TOWARDS A BETTER DIAGNOSIS AND PROGNOSIS IN PERI-IMPLANT DISEASE FROM A MICROBIOLOGICAL PERSPECTIVE. A NARRATIVE REVIEW

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Abstract: With the increasing popularity of dental implants among patients as a treatment alternative for edentulousness of various causes, the occurrence of implant complications is continuously rising. The need to know the latest techniques for managing these complications is vital for clinicians. There is currently no data in the literature on possible biological or mechanical complications of this approach. The aim of this review was to identify, in the specialised literature databases, established pathogenic microorganisms associated with peri-implant disease and to observe their grafting onto the implant surface after the application of implantoplasty techniques. The search was performed in databases such as PubMed, Google Academic, Web of Science and Cochrane Library and was conducted for the last thirty years (1993 - 2023). Different combinations of keywords, treatment alternatives of peri-implant pathology, as well as pathogenic microorganisms, involved in the occurrence of the disease were used for the search. We identified elements of etiopathogenicity (dental plaque and smoking), molecular biology mechanisms involved in peri-implant pathology, and we detailed possible particular developments of invasive peri-implant therapies.

Conclusions implantoplasty is a modern treatment alternative for peri-implant pathology. Using sensitive and specific methods (e.g., sequencing), numerous bacterial species associated with dental implants have been identified. In conclusion, implantoplasty requires careful prospective evaluation from microbiological point of view.

Keywords: *periimplantitis, periodontopathogenic microorganisms, implant surface modification, implantoplasty, periimplant disease, prognosis, diagnosis*

1. Introduction

Periimplantitis is an inflammatory disease characterised by increased probing depth, the presence of bleeding and/or suppuration and progressive loss of peri-implant supporting bone tissue, which may lead to loss of the dental implant [1]. It is a prevalent condition affecting a significant number of people with implants [2]. A history of periodontitis, inadequate biofilm control and lack of regular maintenance therapy are recognised as risk factors for the development of peri-implantitis [3-8]. Various therapies have been described to address peri-implantitis, including non-surgical therapies and resective or regenerative surgical therapies. In many cases, a combination of techniques is used [9].

2. General Aspects and Aetiopathogenesis

2.1 Dental plaque

Regular maintenance and adequate accessibility to achieve plaque control are essential in order to avoid recurrence of peri-implant disease with eventual loss of the implant [10-13]. Martins et al emphasise that patient maintenance and compliance were fundamental to achieving these results, as we know that compliance and regular professional control are essential to achieve peri-implant soft tissue health [10]. A recent study found that full-arch implant-prosthetic restorations have a 16.1-fold higher risk of peri-implantitis than single implant-prosthetic restorations [14] most likely due to the difficulty in performing adequate oral hygiene. [15,16]

This could indicate that fully rehabilitated patients should have an appropriate design of supra-implant prosthetic restorations and perhaps a more restrictive maintenance care programme [17].

The high success rate of dental implants has contributed to their consolidation as a therapeutic alternative for the replacement of missing teeth [18]. Despite the high success rate, inflammatory changes in peri-implant tissues due to bacterial infection are a concern for practitioners and require attention [19]. Bacterial accumulation on the implant surface plays a central role in the etiopathogenesis of peri-implantitis, contributing to progressive loss of supporting bone and poor prognosis [20].

Therefore, the approach to peri-implantitis treatment involves eliminating implant surface contamination, attenuating the inflammatory process and halting the progression of bone loss, which will ultimately improve clinical outcomes after implantoplasty, characterised by a decrease in purulence and bleeding, as well as reduced periodontal pockets, increasing implant survival time [9].

2.2 Smoking as a risk factor

Smoking is an important factor that has been reported to influence treatment outcome [21,22].

However, consistent with a recent study that included 6 smokers out of a total of 25 patients, smoking had no effect on the treatment outcome of implantoplasty [23]. In the present cases, there was no indication that smoking exerted an influence on the surgical outcome after implantoplasty, as peri-implantitis resolution was observed in both smoking patients. However, the small number of smokers does not allow a firm conclusion [17].

3. Molecular biology mechanisms involved in peri-implant pathology

It has been shown that particulate debris resulting from specific therapeutic procedures can act as a biologically active substance and initiate an osteolytic reaction leading to failure of implant-prosthetic rehabilitations [24].

Furthermore, differences in composition, concentration, morphology and size of metal particles exert different cytotoxic effects [25]. Among these factors, particle size and concentration have a greater impact [1, 24] Most wear particles found in failed joint replacements are submicron in size (<1 m) and are more likely to be responsible for the osteolytic response initiated and mediated by macrophages [25-35] Specifically, macrophages can phagocytose wear debris [36-37], leading to the production of proinflammatory signalling molecules such as prostaglandin E2 (PGE2), tumour necrosis factor alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) [38-40].

These cytokines have been shown to be stimulated when particle size falls within a certain range (0.6-4.5 m) [41] To promote successful osseointegration and faster bone healing, implant manufacturers have incorporated various surface treatments, including sandblasting, acid etching, plasma spraying, anodising, etc. [42]

Higher levels of biological and immunological activity in metal particles have been observed in the size range of 1-50 m, and/or at the nanometre level [38-43]

However, these modifications may facilitate the release of wear particles during implant handling, placement, maintenance, peri-implant disease management, etc. This alteration of the implant surface may be influenced by fixture structure, roughness and topographic configuration [43] and could influence peri-implant progression and/or treatment [44]

4. Elements of diagnosis and treatment

4.1 General principles and microbiological background

Several treatment modalities and protocols have been used for the therapy of peri-implant pathology, including mechanical debridement, use of antiseptics, local or systemic antibiotics, chemical compounds, laser, air abrasion, access surgery, resective surgical procedures, and regenerative surgical procedures [42-49].

The results of studies on different treatment modalities for periimplantitis are inconsistent and highly controversial, and establishing a standard protocol is still impossible. Implantoplasty is a clinical procedure performed to smooth the exposed implant wires, establishing a more favourable transmucosal area. This mechanical modification of the implant surface favours the reduction of bacterial adhesion and soft tissue adaptation during the healing process [50]. There are studies that have hypothesised that implantoplasty is effective in promoting peri-implant health and have evaluated the likelihood of successful implant survival rates after implantoplasty [9]. Mucosal recession could be a concern in the aesthetic area. However, in posterior areas or in the case of overdentures, this is not a problem and could be accepted by the patient if explained in advance [17].

Peri-implant bone resorption exposes the implant surface, treated in order to achieve better osseointegration results, as well as the implant coils. This condition represents a favourable niche for bacterial colonisation, as well as for the initiation and progression of peri-implant disease.

Mechanical modification of the implant surface in implantoplasty aims at eliminating these irregularities and achieving a smooth surface with cell viability that prevents bacterial adhesion [51]. This was highlighted in a study which demonstrated that implants treated by means of implantoplasty have less biofilm accumulation, which is also less mature than untreated implants [52].

Similarly, another study demonstrated that implantoplasty reduces the rate of bacterial growth [53]. Despite the significant reduction in roughness achieved by implantoplasty, small irregularities remain on the implant surface that promote bacterial adhesion [52,54].

Differences in implantation protocols can lead to differences in surface roughness of treated implants [55].

Several chemical forms of disinfection, including EDTA, tetracycline, hydrogen peroxide, and chlorhexidine, have been associated with implantoplasty.

However, the benefit of combining chemical disinfection with implantoplasty is still controversial [56]. Furthermore, the literature on the influence of implant surface on implant results is limited. In cases where the peri-implant defect presents a more favourable configuration for regeneration, guided surgery is combined with implantoplasty.

Clinical improvements have been described after treatment of periimplantitis with regenerative techniques associated with implantoplasty [57,58]. However, scientific evidence on the benefits of this combination is limited.

The lack of bactericidal treatments approved by accreditation agencies, due to the lengthy nature of clinical trials of different bactericidal strategies for implants [59-67], has given rise to treatments such as implantoplasty, which can be performed in any dental clinic. Bactericidal treatments under study include silver nanoparticles as an element with high bactericidal capacity [63, 66], functionalisation of titanium with organic compounds such as TESPSA and lactoferrin, among others, and the use of titanium with organic compounds such as TESPSA and [60, 68]. The long-term behaviour of nanoparticles or the complicated and costly anchoring of organic compounds in titanium means that these treatments have not yet reached sufficient maturity for their application [69].

In the recent years, researchers from all the continents investigated, using very comprehensive microbiological assays, the bacterial aetiologies associated with dental implants. [60]

In Table 1 can be observed the most frequent bacterial species associated with periimplantitis.

Table 1: *Bacterial species associated with periimplantitis.*

First Author Year, Country	Microbial assay	Detected bacterial species	Medical importance
Zhou et al., 2022, China [57]	V4 region of the 16S rDNA Illumina HiSeq platform sequencing	*Actinomyces* *Streptococcus* *Fusobacterium* *Prevotella*	these results provide a bacteriological basis for the prevention and treatment of peri-implant mucositis
Pallos et al., 2022, Brazil [58]	V4 hypervariable region of the 16S rRNA Ion Torrent PGM System sequencing	*Stenotrophomonas*, *Enterococcus* and *Leuconostoc* genus, *Faecalibacterium prausnitzii*, *Haemophilus parainfluenzae*, *Prevotella copri*, *Bacteroides vulgatus*, *Bacteroides stercoris bacterial species*	important differences was found in participants with peri-implantitis when compared with those with healthy peri-implant sites.
Grischke et al., 2021, Germany [59]	RNAseq	16.41% of the implants were diagnosed with peri-implantitis with: *Fusobacterium nucleatum subspecies animalis* *Prevotella intermedia*	implants with removable dentures appear: - to be a risk indicator for peri-implantitis - to facilitate expansion of specific periodontopathogens
Ghensi et al, 2020, Italy [60]	metagenomic sequencing	peri-implantitis-related complex composed by the 7 most discriminative bacteria: *P. gingivalis*, *T. forsythia*, *Treponema denticola* *P. endodontalis* *F. fastidiosum* species, *Prevotella intermedia* and *F. nucleatum*	the high-resolution characterization of the plaque microbiome in peri-implant diseases is the first step toward a more comprehensive understanding of the role of the microbiome in peri-implant diseases.

4.2 General information on the implantoplasty technique

It is well known that one of the main problems in oral implantology is peri-implantitis, which is currently the main cause of implant unit loss. This has led to the application of the implantoplasty procedure (Figure 1) at least in the most severe cases. However, there are no protocols, nor are there many studies on the implications of an invasive treatment such as implantoplasty [69-73].

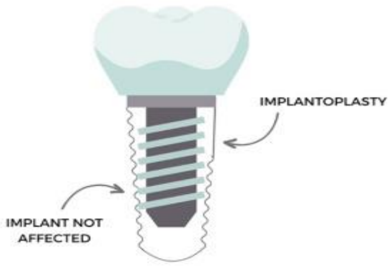

Figure 1. Implantoplasty *vs.* physiological situation

One of the most important steps in the regenerative surgical approach to peri-implantitis is the decontamination of the implant surface.
However, implantoplasty is performed with the aim of completely removing the surface morphology of the osseointegrated implant. Thus, separate surface contamination is not a crucial issue. Despite the fact that IP is an available mechanical method for implant surface decontamination, other mechanical methods are available, and a recent randomised controlled trial showed no radiographic and clinical differences between IP and glycine air abrasion for surgical treatment of peri-implantitis [74]. Final debridement of instrumented surfaces reduces implant roughness; therefore, bacterial biofilm formation and maturation is prevented [75,76] and the risk of reinfection of treated sites is eliminated [77].

5.2 Hazards of invasive peri-implant therapies

"In vitro" studies have shown that performing implantoplasty on dental implants produces debris mostly in the extremely fine size range (<100 nm). Evidence from previous *in vitro* investigations has also indicated that nanosized particles may account for the largest number of debris generated; however, they represent only a very small proportion of the total volume [25,78]. These results indicate that a surgical area that visually appears "particle-free" after implantoplasty may still contain a large number of nanosized debris. It is important to note that, as previously reported in the orthopaedic literature [79, 80], smaller (submicrometric-sized) particles have been shown to be more commonly associated with macrophage activities, including increased cytokine release (e.g., TNF- α IL-1 β IL-6, IL-8, β). [81]

These extremely fine debris are more biologically harmful compared to visible coarse particles, due to biochemical mediators of inflammation, cell recruitment and bone resorption [44]. As such, clinicians should consider alternatives to reduce the widespread release of particles generated during implantoplasty (rubber dam, high-volume evacuation, etc.). Similarly, the risks and benefits of performing implantoplasty for implant surface treatment should be weighed cautiously for each implant/patient.

Differences in number, size, mass, surface area and morphology have also been demonstrated between different manufacturers with different implant designs and surface treatments [82].

Undoubtedly, titanium processing causes a severe loss of mechanical properties due to the reduction of the dental implant surface and the significant plastic deformation produced in titanium. In addition, the effect of machining on the points of anchorage to the host tissue. From this point of view, Lozano et al consider that implantoplasty should be discouraged for cases of narrow dental implants, as there could be a risk of fracture of the dental implant [83,84].

In addition to mechanical damage, damage to chemical stability is also produced. In this contribution, we could verify the loss of corrosion resistance of the machined implant and even more so in titanium residues. As we have seen, loss in corrosion resistance is closely related to an increase in the mechanical stress accumulated in the material [36,37]. It is well known that metals with high stored energy are very sensitive to corrosion. In this study, it was found that scrap, which has the highest stored energy due to the large amount of deformation, is the most corrosive. This is of concern because these particles can remain in the surrounding tissues and can also produce titanium oxide [69].

Implantoplasty on small diameter implants produces a decrease in fracture resistance in all groups of narrow diameter titanium dental implants tested. The design of the implant-abutment connection influences the strength of fixation. Clinicians should be aware that implantoplasty may increase the risk of fracture, especially for implants with a narrow-diameter internal connection [85].

The lower strength of narrow-diameter implants treated by means of implantoplasty should be taken into account during implant placement planning [86]. The risk of plastic deformation increases if the implant is unsplinted and there is considerable bone loss. It has been reported that a marginal bone loss of 3 mm resulted in a 37.2% reduction in mean implant strength, and the value further decreased to 53.8% for a marginal bone loss of 5 mm [87]. Therefore, implants that have undergone this type of treatment should be reviewed periodically [88].

As previously mentioned, achieving optimal surface planarity of a treated implant is the main goal of treatment. In this study, no surface analysis was performed to assess roughness. However, the milling and polishing sequence used was the same as in the study by Costa-Berenguer et al [89], where an average roughness index of 0.1 ± 0.02 µm was observed. This is below the established maximum value of 0.2 µm required for the minimisation of bacterial adhesion [90], Another limitation of this study is that we could not follow the same milling sequence for either the machined or hand-finished group. Therefore, the results for milling and polishing are not strictly comparable. Future studies including more operators and controls for milling time, pressure, and angulation of drilling during the procedure are warranted [91].

We can state with certainty, however, that many other authors have demonstrated that resective implant surgery, including implantoplasty, is an effective therapeutic approach for the treatment of peri-implantitis in terms of eliminating deep pockets, stopping inflammation and progressive marginal resorption [92-94].

However, data on crucial parameters, such as residual implant dimensions after instrumentation with different tool kits, which might influence the resistance of implants to fracture over years of future loading, are still scarce according to the specialised literature.

There are previous studies evaluating fracture resistance which show discordant results. While Chan et al [95] found a considerable loss of fracture resistance after implantoplasty, several other publications showed no relevant loss for this parameter [96,97]. However, these latter studies did not consider thermomechanical loading, but assessed fracture loads immediately, which describes a considerable difference from the clinical situation, when after years of moderate chewing forces loading peaks could induce significant bending forces.

It should be emphasised that the results of Jorio et al. demonstrated for the first time that there was a loss of resistance for uninstrumented implants that had previously been mechanically loaded and thermally cycled compared to intact implants that had not undergone any treatment. This finding proves the unconditional importance of involving cyclic mechanical loading and thermocycling of implants before assessing fracture load.

There was no obvious difference in material loss at any measurement point for the different instrumentation techniques. This indicates that any of the instrumentation sequences evaluated could be used if only the properties of the material are considered. Damage to neighboring teeth is a clinical reality worthy of consideration in the optimisation of these clinical protocols [98].

5.3 Cytotoxicity and peri-implant therapy

Toledano-Serrabona et al. [99,100] recently studied the characteristics of Ti-6Al-4V particles associated with dental implants, demonstrating a certain level of cytotoxicity and inflammatory cell reaction. Surface properties of dental implant topography [101] and the difficulty of osteoblastic growth on dental implant surfaces with implantoplasty have also been studied. At the same time, strategies to prevent infection processes in implantoplasty treatments with the introduction of antibiotics have been studied [102]. The combination of a resective and a reconstructive surgical approach, together with locally administered antibiotic achieved a high rate of disease resolution after one year of surveillance and is a viable option for short-term management of peri-implantitis [102]. The results are encouraging but do not have long-lasting bactericidal action.

Antibiotics also have no effect on the toxicity processes of particles or on the dental implant surface in case of corrosion [60,103].

Indeed, the implantoplasty technique removes biofilms from the titanium surface to prevent periimplantitis and also preserves the osseointegrated dental implant.

However, as we have seen, it reduces corrosion resistance, increases the release of titanium ions into the environment, and reducing the cross-section of the implant through machining will lead to a reduction in mechanical properties. In this respect, it is necessary to continue research into new anodising treatment techniques, such as those published by Harraft et al [104,105] in which titanium is anodised in the form of TiO_2 nanotubes that can contain bactericidal drugs, or others based on citric acid [106], or with Pirahna treatments that, due to their nanotexture, prevent bacterial colonisation [107].

6. Microbiological perspectives in peri-implant disease research

Lozano et al pointed out that one aspect that requires further study is how the titanium surface will behave towards bacteria after implantation. In principle, everything suggests that having a surface with a lower roughness than that of the implant as received will make biofilm formation more difficult [62,63]. It is well known that the roughness of the dental implant, which is fundamental for osseointegration and fixation of the implant onto the bone, is unfavourable for bacterial colonisation [108,109]. Therefore, the reduced roughness caused by the implant machining process would favour the reduction of plaque adhesion. Similarly, the lack of a certain roughness should be studied in terms of the possibility of osteoblasts to adhere, proliferate and differentiate on this surface. This will certainly be a disadvantage for new bone formation.

For all these reasons, Lozano et al suggest that it is imperative to continue studying these biological aspects on titanium surfaces that have undergone implantoplasty [69].

Cytotoxicity and peri-implant therapy are an important issue associated with implantoplasty.

7. Conclusions

Implantoplasty may be considered by many specialists as modern alternative of treatment for peri-implant pathological processes. Within the limitations of the current paper, we have emphasised the key role of some elements of etiopathogenicity such as dental plaque and smoking. In the same time we pointed out that molecular biology mechanisms involved in peri-implant pathology still need to be explored and we detailed possible particular hazards of invasiveness certain peri-implant therapies.

Using sensitive and specific methods (e.g., sequencing), numerous bacterial species associated with dental implants can be successfully identified at early stages and thus, reduce the failure rated if the implants. Therefore, such techniques like implantoplasty require additional studies and careful prospective evaluation especially from the microbiological perspective, in order to significantly increase the survival rate of dental implants.

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