prevalent with a percentage of 87 and 55% respectively [12]. For the treatment of peri-implantitis, different solutions are proposed, such as the non-surgical technique, resective, regenerative and combined surgical techniques, with the aim of stopping the progression of the disease and bone resorption, by removing bacterial infection and controlling inflammation of the implant. fabric [18] . However, procedures common to all the techniques are: debridement, which consists of the removal of granulomatous tissue, the removal of soft biofilm from the supracrestal aspects of the implant, and decontamination of the implant surface under numerous protocols [19]. Based on the above, when evaluating the factors to take into account for selecting the type of treatment are the amount of bone loss, the intra-surgical anatomy of the bone defect, the graft material and the surface of the implant [20]. It is worth mentioning, then, that the treatment of peri-implantitis can be based on the type of morphology of the bone defect [21], and can be considered as a critical factor to determine a successful result under a regenerative approach. Furthermore, the number of residual walls of the bone defect, the angle, shape and depth of the bone defect serve as valid diagnostic tools for the predictability of guided tissue regeneration [21].

Removal of existing inflamed granulomatous tissues and decontamination of the implant surface is essential in any regenerative procedure. For this, it uses a combined approach of devices such as curettes, titanium brushes, implantoplasty drills, and lasers such as Er:yag and $CO_2$ [22]. In the literature there is a great variety of regenerative surgical techniques translated into what type of graft and what type of membrane to use to regenerate the defect. The use of grafts of the autologous, alloplastic, xenograft, etc. type is described. And I get the use of resorbable and non-resorbable membranes. Despite the fact that surgical protocols have better clinical results, they remain unpredictable and limited, without an acceptable general consensus [21,22]. In addition , regarding the type of regenerative technique, there is not enough evidence to decide which is the best regeneration material and whether barrier membranes offer added value or even whether submerged techniques are preferable [20]. For this reason, the PICO question of this systematic review was: What are the regenerative surgical treatments currently described, and their efficacy for the treatment of peri-implant bone defects in patients diagnosed with peri-implantitis?

## Materials and Methods

This systematic review was conducted using the PRISMA ( Preferred Reporting Items of Systematic reviews and Meta-Analyses) guideline to ensure study quality. We used the Cochrane Collaboration Tool for quality and risk of bias assessment of the included studies , and synthesis of the results was done by tabulation.

## Study selection criteria

To be included in this review, the studies had to have an evaluation of the outcome of the regenerative surgical treatment of peri-implant defects, based on clinical and radiographic parameters before and after the intervention, in order to assess the efficacy of the treatment.

**Exclusion Criteria:** All publications that do not meet the inclusion criteria are excluded from the review. To do this, we use filters in the databases.

**Inclusion criteria:**
Study type: randomized controlled clinical trial.
Publication date: from the year 2012 to the year 2022
Language: English and/or Spanish.
Word "peri-implantitis" and/or "regenerative" in the title or abstract.

In addition, they had to meet the following requirements:

a. Patients with at least one osseointegrated implant affected by a pathological condition compatible with the definition of peri-implantitis.
b. Describe a clinical intervention that aims at the regenerative surgical treatment of the condition.
c. Minimum follow-up period of 6 months.

## Search Strategy

A bibliographic search was carried out from 2012 to 2022 in the PubMed and Scopus databases, to find relevant literature regarding regenerative surgical treatments for peri-implantitis, using the descriptors for Health Sciences and the Boolean operators that included the following terms: ( ("surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR (" surgical"[All Fields] AND "treatments"[All Fields]) OR "surgical treatments"[All Fields]) AND ("peri implantitis"[MeSH Terms] OR "peri implantitis"[All Fields] OR ("peri"[ All Fields] AND "implantitis"[All Fields]) OR "peri-implantitis"[All Fields]) AND "randomized controlled trial"[Publication Type] AND "regenerative"[All Fields]) AND ((randomizedcontrolledtrial[Filter]) AND (2012:2022[pdat])). The systematics of the search strategy are summarized in Table 1. The bibliographic search yielded 75 results. Two authors (LT and FR) independently reviewed each of them and selected the articles based on the aforementioned criteria, discarding 5 articles for being duplicates, 56 for not corresponding to a randomized controlled clinical trial, and 3 for not presenting the word "peri-implantitis" and/or "regenerative" in the title and/or in the abstract. Finally, 11 studies were included for this systematic review exemplified in the PRISMA flowchart (Figure 2).

**Table 1:** Systematic of search strategy.

| | |
|---|---|
| Focus question | ¿Which are the currently described surgical regenerative treatments and their efficacy for the treatment of periimplant bone defects in patients diagnosed with periimplantitis? |
| Search strategy | |
| Population | Patients diagnosed with periimplantitis |
| Intervention or exposure | Debridement, decontamination and regeneration. |
| Comparison | Surgical regenerative treatments |
| Outcome | Efficacy of surgical regenerative treatments ( clinically and radiographically) |
| Database search | |
| Electronic | PubMed and Scopus |
| Selection criteria | |
| Inclusion criteria | Randomized controlled clinical trial published between 2012 and 2022, in English and/or Spanish with the word periimplantitis and/or regenerative in the title or abstract. Patients with at least one Osseo integrated dental implant, affected by a pathological condition compatible with the definition of periimplantitis, that describes a clinical intervention that aims to a surgical regenerative treatment with a minimum following period of 6 months |
| Exclusion criteria | All those who do not meet the inclusion criteria. |

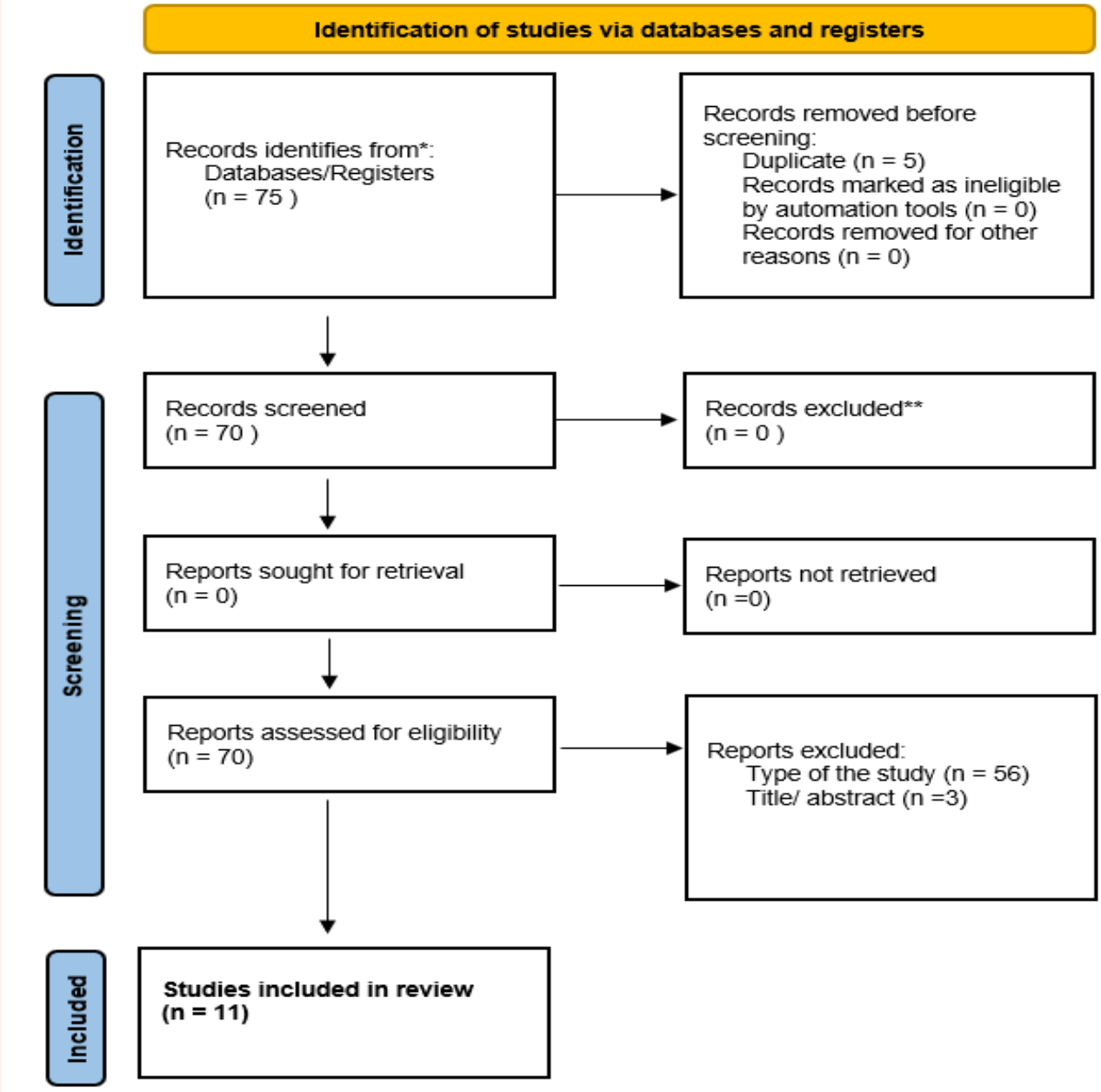


**Figure 1:** *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

### Data extraction

The following data were sought and recorded by the two authors (LT and FR) in a results table: Study title, first author's last name, study follow-up period, number of patients, presence of blinding, control group, test group. and definition of peri-implantitis. In addition, the following variables were recorded: type of filling material, type of membrane (if applicable), disinfection and debridement protocol. To record the results of the treatment, the following clinical and radiographic parameters were considered: probing depth (PS), bleeding on probing and/or suppuration (BoP and/or Sup), clinical attachment level (NIC), gingival recession, type of defect, radiographic bone level. Based on the change of these parameters with respect to the beginning, the improvement of the disease and the effectiveness of the treatment are justified.

## Assessment of risk of bias and quality

Quality and risk of bias assessment was performed on all articles included in this review by the two authors independently. The Cochrane Collaboration tool for risk of bias assessment was used. The following bias-causing parameters were addressed: Random sequence generation (selection bias), Concealment of allocation sequence (Selection bias), Blinding of participants and personnel (Performance bias), Blinding of assessors (Performance bias). detection), incomplete outcome data (attrition bias) selective reporting of outcomes (reporting bias). The risk of bias advice for each study is summarized in Table 2. For quality assessment we included examiner blinding, examiner calibration (measurement bias), standardization of radiographic advice (measurement bias), attrition bias, and reporting bias (Table 3).

**Table 2:** Risk of bias assessment.

| Study Author | Selection Bias | | Performance bias | Detection bias | Attrition bias | Reporting bias | Final determination of bias |
|---|---|---|---|---|---|---|---|
| | Random sequence generation | Allocation sequence hiding | Blinding of participants and personnel | Blinding of assessors | Incomplete outcome data | Selective reporting | |
| Chin-Wei Wang [29] | HIGH | HIGH | LOW | LOW | LOW | LOW | LOW |
| Catrine Isehed [30] | LOW | UNCLEAR | LOW | LOW | LOW | LOW | LOW |
| Sila Cagri Isler [27] | LOW | LOW | LOW | LOW | LOW | LOW | LOW |
| Beatriz de Tapia [25] | LOW | LOW | LOW | LOW | LOW | LOW | LOW |
| Hamidreza Arab [34] | LOW | UNCLEAR | LOW | LOW | LOW | HIGH | HIGH |
| Ahmad Aghazadeh [35] | LOW | LOW | LOW | LOW | LOW | LOW | LOW |
| Frank Schwarz [32] | LOW | LOW | LOW | LOW | HIGH | LOW | HIGH |
| Frank Schwarz [33] | LOW | LOW | LOW | LOW | HIGH | LOW | HIGH |
| Markus Schlee [31] | HIGH | LOW | LOW | LOW | LOW | LOW | LOW |
| Sila Cagri Isler [28] | LOW | LOW | LOW | LOW | LOW | LOW | LOW |
| Roos-Jansaker [26] | HIGH | UNCLEAR | LOW | LOW | HIGH | LOW | HIGH |

| Study Author | Examiner`s blinding | Examiner calibration | Standardized radiographic assessment | Attrition bias | Notification bias |
|---|---|---|---|---|---|
| Chin-Wei Wang [29] | + | + | + | - | - |
| Catrine Isehed [30] | + | - | - | - | - |
| Sila Cagri Isler [27] | + | + | + | - | - |
| Beatriz de Tapia [25] | + | + | + | - | - |
| Hamidreza Arab [34] | + | - | + | - | + |
| Ahmad Aghazadeh [35] | + | + | - | - | - |
| Frank Schwarz [32] | + | + | - | + | - |
| Frank Schwarz [33] | + | + | - | + | - |
| Markus Schlee [31] | + | + | - | - | + |
| Sila Cagri Isler [28] | + | - | + | - | - |
| Roos-Jansaker [26] | + | - | + | + | - |

## Results

The initial search included 75 potentially relevant studies. Of which 4 were removed due to finding duplicates. In addition, 56 were excluded because they did not correspond to a randomized controlled clinical trial and 3 because they did not present the word "peri-implantitis" and/or "regenerative" in the title and/or abstract. Finally, 11 studies were included for this systematic review. Table 4 summarizes the characteristics of the interventions for the treatment of peri-implantitis that were discussed in the RCTs. The 11 RCTs defined peri-implantitis in different ways. Most determined the diagnosis of peri-implantitis as bone loss (PO) of 2 to 3 mm or more and/or at least 2 to 3 exposed implant threads. Only one study defined PO as greater than 30% of the exposed implant surface [25]. In turn, all definitions are accompanied by an increase in probing depth (PS) ranging from 5 to 6 mm or more. One of the studies does not refer to PS in the definition of peri-implantitis [26] and two only consider the existence of a concomitant increased PS [27,28]. Regarding the clinical parameter of bleeding on probing (BoP) and/or suppuration (Sup), both parameters are present in the definitions of all the ECCAs. Regarding debridement therapy, ultrasound is included in four of the ECCAs [29,30,25,31], curettes of different materials (titanium, plastic or with a carbon fiber tip) in all the studies, except for two studies [26,29]. Additionally, the use of a titanium brush was included in one of the studies [25], which precisely studied its complementary effect in debridement therapy.

**Table 4:** Characteristics of regenerative surgical therapies from randomized controlled clinical trials.

| Study | Patients | Definition of periimplantitis | Debridement therapy | Decontamination therapy | Regenerative therapy | Follow up time |
|---|---|---|---|---|---|---|
| Chin-Wei Wang [29] | 24 | BL 2 exposed threads or 2mm, PD ≥ 5mm, BoP and/or Sup in at least 1 implant | Ultrasonic device | Er:yag laser or nothing* | Mineralized allograft (MinerOssÒ), demineralized fibers (GraftonÒ), Acellular dermal matrix (Alloderm GBRÒ) | 1 year |
| Catrine Isehed [30] | 26 | BL ≥ 3mm, PD≥ 5mm, BoP and/or Sup | Ultrasonic device, titanium curettes, Superfloss | Saline irrigation | Enamel matrix derivate 0.3mL (Emdogain) or nothing* | 1 year |
| Sila Cagri Isler [27] | 52 | BL ≥ 2mm, BoP and/or Sup with or without concomitant PD | Titanium curettes | Saline - soaked cotton gauzes | Cancellous xenograft (Bio-OssÒ) y L-PRF membrane or Collagenous membrane (BioGuideÒ)* | 1 year |
| Beatriz de Tapia [25] | 30 | BL ≥ 30% of the implant surface PD ≥ 6mm, BoP and/or Sup | Curettes, Ultrasonic device with Teflon-coated tips, with or without titanium brushes | Irrigation with 3% hydrogen peroxide | Beta tricalcium phosphate and hydroxyapatite (BoneCeramicÒ), Collagen membrane (CytoplastÒ) | 1 year |
| Hamidreza Arab [34] | 10 | BL ≥ 3 exposed threads or 2mm, PD > 5mm | Carbon fiber curettes | Profijet and saline irrigation | Xenograft (Bio-OssÒ), collagen membrane (T-BarrierÒ) or porous titanium granules (PTGs, NatixÒ Tigran tech)* | 6 months |
| Ahmad Aghazadeh [35] | 45 | BL ≥ 3mm, PD ≥ 5mm, BoP and/or Sup | Titanium curettes | Irrigation with 3% hydrogen peroxide and Sterile saline | Autograft from the mandibular ramus region or Xenograft (Bio-OssÒ), collagen membrane (OsseoguardÒ)* | 1 year |
| Frank Schwarz [32] | 24 | BL > 3mm subosseous and ≥1mm supraosseous, PD > 6mm, BoP and/or Sup | Plastic curettes | Er: yag laser or cotton pellets soaked in sterile saline* | Cancellous xenograft (Bio-OssÒ), collagen membrane (BioGuideÒ) | 2 years |
| Frank Schwarz [33] | 17 | BL > 3mm subosseous and ≥ 1mm supraosseous, PD > 6mm, BoP and/or Sup | Plastic curettes | Er: yag laser or cotton pellets soaked in sterile saline* | Cancellous xenograft (Bio-OssÒ), collagen membrane (BioGuideÒ) | 4 years |
| Markus Schlee [31] | 24 | BL ≥ 3mm, PD≥ 6mm, BoP and/or Sup | Ultrasonic device and/or Curettes. | Electrolytic method and/or Airflow Plus Powder in spray* | Autograft from the mandibular ramus region, Xenograft (Bio-OssÒ), Collagen membrane (BioGuideÒ) | 6 months |
| Sila Cagri Isler [28] | 41 | BL ≥ 2mm, BoP and/or Sup with or without concomitant PD | Titanium curettes | Ozone 2100 ppm or Irrigation with sterile saline* | Cancellous xenograft (Bio-OssÒ) with chopped L-PRF membrane, L-PRF membrane | 1 year |
| Roos-Jansaker [26] | 25 | BL ≥ 3 exposed threads or 1.8 mm, BoP and/or Sup | Does not specify | 3% hydrogen peroxide and sterile saline | Porous phycogenic hydroxyapatite (AlgiporeÒ), with or without collagen membrane (OsseoquestÒ)* | 5 years |

* Topical compared in each randomized controlled clinical trial.
- BL: Bone Loss //PD: Probing Depth

Regarding decontamination therapy, various techniques are used such as Er:Yag laser, irrigation or saline soaked gauze, irrigation with 3% hydrogen peroxide, electrolytic method, AirFlow plus spray powder, profijet and ozone. Three studies used the Er:Yag laser [29,32,33], only one used ozone [28], one the electrolytic method [31] and one the profijet [34]. In addition, two used serum as the only decontaminant [27,30] and three 3% hydrogen peroxide [25,26,35]. Within the studies, different methods of decontamination prior to regenerative therapy of peri-implant bone defects are compared. For example, regarding the Er:yag laser, one of the studies wanted to compare its use as an aid to regenerative surgical therapy versus using nothing additional [29], while two others compared it versus the use of cotton balls embedded in serum [32,33]. Another decontaminant that was used in surgical therapy was the electrolytic method, comparing its use alone or in conjunction with Airflow spray powder. Finally, a study describes the use of ozone at 2100 ppm compared to irrigation with saline solution [28]. Regarding regenerative surgical therapy as such, most studies use a bone graft or substitute accompanied by a membrane as a barrier. Only one study did not describe the use of a bone substitute or barrier membrane in regenerative therapy. This used Emdogain ®, an enamel matrix derivative, as a filler for bone defects [30]. The other studies used autografts, allografts, xenografts, and beta-tricalcium phosphate (B-TCP) substitutes with hydroxyapatite (HA) or porous phycogenic hydroxyapatite for defect filling. Most of the studies used resorbable collagen membranes as a barrier between the bone substitute and soft tissue. Only one of the studies used L-PRF membrane [27], another used an acellular dermal matrix, composed mainly of bovine collagen and chondroitin sulfate [29]. And as previously mentioned, another did not use any barrier [30]. Some studies referred to the use of a membrane, comparing whether it was used or not, and others comparing different types of membrane; For example, one study questions whether the use of a membrane provides any additional effect, since it compared the use of a bone substitute with or without a collagen membrane [26]. Another of them compared the use of a xenograft in conjunction with a collagen membrane or with an L-PRF membrane [27]. Other studies referred to the type of padding used; for example, one analyzed the use of autograft of the ramus versus xenograft as a bone substitute for the peri-implant defect [35]. Likewise, another compared the use of xenograft with the use of porous titanium granules [34]. On the other hand, only one study used an enamel matrix derivative (Emdogain ) as a *filler for the bone defect , comparing its use or not in regenerative therapy [30].

Thus, the great variety of regenerative therapies used for the treatment of peri-implantitis is evident; however, the focus of this review is not only to review the currently used therapies, but also whether they are effective for the treatment and resolution of the disease. For this, each study identified different variables to later evaluate if the therapy turned out to be effective. Among them are probing depth (PS), bleeding on probing (BoP) and/or suppuration (Sup), clinical attachment level (NIC), gingival recession (RG) and bone level. In most studies, these variables were compared with respect to the baseline and also between the two study groups. In the study by Chin-Wei Wang et al [29], who operated on suprabony, infrabony, and combined defects with mineralized particulate allograft, demineralized fibers, and acellular dermal matrix, and in decontamination therapy added the use of Er;yag laser in the test group. The study showed an improvement in all the parameters in both groups with respect to the baseline, but tending in favor of the test group. And

this obtained a statistically significant difference compared to the control group in the PS. In the study by Isehed et al [30], the effectiveness of the use of enamel matrix derivative was compared, it did not show a decrease compared to PS, and also did not measure CIN or gingival recession. There was a gain with respect to the bone level only in the test group, but this was not statistically significant with respect to the baseline and neither was it between the two groups. The BoP/Sup decreased in both groups without specifying whether or not there was a statistically significant difference. Sila Cagri Isler [27], treated 2- or 3-walled subbony defects with cancellous xenograft and collagen membrane (test group) or L-PRF membrane (control group). It showed an improvement in all clinical and radiographic parameters, including a statistically significant difference for all with respect to the baseline. In addition, there is a statistically significant difference in favor of the test group (use of collagen membrane) with respect to PS and NIC.

In the study by Beatriz de Tapia [25], infrabony defects with 2 or 3 walls were treated with B-TCP and HA together with a collagen membrane. In the debridement therapy, titanium brushes were used (test group), and it was evidenced that there were improvements in all the parameters, finding statistically significant differences with respect to the baseline in both groups in the parameters of PS and BoP and/or Sup. In addition, it was obtained a statistically significant difference in favor of the test group in PS, thus demonstrating the favorable effect that the use of titanium brushes has in reducing this parameter. It is worth mentioning that in this study the level of clinical insertion was not measured. Hamidreza Ahrab [34], compared the use of porous titanium granules vs. the use of xenograft and collagenous membrane. There were statistically significant differences in relation to the baseline in PS, CIN, and bone level; but without differences between both groups, leading to the fact that the porous granules do not show greater efficacy. The gingival recession parameter in this case was not measured. Ahmad Ahazadeh [35], compared the use of xenograft and collagenous membrane vs/s autograft of the branch and collagenous membrane. CIN and gingival recession were not measured variables. Regarding the PS, there was a statistically significant difference with respect to the baseline, and in favor of the xenograft. Likewise, there was also a statistically significant difference in favor of the xenograft with respect to the bone level. BoP and/or Sup decreased in both groups. This demonstrated that the use of xenograft showed better clinical parameters than the use of branch autograft.

Frank Schwarz [32,33], published 2 clinical trials over 4 years, evaluating the use of Er:yag laser (test group) versus serum-embedded cotton swabs (control group) in decontamination therapy for defects combined regenerated with cancellous xenograft and collagen membrane. In the first study [32], after 2 years, there was improvement in all the parameters, but without statistically significant differences with respect to the baseline and between both groups, concluding that the efficacy of the treatment depends on the type of effect. In the second study [33], at 4 years, there was improvement in all parameters except for gingival recession in the control group, which was increased. In this study, it was not possible to measure the effectiveness of the methods because the number of patients decreased over time, leading to only being able to perform a descriptive analysis. Markus Schlee [31] compared the use of the electrolytic method alone or in conjunction with AirFlow plus powder spray for decontamination therapy and only focused on one variable, bone gain. As regenerative therapy, this study used autograft of the branch, xenograft, and a collagen membrane. Although there was a bone gain with statistically significant differences with respect to the baseline in both groups, there was no statistically significant difference between the two groups, assuming that the use of AirFlow powder does not show greater effectiveness when added to the electrolytic method. Sila Cagri Isler [28] used a cancellous xenograft with chopped L-PRF membranes and two as a barrier, and for decontamination therapy, compared the use of ozone v/s serum. In this study, there was improvement in all clinical parameters with statistically significant differences from baseline. However, ozone shows an improvement in bone gain when evidencing a statistically significant difference in favor of it when evaluating the bone level. Lastly, Roos Jansaker [26] compared the use of porous phycogenic hydroxyapatite with or without a collagen membrane. All the parameters improved with respect to the baseline (without a statistically significant difference), with the exception of gingival recession in the group that did not use a collagen membrane, where it was increased; however, this difference was not statistically significant with respect to the baseline and neither compared to the test group. By way of summary, 5 studies compared regenerative therapy [26,27,30,34,35], 5 compared decontamination therapy [28,29,31,32,33], and 1 compared debridement therapy [25]. It is worth mentioning that only one of the studies does not specify the debridement therapy performed (26) . The results of each study are shown in Table 5.

**Table 5:** Results in relation to baseline and between groups.

| Author | Group | Studied therapy | PD | Dif BL | BoP y/o Sup | Dif BL | CAL (clinical attachment level) | Dif BL | Gingival recesion | DIf BL | Bone level | Dif BL | Effectiveness of treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chin-Wei Wang [29] | TG | Laser Er:Yag | Decrease | SSD | Decrease | SSD | Gain | SSD | Not measured | | Gain | W/o SSD | Yes, Improvement off all clinical and X-ray parameters, tending to favor the Er:yag laser |
| | CG | Nothing | Decrease | SSD | Decrease | SSD | Gain | SSD | | | Gain | W/o SSD | |
| | Dif between G | | with SSD in favor of the TG | | W/o SSD between both groups | | W/o SSD between both groups | | | | W/o SSD between both groups | | |
| Catrine Isehed [30] | TG | Derivate of enamel matrix 0.3mL | Remained | - | Decrease | - | Not measured | | Not measured | | Gain | W/o SSD | No, EMG does not generate an additional effect on the parameters of PD, BoP and/or Sup |
| | CG | Nothing | Remained | - | Decrease | - | | | | | Decrease | W/o SSD | |
| | Dif between G | | Without SSD between both groups | | - | | | | | | W/o SSD between both groups | | |
| Sila Cagri Isler [27] | TG | Collagen membrane (CM) | Decrease | SSD | Decrease | SSD | Gain | SSD | Improved | SSD | Gain | SSD | Both work, but the use of the CM has an impact in terms of PD and CAL |
| | CG | L-PRF membrane | Decrease | SSD | Decrease | SSD | Gain | SSD | Improved | SSD | Gain | SSD | |
| | Dif between G | | with SSD in favor of the TG | | W/o SSD between both groups | | with SSD in favor of the TG | | W/o SSD between both groups | | W/o SSD between both groups | | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Beatriz de Tapia [25] | TG | Curettes, Ultrasonic device with teflon-coated tips with titanium brushes | Decrease | SSD | Decrease | SSD | Not measured | | Improved | W/o SSD | Gain | W/o SSD | Yes, Brush use has a favorable effect on PD reduction at 12 months |
| | CG | Curettes, Ultrasonic device with teflon-coated tips without titanium brushes | Decrease | SSD | Decrease | SSD | | | Improved | W/o SSD | Gain | W/o SSD | |
| | Dif between G | | with SSD in favor of the TG | | W/o SSD between both groups | | | | W/o SSD between both groups | | with SSD in favor of the TG | | |
| Hamidreza Arab [34] | TG | Porous titanium granules | Decrease | SSD | Decrease | W/o SSD | Gain | SSD | Not measured | | Gain | SSD | Yes, But the use of porous titanium granules does not show greater efficacy |
| | CG | Collagen membrane + xenograft | Decrease | SSD | Decrease | W/o SSD | Gain | SSD | | | | SSD | |
| | Dif between G | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | | | W/o SSD between both groups | | |
| Ahmad Aghazadeh [35] | TG | Xenograft | Decrease | SSD | Decrease | W/o SSD | Not measured | | Not measured | | Gain | W/o SSD | Yes, Xenograft shows better results than mandibular ramus autograft |
| | CG | Autograft from the mandibular ramus | Decrease | SSD | Decrease | W/o SSD | | | | | Gain | W/o SSD | |
| | Dif between G | | with SSD in favor of the TG | | W/o SSD between both groups | | | | | | with SSD in favor of the TG | | |
| Frank Schwarz [32] | TG | Er:yag laser | Decrease | W/o SSD | Decrease | SSD | Gain | W/o SSD | Improved | W/o SSD | Not measured | | Yes, but the effectiveness is still dependent on the type of defect |
| | CG | Cotton pellets soaked in sterile saline | Decrease | SSD | Decrease | SSD | Gain | W/o SSD | Improved | W/o SSD | | | |
| | Dif between G | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | | | |
| Frank Schwarz [33] | TG | Er:yag laser | Decrease | - | Decrease | - | Gain | - | Improved | - | Not measured | | Number of patients was not enough to see if the methods are effective or not |
| | CG | Cotton pellets soaked in sterile saline | Decrease | - | Decrease | - | Gain | - | Got worse | - | | | |
| | Dif between G | | - | | - | | - | | - | | | | |
| Markus Schlee [31] | TG | Electrolytic method | Does not specify | | Does not specify | | Not measured | | Not measured | | Gain | SSD | Airflow powder does not show greater effectiveness when added to the electrolytic method |
| | CG | Electrolytic method + Airflow Plus powder in Spray | | | | | | | | | Gain | SSD | |
| | Dif between G | | | | | | | | | | W/o SSD between both groups | | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sila Cagri Isler [28] | TG | Ozone+ sterile saline | Decrease | SSD | Decrease | SSD | Gain | SSD | Improved | SSD | Gain | SSD | Yes, Ozone shows an improvement in bone gain compared to sterile saline |
| | CG | Sterile Saline | Decrease | SSD | Decrease | SSD | Gain | SSD | Improved | SSD | Gain | SSD | |
| | Dif between G | | Without SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | with SSD in favor of the TG | | |
| Roos-Jansaker [26] | TG | Collagen membrane | Decrease | W/o SSD | Decrease | | Decrease | W/o SSD | Improved | W/o SSD | Gain | W/o SSD | The use of membrane in conjunction with bone substitute does not increase the predictability or extent of bone fill |
| | CG | without barrier membrane | Decrease | W/o SSD | Decrease | | Decrease | W/o SSD | Improved | W/o SSD | Gain | W/o SSD | |
| | Dif between G | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | W/o SSD between both groups | | |

*SSD: Statistically significant difference // *TG: Test group // *CG: Control group // *Difference between G Difference between Groups // Dif BL: Difference from baseline.

## Discussion

We know that the field of peri-implantitis treatment is relatively new, so when reviewing the literature available today we can find various types of treatments, including various protocols for debridement, decontamination and regeneration. This is evidenced in this systematic review, which sought to determine which regenerative surgical treatments are currently described and their efficacy for the treatment of peri-implant bone defects. It is essential to have an accurate diagnosis of peri-implantitis in order to treat the disease correctly. To determine it, it is necessary to group different clinical and radiographic parameters that are imperative for a correct diagnosis and thus define whether the therapy was effective or not. In the clinical trials included in this review we were able to observe different definitions of the disease. Most studies agree on the presence of bleeding on probing and/or suppuration, accompanied by a PS greater than 5 to 6 mm. However, the two studies carried out by Sila Cagri Isler et al [27,28], do not specify a measurement of PS for the diagnosis of peri-implantitis, and it may not be present. Therefore, the diagnosis of peri-implantitis is only defined by bone loss and the presence of BoP/Sup. The same occurs in the study carried out by Roos-Jansaker et al [26]. We believe that probing depth is one of the most relevant clinical parameters when defining peri-implantitis; as mentioned in the new classification of periodontal and peri-implant diseases, of the Scientific Journal of the Spanish Society of Periodontics for the year 2018 [11].

This leads to the existence of heterogeneity when classifying peri-implant disease and with it a possible alteration when defining whether the treatment was effective or not. For this reason, we consider it important to unify the diagnosis of peri-implantitis. In relation to this, in 2018 the American Academy of Periodontics (AAP) and the European Federation of Periodontics (EFP) developed a classification system for periodontal and peri-implant pathologies and alterations [11]. It defines peri-implantitis as:

a. Presence of bleeding and/or suppuration after careful probing
b. Increased probing depth compared to previous explorations. In areas with peri-implantitis, probing depth is correlated with bone loss and is therefore an indicator of the severity of the disease.
c. Presence of bone loss beyond changes in crestal bone levels resulting from initial bone remodeling. It is important to note that the rate of progression of bone loss can vary between patients.

The consensus group paid special attention to those situations in which there are no data from previous examinations. In these cases, the group agreed that the diagnosis of peri-implantitis could be based on a combination of:

a. Presence of bleeding and/or suppuration after a delicate probing.
b. Probing depth ≥6 mm.
c. Bone levels located ≥3 mm apical to the most coronal part of the intraosseous component of the implant.

Regarding bone loss, it is present in all definitions of peri-implantitis, but among the studies there are various ways to record it, either clinically or radiographically. It should be noted that the way of measuring it does not coincide between some studies and even others do not specify it. There are studies that diagnose peri-implantitis with a bone loss greater than 2 mm and others with a value greater than 3 mm. Likewise, some studies, to diagnose the disease, consider necessary a bone loss evidenced by the exposure of 2 or 3 threads of the implant or greater than 30% of its surface. The most common radiographic measurement is from the implant platform to the bottom of the defect. It is noteworthy that one study determines the intraoperative defect by measuring from the bone crest to the bottom of the defect, which may cause the peri-implant defect to be underestimated (30) . We consider it important to standardize the radiographic measurement of bone loss so that the evaluation of the efficacy of regenerative therapy is not favored by an incorrect measurement. Some studies also classified the type of operated defect. Including, for example, only 2- or 3-walled infrabony defects. Others did not differentiate the type of defect to be operated on, including suprabony, infrabony, or combined defects. And others simply did not determine the morphology of the defect, focusing only on radiographic bone loss measured in millimeters between two arbitrary points. This is important given that the type of defect is directly related to the type of treatment and the success of regenerative surgical therapy, being much more favorable, for example, the presence of infrabony defects with two to three walls than a suprabony or suprabony defect. horizontal. For this reason, we consider it relevant that in a randomized controlled clinical trial where the type of peri-implant regenerative treatment is evaluated, the type of defect to be intervened is clearly mentioned.

For a correct treatment it is necessary to have the stages of debridement and decontamination, prior to surgical intervention. Regarding debridement, most studies agree on the use of curettes, whether plastic or titanium, and the use of ultrasound. This is favorable because it implies a certain "unification" regarding this part of the treatment in the different studies.

As for decontamination therapy, there are various protocols. In the clinical trials included in this systematic review, there is a study where bone gain was greater in the group where ozone was used, but they do not specify the type of bone defect or how it was measured, which we consider may lead to a bias in the study Outcome.

Regarding follow-up time, the studies included in this review range from 6 months to 5 years. We believe that the follow- up time is an important factor when evaluating the effectiveness of regenerative surgical therapy, since the results vary over time and the success of the therapy is directly related to compliance with maintenance therapy.

Regarding advice on the quality and risk of bias of the studies included in this systematic review, it should be noted that examiner blinding was present in all studies. This helps to avoid detection bias when examining the results. The examiner's calibration is important to deliver results that are most consistent with reality, without generating errors that can falsify the results, either positively or negatively, and thus avoid measurement bias. In this case four studies did not calibrate the examiner.

Regarding the standardization of radiographic advice, 6 of the 11 studies individualized the taking of radiographs, which means that in those studies where it was not standardized, the results could be altered, due to the change in the angulation of the cone with the that the initial and control radiographs were taken, leading to a possible measurement bias.

Regarding attrition bias, associated with incomplete outcome data, three studies presented a high risk of bias, which leads us to think that the reasons for the missing data are related to the true result.

Lastly, notification bias, referring to incomplete selective notification, is evidenced in two studies; because there were reported results that did not have a baseline measurement.

In this systematic review, we consider that detection bias, measurement bias, attrition bias, and notification bias are the most relevant when determining the overall risk of bias for each study. Based on this, 4 studies were defined as having a high risk of bias [26,32,33,34].

## Conclusion

In this review, it was shown that the different regenerative surgical therapies for the treatment of peri-implant defects were effective, achieving an improvement in the clinical and radiographic parameters before and after the intervention. However, it is important to highlight that due to the heterogeneity of the studies regarding the definition of peri-implantitis, the type of defect and the way it is measured, it is not possible to determine the superiority between one regenerative therapy and another. This is why we consider it important to take into account the following recommendations in future clinical trials in order to objectify the effectiveness of the therapy, achieving homogeneity in the studies.

i. Determine the diagnosis of peri-implantitis based on the latest classification of periodontal and peri-implant diseases.

ii. Determine the morphology of the defect to intervene. For this, we consider the classification of Monje eQt al [28], useful and complete , which classifies the morphology and severity of peri-implant bone defects.

iii. Individualize the taking of initial and control radiographs.

iv. Measure the peri-implant defect between two standardized points. We propose taking the implant platform as the coronal reference point and the bottom of the defect as the apical point.

v. Specify intervals of maintenance times during the monitoring period.

## Acknowledgment

The authors thank the authors of the RCTs included in this review and the teaching team of the BMF implantology specialty of the Universidad Mayor, Santiago.

## References

1. Chappuis V, Buser R, Brägger U, Bornstein MM, Salvi GE (2013) Long-term outcomes of dental implants with a titanium plasma-sprayed surface: a 20-year prospective case series study in partially edentulous patients. Clinical implant dentistry and related research 15(6): 780-790.
2. Pjetursson B, Asgeirsson A, Zwahlen M, Sailer I (2014) Improvements in implant dentistry over the last decade: comparison of survival and complication rates in older and newer publications. International journal of oral & maxillofacial implants 29: 308-324.
3. Lindhe J, Meyle J (2008) Group D of the European Workshop on Periodontology. Peri-implant diseases: consensus report of the sixth European workshop on periodontology. Journal of clinical periodontology 35(8): 282-285.
4. Herrera PI (2015) Evaluation of the success and failure of implant treatments in the Faculty of Dentistry of the Andrés Bello University, between 2010 and 2013, through a satisfaction survey.
5. Herreros N, Juan E (2016) Relationship between the characteristics of the patients and the success of dental implants at the time of their connection, installed at the Universidad Mayor.
6. Leyton S (2015) Clinical evaluation of the success rate of implants performed at the Faculty of Dentistry of the Andrés Bello University according to the 2009 Pisa criteria (Doctoral dissertation, Andrés Bello University, Chile.
7. Sánchez CM, Loran AS, Almagro UZE (2019) Bioethical considerations on care competence for implant-prosthetic rehabilitation in the elderly. MediSan 23(2), 342-359.
8. Tamez JEB, Zilli FN, Fandiño LA, Guizar, JM (2017) Factors related to the success or failure of dental implants placed in the specialty of Prosthodontics and Implantology at the University of La Salle Bajío. Spanish Journal of Oral and Maxillofacial Surgery 39(2): 63-71.
9. Schwarz F, Derks J, Monje A, Wang, HL (2018) Peri-implantitis. Journal of Clinical Periodontology 45: S246-S266.
10. Derks J, Tomasi C (2015) Peri-implant health and disease. A systematic review of current epidemiology, Journal of clinical periodontology 42 (Suppl. 16): 158-171.
11. Herrera D, Figuero E, Shapira L, Jin L, Sanz M (2018) The new classification of periodontal and peri-implant diseases. Scientific Journal of the Spanish Society of Periodontics Epoch I Year IV n°11.
12. Monje A, Pons R, Insua A, Nart J, Wang HL, et al. (2019) Morphology and severity of peri-implantitis bone defects. Clinical Implant Dentistry and Related Research 21(4): 635-643.

13. Karoussis IK, Salvi GE, Heitz LJ, Brägger U, Hämmerle CH, et al. (2003) Long-term implant prognosis in patients with and without a history of chronic periodontitis: a 10-year prospective cohort study of the ITI® Dental Implant System. Clinical oral implants research 14(3): 329-339.

14. Roos AM, Renvert H, Lindahl C, Renvert S (2006) Nine-to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. Journal of clinical periodontology 33(4): 296-301.

15. Aglietta M, Siciliano VI, Rasperini G, Cafiero C, Lang NP, et al. (2011) A 10-year retrospective analysis of marginal bone-level changes around implants in periodontally healthy and periodontally compromised tobacco smokers. Clinical oral implants research 22(1): 47-53.

16. Roos AM, Renvert H, Lindahl C, Renvert S (2006) Nine-to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. Journal of clinical periodontology 33(4): 296-301.

17. Thoma DS, Naenni N, Figuero E, Hämmerle CH, Schwarz F, et al. (2018) Effects of soft tissue augmentation procedures on peri-implant health or disease: A systematic review and meta-analysis. Clinical oral implants research 29: 32-49.

18. Canullo, Signorini L, Pistilli R, Patini R, Pistilli V, et al. (2019) A prospective case series on surgical treatment of circumferential and semi-circumferential defects. Braz Oral Res33 (Suppl 1): e072.

19. Sarmiento H, Norton M, Korostoff J, Ko K, Fiorellini J (2018) Surgical Alternatives for Treating Peri-implantitis. The International Journal of Periodontics & Restorative Dentistry 38(5): 665-671.

20. Sanz I, Schwarz F (2015) Combined surgical treatment of resective and regenerative surgery in the treatment of peri-implantitis,Clinical periodontitis 1: 27-23.

21. Sinjab K, Garaicoa CP, Wang H (2018) Decision making for the management of periimplant diseases. Implant Dentistry 27(3): 276-281.

22. Wen SC, Huang WX, Wang HL (2019) Regeneration of Peri-implantitis Infrabony Defects: Report on Three Cases. The International Journal of Periodontics &Restorative Dentistry 39(5): 615-621.

23. Bohač M, Danišovič L, Koller J, Draguňová J, Varga I (2018) What happens to an acellular dermal matrix after implantation in the human body? A histological and electron microscopic study Eur J Histochem 62(1): 2873

24. Najafi B, Patel V, Deutsch RG, Drew HJ, Cappetta EG (2016) Surgical Treatment of Advanced Peri-implantitis With Dual Augmentation Technique: A Report of Two Cases With 15 month Follow-up. Clinical Advances in Periodontics 7(1): 1-7.

25. de Tapia B, Valles C, Ribeiro AT, Mor C, Herrera D, et al. (2019) The adjunctive effect of a titanium brush in implant surface decontamination at peri-implantitis surgical regenerative interventions: A randomized controlled clinical trial. Journal of Clinical Periodontology 46(5): 586-596.

26. Roos JA, Persson GR, Lindahl C, Renvert S (2014) Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: A 5-year follow-up. Journal of clinical periodontology 41(11): 1108-1114.

27. Isler SC, Soysal F, Ceyhanlı T, Bakırarar B, Unsal B (2018) Regenerative surgical treatment of peri-implantitis using either a collagen membrane or concentrated growth factor: a 12-month randomized clinical trial. Clinical Implant Dentistry and Related Research 20(5): 703-712.

28. Isler SC, Unsal B, Soysal F, Ozcan G, Peker E, et al. (2018) The effects of ozone therapy as an adjunct to the surgical treatment of peri-implantitis. Journal of periodontal & implant science 48(3): 136-151.

29. Wang CW, Ashnagar S, Gianfilippo RD, Arnett M, Kinney J, et al. (2021) Laser-assisted regenerative surgical therapy for peri-implantitis: a randomized controlled clinical trial. Journal of periodontology 92(3): 378-388.

30. Isehed C, Holmlund A, Renvert S, Svenson B, Johansson I, et al. (2016) Effectiveness of enamel matrix derivative on the clinical and microbiological outcomes following surgical regenerative treatment of peri-implantitis. A randomized controlled trial. Journal of clinical periodontology 43(10): 863-873.

31. Schlee M, Rathe F, Brodbeck U, Ratka C, Weigl P, et al. (2019) Treatment of peri-implantitis-electrolytic cleaning versus mechanical and electrolytic cleaning-a randomized controlled clinical trial-six-month results. Journal of clinical medicine 8(11): 1909.

32. Schwarz F, John G, Mainusch S, Sahm N, Becker J (2012) Combined surgical therapy of peri-implantitis evaluating two methods of surface debridement and decontamination. A two-year clinical follow up report. Journal of clinical periodontology 39(8): 789-797.

33. Schwarz F, Hegewald A, John G, Sahm N, Becker J (2013) Four-year follow-up of combined surgical therapy of advanced peri-implantitis evaluating two methods of surface decontamination. Journal of clinical periodontology 40(10): 962-967.

34. Arab HR, Shiezadeh F, Moeintaghavi A, Anbiaei N, Mohamadi S (2016) Comparison of two regenerative surgical treatments for peri-implantitis defect using natix alone or in combination with Bio-Oss and collagen membrane. Journal of long-term effects of medical implants 26(3): 199-204.

35. Aghazadeh A, Rutger PG, Renvert, S (2012) A single-centre randomized controlled clinical trial on the adjunct treatment of intra-bony defects with autogenous bone or a xenograft: results after 12 months. Journal of clinical periodontology 39(7): 666-673.