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ROBERTO HARTMANN

EFETIVIDADE E CUSTO-EFETIVIDADE DE TRÊS ALTERNATIVAS DE TRATAMENTO PARA REABILITAÇÃO DO DESDENTADO MANDIBULAR: ENSAIO CLÍNICO RANDOMIZADO COM ACOMPANHAMENTO DE 1 ANO

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EFFECTIVENESS AND COST-EFFECTIVENESS OF THREE TREATMENT ALTERNATIVES FOR REHABILITATION OF THE EDENTULOUS MANDIBLE: ONE-YEAR RANDOMIZED CLINICAL TRIAL

Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Goiás para Obtenção do Título de Doutor em Odontologia, área de concentração em Clínica Odontológica.

Linha de Pesquisa: Perspectivas em Odontologia Clínica.

Orientador: Cláudio Rodrigues Leles

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ATA DE DEFESA DE TESE

Ata Nº **24** da sessão de Defesa de Tese de **Roberto Hartmann** que confere o título de Doutor em **Odontologia**, na área de concentração em **Clínica Odontológica.**

Aos **vinte e três dias do mês de agosto de 2019**, a partir das **14:00**, no **auditório** da **Faculdade de Odontologia**, realizou-se a sessão pública de Defesa de Tese intitulada **"Avaliação comparativa de três alternativas de tratamento para reabilitação do desdentado mandibular: ensaio clínico randomizado com acompanhamento de 1 ano**". Os trabalhos foram instalados pelo Orientador, Professor Doutor **Cláudio Rodrigues Leles (PPGO/UFG)** com a participação dos demais membros da Banca Examinadora: Professora Doutora **Thais Marques Simek Vega Gonçalves (UFSC)**, membro titular externo; Professor Doutor **Mauro Henrique Nogueira Guimarães de Abreu (UFMG)**, membro titular externo; Professora Doutora **Rejane Faria Ribeiro-Rotta (PPGO/UFG)**, membro titular interno; Professor Doutor **Túlio Eduardo Nogueira (PPGO-UFG)**, membro titular interno. Durante a arguição os membros da banca **fizeram** sugestão de alteração do título do trabalho. A Banca Examinadora reuniu-se em sessão secreta a fim de concluir o julgamento da Tese tendo sido o candidato **aprovado** pelos seus membros. Proclamados os resultados pelo Professor Doutor **Cláudio Rodrigues Leles**, Presidente da Banca Examinadora, foram encerrados os trabalhos e, para constar, lavrou-se a presente ata que é assinada pelos Membros da Banca Examinadora, aos **vinte e três dias do mês de agosto de 2019**.

TÍTULO SUGERIDO PELA BANCA

Efetividade e custo-efetividade de três alternativas de tratamento para reabilitação do desdentado mandibular: ensaio clínico randomizado com acompanhamento de 1 ano

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Roberto Hartmann foi Bolsista de Doutorado da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES, e recebeu bolsa do Programa Institucional de Doutorado-sanduíche no Exterior (PDSE) para período de intercâmbio de 6 meses na Universidade de Berna, Suíça – Processo n. 88881.189774/2018-01.

RESUMO

EFETIVIDADE E CUSTO-EFETIVIDADE DE TRÊS ALTERNATIVAS DE TRATAMENTO PARA REABILITAÇÃO DO DESDENTADO MANDIBULAR: ENSAIO CLÍNICO RANDOMIZADO COM ACOMPANHAMENTO DE 1 ANO

Este ensaio clínico randomizado comparou *a efetividade e o custo-efetividade (custo x desfecho centrado no paciente) de* três alternativas de tratamento para a reabilitação do edentulismo mandibular: *overdenture* mandibular retida por implante unitário (Grupo I), *overdenture* mandibular retida por dois implantes (Grupo II) e prótese fixa mandibular suportada por quatro implantes (Grupo III). Foram incluídos 50 desdentados totais os quais receberam inicialmente novas próteses totais convencionais (*baseline*) sendo posteriormente, alocados aleatoriamente para um dos grupos de tratamento. Implantes do tipo hexágono externo (Titamax TI Cortical, Neodent, Curitiba, Brasil) foram instalados seguindo o protocolo de instalação para carga convencional. Equações de Estimações Generalizadas (GEE) foram utilizadas para variáveis de desfecho primário como os custos odontológicos diretos os quais foram identificados, mensurados e valorados; a qualidade de vida relacionada à saúde oral (OHIP-Edent) e a satisfação do paciente com as próteses, em todos os grupos por um período de acompanhamento de 1 ano. A performance mastigatória, complicações protéticas, eventos de manutenção e avaliação peri-implantar (perda óssea marginal, estabilidade dos tecidos peri-implantares, quociente de estabilidade implantar – ISQ) foram avaliadas como desfechos secundários. Dados de 37 participantes: Grupo I (n=11); Grupo II (n=13); Grupo III (n=13) foram coletados sendo semelhantes em relação às características clínicas basais e desfechos do tratamento inicial com prótese total convencional. O custo-efetividade incremental - ICER variou para o Grupo II (comparado ao Grupo I) de R$ 36,20 a R$ 81,46 para um incremento de 1 ponto na satisfação do paciente (valor base = R $ 54,30), para o Grupo III (comparado ao Grupo I) variou de R$ 1321,12 a R$ 2972,52 (valor base = R $ 1981,68). O custo total do tratamento referente as fases cirúrgica e protética foi de R$ 2.370,70 para o Grupo I, R$ 3.185,20 para o Grupo II e R$ 5.739,50 para o Grupo III. Houve diferença significativa entre os custos nos três grupos (p<0,001). Os maiores

impactos no custo total do tratamento foram relacionados aos custos iniciais laboratoriais, de implantes e componentes no Grupo III. Os escores dos questionários de satisfação com as próteses mandibulares e de OHIP-Edent no periodo de 12 meses apresentaram melhora em todos grupos em relação ao baseline. e foram semelhantes na comparação inter-grupos no tempo inicial (com as próteses totais convencionais novas) e 1 ano após a captura das próteses sobre implantes. Nas comparações intra e inter grupos não houve alteração significativa em relação à satisfação com a prótese maxilar. Em relação à performance mastigatória não houve diferença inter-grupos avaliados no mesmo período para os diferentes ciclos (20 e 50 ciclos) com melhora gradativa para todos os grupos até o período de 6 meses e leve queda no período de 12 meses para todos os grupos. Concluiu-se que reabilitação de pacientes desdentados totais com implantes melhorou significativamente os desfechos reportados pelo paciente em todos os grupos de tratamento. Com relação aos aspectos econômicos dos tratamentos, o custo direto odontológico e o tempo clínico dispendido para a realização do tratamento e acompanhamento durante o período de 1 ano na prótese fixa (Grupo III) foi aproximadamente três vezes maior em relação ao Grupo I o que não correspondeu a um ganho proporcional de efetividade assim como o custo adicional da *overdenture* retida por dois implantes não resultou em ganho de efetividade significativo em relação à *overdenture* retida por implante unitário. *A taxa de sobrevida do implante, após um ano de acompanhamento, foi de 100% para todos os grupos.* Levando em consideração as limitações do estudo, as overdenture retidas por implantes se apresentaram como modalidades mais custo-efetiva

Palavras-chave: implante dentário, prótese dentária, ensaio clínico randomizado, análise de custo-efetividade, desfechos de tratamento.

ABSTRACT

EFFECTIVENESS AND COST-EFFECTIVENESS OF THREE TREATMENT ALTERNATIVES FOR REHABILITATION OF THE EDENTULOUS MANDIBLE: ONE-YEAR RANDOMIZED CLINICAL TRIAL

This randomized trial compared the effectiveness and cost-effectiveness (cost x patient centered outcomes) of three treatment alternatives for mandibular edentulism rehabilitation: unit-implant-retained mandibular overdenture (Group I), two-implant-retained mandibular overdenture (Group II) and four-implant-supported mandibular fixed prosthesis (Group III). We included 50 fully edentulous patients who initially received new conventional total dentures (baseline) and were later randomly allocated to one of the treatment groups. External hexagon implants (Titamax TI Cortical, Neodent, Curitiba, Brazil) were installed following the conventional loading installation protocol. Generalized Estimating Equations (GEE) was used to calculate the primary outcome variables were the direct dental costs which were identified, measured and valued; oral health-related quality of life (OHIP-Edent) and patient satisfaction with prostheses in all groups for a follow-up period of 1 year. Masticatory performance, prosthetic complications, maintenance events and peri-implant evaluation (marginal bone loss, peri-implant tissue status, implant stability quotient - ISQ) were evaluated as secondary outcomes. Data from 37 participants: Group I (n = 11); Group II (n = 13); Group III (n = 13) were collected and were similar in relation to baseline clinical characteristics and outcomes of initial treatment with conventional full dentures. Incremental cost-effectiveness - ICER ranged for Group II (compared to Group I) from R$ 36.20 to R$ 81.46 for a 1-point increase in patient satisfaction (base value = R$ 54.30) for Group III (compared to Group I) ranged from R$ 1321.12 to R$ 2972.52 (base value = R$ 1981.68). The total cost of treatment for the surgical and prosthetic phases was R$ 2,370.70 for Group I, R$ 3,185.20 for Group II and R$ 5,739.50 for Group III. There was a significant difference between the costs in the three groups (p <0.001). The greatest impacts on total treatment cost were related to the initial laboratory, implant and component

costs in Group III. The satisfaction questionnaires and OHIP-Edent satisfaction scores in the 12 months improved in all groups compared to baseline. and were similar in intergroup comparison at baseline (with new conventional full dentures) and 1 year after implant prosthesis capture. In intra- and inter-group comparisons there was no significant change regarding satisfaction with the maxillary prosthesis. Regarding masticatory performance, there was no difference between groups evaluated in the same period for the different cycles (20 and 50 cycles) with gradual improvement for all groups up to 6 months and a slight decrease in 12 months for all groups. It was concluded that the rehabilitation of edentulous patients with implants significantly improved patient-reported outcomes in all treatment groups. Regarding the economic aspects of the treatments, the direct dental cost and the clinical time spent to perform the treatment and follow-up during the 1 year period in the fixed prosthesis (Group III) was approximately three times higher than in Group I, which did not correspond to a proportional gain in effectiveness as well as the additional cost of overdenture retained by two implants did not result in significant effectiveness gain over overdenture retained per unit implant. The implant survival was 100% in all groups after the 1-year follow-up. Considering the limitations of the study, implant-retained overdentures were the most cost-effective modalities.

Key words: *dental implant, prosthodontics, randomized clinical trial, cost-effectiveness analysis, treatment outcomes.*

ÍNDICE

INTRODUCTION

Complete edentulous individuals suffer from a chronic detrimental condition since the full restitution of their physiological and psychological functions associated with their oral health is not possible (CARLSSON & OMAR, 2010). In Brazil, the prevalence of tooth loss is 76.6% in the general population, with a median of 6 teeth lost for the population aged 15 or more years old. Epidemiological data from a national oral health survey (BRASIL, 2011) showed that there was an improvement in the oral health status of adults as the demand for dentures. However, the major problem is still concentrated in the population aged 65 to 74, who had an average caries index rate of 27.1 in 2010 (in 2003 the average was 27.8) with a predominance of component lost by decay. There is a high prevalence of edentulism in the 65-74 years age group and the prevalence of complete edentulous is 53.7% of individuals aged 65-74 years are total edentulous (PERES et al., 2013). From 2003 to 2010, the proportion of elderly people who need dentures dropped from 24% to 23% and from 16% to 15% for those who need partial dentures (BRASIL, 2011).

Traditionally, the tissue-supported complete denture is the most common treatment alternative for the fully edentulous subjects, with diverse levels of success regarding patient adaptation to the prosthesis, satisfaction and functional recovery. Most of these patients are satisfied with their dentures and can perform satisfactorily their functional needs, do not demanding other more complex interventions. Nevertheless, many complete denture wearers have substantial complaints related to poor retention and stability of the dentures, resulting in oral pain, discomfort, low confidence, and impaired oral function. These clinical problems are more pronounced for the edentulous mandible, due to the limited retention and stability of the lower denture (VAN WAAS, 1990; CARLSSON, 2006).

On the other hand, taking into account that there is a close relationship between teeth loss and lower socioeconomic conditions, the majority of the edentulous patients worldwide is underprivileged people, especially in underdeveloped and developing countries, most of them will never be candidates for implant therapy

and their expectations are limited to well-functioning complete dentures (CARLSSON & OMAR, 2010). Most patients are well-adapted to their dentures, but prognostic factors are multifactorial and there is a minority of patients who will never adapt to any conventional complete denture, mainly the mandibular denture (CRITCHLOW & ELLIS, 2010). For these difficult patients, other treatments including osseointegrated implants would be recommended as a priority in case of limited healthcare supply, limited resources, and high demand based on normative needs.

The use of dental implants offers an additional improvement of the retention and stability of the dentures for subjects poorly adapted to their dentures, providing more favorable outcomes. The strategy for rehabilitation of fully edentulous arches may vary concerning the number and position of the implants and the type of retention – removable or fixed, and have specific criteria for indication depending on patient clinical factors, technical availability, patient preferences and financial conditions (SILVA, 2013). However, independent of the selected treatment strategy using implants, there are reliable evidences that implant treatments promote significant improvement in the patient's functional, social, psychological, and functional conditions when compared to conventional complete dentures.

Therefore, there is not a unique approach that could be considered the most suitable alternative for all edentulous patients considering both the type of denture retention and the number of implants. For the edentulous mandible, there are proposals for rehabilitation with overdentures supported by up to six implants with different retention systems and prosthodontic designs (KLEMETTI, 2008). However, there are sound evidences that in the mandible, patient satisfaction or function of the prosthesis do not seem to be dependent on the number of implants or type of attachment (KLEMETTI, 2008), however, an overdenture with two implants seems to have the least number of complications and fulfill the needs of most patients (EMAMI et al., 2009).

Consensus statements recommended the two-implant retained mandibular overdentures opposing to a maxillary conventional complete denture as the minimum standard of care that should be offered to edentulous patients as the

first choice of treatment (FEINE et al., 2002; THOMASON et al., 2009). Moreover, there is a large body of evidence from high quality randomized controlled trials that supports that this treatment approach is more effective than a conventional denture regarding several patient-centered outcomes, including patients' overall satisfaction, comfort and masticatory function, nutrition and oral-health related quality of life (THOMASON et al., 2012).

More recently, the use of a single midline implant to retain a mandibular overdenture has been proposed as an alternative to more complex overdenture designs for the treatment of mandibular edentulism (KRENNMAIR & ULM, 2001). This treatment approach aims to be simpler and less costly than both the fixed implant treatment and the overdenture retained by two implants (WALTON et al., 2009). It is assumed to be a more feasible option for geriatric patients due to their reduced functional demands and the favorable local bone condition in the symphyseal region that ensures satisfactory primary implant stability. Previous clinical studies reported favorable results on patient satisfaction and oral health-related quality of life measures (NOGUEIRA eta al., 2018), as well as other clinical and radiographic outcomes such as implant survival rate, marginal bone loss and longitudinal implant stability (ALSABEEHA et al., 2009). Despite differences across clinical studies regarding their experimental design, implant and retention systems, loading protocols and selected outcomes, there is converging evidence on the marked improvements provided by the single implant overdenture compared to the conventional treatment.

The search for less complex and less costly treatments is an important issue, since the incremental cost of implant treatments, when compared to the conventional treatment, remains a recognized barrier to the delivery of implant-supported prostheses, but it is suggested that the use of only two implants can keep the initial cost to a minimum and the differences regarding the whole cost over the expected life span of the patient is relatively small, especially when compared with the initial costs (THOMASON et al., 2009). In conclusion, although mandibular implant-retained overdentures may be more satisfying for edentulous patients than new conventional dentures, the magnitude of the effect is still uncertain, and there is a need for additional evidence including

cost-effectiveness analyses on the impact of mandibular implant overdentures and conventional dentures (EMAMI et al., 2009).

Another option for the rehabilitation of the edentulous mandible is the use of multiple implants in the interforaminal region of the mandible to retain a fixed prosthesis. The use of four implants "ad modum" Branemark with a permanent fixed rigid cross-arch suprastructure has been successfully used since the earliest introduction of osseointegrated implants, with high success rates and predictability regarding implant survival, and favorable patient-reported and clinical outcomes. However many patients may be reluctant to be submitted to this type of treatment, due to the more complex and invasive surgical procedures, and since this treatment modality generates an additional cost due to the more extensive surgical procedure with a higher number of implants, prosthetic components, and laboratory steps.

Also, patient preferences may play a relevant role when choosing theses different alternatives for the edentulous patients, since the perception of potential outcomes of prosthodontic treatment in fully edentulous patients, including benefits, risks and consequences of non-replacement of missing teeth may vary greatly among patients (LELES et al, 2008). Consideration of patients' preferences is an important issue for prosthodontic treatment planning and an essential part of an evidence-based approach which includes the integration of the best available scientific evidence, clinical expertise, and patient values as key factors in the decision-making process in health care. An understanding of the factors that influence patients' preferences in choosing treatment options is required to assist clinicians in deciding on the treatment that best matches patient desires and expectations, and would optimize clinical outcomes and quality of life.

An observational study with patients referred for conventional denture treatment showed that although most conventional dentures have several technical shortcomings, dissatisfaction with dentures was low and most patients were more likely to opt for minimum, low-stress and low-cost interventions (LELES et al., 2011). Therefore, a preference for the combined upper and lower CD was more commonly reported, and preference for implant treatments (including fixed

and removable prostheses) may be influenced by patients' perceived psychosocial benefits, functional performance, technical and financial concerns, post-insertion complaints, prosthesis removability, and longevity. Technical and financial concerns (cost, complexity, surgery risks and duration of treatment) were more relevant for those who preferred implants dentures. Conventional complete dentures are associated with lower expected outcomes by patients, and cost-related issues are the major factors associated with the preferences for implant treatment of edentulous patients (LELES et al., 2011; LELES et al., 2019).

In most cases, decision making regarding the type of treatment is influenced by economic criteria, related to the costs of each alternative and the patient's financial condition. However, even considering the evidence in the literature proving the superiority of implant prostheses over the conventional complete dentures, there are still few studies focused on the economic evaluation of treatment modalities for edentulous subjects.

The relevance of developing studies addressed to economic health assessment is to provide scientific evidence for decision making in the allocation of resources as appropriate as possible (SENDI et al., 1999). In the public health context, it is of utmost importance, since available resources are scarce and limited while health demands are extensive and increasingly high. Hence, misuse or wastes of money are key aspects of low effectiveness, inefficiency, and inequities in health care delivery (MAYNARD & MCDAID, 2003). This is not only relevant in the public health perspective, but also in the private practice, where providing the best care for the individual patient may also take into account the delivery of treatments with the better benefits along with the more efficient use of patient's financial resources.

Within this context, cost-effectiveness analysis is a type of economic evaluation that aims to compare the effectiveness of different competing treatment modalities, ie, indicated for the same clinical condition, and also the costs associated with these interventions. Data on treatment costs and outcomes are combined to generate a cost-effectiveness ratio that is defined as the set of information about the additional cost per improvement in a unit of measure of an

outcome between two or more interventions (BEIKLER & FLEMMIG, 2015). Although cost-effectiveness studies identify an incremental cost relative to an incremental benefit, these benefits are generally measured in terms of clinical outcome and do not capture a patient assessment of this outcome. Thus, the use of economic assessments that assess patient and public preferences provides essential information to healthcare providers and other stakeholders (SRIVASTAVA et al., 2013).

Thus, considering the principles of treatment simplification and the scarcity of studies directed at the interface between effectiveness and economic aspects of implant treatments, this study aims to evaluate the costs and outcomes of three treatment alternatives for rehabilitation of the mandibular edentulism using dental implants: overdenture retained by a single implant, overdenture retained by two implants, and mandibular fixed prosthesis retained by four implants. We also included a broad range of patient-reported outcome measures, and clinical and radiographic outcomes, assessed in both patient-level and implant-level, for inter-group comparisons. This study was planned as a three parallel-group randomized clinical trial alongside a cost-effectiveness analysis.

This study protocol was originally submitted for funding to the PPSUS-2014 Call for Proposals (Programa de Pesquisa para o Sistema Único de Saúde), that is a program by the Brazilian Ministry of Health for the Brazilian states aiming to promote scientific research within the context of the Brazilian Public Health System (Health Unified System – in Portuguese, Sistema Único de Saúde - SUS), for the scientific and technological development of the health system, and to address loco-regional peculiarities and specificities of each Brazilian states and for contributing to the reduction of regional inequalities (http://www.saude.gov.br/acoes-e-programas/ppsus).

Since 2011 the use of osseointegrated implants and subsequent prosthodontic rehabilitation was incorporated in the list of procedures covered by the Brazilian public health system (Portaria SAS 718, Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Atenção Básica – Coordenação Geral de Saúde Bucal). However, despite Brazil is considered one of the largest markets on implants worldwide, its effective incorporation is restricted to the private

practice with limited access to patients with socioeconomic constraints who are entirely dependent on the public healthcare.

Such inclusion of implant treatments in the list of procedures available highlights the importance of economic evaluations to incorporate in clinical practice interventions that are more cost-effective within the local and regional health system. Currently, there are few studies on this topic and, most of them carried out in other countries with limited application to the local scenario. Thus, along with the limited public resources, there coexist problems such as lack of evidence to guide clinical decision making and management of available technologies.

The results of this study, therefore, are of high clinical relevance and may contribute to the decision-making process when choosing between different alternatives for the rehabilitation of the edentulous mandible. The results of this experimental study may provide evidence about the effectiveness of simplified and low-cost interventions for edentulous subjects, especially for older people, who may be affected by the functional and psychological implications related to the use of unstable and uncomfortable mandibular dentures, and are less likely to adhere to complex and invasive implant interventions.

OBJECTIVES

Overall aim:

To perform a randomized clinical trial alongside a cost-effectiveness analysis comparing three parallel-groups (single-implant mandibular overdenture - Group I), two-implant mandibular overdenture - Group II), and four-implant fixed mandibular denture - Group III) concerning different implant treatment alternatives for the edentulous mandible in complete edentulous subjects.

Specific aims:

- To provide a set of maxillary and mandibular conventional complete dentures as the baseline treatment for the included subjects;
- To collect baseline data and randomly assign participants to the study groups;
- To provide implant treatments for the edentulous mandible, including surgical and prosthodontics interventions, according to the assigned study group and following the specific procedures for each treatment alternative;
- To collect data regarding clinical, radiographic and patient-reported outcomes in the 1-, 6- and 12-month follow-ups;
- To collect data regarding direct costs, according to the specific item costs and valuing methods;
- To perform a cost-effectiveness analysis based on comparative analysis of costs and cost-outcome ratios, considering the two-implant mandibular overdenture as the reference intervention for between-group comparisons.

MATERIALS AND METHODS

Study design and setting

This is a three-parallel group randomized clinical trial alongside a cost-effectiveness analysis. The study was initiated in March 2016 and the final 1-year data collection occurred on June 2019. All clinical procedures were performed at the Faculty of Dentistry at the Federal University of Goias. The study protocol was registered at the ClinicalTrials.gov database (NCT03056976) and was previously approved by the local research ethical committee (CAAE: 54455916.2.0000.5083).

The study arms corresponded to three alternatives for implant rehabilitation of the edentulous mandible, opposing to a conventional maxillary complete denture:

1. Single midline implant to retain a mandibular overdenture;
2. Two implants in the interforaminal region to retain a mandibular overdenture in the canine area bilaterally;
3. Four implants in the interforaminal region to retain a fixed mandibular denture.

In summary, all participants received a set of conventional complete dentures and, after the adaptation period, were randomly assigned to one of the three study groups. Implants were inserted using a single-stage surgical approach and conventional loading with a 3-month healing period. Then, the mandibular denture was incorporated into the implants, using specific retention systems and procedures according to the treatment group, and outcomes were assessed after a 1-, 6- and 12-month follow-up.

The summarized description of the study flowchart is shown in Figure 1.

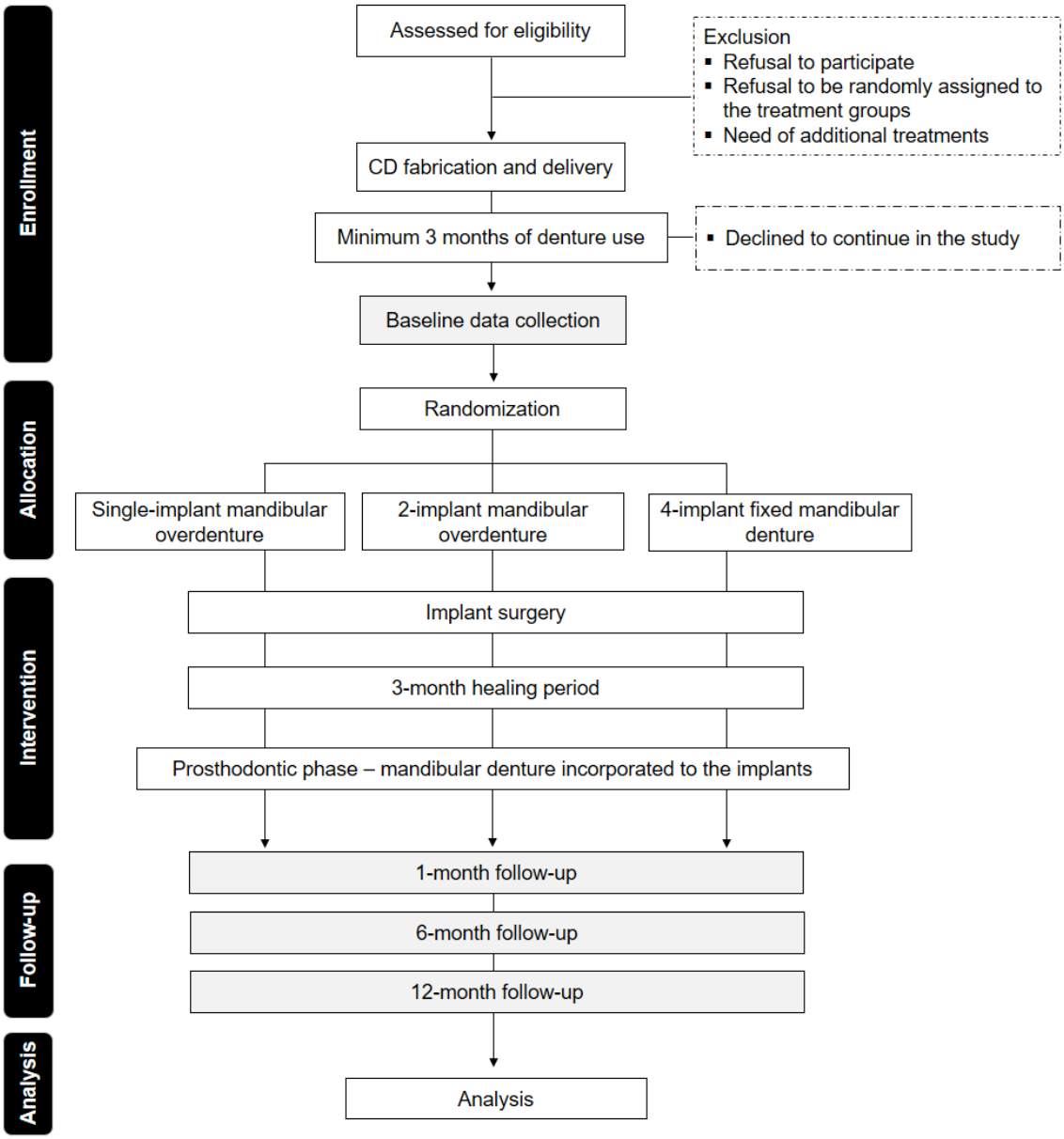

Figure 1. Flowchart of the study.

Study population and sample

The target population consisted of complete edentulous individuals, without restrictions regarding sex and age. Eligible participants were patients with need of new dentures, referred from the Public Health System through the Central Regulation of the Municipal health office. A convenience sampling approach was used by recruiting consecutive participants who fulfill the selection criteria.

Eligible participants were then invited to participate in a screening appointment, which included a detailed explanation of the entire study, from the early stages of treatment to the follow-up and data collection phases. For better clarification of the treatments provided by the study, potential participants received a lecture on aspects of the surgical and prosthodontic procedures, and participants also handled acrylic resin models of the implants and prostheses provided by the study (Figure 2). After the explanation of the characteristics of each treatment alternative and the differences between them, the invited individuals were asked to confirm the interest in participating in the study, and their agreement to be randomly allocated to any of the three treatment options, independent of their individual preferences.

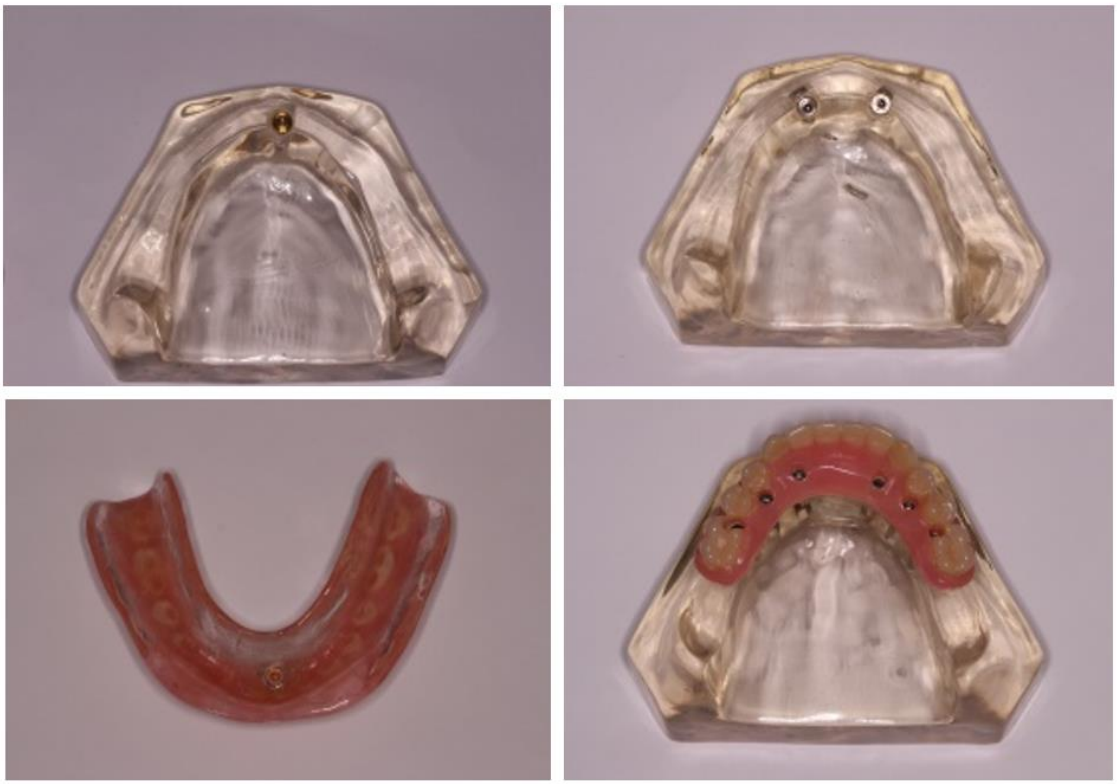

Figure 2. Dental implant models and prostheses.

Sample size

The G*Power software was used to calculate the sample size (available at http://www.gpower.hhu.de/). The required sample size was estimated for the study considering an *a priori* F tests – ANOVA with repeated measures (within-between interactions). The input parameters considered a “small” effect size (Cohen’s d=0.25), minimum power of 0.80 (type II error rate) at a two-sided 0.05 significance level (type I error rate), number of groups = 3, and number of repeated measurements = 4 (Figure 3).

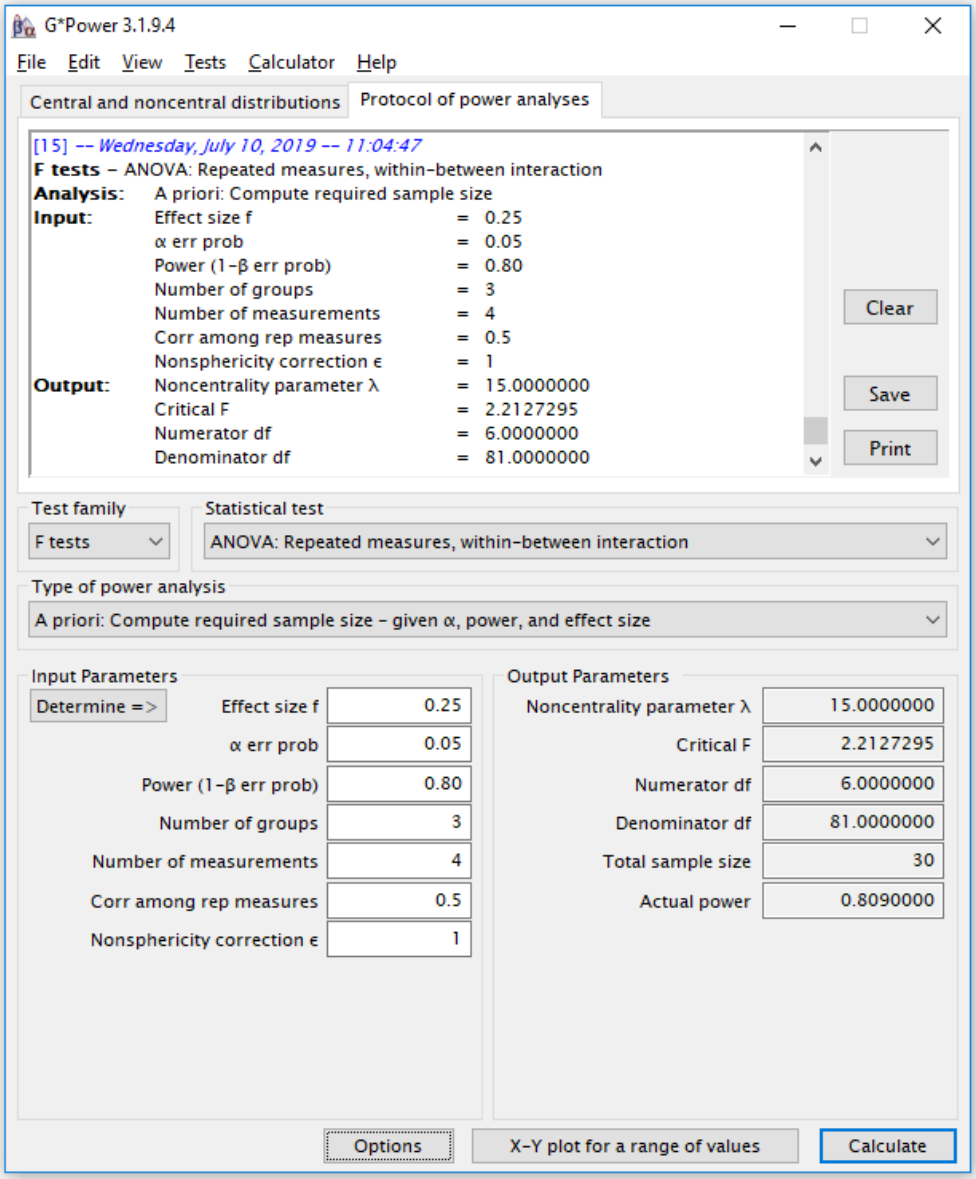

Figure 3. Input and output parameters for sample size calculation.

The minimum sample size was 30 (10 for each treatment group). An increase of 20% to reduce the impact of patient withdraw and loss to follow-up on study power resulted in a minimum final sample of 36 participants, 12 in each treatment group.

Selection criteria

After the initial screening, eligible participants were submitted to anamnesis and clinical examination, as well as a panoramic x-ray exam. The following inclusion criteria may be present:

- complete edentulousness;
- good general health;
- sufficient amount of alveolar bone in the anterior region of the mandible to receive implants of at least 9 mm in length;
- be available to attend the treatment appointments and the follow-up visits;
- satisfactory cognitive function.

As exclusion criteria, we considered the following:

- refusal to receive one of the three treatment alternatives provided by the study;
- smokers;
- local conditions that directly influence the stability, retention, and adaptation of the dentures, such as alterations or anatomical deformations of the jaws, severe mucosal lesions, tumors;
- systemic, psychological or neurological diseases that impair clinical oral care;
- interest in other treatment modalities not provided by the study;
- disorders related to alcoholism or other serious behavioral disorders that compromise their participation in the study.

The height of the alveolar ridge and bone availability for the installation of dental implants was assessed in the panoramic radiography with the use of a transparent template.

The cognitive ability of the participant was measured using the Mini-Mental State Examination – MMSE (FOLSTEIN et al., 1975). The MMSE is a widely used test of cognitive function among the elderly, especially to screen for dementia, which includes tests of orientation, attention, memory, language and visual-spatial skills. This examination was used as a screening tool to evaluate the cognitive condition of participants and confirm the study inclusion criteria of understanding and answer to the questionnaires during the study.

The Brazilian version of the MMSE was used (BRUCKI et al., 2003), which comprises two sections: (1) responses referring to the notion of spatial orientation, memory and attention, and (2) requires the respondent to name objects, follow verbal and written commands, write a sentence spontaneously, and try to reproduce a drawing of a polygon. For each correct answer, a score was assigned and the score obtained was compared to the level of education of the respondent. For illiterates, the minimum required score was 18 points; schooling from zero to three years, minimum score of 20 points; schooling between four and eight years, minimum score of 22 points; and schooling over eight years, a minimum score of 24 points (FOLSTEIN et al., 1975; BRUCKI et al., 2003).

The stratification of the participants' socioeconomic status was based on the Brazilian classification system by socioeconomic level, based on education and ownership of consumer durable goods (ABEP, 2014).

Ethical aspects of the study

Participation in the study was conditioned by the sign of an informed consent term. Confidentiality and anonymity of patient-related information were also guaranteed. Participants were not charged with any costs related to the treatment provided, including diagnostic exams, pre- and postoperative medications, implant surgery, prosthodontic treatment and post-insertion care.

In case of any adverse events or negative outcomes, participants were properly assisted minimize any harm related to the interventions and the best possible care was provided within the context of the university dental clinic were additional treatment was needed.

Complete denture treatment

Conventional denture treatment of the edentulous maxilla and mandible was proceeded according to the following protocol: (1) anamnesis and preliminary impression with stock trays and irreversible hydrocolloid (Jeltrate Dustless, Dentsply, Brazil), (2) final impression with a custom tray, border moulding with impression compound (Green Impression Compound Type 1; Kerr Corporation, Romulus, MI, USA), followed by a zinc-eugenol paste impression (Lysanda, Lysanda Produtos Odontológicos Ltda, São Paulo, Brazil); (3) occlusal registrations, mounting in a semi-adjustable articulator fixed in average settings, and selection of artificial teeth (Trilux, Dental Vip Ltda, Pirassununga, São Paulo, Brazil); (4) try-in visit to assess artificial teeth (Trilux, Dental Vip Ltda, Pirassununga, São Paulo, Brazil) arranged in bilateral balanced articulation; (5) delivery of the dentures; and (6) post-insertion visits for adjustments. All the laboratory steps were performed by the same commercial laboratory.

Patients were followed-up after the delivery of the dentures for adjustments until they report having no complaints related to the denture use. For those who still had minor complaints related to oral comfort of even major problems related to denture functioning, a minimum of 3 months elapsed from denture delivery to data collection at baseline.

At baseline, the quality of the dentures was assessed using the Functional Assessment of Dentures (FAD) instrument, described by Corrigan et al. (CORRIGAN et al., 2002) and validated by Anastassiadou et al. (ANASTASSIADOU et al., 2002), was used to assess the overall quality of the dentures according to the following parameters: freeway space, occlusion, articulation, denture retention, and stability. Additionally, the Kapur index (KAPUR, 1967) was used to evaluate the quality of the maxillary and

mandibular dentures concerning the degree of retention and stability, classified as poor, fair, or good. All the procedure for denture assessment was carried out by a single experienced prosthodontist.

The anterior mandibular ridges were classified according to the criteria described by Cadwood & Howell (CADWOOD & HOWELL, 1988), illustrated in Figure 4. All assessments were performed by the same implant surgeon.

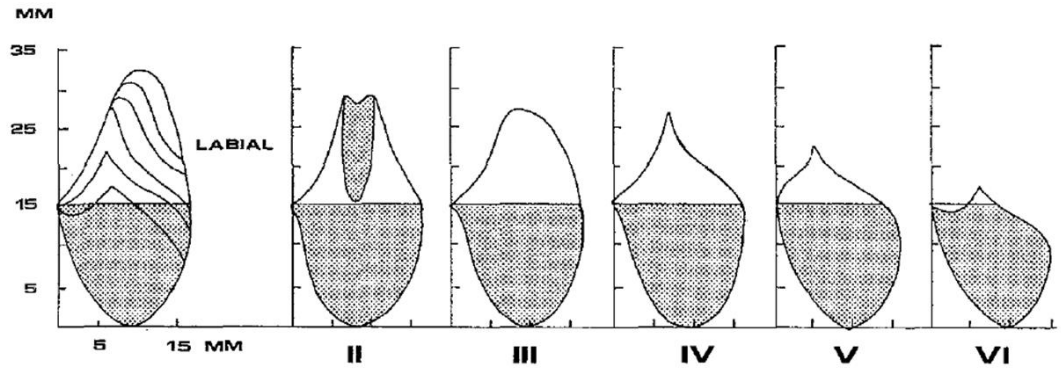

Figure 4. Classification of the edentulous ridges (Cadwood & Howell, 1988): Class I – dentate; Class II – immediately post extraction; Class III – well-rounded ridge form, adequate in height and width; Class IV – knife-edge ridge form, adequate in height and inadequate in width; Class V – flat ridge form, inadequate in height and width; Class VI – depressed ridge form, with some basalar loss evident.

Randomization

After the period of patient adaptation to the dentures, participants were randomly assigned to one of the three treatment groups: Group I: mandibular overdenture retained by a single implant (G-I); Group II: mandibular overdenture retained by two implants (G-II); or Group III: fixed mandibular prosthesis supported by four implants (G-III).

Randomization was performed by an independent member of the research team, not directly involved in patient care. We used a random number generator

(www.randomizer.org) to allocate participants among the treatment groups. Group assignment was performed using block randomization with unsorted and unequal block sizes, with an allocation ratio of 1:1:1. The numbered sequences were concealed in black sealed envelopes until the clinical appointment for baseline data collection.

Masking/blinding

Group assignment was disclosed for the participant only after baseline data collection to avoid selection bias and ensure adequate allocation concealment. Hence, their treatment groups were only revealed for each participant after the assessment of the baseline outcomes, which occurred after the delivery and regular use of the new set of conventional dentures. Considering that the preoperative exams differed for the treatment groups, the full blinding for the three interventions was not possible for those involved with treatment management and collection of data.

Interventions

Pre-surgical stage

Pre-surgical procedures were initiated after a minimum of three months after delivery of the complete dentures, to assure that participants were adapted to the dentures without significant complaints. Firstly, all participants were submitted to the laboratory and radiographic examinations. Blood tests that included complete blood count, prothrombin time, activated partial thromboplastin time, and fasting blood glucose were ordered to evaluate systemic conditions favorable to the surgical procedure. In case of adverse changes, the patient was referred to medical appropriate medical care.

Regarding imaging exams, for all participants the same panoramic digital radiograph of selection criteria was used for assessment of bone availability in the implant region. Additionally, a lateral cephalometric radiograph was required for Group I. A thin lead film was fitted in the midline region of the mandibular

denture for image acquisition to outline the shape and position of the mandibular denture and its relation with the area of the alveolar bone cross-section in the midline region (Figure 5). For the subjects of Groups II and III, a cone beam computed tomography of the anterior region of the mandible was performed, with a tomographic guide in position. (Figure 6)

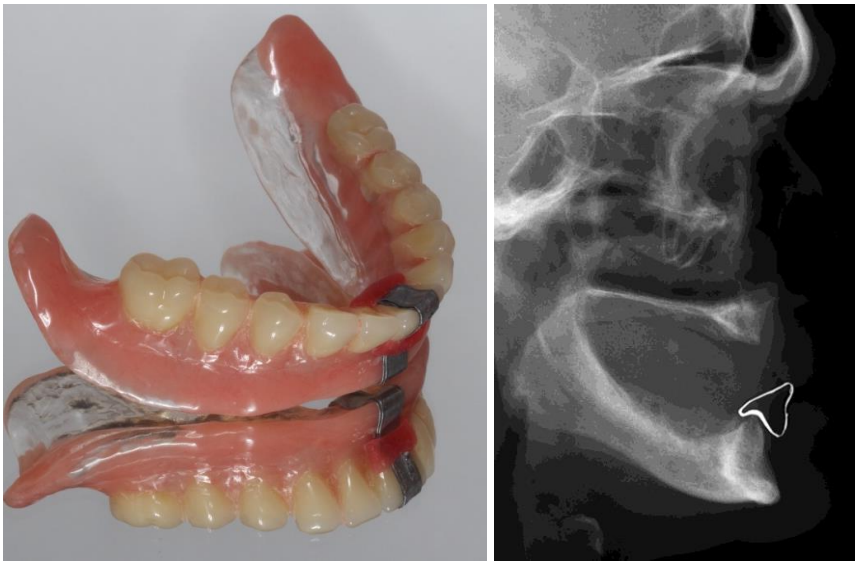

Figure 5. Lead film embracing the mandibular denture prior to image acquisition (left), and lateral cephalometric radiograph.

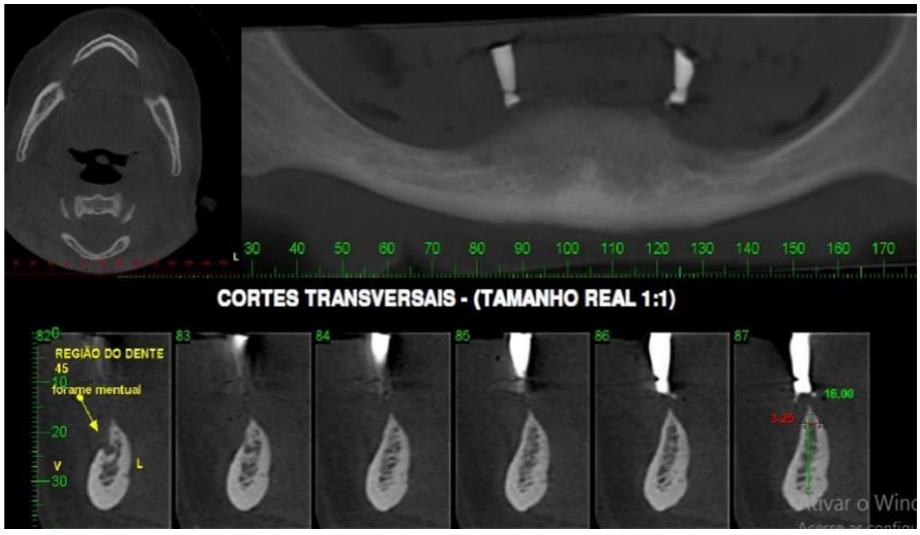

Figure 6. CBCT exam.

The surgical and tomographic guide was fabricated by duplicating the mandibular denture, using an irreversible hydrocolloid mold (Jeltrate Dustless,

Dentsply, Brazil) and self-curing acrylic resin (Vipiflash, Vipi, Brazil). Two perforations were made in the midline area (Group I), canine regions (Group II) or first premolar regions bilaterally, and covered with radiopaque material (gutta percha). The sequence of procedures for fabrication is detailed in Figure 7. The surgical guides were disinfected with 2% chlorhexidine digluconate for 12 hours.

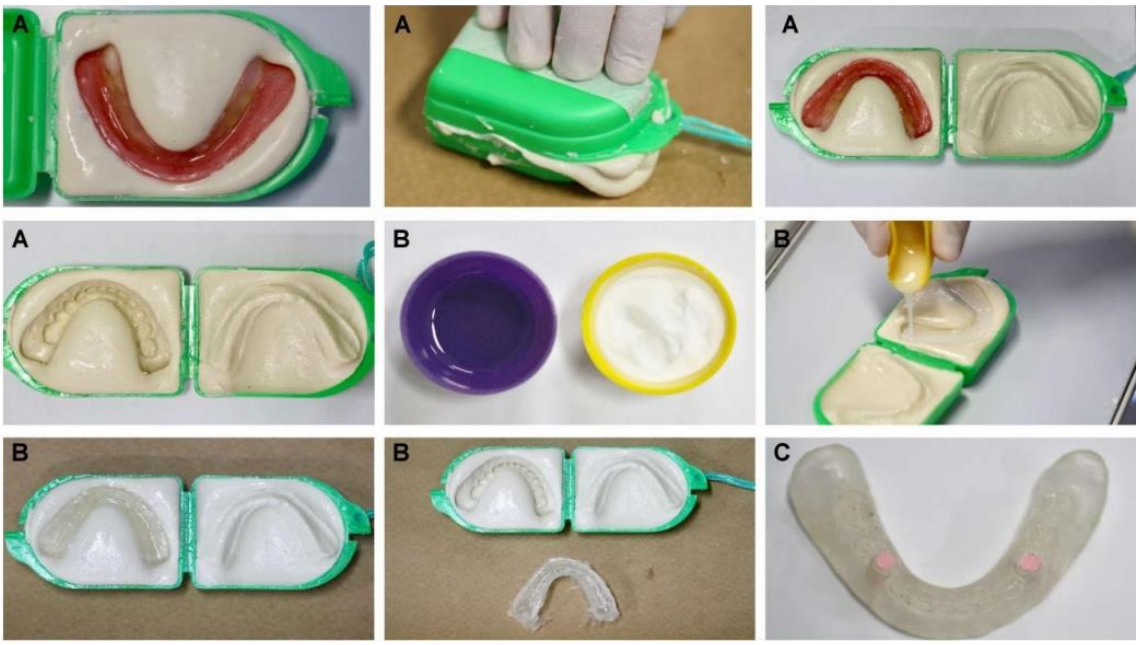

Figure 7. Fabrication of the surgical/tomographic guide: (A) duplication of the mandibular denture; (B) mould filling with self-curing acrylic resin; (C) finished tomographic guide.

Surgical stage

Preoperative 2g amoxicillin was administered for prophylactic purposes one hour before surgery (ESPOSITO et al., 2013), and 4mg dexamethasone for cases with more extensive surgery. The patient made a mouthwash with 0.1% chlorhexidine solution for 1 minute and the extraoral disinfection of the patient's face was performed with a sterile gauze soaked in 4% chlorhexidine digluconate solution.

The surgical procedure consisted of local infiltrative anesthesia using 4% articaine hydrochloride with epinephrine 1:100,000 (DFL Indústria e Comércio SA, Rio de Janeiro, Brazil), crestal incision using a 15C disposable scalpel

blade (Solidor-Lamedid, São Paulo, Brazil), followed by elevation of the mucoperiosteal flap. For the cases requiring regularization of the alveolar bone crest a #702 carbide drill and #1505 tungsten drill were used for bone drilling.

Bone drilling followed the standard procedures recommended by the manufacturer. The implants used for the three study groups were the 3.75 mm diameter external hexagon implant (Titamax TI Cortical, Neodent, Brazil) (Figure 8).

Figure 8. External hexagon implant (Titamax TI Cortical, Neodent, Brazil): 3.75mm implant diameter, 4.1mm diameter of the prosthetic platform with lengths of 9, 11, 13 and 15 mm.

The implant height and the final implant insertion torque were registered. Implant primary stability was also registered (Implant Stability Quotient – ISQ) using a magnetic resonance frequency device (Osstell Mentor, Integration Diagnostics, Göteborg, Sweden) the Osstell instrument (Integration Diagnostic, Gothenburg, Sweden). For each implant, the average of three repeated ISQ measures were registered for the buccal, left and right sides of the Smartpeg transductor.

For Group I a single implant was inserted in the midline region of the mandible, for Group II two implants were inserted in the canine regions bilaterally, and for Group III, four implants were distributed in the anterior region of the mandible between the two mental foramina.

In the final implant position, the implant platform was placed below the gingival margin and a healing abutment was connected to the implant to be at least 1mm above the sutured gingival margin. The suture was performed with simple interrupted stitches to be removed after 7 days. The inner part of the mandibular denture was relieved to avoid overload of the implant and, if needed, the denture was relined with a soft acrylic temporary relining material (Soft Comfort, Dencril, São Paulo, Brazil). One-stage surgical protocol and conventional loading with a 3-month healing period was adopted for the three groups.

Patients were instructed to have a soft food diet and to rinse with a 0.12% chlorhexidine mouthwash for 1 week. Paracetamol 750 mg was prescribed to a maximum of four times daily as needed. For Groups II and III or for patients who had extensive bone regularization, anti-inflammatory nimesulide 100mg was prescribed each 12-hours for a 3-day period.

Prosthodontic stage

During the healing period, the patients were followed-up continuously to assess the need for adjustments in the mandibular denture, substitution of the interim relining material or to solve any other complaints. Then, the prosthetic procedures were initialized at least three months after implant insertion. The distance between the gingival margin and the implant platform was recorded for selection of the prosthetic abutment, and the subsequent prosthodontic procedures were performed according to the study groups. *All procedures were performed by a single operator.*

- Groups I and II

For the overdenture groups, we used a nitrite-coated titanium ball attachment and a nylon matrix – O'ring attachment (Neodent, Brazil) (Figure 9) with a 32 Ncm torque. The height of the ball attachment was selected in order for the platform to be at least 1 mm above the gingival margin. The available abutment heights by the manufacturer were 2, 3, 4 and 5 mm.

Figure 9. Selected retention system for overdentures used in Groups I and II.

Then, the mandibular denture was relived in the implant region do accommodate the denture in position without interferences. The female component was incorporated into the denture using self-curing acrylic resin (Duralay, Reliance Dental, USA) with a 3–5 min period for curing before removal. The patient was asked to keep the opposing dentures firmly occluded in the intercuspal position during this procedure. Subsequently, the excess material was trimmed and the area was polished when needed. All participants received postoperative care and oral hygiene instructions, as well as for instructions on how to insert and remove the overdenture.

The clinical sequence for the prosthodontics stage for groups I and II are detailed in Figures 10 and 11, respectively.

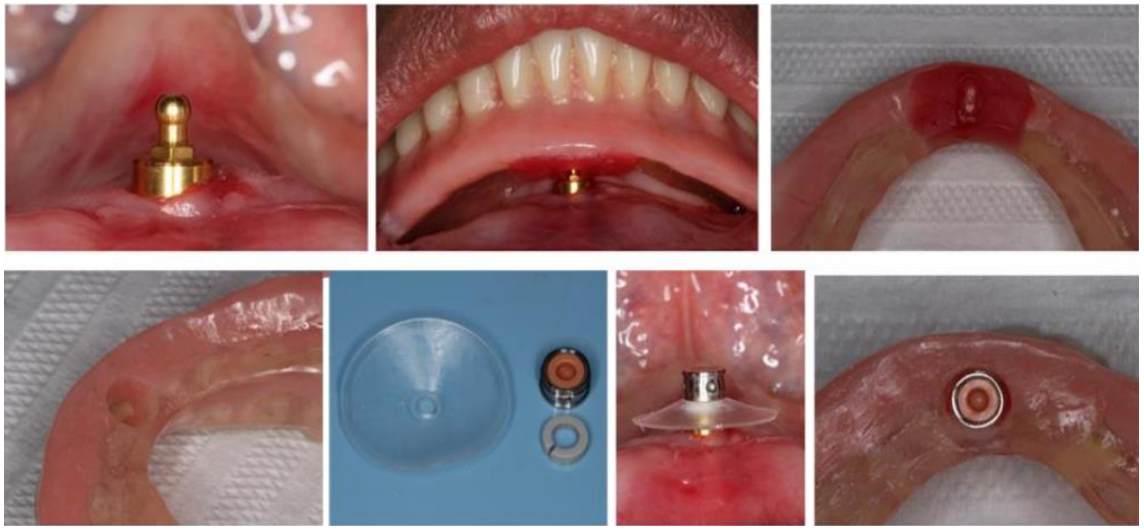

Figure 10. Procedures for incorporation of the retention system to the single-implant overdenture (Group I).

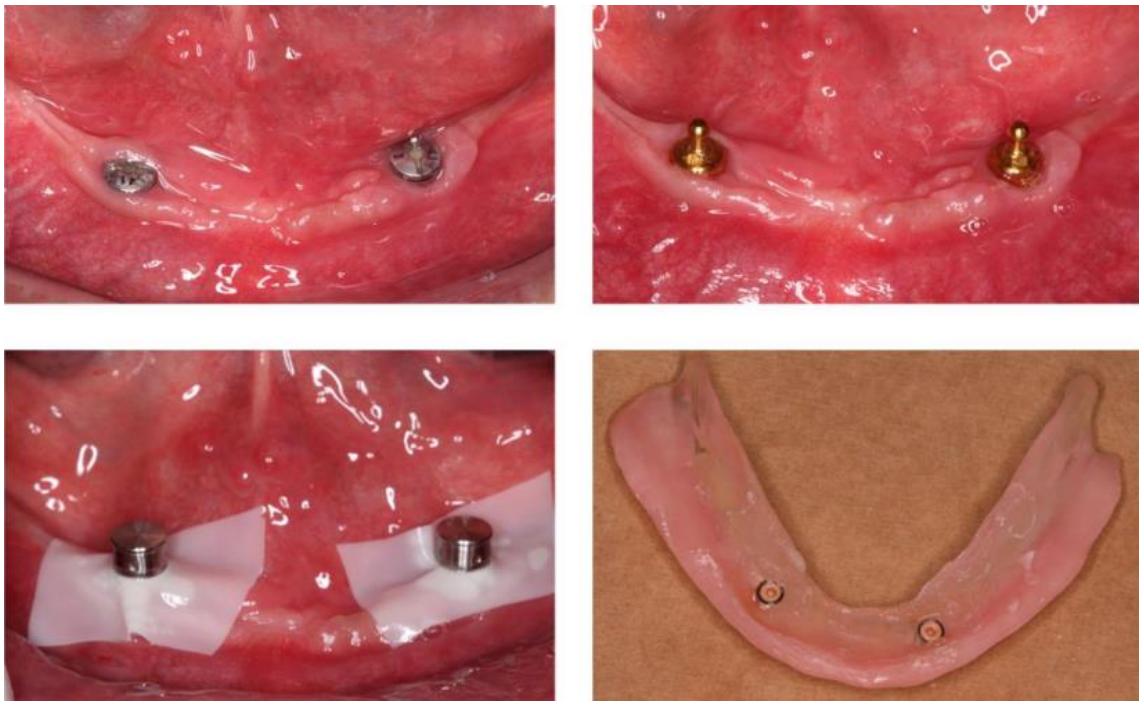

Figure 11. Procedures for incorporation of the retention system to the two-implant overdenture (Group II).

- Group III

For patients receiving the 4-implant fixed mandibular denture we proceeded the following protocol: (1) selection and insertion of mini-conical abutments (Figure 12) with a 32 Ncm torque (Neodent, Curitiba, Brazil); (2) impression transfer

with cylindrical impression copings and open tray moulding technique with condensation silicone rubber; (3) fabrication of a master cast; (4) waxing and casting of the metal infrastructure of the Co-Cr framework using a castable polymer coping for laboratory use; (5) intraoral try-in of the metal framework; (6) occlusal registration and articulator mounting; (7) teeth arrangement and intraoral try-in; (8) denture processing with heat-cured acrylic resin; (9) delivery of the prosthesis. The final aspect of the prosthesis in position is shown in Figure 13, and the radiographic aspect in Figure 14.

Figure 12. Implant mini-conical abutment used in Group III.

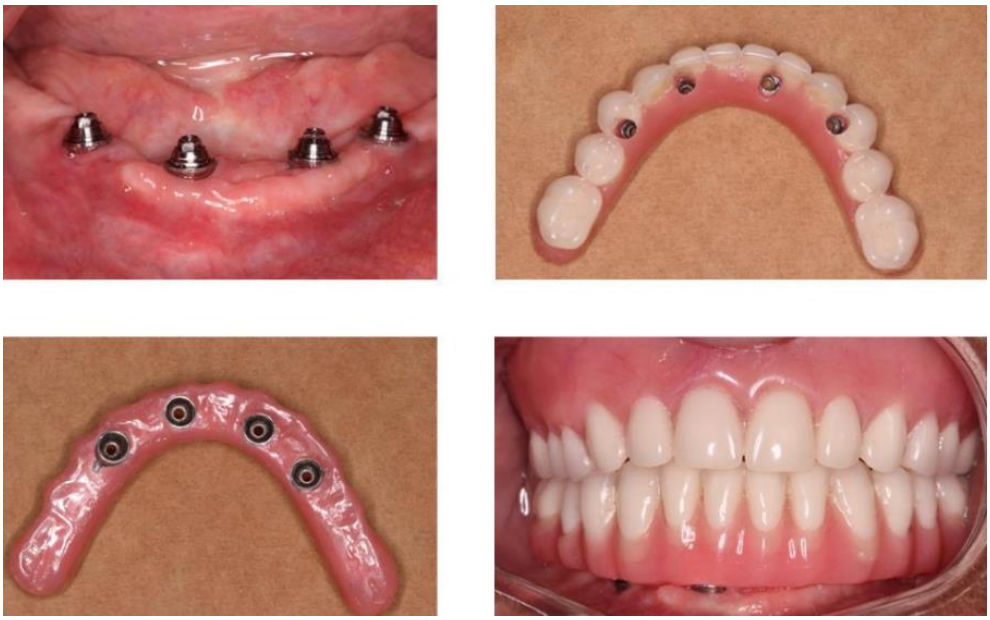

Figure 13. The final aspect of the prosthesis – retention system and the 4-implant fixed mandibular denture in position (Group III).

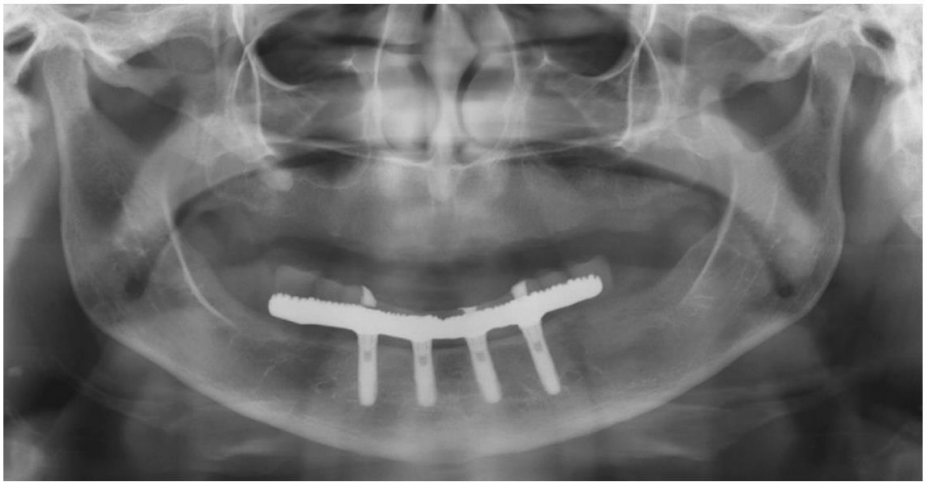

Figure 14. The final radiographic aspect of the prosthesis (Group III).

After insertion of the mandibular prosthesis, patients were instructed on the appropriate oral hygiene measures and the need of post-insertion routine care.

Outcomes

Time points for outcome measurement

Patients were assessed at different time points throughout the study. Time points were considered as a factor variable for longitudinal data analysis, defined as follows:

- Baseline: data were collected after the participants were adapted to their conventional dentures (minimum 3-months after denture delivery), before group randomization and implant treatment;
- Immediate follow-up: corresponding to 1-month post-delivery of the implant-retained prosthesis;
- Mid-term follow-up: 6 months after delivery of the implant-retained prosthesis (approximately months after implant surgery);
- Long-term follow-up: 1-year of implant-retained prosthesis use.

Patient-reported outcome measures

- Oral Health-related Quality of Life (OHRQoL) Impacts: OHRQoL impacts were measured using the cross-culturally adapted Brazilian version of the Oral Health Impact Profile for edentulous subjects (OHIP-Edent) (SOUZA et al., 2007). It contains 19 items divided into four different subscale domains: (I) masticatory discomfort and disability (four items), (II) psychological discomfort and disability (five items), (III) social disability (five items) and (IV) oral pain and discomfort (five items). The items are answerable on a 3-point Likert scale and responses will be summed to obtain an overall OHIP-Edent score and for each of the four domains. Higher scores represent worse OHRQoL.

- Satisfaction with the dentures: a 10-cm uninterrupted Visual Analogue Scale was used to assess the participants' ratings of their satisfaction with the maxillary and mandibular dentures considering the following parameters: "general satisfaction," "comfort," "stability," "aesthetics," "ability to speak," and "ability to chew". The respondent was asked to indicate his/her level of satisfaction with each parameter by marking a point along the scale, in which one end means "completely unsatisfied" and the other end means "completely satisfied". Then, an assistant converted each rating into a value between 0 and 100 by placing a transparent template with numbered intervals from 0 to 100 mm (HEYDECKE et al., 2003).

Clinical, radiographic and functional outcomes

- Masticatory Performance: it was measured using a mixing ability test with a two-coloured chewing gum. The selected gum was the Vivident Fruitswing "Karpuz/Asai Üzümü" (Perfetti van Melle, Turkey), a two-coloured gum comprising a green and a dark violet layer measuring 43×12×3 mm (Figure 15). Two subsequent tests were performed randomly with 20 and 50 chewing cycles. Subjects were instructed to chew in their preferred chewing side and, as the subject chew, the operator counted the number of chewing cycles by observing the mandibular movements in the anterior plane and

evaluating the up-and-down movements. Subsequently, the chewed gum was placed inside a transparent plastic bag, flattened to a wafer with a 1 mm thickness and then labeled with an identification code to allow blind assessment (Figure 16). Both sides of the specimen were scanned using a flatbed scanner at a resolution of 300 dpi (HP Photosmart C4780, Hewlett Packard Corp., Brazil). For quantification of the masticatory performance, an electronic colourimetric analysis was performed as described elsewhere (SILVA et al., 2018). In summary, colourimetric analysis was performed using the freeware ViewGum© software (dHAL Software, Greece, www.dhal.com). Images were transformed into the HSI (Hue, Intensity, Saturation) space using an image processing application to analyze separately the hue, intensity, and saturation. Then, the hue value was calculated for each pixel in the semiautomatically segmented images to obtain a representative measurement of the mixture by concentration only on the hue component. The circular variance of the hue (VOH) was considered the measure of mixing. The smaller is the VOH value, the greater was the mixing of the two-coloured layers of the chewed gum, which in turn means better chewing performance of the subject (Figure 17).

Figure 15. Two-colour chewing gum used for the masticatory performance tests.

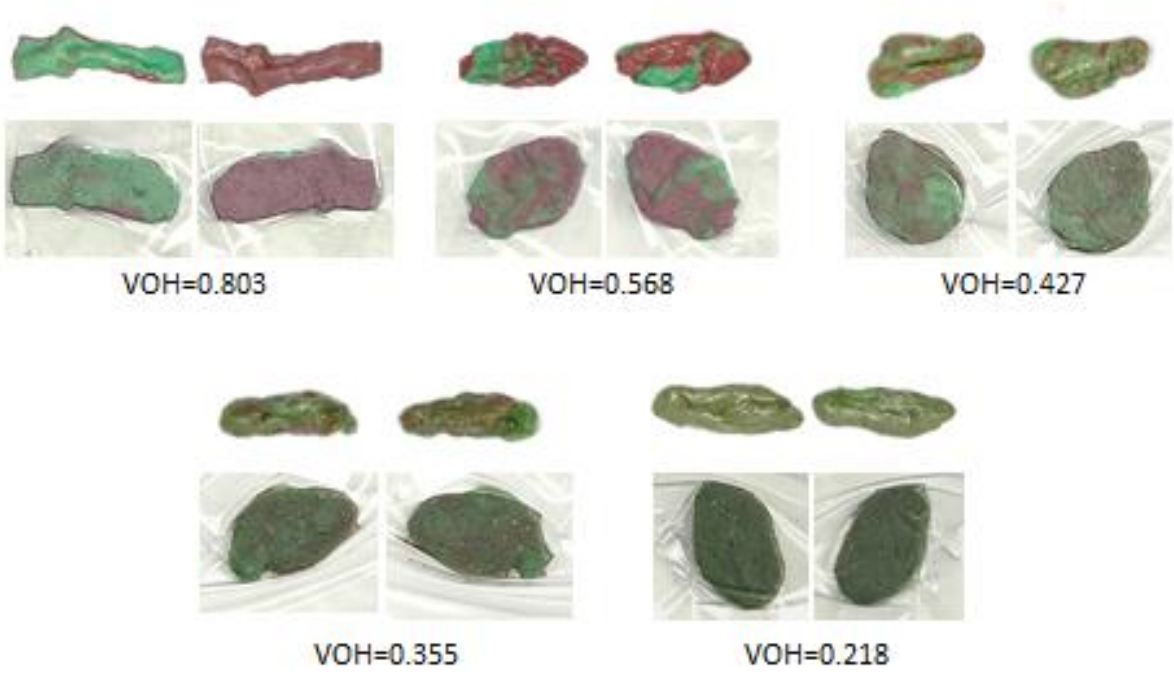

Figure 16. Images of the chewed gum specimens ordered in ascending grades of colour mixture. The original chewed gum and flattened specimens prepared for the electronic colourimetric analysis (the two-sided scanned specimen is shown). The corresponding VOH values represent the mixing ability measure using the ViewGum software.

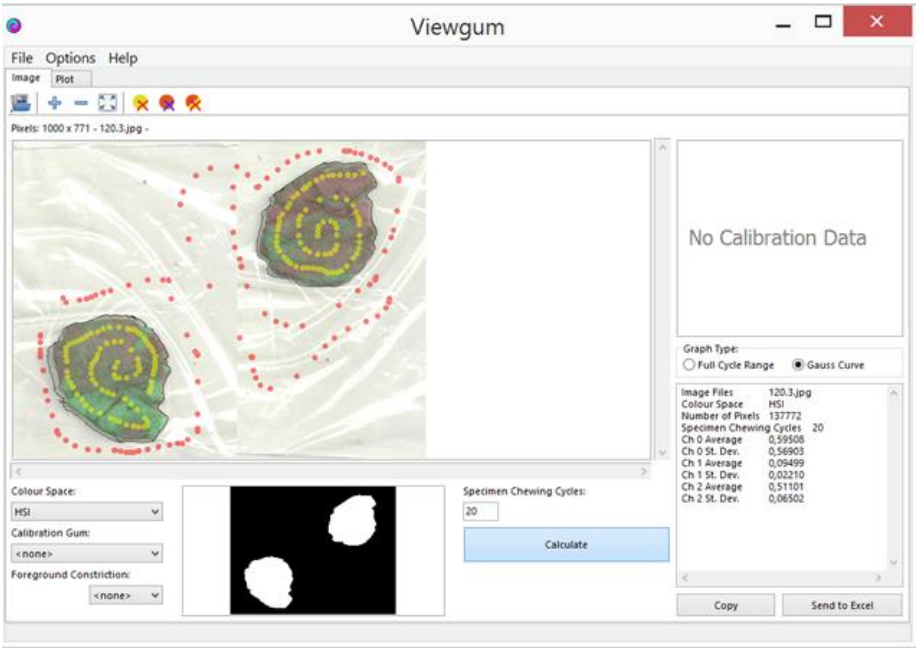

Figure 17. Printed screen of the ViewGum © software after loading two images of the chewed gum for 20 chewing cycles. Image foreground (yellow dots) and background (red dots). After calculating the targeted area, the results were

shown on the right side. Variance of Hue (VOH) displayed in the software output was used as a measure of the degree of mixing of the two colours.

- Implant survival and success: before- and after-loading implant survival were registered. Survival was defined as implant and prosthesis present in the mouth independent of biological and/or technical complications. Success was defined as being free of all these complications over the entire observation period (SMITH & ZARB, 1989).

Peri-implant bone changes: digital periapical radiographs of the implants were taken at the 1-, 6- and 12-month follow-up using periapical radiographic equipment (Heliodent 70, Siemens, Bensheim, Germany), with anexposure time of 0.5s. For acquisition of the digital images a phosphate plate system and digital scanner (EXPRESS™, Instrumentarium Dental, Tuusula, Finland) was used. A modified anterior positioner was used to allow the parallelism between the implant and the radiographic sensor. The radiographic images were considered satisfactory according to the following criteria: clear visualization of at least 3 threads in the coronal region of the implant neck in both sides of the implant (mesial and distal), absence of large image distortions perceived by the elongation or shortening of the implant and the distance between the implant threads, and absence of overlaps of bone structures. Implant bone level was defined as the distance between the first bone-implant contact and the implant platform, measured in the right and left sides. For the software calibration the implant platform was used (4.1 mm) and all measures were performed by a single operator**.** Peri-implant bone changes were calculated by subtracting the bone levels obtained in the different follow-up periods (6- and 12-month follow-ups) compared to baseline (1-month follow-up). The variation of the bone level over time was defined as the "marginal bone change". The Image J software (Image J 1.37v, National Institute of Health, Bethesda, MD, USA) was used for the linear measurements (Figure 18) **(**PETERSSON et al., 2001).

Figure 18. Measurement of the peri-implant bone level.

Implant stability: the Implant Stability Quotient (ISQ) was measured immediately after implant insertion and at the subsequent evaluations using the Osstell instrument (Integration Diagnostic, Gothenburg, Sweden). For each implant, the average of three repeated ISQ measures were registered for the buccal, left and right sides of the Smartpeg transductor. ISQ values are based on the resonance frequency parameters that are automatically converted into the ISQ values ranging on a 0-100 continuous scale. (FERREIRA, 2010; OLIVEIRA, 2010)

- Clinical aspects of the peri-implant region: the following parameters were assessed at 1-month follow-up (baseline) and the 6- and 12-month follow-up:

    - Distance between the gingival margin and the implant platform (Implant platform position – IPP): measured at the buccal, lingual, right and left aspects of the implant, measured with a millimeter

periodontal probe; positive values mean that the implant platform was at a supragingival level and negative values mean subgingival level.

- Oral hygiene:
  - Silness and Löe Plaque Index (1964): scores "0" (absence of plaque), "1" (plaque identified only by using a probe along the cervical surface of the prosthetic abutment), "2" (plaque identified by the naked eye), and "3" (abundant plaque).
  - Ramfjord's calculus score (1967): scores "0" (no calculus), "1" (discrete supra-gingival calculus limited to the gingival margin), "2" (moderate sub and supra-gingival calculus), and "3" (abundant sub and supra-gingival calculus).
  - Gingival Index (Löe, 1967): scores "0" (total absence of visual inflammation signs), "1" (mild color and texture alterations), "2" (visual inflammation and bleeding in the gingival margin after probing), and "3" (marked inflammation due to spontaneous bleeding).

- Prosthodontic events: the incidence of procedures for maintenance and repair of the prosthesis was registered throughout the clinical trial. Data included the frequency, date of occurrence, and types of events that occurred. Clinical complications included overdenture and teeth fracture, any need for repair and/or adjustment of overdentures and retention system components, such as loosening of the abutment, elimination of painful mucosal points, replacement of abutment and retentive matrices, and the need of relining of the prostheses.

Data analysis

Preliminary data analysis included descriptive statistics of the patients' features and primary outcomes. For hypothesis testing, as a first step, bivariate tests were used for pairwise comparison of outcome measures between baseline and the 6- and 12-month follow-ups. Normal distribution of data was tested using the Shapiro-Wilks test for normality. Departures from normality were assumed when

the test rejects the hypothesis of normality when the p-value is less than or equal to 0.05.

Further, the Generalized Estimating Equations (GEE) for repeated data was used to fit the repeated measures regression in order to identify the effects of time points and treatment groups on the outcome variables. Longitudinal associations were estimated considering the repeated outcome measurements at different time points (baseline, 6- and 12-month follow-ups) as the within-subjects variable, while the treatment groups (Groups I, II and III) were set as the between-subjects factor. The tested model effect included the main effects and the highest-level interaction term for all selected independent variables. Longitudinal multiple regression models were fitted to changes from baseline as the reference time point.

In addition, the estimates of effect sizes (ES) for each group were calculated to quantify the size of the difference provided by the three treatments. Hence, the "Effect Size" was used to quantify the size of the difference between the baseline and the 12-month follow-up, which measures the effectiveness of the intervention after 1 year relative to the initial condition.

For non-normally distributed data, ES was derived from the Wilcoxon signed-rank test comparing the differences in treatment outcomes between baseline and the 12-month follow-up. The Z-value of the test was divided by the square root of N (the number of observations over the two time points). Cohen's benchmarks were used for interpretation of the ES, where |0.1| was considered a small effect, |0.3| a medium effect and |0.5| a large effect.

For normally distributed data, ES was calculated based on Cohen's *d* effect size index for repeated measures (paired t-test): [$d = (mean_1 - mean_2) / s$], where *"s"* is the standard deviation of either group. The calculated effect sizes were classified as small (d = |0.2|), medium (d =|0.5|), and large (d ≥ |0.8|).

The incidence of clinical complications and maintenance events were registered throughout the complete follow-up period. Clinical complications included implant failure, peri-implant tissue problems, and overdenture fracture, whereas maintenance events comprised any need for repair and/or adjustments of the

dentures and of the retention system, such as elimination of mucosal sore points, abutment loosening, matrix and abutment replacement, and denture rebase and relining. Incidence rates (number of new cases per population at risk in a given time period) were calculated for each clinical event, as well as the incidence density rate, i.e. the person-time incidence rate in a monthly interval (number of new cases per the sum of the person-time of the at-risk population). The incidence density rate was calculated because more than one event may occur for the same individual in the follow-up period and because of the likelihood of having a different number of patients at-risk throughout the follow-up period due to treatment failure, withdrawal, and loss of follow-up.

All statistical analyses were performed using the IBM-SPSS 24.0 software and the significance level at $p < 0.05$.

Dahlberg, G. (1940). Statistical methods for medical and biological students, 122-132. London: George Allen & Unwin Ltd.

Cost-effectiveness analysis

The cost-effectiveness analysis was planned from the perspective of the health provider, simulating a clinical treatment in a private clinical setting. We included only direct cost items comprising all relevant expenditures and human resources that could be attributed to the delivery of the specific treatments. Cost items were identified and quantified alongside all clinical and laboratory phases of patient care, from baseline assessment after complete denture treatment up to the 12-month follow-up, using a “bottom-up” costing estimation method. We used the Brazilian currency (BRL$) for cost estimation with no discounting. Costs related to the implementation of the prosthodontic and surgical care, such as acquisition and depreciation of equipment and items of lasting value, professional training, transportation fares, and administrative expenses were not included in the cost estimation. The methods for cost estimation are detailed in Table 1.

Table 1. Description of cost items and methods for quantification, cost estimation methods and sources of valuing the direct cost items.

Item	Quantification of costs	Estimation method	Source of valuing
Manpower	(Month salary / monthly working time) x clinical time for treatment	Time in minutes	Reference salary
Consumables	Total cost items / number of patients	Microcosting	Mean market prices
Prosthetic laboratory	Prices per unit	Gross costing	Mean market prices
Implants and prosthetic components	Prices per unit	Microcosting	Catalogue prices

The quantification and valuing of human resources (dentist and auxiliary person) were performed by recording the clinical time of each appointment during the whole treatment period for all groups. Clinical time was registered in minutes and converted in “overall working hours for treatment”. Costs of labour force were valued considering as follows: the cost of working hours of the dentist and the auxiliary person was calculated based on the minimum wage stipulated by the 2018 indexes of the National Federation of Dental Practitioners (FNO) – R$ 5,622.00 for the 8-hour daily work routine (Lei 3999/61). We also added a 40% bonus for unhealthiness work and 23% for the specialization degree of the dentist (Table 2).

Table 2. Base values for manpower costs – dentist and auxiliary (in BRL$).

	Dentist (monthly)	Auxiliary (monthly)	Sum
Base salary	R$ 5.622,00	R$ 1.258,21	R$ 6.880,21
Additional for unhealthiness work (40%)	R$ 2.248,80	R$ 503,28	R$ 2.752,08
Additional for specialization (23%)	R$ 1.293,06		R$ 1.293,06
Total per month	R$ 9.163,86	R$ 1.761,49	R$ 10.925,35
Total per week	R$ 2.290,97	R$ 440,37	R$ 2.731,34
Total per day	R$ 458,19	R$ 88,07	R$ 546,27
Total per hour (8h daily)	R$ 57,27	R$ 11,01	R$ 68,28
Total por hora (+100%)	R$ 114,55	R$ 22,02	**R$ 136,57**

The incremental cost-effectiveness ratio (ICER) was calculated as the overall parameter for the cost-effectiveness analysis:

$$ICER = (CostA - CostB) / (EffectA - EffectB)$$

, where “cost” was set as the overall treatment cost described in monetary units and “effect” the outcome measures in terms of patient-reported outcomes for the study groups. ICER compares two treatment modalities to determine which of them provides a more cost-effective relationship and also provides to decision-makers information on which alternative would offer more potential benefit, and where resources should be allocated when they are limited.

For calculation of the incremental cost and effectiveness, Groups I and III were assigned as treatment “A” (the new technology) and Group II (2-implant overdenture) was assigned as treatment “B” (the usual technology). The

effectiveness of each treatment was calculated by the difference between the overall outcome measured at the 12-month follow-up and at the baseline assessment (difference in effectiveness throughout the 1-year period due to the treatment provided). ICER was calculated considering the outcome patient satisfaction with the mandibular denture and was interpreted as a common effect that measures the difference in magnitude between the two alternatives using data retrieved from a clinical trial, expressed in terms of the incremental cost per unit of effect.

Since the estimated costs and outcome measures may vary across different clinical settings and considering that the use of different techniques may occur in a real-world condition, a sensitivity analysis was conducted to evaluate the impact of changes in various key parameters on the cost-effectiveness results. A non-probabilistic one-way sensitivity analysis was performed by imputing values to the outcome measures within the lower and upper limits of a 20% change of both the mean values of satisfaction scores (effectiveness) and costs.

Two hypothetical scenarios were generated by combining these 20% limits to simulate extreme conditions for the ICER estimation: (1) a best scenario that combines the worst possible outcome for Group I group and the best possible outcome for Groups II or III – that represent the higher incremental effectiveness and the lowest ICER value for a fixed treatment cost, and (2) a worst scenario that combines the best possible outcome for Group I and the worst possible outcome for Groups II or III – that represent the lower incremental effectiveness and the highest possible ICER value for a fixed treatment cost.

For the cost-effectiveness analysis, the Microsoft Office Excel software was used to construct the spreadsheets for cost estimations and ICER calculations.

RESULTS

The total number of potentially eligible individuals invited to participate in the study was 78 edentulous subjects. They were assessed for eligibility and 28 did not fulfill the selection criteria and were excluded due to the following reasons:

- General health conditions that limited patient availability to be submitted to implant surgery within a reasonable time period (n=8);
- No interest in receiving implant treatment (only interested in replacement of the existing complete dentures (n=6);
- Smokers (n=5);
- Excluded due to low cognitive function as assessed by the MMSE (n=4);
- Presence of oral lesions requiring pre-prosthetic surgical intervention (n=2);
- Limited alveolar bone availability in the anterior mandible – lower than 9 mm (n=2);
- Presence of remaining teeth roots (n=1).

The remaining 50 subjects were enrolled for the complete denture treatment stage. Treatment was provided as described previously. The duration of fabrication of the complete dentures, from the complete anamnesis and clinical examination until delivery of dentures ranged from 17 to 63 days (mean = 36.3; SD = 9.9).

After denture delivery, patients were followed-up for adjustments and adaptation to the dentures until baseline data collection. The time elapsed after denture delivery ranged from 1.15 to 14.3 months (mean = 4.8; SD = 3.7). Baseline data collection occurred when the participant had no major complaints related to the complete dentures or when a minimum 3-month period elapsed from denture delivery appointment.

Then, participants were invited again to continue in the study and were informed about the next phases of the study interventions, including the random assignment to the treatment groups and the subsequent exams and surgery for

implant insertion. At this point, four participants were excluded from the study due to the following reasons: three were satisfied with their complete dentures and judged that they did not need any additional treatment, and other participant died 2 months after denture delivery due to pancreatic cancer.

The remaining 46 participants were assessed at baseline and were randomly assigned to the treatment groups using unequal sized block randomization. The resulting sample sizes were: Group I = 14; Group II = 17; and Group III = 15.

However, after being randomized other five participants withdraw the study – 3 from Group II and 2 from Group III. In addition, after the implant treatment, two participants died due to cardiovascular disease – one before the 1-month follow-up and other between the 1- and 6-month follow-up, from Groups I and II, respectively.

The remaining 39 participants submitted to implant surgery had the implant and prosthodontic treatment completed. Before the 6-month follow-up one patient from Group I was dissatisfied with treatment and withdraw the study due to additional treatment with a higher number of implants to retain a fixed denture. Therefore, the final sample comprised 37 participants – 11 in Group I, 13 in Group II, and 13 in Group III. All these patients completed the 12-month follow-up and the complete patient flowchart is detailed in Figure 19.

Analysis of baseline data

Baseline data analysis included all participants (n=37) who achieved the final follow-up after 12 months of treatment completed – 11, 13 and 13 participants for Groups I, II and II, respectively.

There were 18 female (48.6%) and 19 male participants (51.4%). Age ranged from 39.2 to 77.2 years at the first appointment after patient selection – mean=63.5; SD=8.8 years-old. Twenty-three participants were married (62.2%) and regarding working status, 22 (59.5%) were retired. Most of the participants (n=29; 78.4%) had low educational level – lower than 8 years of formal education and all participants were from the lower socioeconomic stratum.

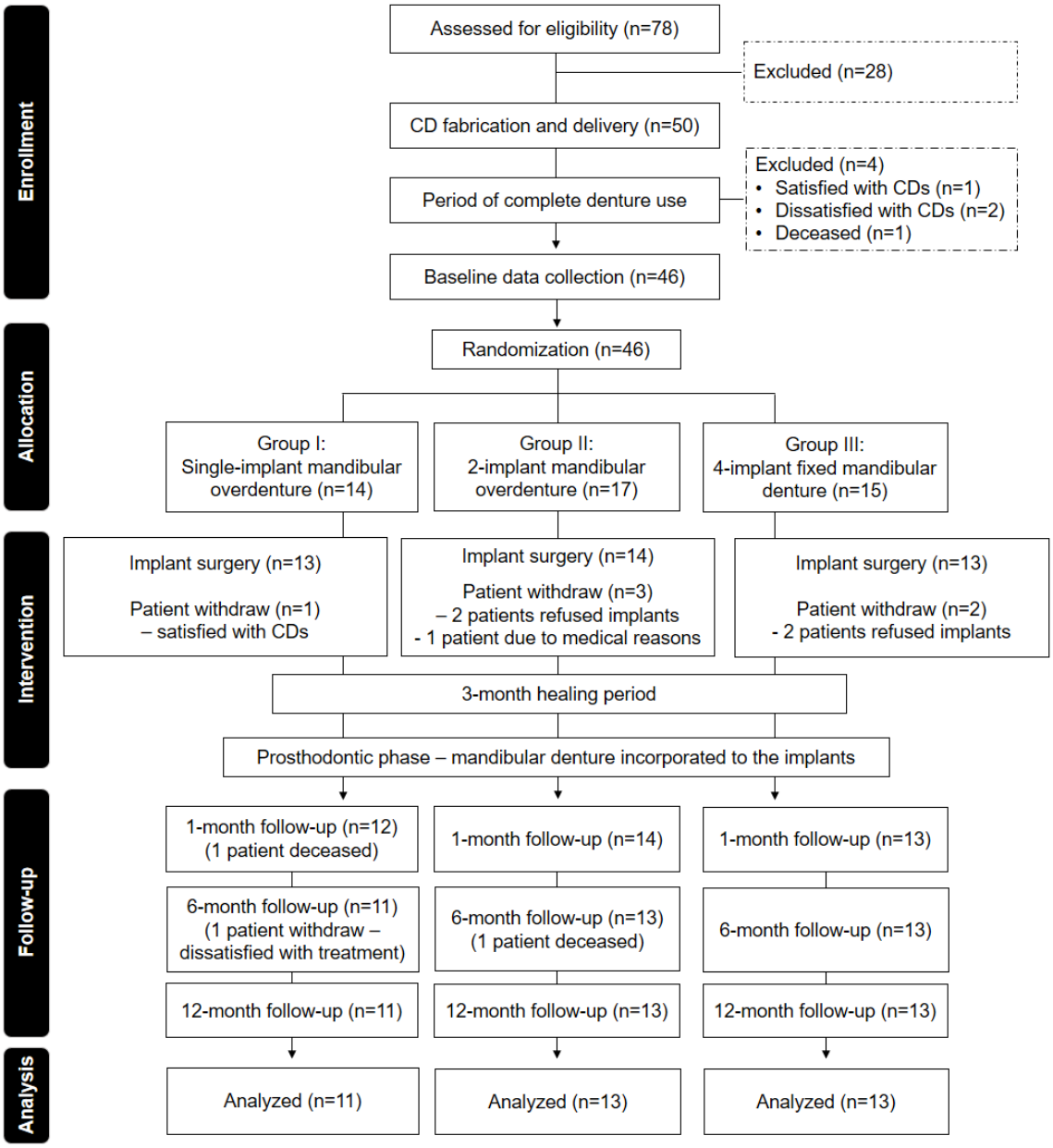

Figure 19. Patient flowchart throughout the study.

There was no differences among groups regarding participants' sex (Chi-square=0.218; p=0.897) and age groups – < 65, 65–74 and ≥75 years-old (Chi-square=7.15; p=0.128).

Table 3 shows participant's features concerning edentulism and denture use at the time they were enrolled in the study. No differences were found among groups regarding the previous use of maxillary and mandibular dentures, and time of edentulism (p>0.05). However, there were more participants with current

use of both dentures in Group III, and using only the maxillary denture in Group II. This difference was barely significant (p=0.048). No group differences were found regarding patient satisfaction with the old dentures and OHIP-Edent scores before complete denture treatment (p>0.05).

Table 3. Patients' features regarding edentulism and denture use.

	Group I	Group II	Group III	p-value
Previous use of CD				
Maxillary	10 (90.9%)	12 (92.3%)	10 (83.3%)	0.750*
Mandibular	8 (72.7%)	10 (76.9%)	10 (83.3%)	0.826*
Current use of CD				
Maxillary and mandibular	6 (54.5%)	6 (46.2%)	11 (84.6%)	0.048*
Maxillary only	2 (18.2)	6 (46.2%)	0 (0.0%)	
No dentures	3 (27.3%)	1 (7.7%)	2 (15.4%)	
Time of edentulousness (years)***	20.5 (±17.0)	21.3 (±12.5)	19.2 (±14.6)	0.149**
Kapur index***				
Quality of dentures	3.4 (1.6)	3.1 (1.6)	3.1 (2.1)	0.925**
Quality of supporting tissues	15.4 (2.7)	13.8 (3.3)	14.4 (3.2)	0.416**
Satisfaction with the old dentures***				
Maxillary	52.7 (37.3)	59.2 (35.9)	59.0 (23.2)	0.584**
Mandibular	28.0 (34.1)	45.0 (38.2)	16.5 (14.8)	0.328**
OHIP-Edent scores***	23.6 (16.6)	16.5 (15.8)	19.1 (8.0)	0.864**

CD: Complete dentures
* Chi-square test
** Kruskal-Wallis test
*** Mean ± Standard Deviation

After complete denture treatment and baseline data collection prior to group randomization, patients were assessed regarding the characteristics of the newly worn dentures fabricated as part of the clinical trial. The results about the quality of the dentures and patient perception of treatment are detailed in Table 4. Subsequent to baseline data collection, participants (n=46) were randomized to the study groups and received implants in the anterior mandible (n=39).

Considering patient exclusion due to withdrawal, Table 5 describes the clinical features of the 37 participants who completed the 12-month follow-up. Table 6 shows the characteristics of the implants inserted according to the study groups.

Table 4. Baseline variable measured after use of the new dentures, according to the treatment groups. Values are expressed as median and interquartile range.

	Group I	Group II	Group III	p-value*
Quality of the dentures				
FAD score	3.0 (2.3)	3.0 (3.0)	3.5 (2.0)	0.796
Kapur index	7.0 (4.0)	5.6 (2.3)	6.2 (4.0)	0.297
Kapur index – maxillary	4.3 (2.0)	3.4 (3.0)	3.5 (3.0)	0.347
Kapur index – mandibular	3.0 (3.0)	2.1 (1.3)	2.6 (2.0)	0.532
Satisfaction with the new dentures				
Maxillary	100 (11.7)	95 (12.5)	100 (3.3)	0.186
Mandibular	76.7 (70.0)	63.3 (70.8)	81.7 (33.3)	0.825
OHIP-Edent scores	9.0 (12.0)	9.0 (11.0)	7.0 (8.0)	0.988

* Kruskal-Wallis test
FAD: Functional Assessment of Dentures

Table 5. Patients' features regarding clinical and pre-surgical aspects for implant planning (percentage in parenthesis)

	Total	Group I	Group II	Group III	p-value
Prosthodontic Diagnostic Index (PDI)					
Class I – II	6 (16.2)	3 (27.3)	2 (15.4)	1 (7.7)	0.648*
Class III – IV	31 (83.8)	8 (72.7)	11 (84.6)	12 (92.3)	
Classification of the alveolar ridge – anterior mandible					
Class III – IV	29 (78.4)	9 (81.8)	10 (76.9)	10 (76.9)	0.947*
Class V – VI	8 (21.6)	2 (18.2)	3 (23.1)	3 (23.1)	
Height of the anterior mandibular ridge (in millimetres)**	22.2 (5.6)	20.9 (4.1)	21.9 (6.0)	24.0 (6.4)	<0.001***

* Chi-square test
** For groups II and III calculated as the mean value of the multiple implant regions (data expressed as mean and standard deviation)
*** One-way ANOVA

Table 6. Main features of the inserted implant, according to the study groups.

	Group I	Group II	Group III	p-value
Number of implants inserted	11	26	52	
Dimension of the implants*				
3.75 x 9 mm	2 (18.2)	4 (15.4)	8 (15.4)	0.505
3.75 x 11 mm	1 (9.1)	4 (15.4)	8 (15.4)	
3.75 x 13 mm	3 (27.3)	7 (26.9)	5 (9.6)	
3.75 x 15 mm	5 (45.5)	11 (42.3)	31 (59.6)	
Final insertion torque**				
Mean (SD)	92.3 (18.1)^{A}	61.2 (28.7)^{B}	69.2 (27.0)^{B}	0.015
Min – Max	45 – 100	10 – 100	23.8 – 100	
ISQ value				
Mean (SD)	83.2 (3.7)	83.3 (3.5)	81.5 (3.3)	0.389
Min – Max	75.7 – 88.7	76.5 – 89.7	77.0 – 86.6	

* Data expressed as frequency (percentage); p-value for Chi-square test
** Different letters correspond to subsets of Tukey HSD test after One-way ANOVA

Analysis of patient-reported outcome measures

Oral health-related quality of life (OHRQoL)

OHIP-Edent scores were used to assess the impacts of the oral conditions on patient's oral health-related quality of life measures. Data from baseline and longitudinal assessments are summarized in Figure 20, concerning the overall OHIP-Edent scores. In addition, Table 7 shows the summary data for the overall score and for the specific domains of the questionnaire, for the overall sample and groups of treatment.

Results showed an overall improvement (lower OHIP-Edent scores) at the longitudinal assessments compared to baseline. The more evidenced differences were found for the overall OHIP-Edent score, and for Group III. It also showed higher effect sizes for Groups II and III compared to Group I.

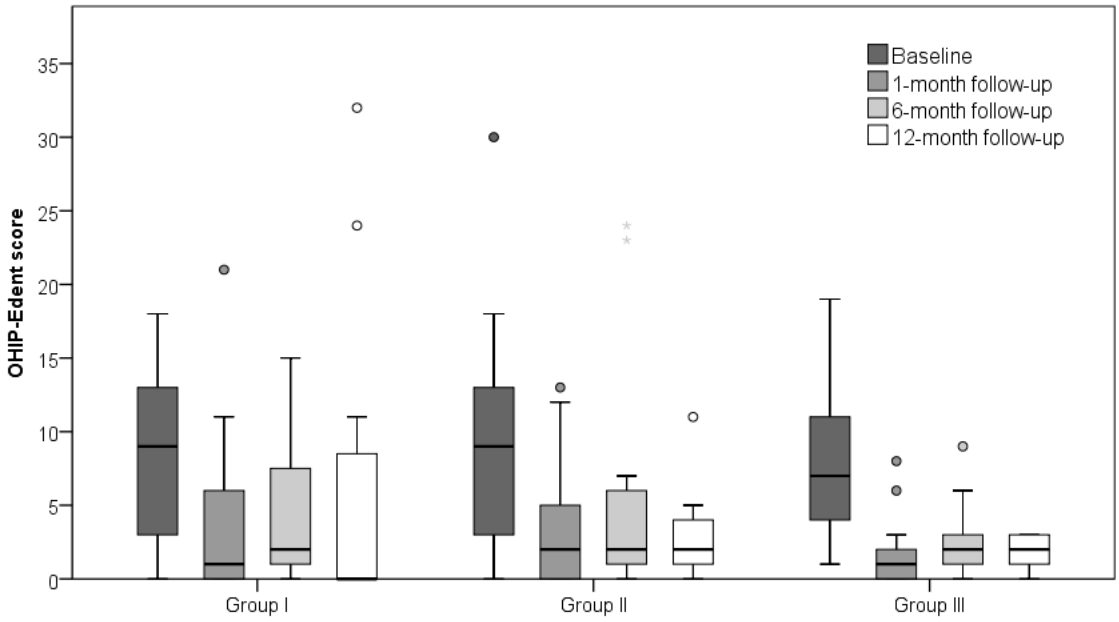

Figure 20. Distribution of OHIP-Edent scores according to the treatment groups and assessed time points.

The test of the main models effects (treatment groups and time points) in GEE analysis resulted in no differences between treatments (Wald Chi-square=1.88; df=2;p=0.390) and significant effect of time points on OHIP-Edent scores (Wald Chi-square=22.2; df=3; p<0.001) – there was a significant difference between the baseline assessment and the 1-month (p<0.001), 6-month (p<0.001) and 12-month (p=0.021) follow-ups. No significant effect of the group/time interactions was observed and was not included in the specification of the final model effect.

Table 7. Descriptive data of OHIP-Edent overall and domain scores (median and interquartile range values), according to the treatment groups and time points.

	Group	Baseline	1-month	6-month	12-month	p-value**	Effect Size
OHIP-Edent (overall)	I	9.0 (12.0)	1.0 (7.0)	2.0 (10.0)*	0.0 (11.0)	0.070	0.22
	II	9.0 (11.0)	2.0 (5.5)*	2.0 (5.5)	2.0 (3.5)*	0.020	0.40
	III	7.0 (8.0)	1.0 (5)*	2.0 (2.5)*	2.0 (2.0)*	0.001	0.42
MRC domain	I	3.0 (5.0)	0.0 (3.0)	0.0 (2.0)*	0.0 (3.0)	0.141	0.29
	II	3.0 (4.5)	1.0 (2.5)*	0.0 (2.0)	1.0 (2.0)	0.373	0.32
	III	2.0 (3.5)	0.0 (1.0)*	0.0 (0.0)*	0.0 (5.0)*	<0.001	0.54
PDD domain	I	2.0 (3.0)	0.0 (2.0)	0.0 (5.0)	0.0 (3.0)	0.179	0.00
	II	1.0 (2.5)	0.0 (0.0)*	0.0 (1.5)	0.0 (2.0)	0.075	0.26
	III	0.0 (2.0)	0.0 (0.0)*	0.0 (1.5)	0.0 (0.5)	0.084	0.12
SD domain	I	0.0 (2.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.249	0.03
	II	0.0 (1.5)	0.0 (0.0)	0.0 (0.5)	0.0 (0.0)	0.082	0.36
	III	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.392	0.21
OPD domain	I	3.0 (3.0)	0.0 (4.0)	2.0 (3.0)	0.0 (5.0)	0.166	0.21
	II	3.0 (4.0)	1.0 (3.5)	1.0 (3.5)	1.0 (1.5)*	0.100	0.42
	III	3.0 (3.0)	1.0 (2.0)*	1.0 (1.0)*	2.0 (1.5)*	0.001	0.41

* Significant difference compared to baseline (Wilcoxon Signed Ranks Test)
** Non-parametric Friedman test

Satisfaction with the dentures

Figures 21 and 22 show the distribution of patient satisfaction scores for the maxillary and mandibular dentures, respectively, as well as the variation in satisfaction according to the study time points and differences among treatment groups.

Bivariate analysis in Table 8 revealed no differences in between-group and within-group comparisons regarding the maxillary denture, whilst significant differences were found for the mandibular denture in the within-group comparisons between baseline and the longitudinal follow-ups ($p<0.05$) for all time points and treatment groups (Table 8). Although all groups showed significant improvement in the 12-month follow-up compared to baseline, Group

III showed a higher effect size value (ES=0.57 – large effect), followed by Group II (ES=0.43 – medium effect) and Group I (ES=0.36 – medium effect).

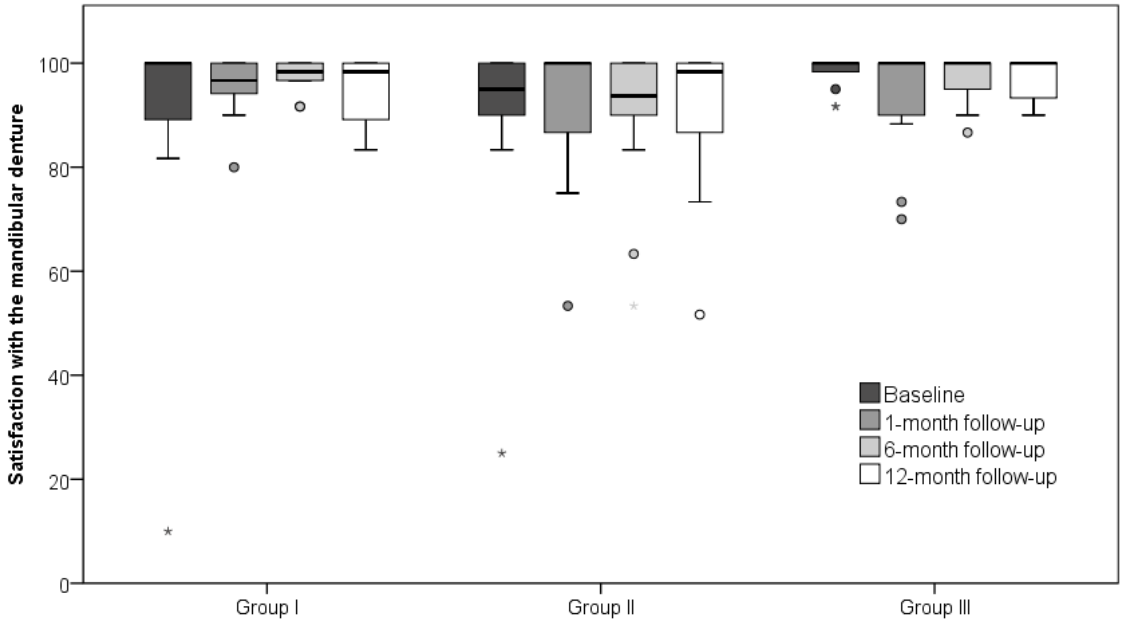

Figure 21. Distribution of the scores of patient's satisfaction with the maxillary denture according to the treatment groups and assessed time points.

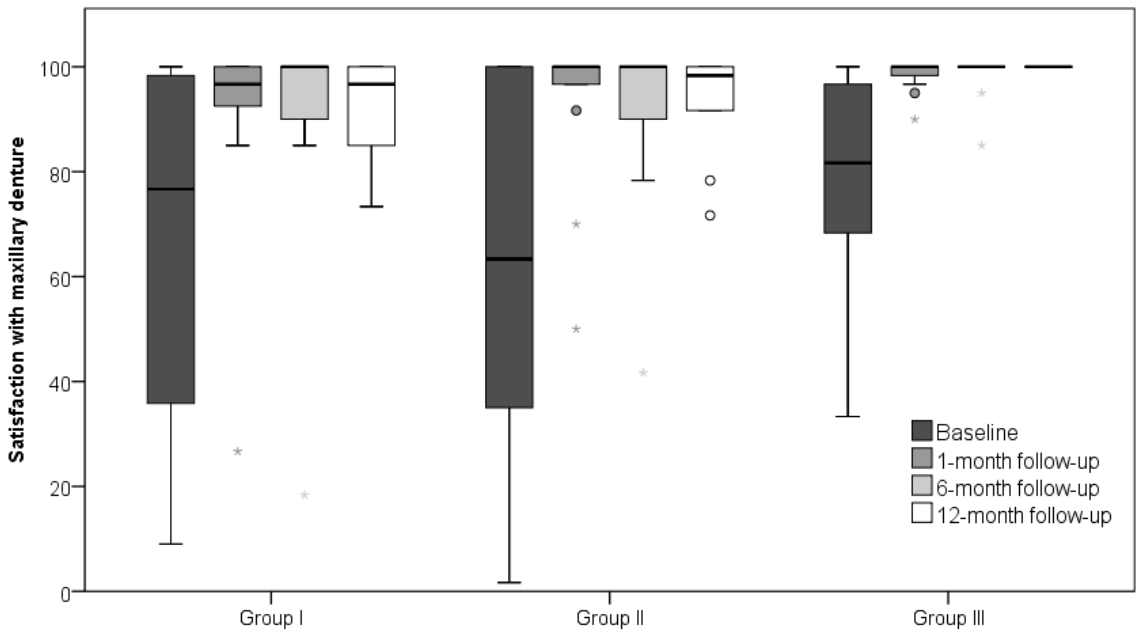

Figure 22. Distribution of the scores of patient's satisfaction with the mandibular denture according to the treatment groups and assessed time points.

Table 8. Descriptive data of patient satisfaction with the maxillary and mandibular, according to the treatment groups and time points. Data are expressed as median and interquartile range.

		Time points					
Satisfaction score	Group	Baseline	1-month	6-month	12-month	p-value**	Effect Size
Maxillary CD	Group I	100 (11.7)	96.7 (6.7)	98.3 (3.3)	98.3 (11.7)	0.624	0.16
	Group II	95 (12.5)	100 (13.3)	93.7 (13.3)	98.3 (18.3)	0.920	0.02
	Group III	100 (3.3)	100 (10.8)	100 (5.8)	100 (8.3)	0.352	0.23
	p-value***	0.186	1.000	0.343	0.901		
Mandibular CD	Group I	76.7 (70.0)	96.7 (8.3)*	100 (11.7)*	96.7 (18.3)*	0.056	0.36
	Group II	63.3 (70.8)	100 (5.8)*	100 (15.0)*	98.3 (15.0)*	0.007	0.43
	Group III	81.7 (33.3)	100 (2.5)*	100 (0.0)*	100 (0.0)*	<0.001	0.57
	p-value***	0.825	0.319	0.156	0.050		

* Significant difference compared to baseline (Wilcoxon Signed Ranks Test)

** Non-parametric Friedman test

*** Non-parametric Kruskal-Wallis test

Table 9. Parameter estimates for the Generalized Estimating Equations models for patient satisfaction with the maxillary and mandibular dentures as dependent variables.

Dependent variables	Maxillary denture				Mandibular denture			
Parameter	B (95% CI)	Wald Chi-Square	df	p-value	B (95% CI)	Wald Chi-Square	df	p-value
(Intercept)	4.53 (4.43 – 4.62)	9767.5	1	<0.000	4.19 (3.99 – 4.39)	1685,1	1	<0.001
Treatment groups								
Group III	0.01 (-0.50 – 0.071)	0.108	1	0.742	0.12 (-0.03 – 0.27)	2.429	1	0.119
Group II	-0.03 (-0.12 – 0.05)	0.659	1	0.417	0.01 (-0.16 – 0.19)	0.019	1	0.891
Group I	Reference				Reference			
Time points								
12-month follow-up	-0.01 (-0.09 – 0.08)	0.013	1	0.909	0.29 (0.15 – 0.42)	16.324	1	<0.001
6-month follow-up	0.03 (-0.05 – 0.11)	0.612	1	0.434	0.29 (0.16 – 0.43)	17.965	1	<0.001
1-month follow-up	0.02 (-0.05 – 0.08)	0.271	1	0.602	0.31 (0.18 – 0.44)	20.794	1	<0.001
Baseline	Reference				Reference			

Results of GEE analysis in Table 9, considering the hierarchical structure of longitudinal data, also confirm the results of the bivariate analyses. No significant effect was observed in the tests of overall model effects for the maxillary denture concerning the treatment groups (Wald Chi-square=1.32; df=2; p=0.528) and time points (Wald Chi-square=2.34; df=3; p=0.505). Conversely, for the satisfaction with mandibular denture significant effect were found for both the treatment groups (Wald Chi-square=6.38; df=2; p=0.041) and time points (Wald Chi-square=22.0; df=3; p<0.001). Independent of the treatment groups, significant positive effects were observed from baseline to all the longitudinal assessments (p<0.001), as observed in Table 9. In addition, no significant effects were found for the interaction between the independent variables and, therefore, the interaction between factors were not included in the final models.

Masticatory Performance (MP)

Preliminary analysis of VOH measures revealed that the distribution of data was normally distributed for the treatment subgroups. Therefore, descriptive and bivariate analysis were based on parametric parameters, and for GEE we used linear model type and link function for the regression estimates.

Table 10 shows the results of the bivariate between-group contrasts according to the treatment groups and number of masticatory cycles, and the within-groups contrast comparing the different time points. All-group subjects were considered for analyses.

Table 11 describes the within- and between-groups comparison of mean values o MP. There were significant differences in all paired comparisons between baseline and the 1-, 6- and 12-month follow-ups, except for the comparison between baseline and 1-month follow-up for Group I in 20 cycles (p=0.352) and Group III in 50 cycles (p=0.106). No between-group differences were found in all time points for both 20 and 50 cycles. The effect sizes calculated for comparison between group means ranged from medium (-0.69; -0.74) to large (> -0.94).

Table 10. Bivariate comparisons of mean values of masticatory performance according to the factors of variation.

Factor			Mean (SD)	p-value
Number of cycles	20		0.475 (0.16)	<0.001*
	50		0.356 (0.14)	
Treatment groups	Group I		0.446 (0.17)	0.059**
	Group II		0.414 (0.16)	
	Group III		0.391 (0.14)	
Time points	20 cycles	Baseline	0.607 (0.11)	<0.001***
		1 month	0.480 (0.14)	
		6 months	0.358 (0.12)	
		12 months	0.445 (0.14)	
	50 cycles	Baseline	0.468 (0.12)	<0.001***
		1 month	0.350 (0.12)	
		6 months	0.260 (0.11)	
		12 months	0.331 (0.11)	

* Independent t-test
** One-way ANOVA
*** Repeated-measures ANOVA

Table 11. Descriptive data of masticatory performance (VOH values) according to the number of chewing cycles, treatment groups and time points of follow-up. Data are expressed and means (and standard deviations).

	Group	Baseline	1-month	6-month	12-month	Effect Size
20 cycles	I	0.604 (0.14)	0.549 (0.16)	0.356 (0.14)*	0.500 (0.16)*	-0.69
	II	0.634 (0.09)	0.482 (0.15)*	0.388 (0.14)*	0.427 (0.14)*	-1.88
	III	0.584 (0.09)	0.440 (0.13)*	0.347 (0.11)*	0.420 (0.14)*	-1.49
	p-value**	0.529	0.202	0.692	0.293	
50 cycles	I	0.509 (0.14)	0.381 (0.12)*	0.280 (0.15)*	0.387 (0.12)*	-0.94
	II	0.477 (0.08)	0.353 (0.16)*	0.253 (0.10)*	0.322 (0.14)*	-1.41
	III	0.426 (0.12)	0.359 (0.13)	0.256 (0.11)*	0.337 (0.12)*	-0.74
	p-value**	0.216	0.813	0.812	0.241	

Data distribution depicted in Figure 23 shows that there is a progressive improvement in masticatory performance (decreasing VOH values) from baseline to the 6-month follow-up for all treatment groups, considering both the

tests for 20 and 50 cycles. It was also evident a small increase in VOH values from 6- to 12-month follow-ups, suggesting a slight declining in masticatory performance after 1 year.

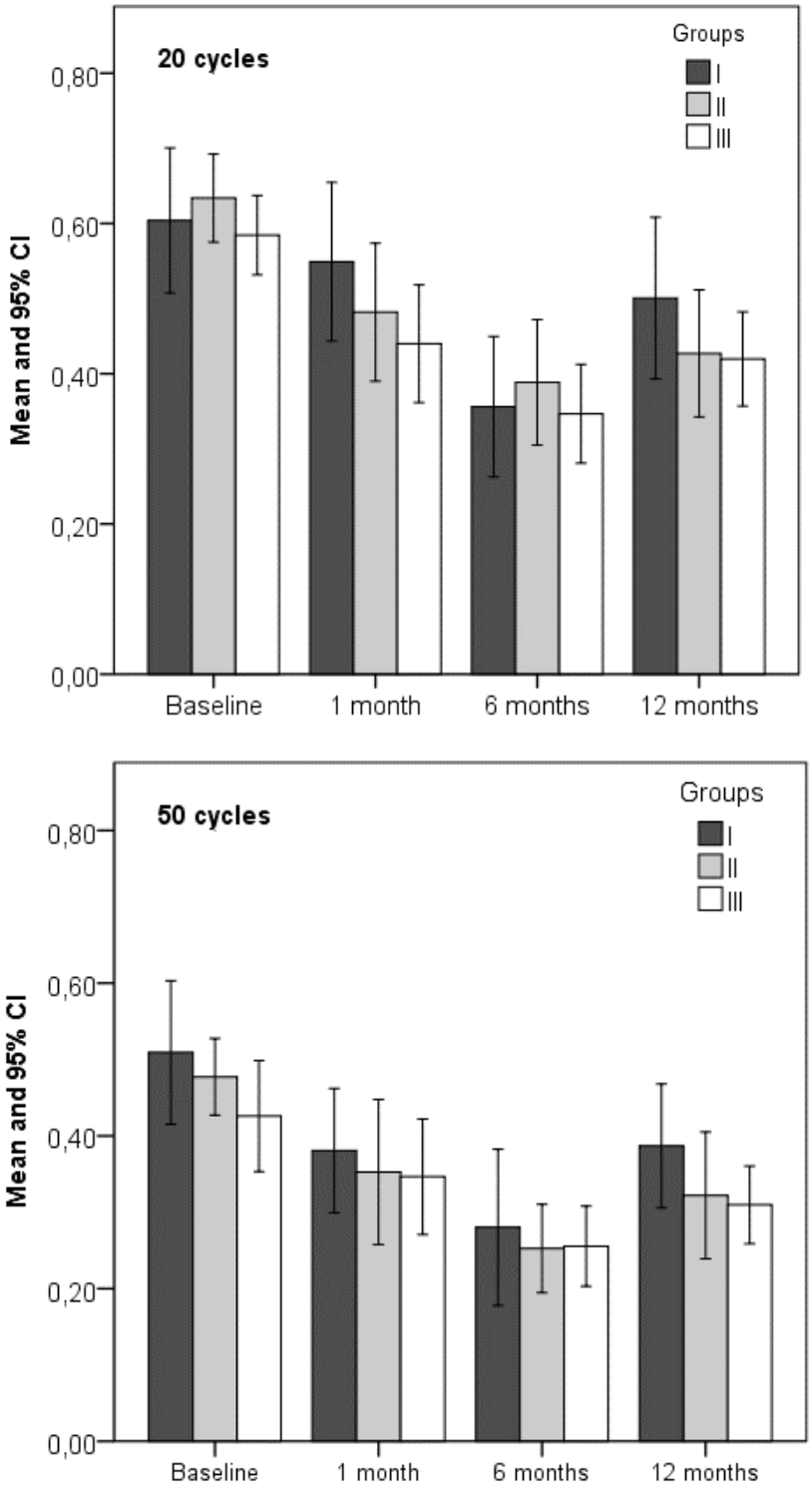

Figure 23. Mean values of Masticatory Performance according to the treatment groups, time points and number of chewing cycles – 20 (upper) and 50 (lower).

The test of model effects in GEE analysis (Table 12) revealed a significant effect for the variation in time points ($p<0.001$) and the number of chewing cycles ($p<0.001$), and a non-significant effect of the treatment groups ($p=0.168$). Table 10 details the parameter estimates of the GEE regression model for masticatory performance as influenced by the independent variables. Results confirm the significant improvement in all longitudinal assessments compared to baseline ($p<0.001$), as well as the higher VOH values for 50 cycles ($p<0.001$). In addition, although there was no significant effects on the treatment group factor, the was a barely non-significant effect between Groups I and III.

Table 12. Parameter estimates for the Generalized Estimating Equations model for masticatory performance as dependent variable.

Parameter		B (95% CI)	Wald Chi-Square	df	p-value
(Intercept)		0.627 (0.563 – 0.691)	365.0	1	<0.001
Treatment groups	Group III	-0.055 (-0.115 – 0.006)	3.17	1	0.075
	Group II	-0.029 (-0.100 – 0.042)	0.65	1	0.422
	Group I	Reference			
Time points	12-month follow-up	-0.146 (-0.184 – -0.108)	55.86	1	<0.001
	6-month follow-up	-0.225 (-0.265 – -0.185)	121.28	1	<0.001
	1-month follow-up	-0.115 (-0.164 – -0.065)	20.72	1	<0.001
	Baseline	Reference			
Number of cycles	50	-0.119 (-0.135 – -0.104)	233.80	1	<0.001
	20	Reference			

Peri-implant bone changes

Table 13 shows the summary values of the peri-implant bone levels for implants in Groups I and II at baseline and after 12 months. Significant changes were found for Group I ($p=0.002$), as shown in Figure 24. GEE analysis in Table 14 revealed that changes were significantly higher for Group I compared to Group II (left and right sides). No significant effects were also found for the time point variable (baseline *vs* 12 months).

Table 13. Descriptive data of the distance between the implant platform and the peri-implant bone level (in millimetres), according to treatment group, implant-level measurements, and time points (baseline and 12-month follow-up). Data are expressed and means (and standard deviations).

Groups	Baseline	12-month	p-value*
Group I	-0.35 (1.05)	-0.72 (0.88)	0.002
Group II (all implants)	-0.43 (0.95)	-0.33 (0.82)	0.489
Group II – Left	-0.45 (1.04)	-0.30 (0.99)	0.845
Group II – Right	-0.41 (0.87)	-0.37 (0.64)	0.349

* Wilcoxon test

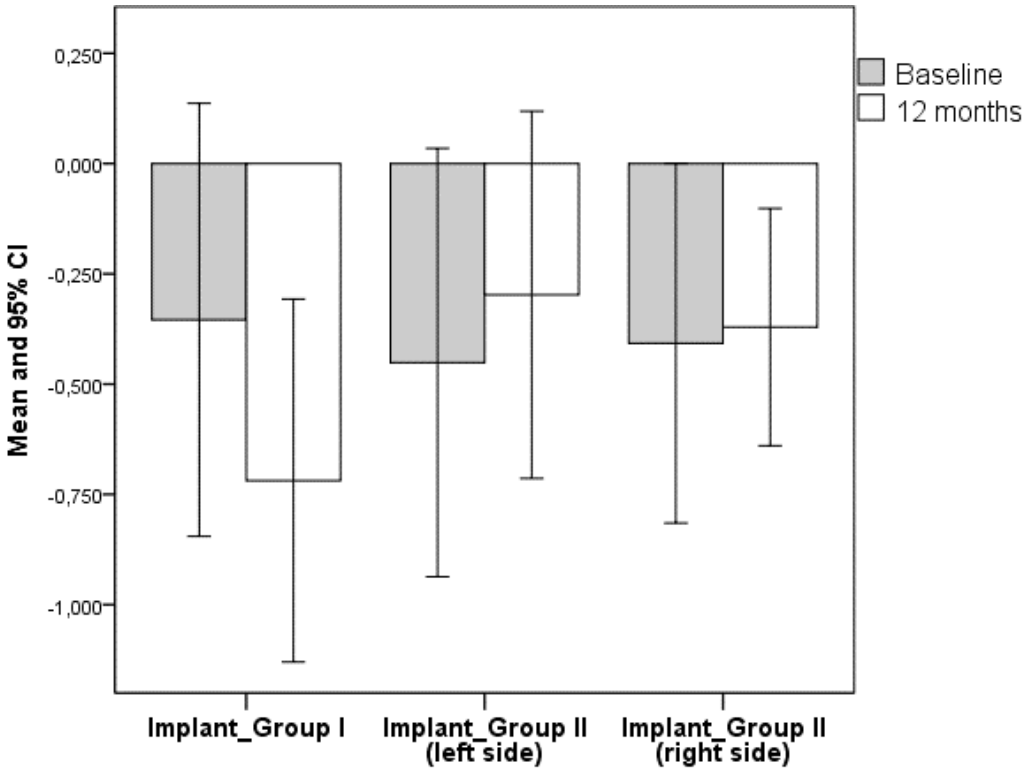

Figure 24. Measures of the distance between the implant platform and the peri-implant bone level. Negative values mean that implant platform is located supra-crestally.

Table 14. Parameter estimates for the Generalized Estimating Equations model for peri-implant bone level as dependent variable.

Parameter		B (95% CI)	Wald Chi-Square	df	p-value
(Intercept)		-0.512 (-0.634 – -0.390)	67.42	1	<0.001
Implant	Group III (Right)	0.151 (0.140 – 0.162)	712.5	1	<0.001
	Group II (Left)	0.171 (0.160 – 0.182)	913.4	1	<0.001
	Group I	Reference			
Time points	12-month follow-up	-0.049 (-0.294 – -0.195)	0.156	1	0.693
	Baseline	Reference			

Implant survival and success

Implant survival was 100% in all groups after the 1-year follow, which corresponds to 15 months after implant insertion and 12 months after implant loading. Similarly, no biological or technical complications were observed during the follow-up periods.

Implant stability

Figure 25 shows the variation in mean ISQ values for implants inserted in the different treatment groups, according to the measurements proceeded in the different time points. In GEE analysis, the tests of model effects showed significant effects of the time point factor ($p<0.001$) and the interaction between time points and treatment groups ($p<0.001$).

Table 15 details the parameter estimates for the final GEE regression model. There was a significant decrease from the initial ISQ values compared to the reopening values ($p=0.019$) and between Groups I and III at the reopening ($p=0.004$) and the 12-month follow-up ($p=0.007$).

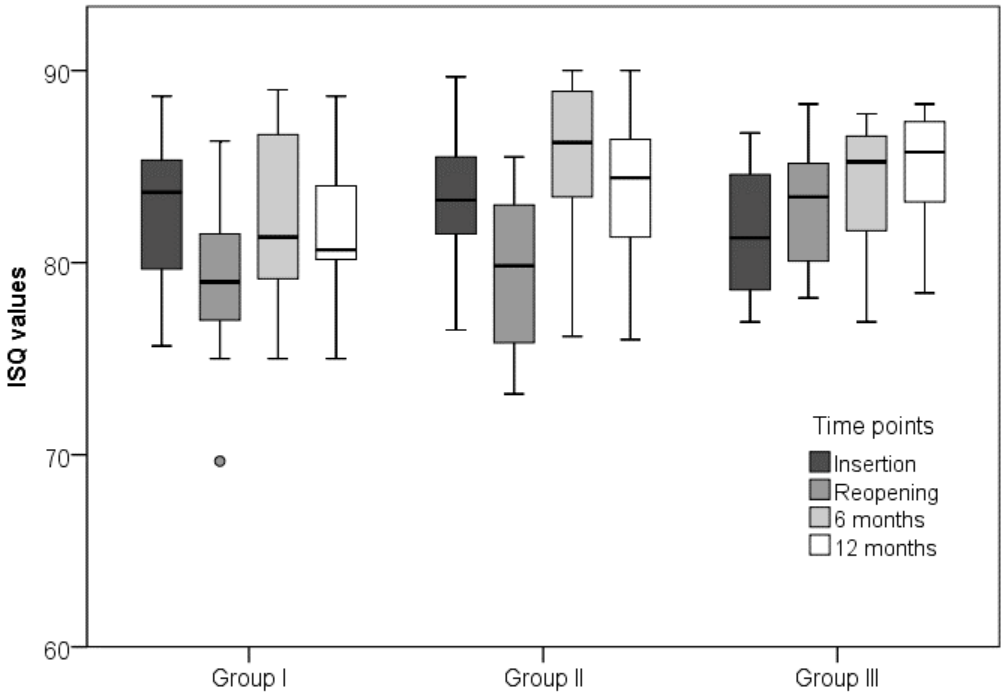

Figure 25. Distribution of ISQ mean values according to the treatment groups and time points for assessment.

Table 15. Parameter estimates for the Generalized Estimating Equations model for mean ISQ values as the dependent variable.

Parameter		B (95% CI)	Wald Chi-Square	df	p-value
(Intercept)		82.8 (80.8 – 84.8)	6691.0	1	<0.001
Treatment groups	Group III	-11.26 (-3.80 – 1.29)	0.935	1	0.334
	Group II	0.53 (-2.09 – 3.17)	0.159	1	0.690
	Group I	Reference			
Time points	12 months	-1.35 (-4.09 – 1.40)	0.928	1	0.335
	6 months	-0.54 (-4.34 – 3.25)	0.078	1	0.780
	Reopening	-3.80 (-6.97 – -0.63)	5.534	1	0.019
	Insertion	Reference			
Treatment groups x time points	I x III (12 months)	4.68 (1.30 – 8.06)	7.359	1	0.007
	I x III (6 months)	3.21 (-1.12 – 7.54)	2.109	1	0.146
	I x III (reopening)	5.25 (1.71 – 8.78)	0.461	1	0.004
	I x III (insertion)	Reference			
	I x III (12 months)	2.06 (-1.39 – 5.51)	1.373	1	0.241
	I x III (6 months)	2.81 (-1.54 – 7.16)	1.606	1	0.205
	I x III (reopening)	0.03 (-4.02 – 4.07)	0.000	1	0.989
	I x III (insertion)	Reference			

Clinical outcomes

The clinical aspects of the peri-implant region was assessed at the appointment of implant loading (initial) and after 6 and 12 months. The main findings are described in Table 16 concerning the distance between the gingival margin and the implant platform (Implant platform position – IPP), Plaque Index and bleeding on probing. Only a few patients had discernible calculus accumulation and suppuration was not found in any case, and, therefore, no summary data was presented. Similarly, no significant changes were observed concerning the plaque index in the longitudinal assessments.

Table 16. Clinical assessed outcomes according to the treatment groups and time points. Sample size at the implant level: Group I – n=13; Group II – n=26; Group 3 – n=52.

		Clinical outcomes		
Groups	Time points	Mean IPP*	Mean Plaque index*	Bleeding on probing (%)**
Group I	Initial	-0.61 (0.78)	1.27 (1.01)	0 (0.0)
	6 months	-0.53 (0.58)	0.72 (0.79)	0 (0.0)
	12 months	-1.07 (0.51)*	1.36 (1.21)	1 (9.1)
Group II	Initial	-0.57 (0.65)	1.08 (0.95)	0 (0.0)
	6 months	-0.87 (0.59)	0.92 (1.02)	2 (7.7)
	12 months	-0.77 (0.84)	0.92 (0.81)	0 (0.0)
Group III	Initial	-1.13 (0.86)	1.15 (0.78)	0 (0.0)
	6 months	-0.94 (0.45)	1.35 (0.86)	1 (1.9)
	12 months	-1.20 (0.62)	1.45 (0.87)	2 (3.8)

* Wilcoxon Signed Ranks Test (compared to initial values)
** Cochran's Q (all paired contrasts with initial values were non-significant)

Figure 26 shows the distribution of measurements of the position of the gingival margin. Only a significant change at the 12-month follow-up in Group I compared to baseline was observed.

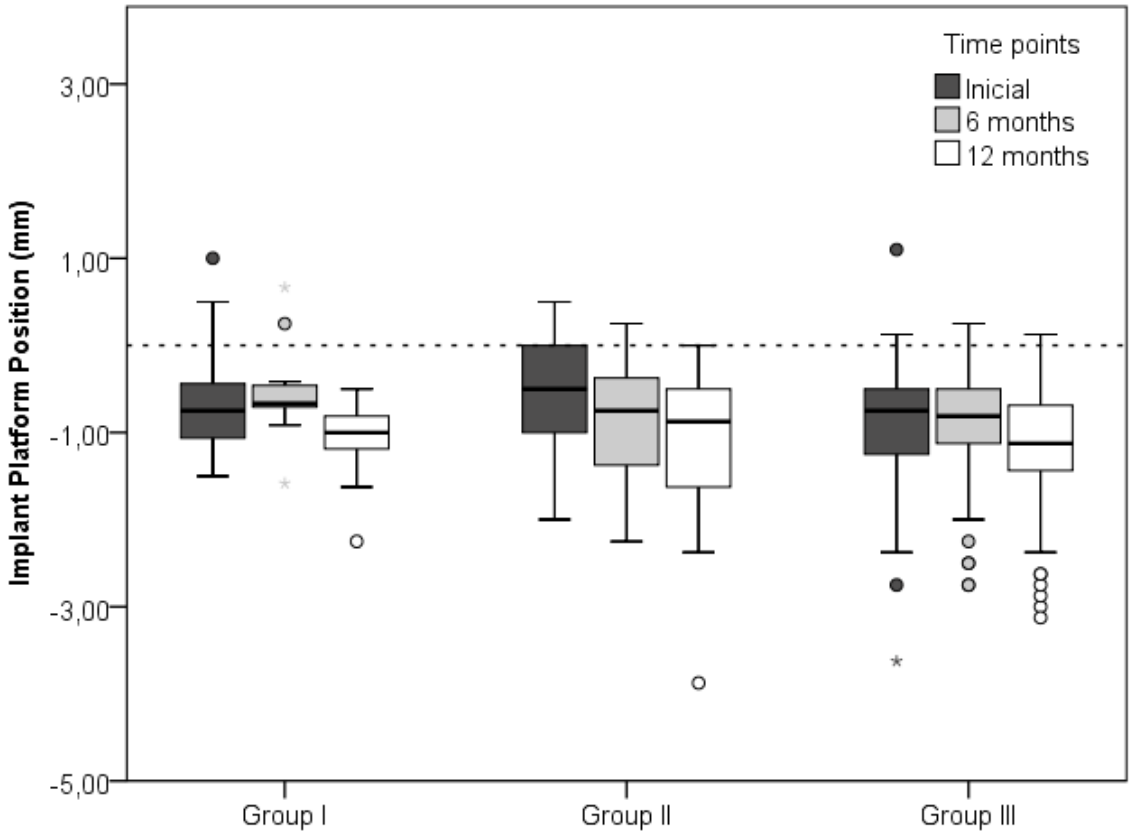

Figure 26. Changes in the position of the gingival margin according to time points and treatment groups.

Incidence of prosthodontics complications

We calculated the incidence of prosthodontics events throughout the entire observation period for the three study groups. Although the study time points for all outcomes were limited to the 12-month follow-up, results from prosthodontics complications were extended for longer periods until the last patient visit for routine recall or to solve any prosthodontics complaint. Figure 27 shows the variation of the individual complete time of follow-up for estimation of the incidence of prosthodontics events.

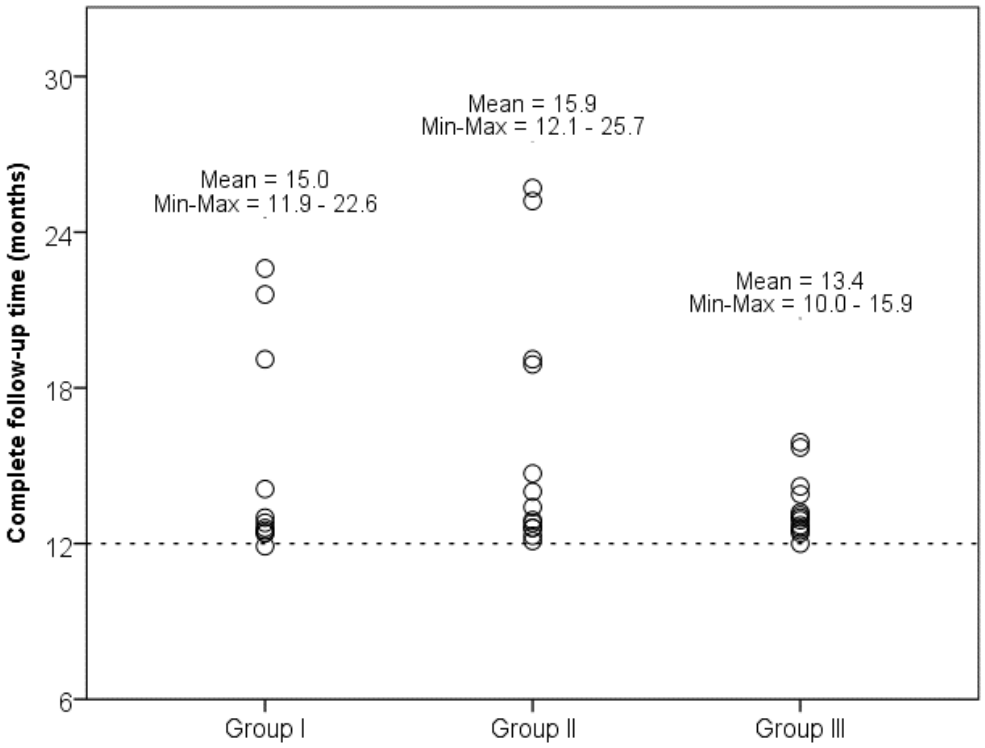

Figure 27. Individual complete time of follow-up for estimation of the incidence of prosthodontics events for Groups 1 (n=11), II (n=13) and III (n=13).

Table 17 describes the total number of events for each prosthodontics complication, the percent incidence, and the incidence density. For calculation of the incidence density (number of new cases per the sum of the person-time of the at-risk population), we considered the total person-time (in years) for Group I = 13.6, Group II = 16.9, and Group III = 14.3. There was a high number of replacement of retentive matrices in Groups I (72.7%) and II (123.1%), although the high incidence in Group II was related to the multiple events per patient – 2 patients had 3 replacements of the two matrices, and 1 patient had 4 replacements of the two matrices. Considering the incidence of patients who had replaced matrices, the incidences were 5 out of 11 in Group I (45.5%) and 7 out of 13 in Group II (53.8%). The incidences of overdenture fracture were 18.2% for Group I and 15.4% in Group II, with no significant difference between groups (Fisher Exact test= 0.40; p=1.00). A significantly higher incidence of teeth fracture of the mandibular denture (46.2%) was found for Group III compared to Groups I (9.1%) and II (7.7%) (Chi-square test=7.12; p=0.028).

Table 17. Summary data on the occurrence of prosthodontic complications.

	Number of patients			Number of events			Incidence (%)			Incidence density (%)		
Grupos de tratamento	I	II	III	I	II	III	I	II	III	I	II	III
Replacement of the retentive matrices	5	7	–	8	16	–	72.7	123.1	–	59.0	94.4	–
Overdenture fracture	2	2	–	2	2	–	18.2	15.4	–	14.7	11.8	–
Tooth fracture – maxillary denture	0	1	1	0	1	1	0	7.7	7.7	0	5.9	7.0
Tooth fracture – mandibular denture	1	1	5	1	1	6	9.1	7.7	46.2	7.4	5.9	41.9
Soft tissue surgery	1	0	0	1	0	0	9.1	0	0	7.4	0	0
Abutment loosening	0	1	0	0	1	0	0.0	7.7	0	0	5.9	0

Economic analysis

Treatment costs:

The costs of treatments were estimated throughout the entire study. The construction of a detailed spreadsheet included all consumable items, implants, and prosthetic components, and laboratory services. Valuing labour workforce was initially based on the clinical time needed for performing all clinical procedures during complete denture treatment, implant treatment (surgical and prosthodontics) and post-insertion care. Table 18 shows the summary of clinical time (in minutes) according to the study groups and treatment phase.

Table 18. Clinical time for treatment (in minutes) for the complete denture, implant and post-insertion phases, according to the study groups

Study group	Treatment phase	Mean	Std. Deviation
Group I (n=10)	Complete denture	174.7	29.5
	Implant	162.1	57.2
	Post-insertion	31.8	43.9
	Total	368.6	92.0
Group II (n=12)	Complete denture	181.7	46.5
	Implant	204.3	71.3
	Post-insertion	41.3	68.5
	Total	427.3	127.7
Group III (n=12)	Complete denture	177.4	57.2
	Implant	327.7	109.3
	Post-insertion	40.8	42.2
	Total	545.9	153.7

Table 19 shows the detailed cost estimates for the study groups. The overall costs were R$ 2.370,66 for Group I, R$ 3.185,21 for Group II and R$ 5.739,52 for Group

III. The greater impact on treatment costs was the cost of implants and prosthetic components, as well as the laboratory cost for Group III, as seen in Figure 28.

Table 19. Cost estimates for the treatment groups, according to the treatment stages and cost items (data are mean costs).

Parameter	Cost items	Group I	Group II	Group III
Direct costs: CD stage	Consumables	R$ 207,54	R$ 201,90	R$ 213,80
	Laboratory	R$ 393,00	R$ 385,90	R$ 380,08
	Manpower	R$ 73,16	R$ 55,44	R$ 88,44
Direct costs: Implant stage	Consumables	R$ 162,85	R$ 128,09	R$ 409,03
	Laboratory	R$ 10,91	R$ 0,00	R$ 951,54
	Implants and prosthetic components	R$ 697,00	R$ 1.368,71	R$ 2.324,69
	Exams	R$ 62,20	R$ 223,00	R$ 223,00
	Manpower	R$ 764,01	R$ 822,17	R$ 1.148,94
Sub-total (per stage)	Complete denture stage	R$ 673,70	R$ 643,24	R$ 682,32
	Implant stage	R$ 1.696,96	R$ 2.541,97	R$ 5.057,20
Total cost	All items	R$ 2.370,66	R$ 3.185,21	R$ 5.739,52
Incremental cost - (%)	Reference: CD treatment	252 %	395%	741%
	Reference: Group I	-	34.4%	142.1%
	Reference: Group II	-25.6%	-	80.2%
	Reference: Group III	-58.7%	-44.5%	-

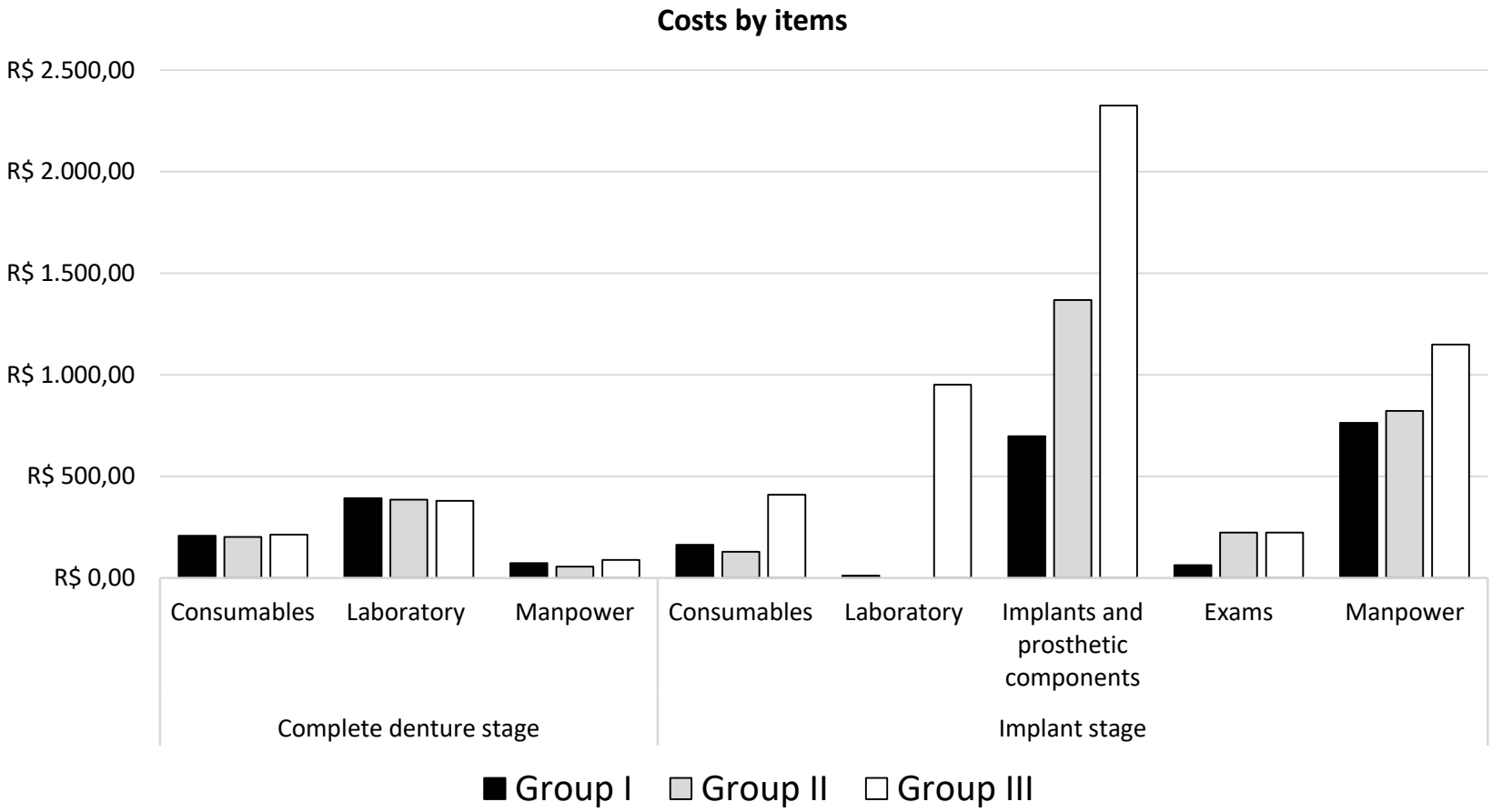

Figure 28. Estimated cost of item for the complete denture and implants phases of treatment according to the study groups.

Percent incremental costs were estimated for each of the two competing treatment groups, by calculating the difference between the overall cost of each pair of groups and the proportion of this difference compared to the reference group cost, as follows:

$$\% \text{ Incremental Cost} = [\ Cost_A - Cost_B\ ] * 100 / Cost_B$$

Hence, Table 19 also shows that the percent incremental cost in relation to the complete denture phase range from 252% for Group I to 741% in Group III (Figures 29 and 30). The other incremental cost ratios are detailed in Table 20.

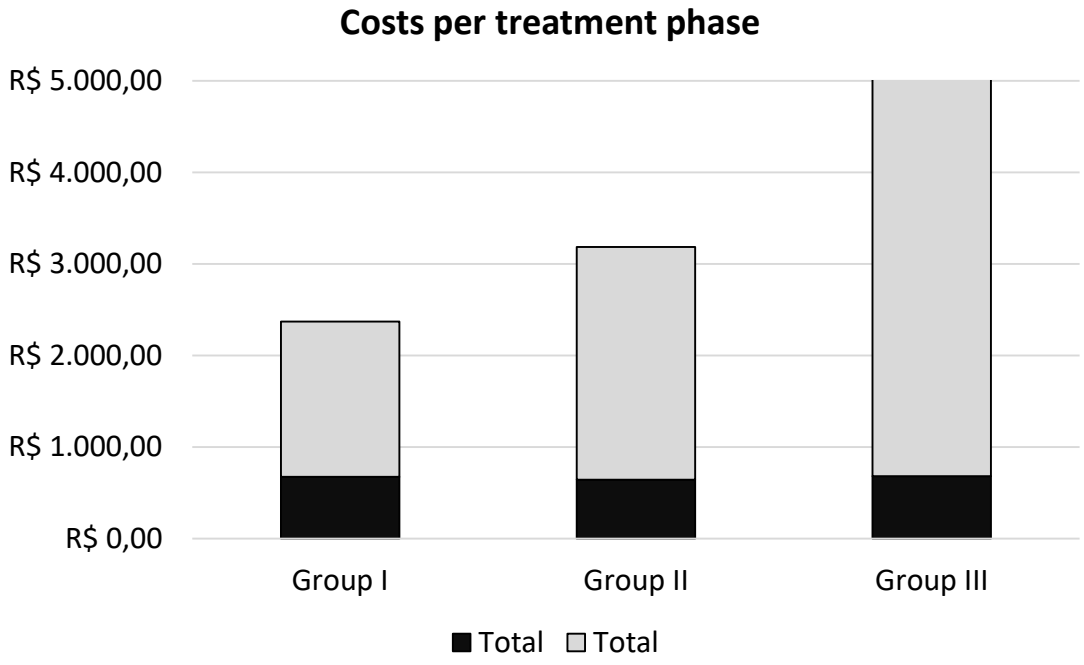

Figure 29. Costs of complete denture and implant treatment phases.

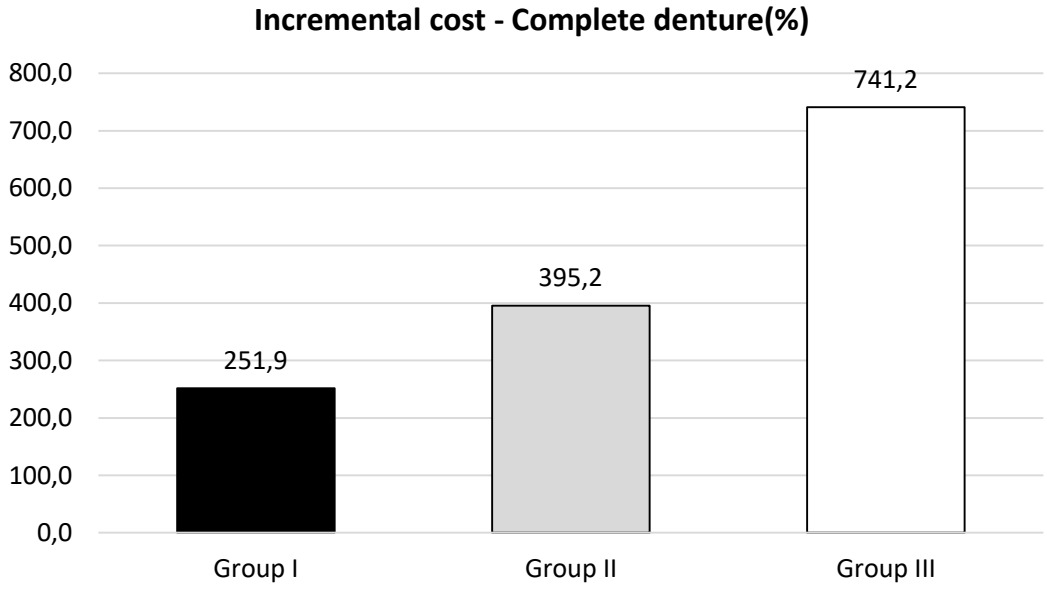

Figure 30. Percent incremental costs of implant treatment phases, compared to the complete denture phase.

Cost-effectiveness analysis

The cost-effectiveness analysis was based on the calculation of the incremental cost-effectiveness ratio (ICER) as the cost-outcome measure for comparison between treatments. We used patient satisfaction (DONADEDIAN, 1988) with the mandibular denture as the primary outcome (effectiveness measure) and overall direct cost for each treatment group.

Table 20 shows the summary of cost and outcome measures and ICER results for the following two-group comparisons:

1. Before-and-after within-group comparison for the initial complete denture treatment and each of the final implant treatment groups;
2. Between-group comparison for each two competing implant treatments using Group I as the reference strategy and Groups II and III as the tested strategies;
3. Worst and best scenarios by the combined ±20% change of costs and effectiveness for calculation of extreme ICER values.

Table 20. Cost-effectiveness analysis.

Groups	Outcome			Costs							
	Baseline outcome measure	12-month outcome measure	Incremental effectiveness	Cost CD phase	Cost Implant phase	Incremental cost (Implant – CD)	Total cost	ICER Ref.= CD	ICER Ref.= Group I	Worst scenario*	Best scenario*
Group I	76,7	96,7	20	R$ 673,7	R$ 1697,0	R$ 1023,3	R$ 2370,7	R$ 51,16	-		
Group II	63,3	98,3	35	R$ 643,2	R$ 2542,0	R$ 1898,7	R$ 3185,2	R$ 54,25	R$ 54,30	R$ 81,46	R$ 36,20
Group III	81,7	100,0	18,3	R$ 682,3	R$ 5057,2	R$ 4374,9	R$ 5739,5	R$ 239,06	R$ 1981,68	R$ 2972,52	R$ 1321,12

CD – Complete denture
ICER – Incremental Cost-Effectiveness Ratio
* Worst and best scenario based on a 20% combined increase/decrease in cost and effectiveness

Results suggest that the incremental costs for Group II compared to group I are considerably lower than Group III and, as the gain in effectiveness ranges from low to moderate in Groups II and III, respectively, compared to Group I, it may be concluded that the incremental costs for Group III is not proportional to the respective gain in effectiveness. Whilst the ICER for Group II (compared to Group I) ranged from R$ 36,20 to R$ 81,46 for an incremental 1-point in patient satisfaction (base value = R$ 54,30), the same parameter for Group III (compared to Group I) ranged from R$ 1321,12 to R$ 2972,52 (base value = R$ 1981,68). Therefore, results suggest that the use of implants to retain a mandibular overdenture, irrespective to the use of one or two implants, are more cost-effective than the fixed implant treatment for the edentulous mandible.

DISCUSSION

This study comprised a parallel-group randomized clinical trial testing the effectiveness, comparing prosthodontics, peri-implant outcomes and costs of three treatment alternatives for the edentulous mandible opposing to a maxillary conventional complete denture. The study was planned to include three alternatives with different levels of complexity and related costs. The rationale was to investigate whether changes in the number of implants and use a removable versus a fixed prosthesis have a significant effect on patient response to treatment. As a second objective, we tested the difference in the incidences of prosthodontics complications and negative peri-implant outcomes. Finally, we investigated if the results achieved using more complex interventions are proportional to the costs associated with treatment.

Overall results revealed that all treatment groups had improved outcomes after the transition from the baseline condition (recently worn new complete dentures) until the 12-month follow-up after the incorporation of the mandibular prostheses to the implants. In addition, findings suggest that overdentures retained by one or two implants (Groups I and II) are quite similar, whilst a 4-implant fixed prosthesis (Group III) results in slight better patient-reported outcomes and fewer adjustments and repairs in the long term. It may also be hypothesized that the initial costs may be compensated by the lower maintenance cost in longer follow-up periods compared to the lower initial costs of the overdenture treatments and higher maintenance costs.

Although the treatments for Groups II and III are well-recognized as effective treatments with sound clinical evidence, this study included a patient group treated with a single-implant mandibular overdenture, which is a treatment option with limited evidences from robust clinical trials. The aim was to reduce the complexity and costs to a minimum to test its viability as an alternative for the effective incorporation of implant treatment in different settings within Brazilian context, including private practice, public health system and other subsided healthcare services.

The use of a single-implant overdenture may also be justified by means of simplification of the intervention for patients demanding less invasive

procedures, for whom simplicity would be preferable to complexity. It is also essential in scenarios where more efficient use of available resources, to achieve better benefits with lower costs – not only monetary but also in terms of time and effort for the patient and health provider. A systematic review from Nogueira et al. (NOGUEIRA et al., 2017) showed that the available evidence on single-implant mandibular overdenture suggests a considerable improvement in patient-reported outcomes. The results also suggest that the instruments used to measure patient satisfaction and OHRQoL were able to detect the changes between treatments; however, poor reporting and lack of standardised instruments and scale measures make it difficult any attempt to combine data from these studies in a meta-analysis (NOGUEIRA et al., 2017).

One important limitation of this study was the use of an o'ring-ball attachment system for overdenture patients. This system is manufactured by a Brazilian company and is one of the common and less costly types available in the market. There are few studies comparing the attachments for single-implant overdentures. Nascimento et al. (NASCIMENTO et al., 2015) published a photoelastic laboratory study testing six types of attachments for a single overdenture and found a favourable concentration and distribution of stress to the implant in the single-implant mandibular overdenture, suggesting that the greatest part of the occlusal load is consistently transferred to the denture-bearing mucosa and although slight differences were observed among different retention systems, results suggest that all tested attachments may produce an acceptable level of stress to the implant and surrounding tissues (NASCIMENTO et al., 2015). Loss of retention and matrix replacement was one of the most common maintenance events in the overdenture groups, as observed in a study comparing overdentures retained by 1 or 2 implants (KRONSTROM et al., 2017). In general, studies show great variation in the incidence of matrix replacement, although no comparison of the different types of retention systems and no time-to-event analysis is available.

The importance of attachment performance in overdenture treatment cannot be neglected. Therefore, clinicians should be aware of its properties to achieve the main goal of treatment, which is the retention and stability of the denture. Many designs of attachments are commercially available and the selection of a

specific product depends on many criteria and patient-physician requirements: impact on implant survival rate and marginal bone loss, soft tissue complications, retention, stress distribution, space requirements, maintenance complications and patient satisfaction (TRAKAS et al., 2006). Cost and commercial availability may also be considered as another important factor in choosing the appropriate overdenture attachment type. The retention system used in this study has been replaced by others, as implants companies worldwide have been developing other more reliable and durable attachments with newly developed materials

From the perspective of the study design, this study is a randomized clinical trial used as a method of longitudinal cost-effectiveness comparison of three different treatment modalities that compete to solve the same clinical problem. The study was registered in the Clinical Trials database, with registration number NCT03056976, and this report follows the CONSORT Guidelines for this type of study. To assure proper external validity, we adopted means of training of examiners and performers (prosthetic and surgical stages, clinical outcomes, reported by patients, chewing performance and radiographic evaluations), randomization, blinding the preoperative stage and in the masticatory performance evaluation, and standardization of the evaluation stages (baseline, 1 month, 6 and 12 months). However, operator was not blinded in relation to collection of longitudinal data from questionnaires (satisfaction, OHIP-Edent). We also adopted patient-related outcomes as the measures of effectiveness as important predictors of positive prognosis for the rehabilitation of total edentulous individuals.

For multivariate statistical analysis we used generalized estimating equations (GEE), which use is preferred over repeated measures ANOVA for randomized clinical trials. GEE is indicated due to the non-constant variance over time, “time” is a factor variable to be tested, hierarchical data are frequently not normally distributed, and longitudinal evaluations depend on the previous situation, a fact that is typical in health research because patients change their clinical condition during treatment, and the measured status is dependent on the previous status over time. GEE is also a method for longitudinal data analysis of nominal and continuous outcomes, even when the variable does not

present normal distribution or sphericity. Moreover, even in the case of missing data due to loss of information from any individual in the sample, it is possible to include all individuals in analyses, a situation that can avoid some kind of selection bias. Another advantage of GEE over Repeated-measures ANOVAMR is the need for a smaller sample size to be able to evidence the same effect size, with an 80% power (GUIMARAES & HIRAKATA, 2012).

Study sample considerations

We applied very restricted criteria for patient selection. Nearly one third of recruited eligible subjects were excluded due to conditions that would affect patient response to treatment or the presence of confounders that could influence implant prognosis. Since patient randomization occurred after baseline treatment with conventional dentures, patient withdrawal after being assigned to one of the study groups seemed not to be related to the group allocation – most of them were due to refusal to receive implant and/or satisfied with their conventional dentures. However, patient withdrawal after the prostheses were incorporated into the implants occurred only in Group I (n=1) due to dissatisfaction with treatment. The other patients, disregarding their satisfaction status continued using their prostheses and none abandoned the study due to poor outcomes. Although this may be regarded as a higher risk of treatment failure in Group I, the small sample size and occurrence of withdrawal do not allow any strong inference.

Other problem related to sampling strategy was that all subjects were enrolled to implant intervention at the beginning of the study. This means that even participants highly satisfied with their dentures (and not actively demanding implants) were included. In fact, most participants had already experienced a marked improvement in their self-perceived outcomes in the transition between the old and the new dentures, and, therefore, the magnitude of improvement after insertion of implants may not be as high as expected.

An interesting systematic review on oral health-related quality of life in subjects with implant-supported prostheses, by Reissmann et al. (REISSMANN et al.,

2017), reported that studies in edentulous patients indicate that treatment with implant overdentures improves OHRQoL, and improvement is slightly higher than for conventional CD. They argued that one possible reason might be that patients requesting implant treatment typically experienced more problems related to their oral health and, accordingly, the expected improvement in outcomes may be greater than in patients with initially less impaired outcomes. Therefore, in patients who are satisfied with their current conventional dentures, implant placement does not add a substantial amount of satisfaction, and this may be the explanation for the moderate effect size observed in our study after implant treatment.

In our study, as in most of the identified randomized clinical trials included in the systematic review (REISSMANN et al., 2017), study participants were not well representative for all typical edentulous subjects of the population sample, since they were recruited based on the consent for implant treatment – those who refused implants at the recruitment stage were excluded from the study. Consequently, participants who had a request for implant treatment were more likely to have substantially impaired OHRQoL and, accordingly, the effects if implants on patient-reported outcomes would be greater in patients who request implants than in those who do not.

Patient baseline characteristics

We tested the differences in baseline characteristics of participants across groups for two reasons. First, because randomization is often not perfect and the two groups are not starting the same, especially considering that our sample size was relatively small – in larger samples the differences between randomized groups would be minimal. And second, the baseline measurements were used to run repeated measures (i.e., dependent samples) in statistical procedures such as GEE, which are more powerful to assess the change scores, which reduce the problems associated with between-subject variability in baseline scores. Therefore, although there have differences across groups at baseline, this problem may be overcome by the use of mixed-model effects regressions for the analysis of longitudinal data.

In general, participants of this study were of the lower socioeconomic statuses, referred from the public health system, with limited access to private oral healthcare on a fee-for-service payment model. As for these patients financial constraints is a relevant barrier to the placement of implants, and as lower OHRQoL is associated with socioeconomic status and poorer oral health conditions, it may be hypothesized that these participants were more likely to respond more positively to treatments, especially if they receive more extensive and costly treatment, as they received in Group III. In a previous qualitative study of our research group (NOGUEIRA et al., 2018) that included patients receiving single-implant mandibular overdentures, we found that patients expressed gratitude for and satisfaction with the care received and reported that, in addition to being satisfied with the results of the treatment itself, they felt grateful for having the opportunity to be treated. It is important to note that all treatments provided were free from charge for the participants, and many of these patients would hardly be candidates for implants in a regular private service due to limited financial resources.

Although we had not assessed patient preferences concerning the offered treatments, and excluding treatment costs as an influential variable on preferences, those with higher levels of education and higher incomes were more likely to opt for implant treatment, particularly fixed prosthesis (LELES et al., 2019). These variables are closely related to individual access to information and affordability of consumption items. Therefore, the role of treatment cost on clinical decision-making also reinforces the importance of cost-effectiveness studies comparing competing treatment options for the edentulous patient (LELES et al., 2019).

Concerning group differences at baseline concerning implant primary stability and height of the anterior mandibular ridges at the implant sites, these factor seem not be a relevant aspect for the clinical outcomes of the treatment groups.

Changes in post-insertion patient-reported outcome measures

Outcome assessment after implant treatment revealed that all interventions showed a positive response regarding the patient-reported outcomes (PROMS) based on the satisfaction questionnaires and the OHIP-Edent instrument. Results showed an overall improvement (lower OHIP-Edent scores) in longitudinal evaluations compared to baseline (new conventional complete dentures). In the first stage of treatment, the 50 patients included in the sample were rehabilitated with new complete dentures, and post-insertion adjustments were performed to resolve any complaints to ensure that patients were adapted to their prosthesis. In general, they reported an improvement in the oral condition when compared to the initial condition before the study, and these reports were confirmed by obtaining higher treatment satisfaction scores and decreasing OHIP-Edent scores when comparing the two moments: initial condition of the patient, before any intervention provided by the study, and after rehabilitation with the new conventional dentures.

There is significant body of evidence that shows that implant-supported overdentures in mandibular fully edentulous patients can lead to improved satisfaction, improved OHRQoL or other surrogate PROMS compared with conventional complete dentures (DE BRUYN et al., 2015). In the last years the two-implant-retained overdenture has been regarded as the first choice of treatment for the edentulous mandible (FEINE et al., 2002).

A clinical prospective study (De KOK et al., 2011) compared prosthetic outcomes, patient satisfaction, and survival rates of implants between two-implant-supported overdentures and three-implant-supported fixed dentures. Both the treatment modalities significantly and similarly improved patient satisfaction and oral health-related quality of life, and prosthetic complications were relatively rare for both treatments (De KOK et al., 2011). A recent review by YAO et al. (YAO et al., 2018) also concluded that, in general, fixed implant dentures and implant overdentures show no significant differences when compared for PROMS, with a slight trend of the fixed prosthesis being superior to overdentures in most included studies. However, conflicting results were observed in many aspects such as chewing function, phonetics-related function, overall satisfaction and aesthetic. These inconsistent results across the original

studies were observed regarding PROMS when comparing both treatments for fully edentulous patients.

The systematic review by De Bruyn et al. (DE BRUYN et al., 2015) reported that non-standardised questions and different scoring methods compromise the validity and reliability of PROMS to assess the impact of implant-related treatments. Problems related with poor reporting of the criteria for patient recruitment and heterogeneity in the original studies are also crucial. For example, it is not always clear if patients in the studies had actively sought implant treatment, if they had been dissatisfied with their existing prostheses, or if they had paid for the treatment or not. Yao et al., (YAO et al., 2018) also found inconsistent results for PROMS when comparing implant fixed and removable prosthesis for fully edentulous patients. Due to heterogeneities among study methodologies and populations, and diversity of measurement tools (with some instruments not being properly validated). They also suggested that a guideline for standardizing the assessment of PROMs in clinical research is needed in order to produce more meaningful evidence-based information. (YAO et al., 2018).

These finding are similar to our study, concerning a number of outcomes. Most patients reported marked improvement irrespective to the treatment group they were assigned. However, some patients still report episodic complaints and low levels of satisfaction in the recall appointments for data collection. Data from clinical studies suggest that patient satisfaction seems to be highly individual and full satisfaction with an implant overdenture will never be guaranteed. It may be advisable that a conventional denture may suffice for patients who have no complaints with functional comfort or stability of their prosthesis, and the decision to propose an overdenture should be based on proper individual assessment (DE BRUYN et al., 2015). In general, the absolute advantage of either fixed or removable overdentures is not evident from patient-reported outcomes, and patient satisfaction does not seem to be affected by the number of implants nor by the prosthesis retention system to retain an overdenture, while factors such as patients' preferences and their expectations might play a significant role (YAO et al., 2018). Other patient-related factors, therefore, may be considered as determinants of patient preference and clinical decision. For

example, some patients seem to prefer straightforward implant surgery over complex surgery that includes bone grafting, and since are easier to maintain oral hygiene, this might be of significance when selecting a treatment for patients with difficulties in conducting oral hygiene such as the elderly, patients with disabilities or Parkinson's disease (DE BRUYN et al., 2015; YAO et al., 2018).

Functional and clinical outcomes

Findings of our study suggest that all treatments resulted in the improvement of masticatory function after the insertion of implant-retained prostheses. Although the overall effect of the experimental group factor was not significant, a slightly better performance seems to occur with a greater number of implants (Group I *vs* II) and from removable to fixed prostheses. The objective benefits in masticatory performance of implant-supported (removable) or retained (fixed) dentures compared to conventional dentures have been substantiated for patients with resorbed mandibles and/or difficulty adapting to conventional removable complete dentures (FUEKI et al., 2007).

We used a mixing ability test with a two-colour chewing gum, which was proved to be reliable and capable to measure intra-individual differences in masticatory performance of complete denture wearers, by both visual and opto-eletronical analysis (SILVA et al., 2018). This is an alternative to the food comminution test for dentate subjects, correlates significantly with the sieving method, and the electronic assessment of the chewed gum is also a discriminative tool to assess chewing efficiency in clinical and research settings (SCHIMMEL et al., 2015).

Findings also suggest previous studies that showed that masticatory performance seems to be improved with the continuous use of newly inserted dentures and negatively influenced by advanced age (LELES et al., 2019), and that masticatory performance improved significantly after 12 months, irrespective to the insertion of an implant-retained mandibular overdenture, although patients receiving implant treatment may perform better than complete denture patients in the shorter follow-up period (NOGUEIRA et al., 2019).

A review by Boven et al., (BOVEN et al., 2015) reported that treating complete denture wearers with implants to support their denture improves their chewing efficiency, increases maximum bite force, and it clearly improves satisfaction. Patients receiving overdentures could chew better and eat more tough foods (such as raw fruit, vegetables, and nuts), although there is no evidence that it improves dietary intake as measured by interviews, questionnaires and blood samples. This suggests that diet is a habit and it seems that by just improving the dental situation, the dietary habit does not change. As expected, bite force improved after implant treatment. However, improvements due to the stabilization of the dentures by implants after 1 year seemed to decrease slightly but were stable over time, at least for 10 years (BOVEN et al., 2015).

Our study found a slight decrease in masticatory performance in the 12-month follow-up, possibly due to the need for adjustments associated to the loss of retention of the retentive inserts of the overdentures, as observed in a previous prospective study with patients treated with single-implant mandibular overdenture (NOGUEIRA et al., 2018). Therefore, although there were marked improvements in patient-perceived outcomes after the transition from the conventional denture to a single-implant mandibular overdenture, the high incidence of prosthodontics complaints in longitudinal follow-up reinforces the need for regular treatment recalls for proper management of prosthodontic complications and preservation of the treatment benefits in the long term (NOGUEIRA et al., 2018).

Regarding implant survival, our study had no implant failure, and the one-year follow-up revealed no significant factors that would affect implant survival in the long-term. A systematic review (Kern et al., 2016) analyzed the post-loading implant loss for implant-supported prostheses in the edentulous maxilla and mandible, regarding a potential impact of implant location (maxilla vs. mandible), implant number per patient, type of prosthesis (removable vs. fixed), and type of attachment system (screw-retained, ball vs. bar vs. telescopic crown). They concluded that the risk for implant loss in the edentulous mandible is significantly lower than in the maxilla ($p<0.001$). Regarding the direct comparisons of implant numbers in the mandible, higher numbers of implants showed a clear tendency for lower implant loss rates, and the concept of a

single implant in the mandible midline (which represents the absolute minimal treatment concept.) is an ongoing and intensively discussed topic. The high survival rates of the single-implant overdenture are based on few studies, and a 5-year survival estimation of 92.1% seems to be satisfactory (HARDER et al., 2011). Nevertheless, implant loss rates for two and four implants with an overdenture were significantly lower, and seems to be consolidated by the analyses of this systematic review, regarding post-loading implant survival, exclusively (Kern et al., 2016).

Cost-effectiveness

The underlying hypothesis of this study was that less complex and less costly interventions would perform similarly to more extensive and costly interventions. The expression “less is more”, frequently invocated by clinicians, as part of the disseminated concept of Brånemark’s philosophy of care is a synthesis of the expectations of many patients and clinicians. The idea that “simplicity is preferred to complexity” may also imply the need for more efficient use of available resources to achieve better benefits with lower costs – not only monetary but also in terms of time and effort for the patient and health provider (LELES & NOGUEIRA, 2015).

Resource allocation is a central part of the decision-making process in any health-care system. Resources – money, manpower, time, equipment, facilities, etc. – have always been finite and scarce, while demands are increasingly high. This means that people and society do not have enough resources to produce all the things people would like to have. Hence, the main economic challenge is to provide the best possible allocation of resources along with the provision of the most effective and beneficial technologies, minimizing the waste of resources, inefficiency, and inequalities in access to health care (MAYNARD & McDAID, 2003).

Economic analysis is scarce in the field of prosthodontics and dental implants. A review by Vogel et al. (VOGEL et al., 2013) presented an overview of the cost-effectiveness of dental implants compared with other conventional treatment

options for the partially and fully edentulous patients. They concluded that for single-tooth replacement, a single implant was a cost-effective treatment option in comparison with a traditional three-unit fixed dental prosthesis. For the replacement of multiple teeth, dental implants (fixed or removable prostheses) were associated with higher initial costs but better improvements in oral health-related quality of life compared with other treatment options (VOGEL et al., 2013). The idea that dental implants lead to higher costs but at the same time improved outcomes in comparison with other treatment options raises questions relating to the cost-effectiveness of dental implants, especially when crown lengthening, endodontic therapy, and post-core buildup become necessary to restore a compromised tooth. However, for the edentulous patient, the competing treatments are limited to conventional and implant treatment options, and the implant-related alternatives comprise a wide range of interventions, from extremely simple to extremely complex and costly treatments.

Considering that most patients live well with their conventional dentures, and even having minor to moderate complaints they stay using the dentures for years, the decision to change for new dentures or receive implants to improve denture functioning is based on individual predisposing factors, perceived needs, and financial capacity (LELES & FREIRE, 2004). In our study, patients had no cost of treatment and decisions were based on voluntary inclusion and random allocation to treatment groups. It is very distinct from a real clinical setting, where the limits of the range of solutions are defined by the dentist and patient adherence depends on patients' perception of need and they can afford the costs of treatment.

Nevertheless, even when patients can pay for treatment costs, there are unrecoverable costs that are the opportunity costs, which are costs of a potential benefit foregone (DRUMMOND et al., 2005). Cost opportunity is relevant because people have different values about costs. This means that in a situation in which a choice needs to be made between several mutually exclusive alternatives given the patients' limited resources, they make different judgments about value for money, and they have to decide whether a health procedure is worth doing compared with other things they could do with the same resources (i.e., spending on X takes away the opportunity to spend on Y).

In summary, the real cost of an intervention is not measured solely by the monetary budgets, but rather the value of the benefits achievable in one intervention that was chosen (for example, an implant-supported prosthesis) compared to another alternative that was foregone (for example, buying a new car) (LELES & NOGUEIRA, 2015).

This is particularly relevant in cases of high costly treatment with implants. However, the lack of sound evidence on the cost and consequences of implant interventions makes it difficult to identify clearly the most cost-effective course of action without a systematic analysis of all relevant costs (direct and indirect) and the consequences of treatments. As a consequence, decisions are often based on personal preferences or subjective data from clinical experience.

Our study showed that there were small incremental costs for Group II compared to group I, and a high incremental cost from Groups I and II compared to Group III. However, the gain in effectiveness from the conventional to the implant treatments was similar for the three groups, and we concluded that the incremental costs for Group III was not proportional to the respective gain in effectiveness and, therefore, results suggest that the use of implants to retain a mandibular overdenture, irrespective to the use of one or two implants, are more cost-effective than the fixed implant treatment for the edentulous mandible. This does not mean that one treatment is recommended over another, whereas the results of an economic analysis aim to provide information for patients, health providers, and stakeholders, about the relations between costs and probable outcomes. As remarked by Tunis (TUNIS, 2004), the potential use of economic analysis in healthcare decision making has strong natural appeal as it becomes clear how an individual's healthcare decisions can affect, through insurance coverage, the ability of others to obtain the care they need.

Cost-effectiveness analyses relate outcomes to costs and provide information about the additional costs per improvement in outcome between two or more interventions. Incremental cost-effectiveness ratios (ICERs) relate the difference in costs C to the difference in effectiveness E between alternative interventions 0 and 1 in terms of ICER = (C1 – C0)/(E1 – E0). Cost-effectiveness analyses

are most valuable for assessing interventions that cost more and are more effective than alternative interventions (KLINGE et al., 2015). A number of studies investigated the cost-effectiveness of different implant-supported overdentures (ATTARD et al., 2003, 2005; CHAFFEE et al., 2002; HEYDECKE et al., 2005; TAKANASHI et al., 2004; ZITZMANN et al., 2005, 2006). A systematic review of these studies by Vogel et al., (VOGEL et al., 2013) concluded that although implant-retained overdentures may be associated with high initial treatment costs, they are more likely to represent a cost-effectiveness option in comparison to complete dentures.

Finally, evidence on the efficiency of an implant-supported prosthesis in various clinical conditions and settings demand more economic evaluations, using more robust methods in health economics and the reporting should follow the guidelines of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement (HUSEREAU et al., 2013) for more reliable comparison across studies.

CONCLUSIONS

Within the limits of this randomized clinical trial comparing different implant treatment alternatives for the edentulous mandible in complete edentulous subjects, the following conclusion may be drawn:

- Patients experienced marked improvement after the provision of a set of new complete dentures.

- The adherence of participants to the clinical trial was affected by a sort of individual factors related to patient intention to receive implants as an additional intervention to improve the function of their existing dentures.

- All treatment alternatives were safe and highly predictable concerning the surgical stage of implant treatment.

- Overall results regarding patient-reported outcome measures revealed that all treatment groups had improved outcomes after the transition from the baseline condition (recently worn new complete dentures) until the 12-month follow-up after the incorporation of the mandibular prostheses to the implants.

- Overdentures retained by one or two implants (Groups I and II) performed quite similarly, whilst a 4-implant fixed prosthesis (Group III) results in slight better patient-reported outcomes.

- The fixed mandibular denture (Group III) was associated with fewer adjustments and repairs in the long term.

- The reduction of the complexity and costs to a minimum using a single implant-retained overdenture was an effective alternative for improvement of the implant pre-treatment condition.

- Longitudinal assessment of peri-implant outcomes revealed no significant negative changes after one year.

- Cost-effectiveness analysis showed that the incremental costs for Group II compared to group I are considerably lower than Group III and, as the gain in effectiveness related to patient satisfaction ranges from low to moderate in Groups II and III, respectively, compared to Group I, it may be concluded that the incremental costs for Group III is not proportional to the respective gain in effectiveness.

- The economic analysis suggests that the use of implants to retain a mandibular overdenture, irrespective to the use of one or two implants, is more cost-effective in terms of patient satisfaction than the fixed implant treatment for the edentulous mandible.

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APPENDIX