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Supracrestal implant placement improves peri-implant health in T2DM patients: A randomized clinical trial

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ABSTRACT

Objective: This study, designed as a randomized controlled trial, investigated how the vertical placement of implants influences peri-implant conditions in patients with type 2 diabetes mellitus (T2DM) treated with mandibular overdentures.

Material and Methods: Twenty-two edentulous individuals with T2DM received two implants each in the anterior mandible following a split-mouth design: one placed at the crestal level (CL) and the other at a supracrestal level (SL). Clinical, immunoenzymatic, and tomographic assessments were conducted at prosthesis placement (baseline) and after 6, 12, and 24 months.

Results: Probing depth (PD) and clinical attachment level (CAL) were consistently higher in CL group than SL in all evaluated periods ($p < 0.05$). Immunoenzymatic assay showed that CL implants demonstrated higher concentrations of IL-4, at 6, 12 and 24 months, and IL-21 at 24 months, when compared to SL implants ($p < 0.05$). Radiographically, the bone loss was similar in both groups ($p > 0.05$). Higher bone loss was detected in the first year of implant loading compared to the second year in both SL and CL group ($p < 0.05$). In the SL group, the mean bone loss increased by 31.22 % from baseline to 24 months, corresponding to a change of 0.74 mm. In the CL group, the initial variation was 1.21 mm (69.94 %) over the same period.

Conclusion: These findings suggest that supracrestal implant placement may offer clinical and immunoinflammatory advantages in patients with T2DM, promoting better peri-implant health and reduced bone loss over time. Within the limitations of this study, SL positioning appears to be a favorable strategy for implant-retained overdentures in diabetic individuals. The clinical trial registry number is NCT03988140.

Clinical significance: Rehabilitating diabetic patients with dental implants can be challenging. This study demonstrates that supracrestally placed dental implants exhibit better clinical behavior in maintaining peri-implant health.

1. Introduction

Although the occurrence of type 2 diabetes mellitus (T2DM) has expanded, the number of deaths has decreased, likely because of advances in clinical therapies of diabetes, elevating the patient life expectancy of this patient profile [1,2].

Diabetes is a risk factor for periodontal diseases [3], which has increased the rate of tooth loss [4]. Considering the longer life expectancy of diabetics and the higher incidence and progression of periodontitis with later tooth loss in these individuals, dental rehabilitation with implant-supported prostheses will become more required in diabetic individuals. Notably, implant-retained overdentures may be considered an interesting therapeutic alternative, considering that this category of prosthesis can provide high levels of satisfaction, improvement in masticatory ability, nutritional state, and quality of life [5–7]. However, it is known that diabetic individuals present a higher risk for the progression of peri-implant diseases and augmented rates of implant failure [8–12].

Some data from clinical trials have indicated that using machined-collar implants inserted supracrestally may promote reduced marginal bone loss [13–16]. In line, it has been supported that the position of the implant-abutment interface may interfere with the magnitude of local inflammation, with higher intensification of peri-implant neutrophil

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accumulation as the implant-abutment interface is deeper, which contributes to the level of implant-associated alveolar bone loss [13,17]. Previous study [18,19] conducted with overdentures to rehabilitate diabetic patients demonstrated that different levels of glycosylated hemoglobin A1c (HbA1c) did not interfere with the implants' success. However, bone metabolism during the osseointegration period is different [18]. In this way, it would be relevant to examine whether this therapeutic approach could be considered in the rehabilitation of individuals with T2DM, since these individuals may be more predisposed to peri-implant variations, both considering the marginal bone remodeling and considering the local changes in immunoinflammatory reaction.

This study hypothesizes that implants placed supracrestally in T2DM individuals rehabilitated with overdentures may reduce bone remodeling and improve clinical parameters compared to crestal implants. Thus, this split-mouth randomized controlled trial aimed to evaluate the impact of crestal level or supracrestal implant platforms in T2DM patients treated with implant-retained overdentures.

2. Materials and methods

2.1. Study design

This study was designed as a prospective, split-mouth, randomized controlled trial to assess the influence of implant platform at the crestal level or supracrestally in T2DM patients on the clinical parameters, tomographic, and immunoinflammatory peri-implant results.

Diabetic edentulous patients who sought treatment at the Paulista University dental clinic were recruited between November 2014 and August 2016. The clinical practices and assessments were conducted between April 2016 and September 2018. Data entry and statistical evaluations were completed by the end of October 2018.

The inclusion criteria were patients between 50 and 80 years old, edentulous in the mandible with earlier mandibular dentures for at least 6 months, and a diagnosis of T2DM. Diabetic patients were included after undergoing a blood test at the same Clinical Analysis Laboratory to obtain the HbA1c level and medical authorization to carry out the proposed treatment (thirty days prior to study initiation). In addition, they had to have been diagnosed with T2DM for at least 5 years and could control their blood glucose levels through diet, use of hypoglycemic agents, and/or insulin. Exclusion criteria were smoking; pregnancy and lactation; systemic circumstances that could influence bone tissue (e.g., immunologic disorders); consumption of immunosuppressive, anti-inflammatory and anti-resorptive drugs; requirement of bone grafts; earlier regenerative procedures in the region; major diabetic problems (i.e., neuropathy, vascular diseases, and nephropathy).

All patients were notified of the possible risks and benefits of their involvement in the research and signed an informed consent form. This experiment was accepted by the ethics committee of Paulista University (Protocol 077310/2014). The clinical trial registry number is NCT03988140.

2.2. Sample size calculation

The sample size was determined using $\alpha=0.05$ and 80 % power. For the variability ($\sigma=SD$), a value of 1.5 mm was applied, with clinical attachment level (CAL) recognized as the primary outcome variable. The minimum clinically significant value (δ) established was 1 mm. A minimum sample of 20 participants per group was established. Considering that some individuals may be lost throughout follow-up, 22 subjects were registered in the research. The primary variable achieved a 0.94 power value with the current data (SPSS 21[1]).

2.3. Experimental groups

Based on a split-mouth model study, two dental implants used to retain the overdenture of patients were randomly assigned using a computer-generated list into one of the groups: 1) One of two implant was placed at supra crestal level (SL) and 2) the other implant was placed at crestal level (CL). The computer-generated list was kept in a sealed, opaque brown envelope under the supervision of a person not involved in the assessments. The operator was informed of the allocation only at the time of implant placement.

2.4. Treatment protocol

Fasting plasma glucose (FPG) and glycated haemoglobin A1c (HbA1c) were assessed at baseline, 6, 12, and 24 months. A single laboratory (Clinical Analysis Laboratory, Paulista University) performed blood evaluations of the subjects. FPG was quantified using the glucose oxidase technique (milligrams per deciliter), and HbA1c (percentage) was assessed by high-performance liquid chromatography.

The same operator (AC) performed surgeries. Patients had already used adequate prostheses, so a prosthesis was duplicated to make an acrylic resin guide. All subjects received 3.5 mm diameter dental implants—surface blasted with TiO2 particles and a machined collar of 1mm—in the interforaminal area of the mandible. The surgical steps were based on the protocol recommended by the implant company.

Amoxicillin (2 g/1 hour before the procedure), postoperative sodic dipyrone (500 mg, 6/6 h/2 days), and 0.12 % chlorhexidine mouthwash (12/12h/7 days) were indicated.

A two-stage protocol was employed, and the prostheses were positioned at 4 months, using the O'ring as a prosthetic retention system [20, 21]. After 7 and 14 days, the subjects returned to occlusal adjustments and confirmation of prosthetic adaptation. The prostheses were produced entirely of acrylic resin. Edentulous areas in the antagonist maxilla were rehabilitated with muco-supported prostheses.

Post-operative visits happened every 15 days throughout the first month and then quarterly until the end of the study (24 months after implant loading). Healing complications and implant failure, if present, were recorded. Patients were also submitted to prophylaxis, polishing, and instruction in oral hygiene practices.

2.5. Clinical examination

The same examiner (BG) completed all clinical measurements. To perform the intra-examiner calibration, the examiner measured the peri-implant CAL of 15 non-study subjects with dental implants twice within 24 h. The intra-class correlation was computed as 93 % reproducibility.

Using a probe North Carolina/Colorvue[2], the following parameters were measured (four sit/implant) at baseline (after prosthetic rehabilitation), 6, 12 and 24 months (Fig. 1): 1) Modified Plaque Index (MPI/%): dichotomous modified plaque index along the mucosal margin around implants [22], 2) Modified Bleeding on Probing (MBoP %): dichotomous index of bleeding during probing around implants [23], 3) Peri-implant Probing Depth (PPD/mm): distance from the bottom of the peri-implant sulcus/pocket to the mucosal margin; 4) Mucosal Margin (MM/mm): distance from the implant platform to the peri-implant margin (CL group) and distance from the machined collar maintained supracrestally to the peri-implant margin (SL group); 5) Clinical attachment level (CAL/mm): considered by adding PPD and MM.

2.6. Immunoinflammatory profile assessment

The same examiner (BG) collected peri-implant crevicular fluid from

[1] IBM, Armonk, NY, USA

[2] Hu-Friedy, Chicago, IL, USA

Fig. 1. Schematic drawing illustrating the clinical parameters evaluated. The figure demonstrated that the clinical parameters were measured in the CL (crestal level) and SL (supracrestal level) groups. PPD: Peri-implant Probing Depth the distance from the bottom of the peri-implant sulcus/pocket to the mucosal margin; MM: Mucosal Margin distance from the implant platform to the peri-implant margin (CL group) and distance from the machined collar maintained supracrestally to the peri-implant margin (SL group).

implants using filter paper strips[3] at baseline, 6, 12, and 24 months, as described earlier [23]. The fluid volume was computed using a calibrated device[4], and peri-implant fluid samples were stored at −20 °C. The levels of interleukin (IL)-4, IL-6, IL-10, IL-17, IL-21, IL-23, IL-33, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ in the peri-implant fluid were established using human plex[5] and the multiplexing apparatus.[6] The samples were separately assessed, corrected according to volume, and the concentrations were projected from the standard curve using a five-parameter polynomial equation and specific software.[7] Thus, each mediator's mean concentration (pg/ml) was determined.

2.7. Tomographic evaluation

Cone Beam Computed Tomography (CBCT) scans were done before implant surgery for planning. In addition, CBCTs were taken at baseline, 6, 12 months, and 24 months following implant loading for radiographic measurements. All scans were taken using the same equipment[8] The exposure settings selected were FOV of 240 × 190 mm, 74 kV, and 10 mA, using a 10.68-second acquisition time, providing a low-dose protocol with a low radiation exposure [24]. CS3D Imaging[9] was used to reconstruct the images and complete the analysis. The parameter Crest Height Bone Marginal Peri-implant was measured in all images. This parameter represents the linear measurement achieved by a parallel line to the implant surface from the implant platform to the bone crestal (mesial, distal, buccal, and lingual) in the sagittal and coronal slices, each 2 mm. The scans were viewed by a single research investigator (PHFD) who made all radiographic measurements. For the intra-examiner calibration, 15 non-study implants used in rehabilitation with overdentures were selected and analyzed tomographically. The examiner measured all subjects' Crest Height Bone Marginal Peri-implant twice within 24 h. The intra-class correlation was determined to be 90 % reproducibility.

2.8. Statistical analysis

Exploratory analyses were performed. For the comparison between groups and times, generalized linear models were used to evaluate the effect of the group, time and group versus time interaction according to the split-mouth design and repeated measures over time. After log transformation of data, the statistical methodology was applied using ANCOVA test, the baseline was a covariate in the model. Multiple comparisons were made by decomposing the interaction by the Tukey-Kramer test. For the variables MPI, MBoPI, MM and immunoinflammatory markers, the Friedman and Wilcoxon tests were used, due to the lack of model adjustment. An experimental significance level was established at 5 % for all statistical evaluations. Statistical tests were performed using the SAS 9.3 program.[10]

3. Result

The demographic characteristics of the sample at the initial stage of the study were 60 % males and 40 % females, with a mean age of 68.23 ±8.55 years, a diagnosis of T2DM for 14.55±7.29 years, an HbA1c (%) of 7.73±1.59, and an FPG (mg/dL) of 127.32±26.85. HbA1c and FPG levels did not show differences throughout the study ($p > 0.05$, Table 1). All edentulous mandibles were considered Class III [25]. The patient selection is shown in a flow diagram (Fig. 2).

3.1. Clinical and immunoinflammatory markers outcomes

Both groups present similar MPI and MBoP values throughout the follow-up time, in addition to not exhibiting intragroup changes over time ($p > 0.05$, Table 2). PPD and CAL present higher values for the CL group than SL in all evaluated periods ($p < 0.05$). At 24 months, PPD (p

[3] Periopaper, Oraflow, Plainview, NY, USA
[4] Periotron 8000; Oraflow
[5] Human Th17 HTH17MAG-14K, Millipore Corporation, Billerica, MA, USA
[6] MAGpix™ MiraiBio, Alameda, CA, USA
[7] Xponent® Millipore Corporation, Billerica, MA, USA
[8] KODAK 9000 EXtraoral Imaging system, Carestream Health, Rochester, NY, USA
[9] Carestream Dental, Atlanta, GA, USA
[10] Cary, NC, USA

Table 1
FPG and HbA1c of the study population throughout the time (Mean ± SD).

Period	HbA1c (%)	FPG (mg/dL)
Baseline	7.73 ± 1.59	126.67 ± 32.08
6 months	7.73 ± 1.34	123.33 ± 29.96
12 months	8.32 ± 1.83	120.00 ± 21.10
24 months	7.92 ± 1.47	127.32 ± 26.85

There was no statistically significant difference ($p > 0.05$).

< 0.05; Table 3) and CAL values were higher than the others time-period in both groups ($p < 0.05$; Table 3). No intra-group differences for MM were detected ($p > 0.05$; Table 3).

Immunoenzymatic assay showed that CL implants demonstrated higher concentrations of IL-4, at 6, 12 and 24 months, and IL-21 at 24 months, when compared to SL implants ($p < 0.05$). At 6 and 24 months the levels of IL-6 were higher than other time-points in the CL implants ($p < 0.05$). Concerning the amounts of IFN-γ, IL-17, IL-10, IL-33, IL-23 and TNF- **α** it was not found any intra or inter-group difference ($p > 0.05$, Table 4).

3.2. Tomographic analysis

Inter-group analysis did not show significant differences within the same time-period ($p > 0.05$).

SL implants presented higher bone loss in 12 months than at baseline. At 24 months, bone loss was higher than at baseline and the 6-month period ($p < 0.05$). No difference in bone level between the first and the second year of loading was observed. On the other hand, CL implants revealed additional changes in bone loss at 12 and 24 months compared to 6 months and baseline ($p < 0.05$; Table 5). In the SL group, the mean bone loss increased by 31.22 % from baseline to 24 months, corresponding to a change of 0.74 mm. In the CL group, the initial variation was 1.21 mm (69.94 %) over the same period.

Higher bone loss was detected in the first year of implant loading compared to the second year in both supracrestal and crestal implants ($p < 0.05$). No significant difference in peri-implant bone loss was detected in the second year of implant loading when compared with 1 year in both groups ($p > 0.05$, Table 5).

4. Discussion

It is well established that preserving peri-implant bone is essential for efficacious results in implant dentistry [26]. According to the data of the current investigation, the tomographic evaluation showed that SL implants presented lower bone remodeling when compared to CL implants,

Table 2
Percentage of modified plaque and bleeding on probing index (Mean ± SD) at experimental sites throughout the study.

Parameter	Group	Baseline	6 months	12 months	24 months
MPI	SL	19.05 ± 34.37	14.31 ± 31.19	22.62 ± 32.50	28.57 ± 32.87
	CL	15.00 ± 31.83	26.25 ± 40.94	32.50 ± 40.64	27.50 ± 37.96
MBoPI	SL	9.76 ± 24.26	16.67 ± 29.93	14.29 ± 23.15	14.29 ± 23.15
	CL	7.53 ± 11.74	18.75 ± 33.32	16.25 ± 29.55	16.25 ± 24.70

There was no statistically significant difference ($p > 0.05$).

Table 3
Peri-implant clinical parameters (Mean ± SD) in SL and CL implants throughout the experiment.

Parameter	Group	Baseline	6 months	12 months	24 months	p-value
PPD (mm)	SL	2.07 ± 0.50 Bb	1.96 ± 0.60 Bb	2.05 ± 0.58 Bb	2.34 ± 0.54 Ba	<0.001
	CL	2.55 ± 0.50 Ab	2.52 ± 1.15 Ab	2.55 ± 1.21 Ab	2.83 ± 1.05 Aa	
CAL (mm)	SL	2.07 ± 0.50 Bb	2.02 ± 0.64 Bb	2.1 ± 0.62 Bb	2.47 ± 0.67 Ba	0.0001
	CL	2.56 ± 0.50 Ab	2.53 ± 1.15 Ab	2.60 ± 1.23 Ab	2.88 ± 1.06 Aa	
MM (mm)	SL	0.00 ± 0.00 Aa	0.06 ± 0.23 Aa	0.06 ± 0.23 Aa	0.14 ± 0.29 Aa	0.1021
	CL	0.01 ± 0.06 Aa	0.01 ± 0.06 Aa	0.05 ± 0.22 Aa	0.05 ± 0.22 Aa	

Different letters indicate statistical significance. Uppercase letter compares difference between groups (within same time) Lowercase letters compare longitudinal data (within same group).

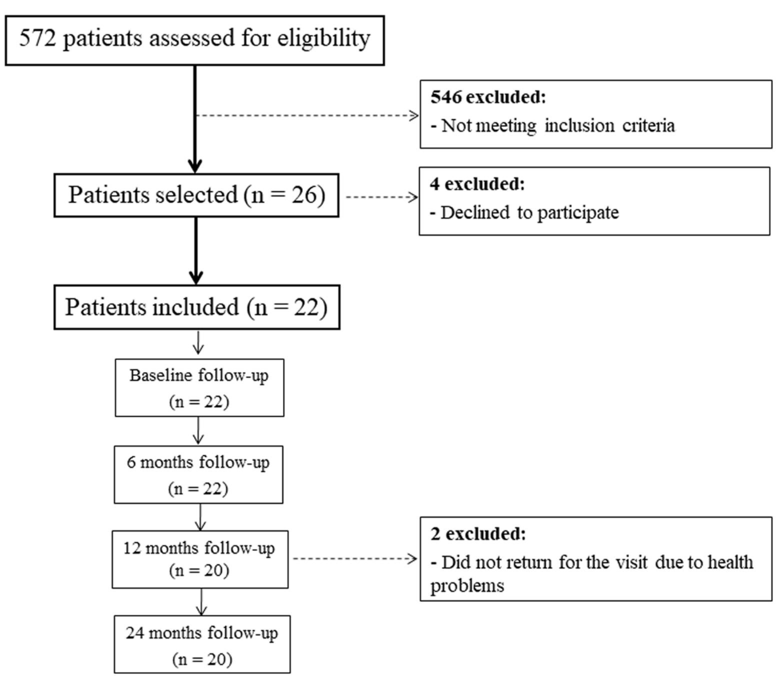

Fig. 2. Flowchart of the study.

Table 4
Level of immunoinflammatory markers (Mean ± SD) for both groups throughout the time (pg/ml).

Mediator (pg/ml)	Group	Baseline	6 months	12 months	24months
IFN-γ	SL	1.61 ± 0.79	1.79 ± 1.50	2.10 ± 1.81	1.45 ± 1.42
	CL	0.50 ± 0.49	1.74 ± 1.48	0.99 ± 0.98	0.77 ± 0.59
IL-10	SL	0.31 ± 0.16	0.55 ± 0.51	0.27 ± 0.22	0.46 ± 0.43
	CL	0.56 ± 0.51	0.70 ± 0.61	0.77 ± 0.60	0.80 ± 0.76
IL-17	SL	1.29 ± 0.61	1.46 ± 1.31	0.73 ± 0.60	1.56 ± 1.43
	CL	1.81 ± 1.88	2.34± 2.18	0.90 ± 0.87	5.38 ± 2.48
IL-33	SL	0.27 ± 0.15	0.34 ± 0.35	0.21 ± 0.15	0.33 ± 0.33
	CL	0.26 ± 0.35	0.34 ± 0.34	0.18 ± 0.17	0.64 ± 0.61
IL-21	SL	1.22 ± 0.64	1.78 ± 1.62	1.13 ± 1.05	1.98 ± 1.85
	CL	1.16 ± 1.54	1.33 ± 1.20	0.78 ± 0.25	3.10 ± 2.86 †
IL-4	SL	0.07 ± 0.09	0.02 ± 0.02	0.01 ± 0.01	0.01 ± 0.01
	CL	0.04 ± 0.07	0.05 ± 0.05 †	0.04 ± 0.02 †	0.03 ± 0.03 †
IL-23	SL	0.08 ± 0.04	0.12 ± 0.11	0.06 ± 0.04	0.10 ± 0.09
	CL	0.10 ± 0.10	0.14 ± 0.14	0.05 ± 0.02	0.18 ± 0.17
IL-6	SL	0.65 ± 0.35	0.66 ± 0.48	0.35 ± 0.34	0.90 ± 0.79
	CL	0.77 ± 0.74	2.76 ± 2.60 *	0.48 ± 0.41	1.42 ± 1.36 *
TNF-α	SL	0.30 ± 0.15	0.55 ± 0.52	0.38 ± 0.27	0.35 ± 0.31
	CL	0.34 ± 0.36	0.71 ± 0.67	0.20 ± 0.06	0.91 ± 0.82 †

* Indicates difference when compared to the other re-evaluation periods (Friedman test, $p < 0.05$).
† Indicates difference between groups (Wilcoxon test, $p < 0.05$).

which is in line with previous investigations that highlighted advantages in supracrestal implants with machined surface exposed [13,14].

Schwarz et al. [14]. measured the impact of distinct insertion depths of dental implants on crestal bone-level alterations, comparing implant shoulders positioned at either epicrestal, supracrestal, or subcrestal positions. Supracrestal positioning was frequently related to a small bone gain over the epicrestal group. Cochran et al. [13] reported a slight bone gain when the implant shoulder was above the crest. Accordingly, van Eekeren et al. [27] revealed higher bone loss in the implant/abutment connection at the crestal bone level than in the implant/abutment connection above the crestal level. These data sustain the hypotheses that the supracrestal implant-abutment interface could prevent the peri-implant marginal bone loss, benefiting the formation of the biologic width and distancing the microgap from the bone crest [28,29]. Our results align with these reports, indicating that supracrestal implant placement can also be beneficial in patients with type 2 diabetes, a population traditionally considered at higher risk for peri-implant bone loss. Interestingly, the magnitude of bone remodeling observed in our diabetic cohort was comparable to, or even more favorable than, that described in some studies involving non-diabetic subjects, particularly when implants were placed supracrestally. This finding may suggest that, despite systemic metabolic challenges, surgical and prosthetic strategies—such as supracrestal positioning—could mitigate the impact of diabetes on peri-implant bone stability.

The present study revealed that the benefits achieved by implants with a machined collar placed supracrestally occurred in the first year of loading. Although there is no difference between SL and CL implants, there is a tendency of bone level at SL implants to have higher stability at the first year of function. It is known that the main peri-implant bone loss occurs throughout the first year after abutment connection and that reduced annual crestal bone loss might happen thereafter [26,30]. The favorable results achieved by SL in terms of marginal bone loss agreed with the clinical evaluations of the current study, which revealed lower PPD and CAL means in SL implants during the 24 months. Limited evidence is offered concerning the impact of vertical implant position on peri-implant soft tissues, including evaluations of the health around implants over time, especially in diabetic patients. It is relevant to emphasize that reduced PPD and CAL on a long-term basis seem to be important to maintaining the health of peri-implant tissues over time. Monje et al. [31] suggested that probing pocket depth is the most accurate prognostic indicator of peri-implant disease progression. In addition, Kröger et al. [32] characterized the submucosal microbiome of peri-implant sites. They demonstrated an association between deeper peri-implant probing depths and increasing levels of microbial dysbiosis, supporting that peri-implant clinical parameters are relevant in shifting healthy implant conditions to peri-implant diseases.

Stable peri-implant bone is a prerequisite to guarantee predictable sustenance of the surrounding soft tissues [33]. Thus, the diminished PPD and higher CAL observed in the supracrestal implants may be related to the stability of bone level in these implants at the first year, as verified in the present study. The significance of peri-implant bone and soft tissue preservation is relevant mainly in T2DM individuals, considering the augmented potential for establishing peri-implant diseases in this patient profile. In addition, a study on diabetic patients with crestal implant-supported overdentures found that glycemic control has a positive influence on peri-implant clinical outcomes [19]. Highlighted that in the present study, HbA1c and FPG levels remained stable throughout the follow-up period, which aligns with the favorable peri-implant tissue maintenance observed in both groups.

The immunoenzymatic assay of the present study revealed augmented amounts of IL-21, at 24 months, and higher, of IL-4 at 6, 12 and 24 months, in CL implants compared to SL. Although the clinical parameters suggest a healthy peri-implant condition in the present study, it could be hypothesized that the pro-inflammatory profile detected in the peri-implant fluid of CL implants would contribute to an at-risk-for-harm condition, predisposing peri-implant disturbances [34]. Likewise, CL implants presented elevated levels of IL-6 at 6 and 24 months related to baseline, what could justify the higher levels of IL-4 in this group in comparison with SL groups, once the release of pro-inflammatory cytokines usually leads to up-regulation of anti-inflammatory cytokines such as IL-4 [33]. Besides, IL-6 has been stated as a marker of peri-implant disease [34], and its release is also linked to the stimulation of TNF, IL-1 and IL-8 production and to the decrease of IL-10 and IL-13, that could reinforce the hypothesis of an at-risk condition on CL implants [35].

A significant aspect to be discussed is that IL-21 was found in higher concentration in CL implants at 24 months. This finding is also a relevant information regarding the potential risk of disease development in this group. Il-21 levels were significant increased in mucositis sites [36]. Interestingly, IL-21 has direct osteoclastogenic potential independently of RANKL and may promote osteoclastogenesis through the PI3K/AKT signaling pathway [37,38]. Based on our results, CL implants could be

Table 5
Changes (mean ± SD) in the bone crestal level from baseline in both groups (mm).

Group	Baseline	6 months	12 months	24 months
SL	2.37 (0.97) Aa	2.57 (0.88) Aab	2.91 (0.0.87) Abc	3.11 (0.85) Ac
MD / Change (%)	ref	−0.2 /8.4 %	−0.54/22.78 %	−0,74/ 31.22 %
CL	1.73 (0.87) Aa	2.18 (1.02) Ab	2.51 (0.89) Ac	2.94 (1.14) Ac
MD / Change (%)	ref	−0.45/26.01 %	−0.78/45.08 %	−1.21/69.94 %

$p < 0.05$. Different letters indicate statistical significance. Uppercase letter compares difference between groups (within same time) Lowercase letters compare longitudinal data (within same group).
MD Mean difference from baseline.
% Change percentage in the bone crestal level from baseline.

hypothesized to negatively modulate the local pattern of immunoinflammatory biomarkers, even in a clinically healthy peri-implant situation, favouring the marginal implant bone level, as observed in this trial. In agreement, Broggini et al. [17] demonstrated that the extent of inflammation is proportionally dependent upon implant-abutment interface position, with progressive increase of peri-implant neutrophil growth as the implant-abutment interface is deeper, which also contributed to the level of implant-associated alveolar bone loss.

Although the clinical outcomes of this trial have revealed lower peri-implant probing depth means in SL implants during all experimental periods, the values of peri-implant probing depth were <3 mm and the modified bleeding on probing was maintained in low levels throughout the study, meaning that the assessed implants were healthy from a clinical point of view. Notably, all subjects were scheduled for supportive therapies during the experimental period. The importance of maintenance therapy for the prevention of peri-implant disorders has been highlighted by several studies [39,40]. In a clinical investigation, Costa et al. [39] reinforced that the regular appointments for preventive peri-implant maintenance decreased the risk of peri-implantitis from 43.9 % to 18 % at the patient level. Although some data have proposed that the rational interval of supportive peri-implant maintenance should be 5 to 6 months, considering its imperative impact to prevent peri-implant diseases, the recall period for peri-implant maintenance must be adapted according to patients' risk profiling, as diabetic individuals, focused on in the current study [39,40]. Taking into account that the strict enrollment of the peri-implant maintenance is not always adhered to patients, and considering the positive clinical outcomes achieved by supracrestal implants in this trial, it could be hypothesized that biological complications in long-term might be avoided using implants with machined collar placed supracrestally, mainly in T2DM individuals.

It is essential to highlight that although the comparisons of bone remodeling and clinical parameters of supra-crestal and crestal level implants have demonstrated significant differences, additional studies are important to confirm these findings, and further trials with more extended re-evaluation periods and varying the glycemic level are required to support the clinical relevance of these data in the long-term, especially considering that the longitudinal influence of the vertical implant position in T2DM patients is unclear in the literature.

The limitation of this trial is that only implants with an external hexagon were utilized in the present clinical trial. Previous studies demonstrated an augmented marginal bone loss in external hexagon implants compared to implants with Morse-taper connections [41,42]. It is important to mention that in all these studies [41,42], the external hexagon implant platform was positioned at the crestal level or slightly below the bone crest. It could be hypothesized that the supracrestal placement of external hexagon implants, as investigated in this trial, may also favor, among other aspects, biomechanical characteristics around implants, minimizing the peri-implant remodeling in implants placed supracrestally.

While studies have confirmed clinically successful implant placement even in people with diabetes lacking reasonable glycemic control [15,18] it seems that poor glycemic status is the most significant aspect to promote dental implant complications, including peri-implant bone loss and peri-implant tissue maintenance [43,19]. It is important to highlight that only modest changes over time were observed in glycemic levels as well as in clinical and radiographic evaluations throughout our study, underscoring the need for careful attention when significant variations in these parameters are detected, especially in patients with T2DM. The number of patients with T2DM has significantly increased in recent years due to population growth and aging, the increased prevalence of obesity and sedentary lifestyle, as well as the greater survival of patients with DM [1,2]. Thus, investigations focusing on determining the better approach to rehabilitate this patient profile, as proposed in the present study, are highly relevant.

In conclusion, implants with a machined collar installed supracrestally in T2DM individuals rehabilitated with overdentures presented better clinical and tomographic results and downregulation of some pro-inflammatory mediators than implants placed at the crestal level. Considering evidence highlighting that diabetic patients have a greater predisposition to peri-implant diseases and implant complications [10,12], using supracrestal implants seems to benefit the maintenance of peri-implant tissue level. It influences the long-term success of implants in patients with type 2 diabetes mellitus. However, it is crucial to emphasize that these findings support that patients with well-controlled T2DM can be successfully rehabilitated with mandibular overdentures using either CL or SL implants, as both apical-coronal positions remained clinically healthy throughout the study period.

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CRediT authorship contribution statement

Alexandre Conte: Investigation. **Bruna Ghiraldini:** Investigation. **Pedro H F Denófrio:** Investigation. **Raissa Micaella Marcello-Machado:** Supervision, Conceptualization. **Monica G Corrêa:** Writing – original draft, Project administration, Data curation. **Suzana P Pimentel:** Supervision, Conceptualization. **Marcio Z Casati:** Writing – original draft, Supervision, Conceptualization. **Vanessa Gallego Arias Pecorari:** Validation, Formal analysis. **Fabiano R Cirano:** Writing – review & editing, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

Permission Note

The manuscript has been submitted solely to the Journal of Dentistry and has not been published previously. All authors were involved in the work leading to the publication of the paper, which was read, approved by all of them and declare that they have no conflict of interest. Finally, we confirm that the submitted work is original including the images. If accepted, the manuscript will not be published elsewhere in the same form, in any language, without the written consent of the publisher.

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