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Cohort Study

IMPLANT SURVIVAL RATES AND PERI-IMPLANT STATUS IN HIV-POSITIVE PATIENTS VERSUS HEALTHY SUBJECTS: A PROSPECTIVE COHORT STUDY AT 5-YEAR FOLLOW-UP

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ABSTRACT

The increasing application of dental implants underscores a research gap in understanding how Human Immunodeficiency Virus (HIV) and antiretroviral therapy (ART) influence peri-implant health. This 5-year prospective study compares HIV-infected patients on ART (Test Group = TG) with healthy controls (Control Group = CG). The study involves 57 healthy patients (CG) and 61 HIV-infected subjects under ART (TG). 116 (CG) and 129 (TG) single dental implants were placed. Check-ups occurred at 3, 6, 12 months, and annually. Outcomes include implant survival, surgical complications (primary), and peri-implant parameters such as Marginal Bone Loss (MBL), Periodontal Screening and Recording (PSR), Plaque Index (PI), Bleeding on Probing (BoP) and Peri-implant Probing Depth (PPD) (secondary). Lost implants, MBL, and surgical complications were recorded during follow-ups. Peri-implant parameters were detected at the end of the monitoring period. Importantly, no significant differences in implant survival or surgical complications between CG and TG were observed, providing reassurance about the safety of dental implants in HIV patients. However, TG displayed unfavorable peri-implant hard and soft tissue parameters, emphasizing potential challenges in HIV patient outcomes. Conclusion: HIV patients under ART may experience increased MBL and poorer peri-implant soft-tissue conditions. No significant differences in implant survival rates and surgical complications were found between healthy and diseased patients.

KEYWORDS: *human immunodeficiency virus, antiretroviral therapy, periimplantitis, bone loss, dental implants*

INTRODUCTION

Human Immunodeficiency Virus remains a persistent global health challenge, affecting millions of individuals worldwide (1). Thankfully, remarkable progress in medical treatments, mainly through ART, has transformed HIV from

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a once-debilitating disease into a manageable, chronic condition. As a result, people living with HIV are experiencing longer lifespans and improved overall quality of life. However, this positive shift in HIV management has given rise to a pressing need to address the unique healthcare needs of these individuals, including their oral health (2-4).

Dental implants have become an effective and popular solution for replacing missing teeth (5, 6). Yet, despite the growing application of dental implants, there remains a notable gap in research and understanding concerning the impact of HIV infection and its management through antiretroviral therapy on peri-implant health (7, 8).

Peri-implant health, a critical aspect of dental implant success, encompasses the condition of the tissues surrounding dental implants. Maintaining optimal peri-implant health could be crucial for ensuring the long-term success and stability of dental implants (9-11).

Several studies tried to investigate the effect of ART on peri-implant health in individuals affected by HIV (12, 13). Collectively, the existing evidence suggests that well-controlled HIV infection, coupled with diligent adherence to ART, could yield favorable peri-implant outcomes (14,15). ART is pivotal in restoring and maintaining immune function by suppressing viral replication and bolstering CD4 cell counts. This enhanced immune function may significantly help improve peri-implant health, as it strengthens the body's abilities to fight infection and aid the healing process around dental implants (16).

As suggested by Gherlone et al. (17) in their prospective longitudinal study at-year follow-up, while HIV infection and associated immune suppression might theoretically hinder soft tissue healing, empirical research has revealed that HIV-infected patients on ART exhibit rates of soft tissue complications, such as peri-implant mucositis and peri-implantitis, comparable to those observed in non-HIV-infected individuals (17). Given the potential for heightened susceptibility to infections, including peri-implant infections, among HIV-infected patients, it is paramount to underscore that well-controlled HIV infection and consistent ART usage appear to mitigate this risk to a level akin to that of non-HIV-infected individuals (18).

For all patients with dental implants, including those living with HIV, vigilant monitoring of peri-implant health and regular professional maintenance could be crucial. Routine dental check-ups enable the early detection and prompt treatment of potential complications, thereby ensuring the enduring success of dental implant therapies (19-21).

The aim of this prospective longitudinal study was to compare, at five years follow-up, HIV-infected patients under ART (TG) with a control group of healthy patients (CG) concerning implants survival rate, surgical complications (first outcomes), and peri-implant parameters (secondary outcomes). The null hypothesis was that no statistically significant differences existed between tested groups (CG and TG) concerning implant survival rate, surgical complications, and peri-implant parameters (MBL and PSR, PI, BoP, PPD).

MATERIALS AND METHODS

Study design

The study was designed as a prospective longitudinal study comparing healthy (CG) and HIV-infected patients on ART (TG). All procedures were in accordance with institutional and/or national research committee ethical standards and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. The ethics committee approval number is 190/INT/2021.

The methodology and reporting of this study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology for Clinical Trials (STROBE-CT) guidelines (STROBE-CT Guidelines).

The study was conducted at the Department of Dentistry and Dental Prosthetics of the IRCCS San Raffaele Milan in association with the subsidiary Department of Dentistry and Dental Prosthetics of the San Luigi Turro Hospital in Milan, where patients were recruited from May to September 2018. The relevant dates for the study include the recruitment period from May to September 2022, with a follow-up period of five years.

Participants

a) Eligibility criteria and participant selection.

Any healthy or HIV-infected patient (on ART) with only systemic disease requiring single-unit implant-retained prosthetic rehabilitation with enough residual bone height for axial implant placement in basal bone without the aid of regenerative procedures, over 18 years of age and able to sign an informed consent form was eligible for inclusion. The exclusion criteria were:

- general contraindications to dental implant placement (22);
- suffering from diseases other than HIV on ART;
- pregnancy or lactation (23);
- untreated periodontitis (24);

- unrealistic expectations;
- substance abuse (25);
- unwilling to comply with monitoring checks and professional hygiene maintenance protocols planned during the follow-up;
- participation in other clinical trials that interfered with the current protocol.

b) Matching criteria for matched studies.

According to the presence or absence of HIV, the sample was divided into two groups: healthy (CG) and HIV-infected patients on ART (TG). Patients were recruited and treated by different doctors and different operators:

- 3 dentists were in charge of patient recruitment and follow-ups;
- 3 oral surgeons performing implant placement;
- 2 prosthodontists who performed the restoration;
- 3 hygienists oversaw the professional oral hygiene sessions scheduled in the protocol.

Each participant in the study was provided with comprehensive explanations, encouraged to pose any pertinent questions, and required to sign a written informed consent form before inclusion. This process ensured the understanding and acceptance of clinical procedures.

Variables

Definitions were provided for outcomes, exposures, predictors, potential confounders, and effect modifiers. Diagnostic criteria, when applicable, were outlined.

Data sources/measurement

For each variable, sources of data and methods of assessment were detailed. Implant design and length were guided by Cone Beam CT scans (26, 27). Surgical procedures were explained, including local anesthesia, flap elevation, implant insertion, and follow-up protocols.

Implant-prosthetic protocol

After an initial objective examination, comprehensive radiographic investigations were performed, including intra-oral radiographs, orthopantomographs, and Cone Beam CT scans. Surgical procedures were conducted under local anesthesia, using an opticain solution with 1:80,000 adrenaline (AstraZeneca, Milan, Italy).

The initial crestal incision was slightly inclined towards the palatal side to ensure that the keratinized mucosa would uniformly cover both sides of the surgical flap. Vertical release incisions were made on the distal and mesial aspects to expose the buccal bone ridge and avoid vestibular bone cortical fenestrations during implant placement. A full-thickness flap was carefully elevated. A lanceolate drill was used to penetrate the cortical bone, followed by a pilot drill with a 2.00 mm diameter to create an implant insertion pathway and verify the implant direction. Progressive diameter drills were employed until the final implant diameter was achieved. The site was intentionally over-prepared vertically and slightly under-prepared transversely. This approach aimed to enhance primary mechanical stability for the implants (28). In cases where implant seating was incomplete, a manual screwdriver was used to position the implant neck at the bone level. The inserted implants were of two types, TTi and K-line (Winsix, Ancona, Italy), having a micro roughened surface, achieved through sandblasting.

The main difference between the two implant lines, both characterized by internal connection, consists in the macromorphology: TT implants with a tapering conical implant body, while K implants with a conical shape. The first, featuring a strongly tapered apical region with an osteotomy effect, was applied in cases of lower bone density, i.e., typical of the upper jaw, while the second, in cases of a prevalence of cortical bone tissue, i.e., mainly in the mandible and usually in the anterior sectors. The choice of implant design, length, and diameter was guided by a morphological evaluation of the residual bone ridge identified by a Cone Beam CT scan examination.

Implants were submerged, and suturing was performed using 3-0 non-resorbable sutures (Vicryl, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA) and intra-oral X-rays were taken to verify the accurate positioning of the implants.

For adequate coverage against possible bacterial infections, each patient received a prescription for antibiotic therapy (amoxicillin and clavulanic acid or clarithromycin in cases of allergies; 1 g every 12 hours for 6 days from the day before surgery). Domiciliary analgesic therapy as needed was prescribed. Patients were also advised to rinse their mouths with a chlorhexidine digluconate-containing solution (0.2%) twice daily for ten days. Sutures were typically removed one week after the surgical procedure. In cases where an insertion torque of 25 Newtons or higher was achieved, implant loading was immediately performed (29, 30).

Preliminary alginate impressions and simultaneous relining of temporary acrylic restorations were conducted. In cases where immediate loading criteria were not met, a custom-made resin removable partial denture was provided during the healing phase, and implants were exposed approximately four months after the surgical procedure. Cap screws were replaced with healing screws, pick-up impressions were taken, and provisional crowns were fitted for each patient. Screw access holes were sealed using provisional resin (Fermit, Ivoclar Vivadent, Naturno, Italy).

After thorough assessments of the provisional devices, four months later, they were replaced with either a metal-ceramic or stratified zirconia implant-supported final crown. The choice was made based on anatomical location, aesthetic considerations, and patient preferences. The definitive impression was obtained using the pick-up technique with a customized spoon after the definitive screw-retained crown was delivered. The impression material was used as Polyether (Impregum Penta, 3M Italia, Pioltello, Italy). To ensure a precise fit between the metal framework and implants, intra-oral x-rays were performed.

Follow-up

Patients were placed on a recall schedule that included check-ups at three, six, and 12 months and once a year during the follow-up period; in addition, patients were subjected to professional oral hygiene sessions every six months (31, 32). In the event of complications in the interval between scheduled visits, the practice was available to the patients for further checks.

Bias

During the study, a potential source of bias was introduced by the varying experience levels among the operators involved in patient recruitment, surgical procedures, and follow-ups. The three dentists responsible for recruitment and follow-ups, the three oral surgeons performing implant placement, and the two prosthodontists involved in restoration may have had different levels of expertise and proficiency in their respective roles. This variation in skill levels could have led to differences in the quality and precision of the procedures performed, potentially influencing the study outcomes.

Efforts were made to standardize the protocols and provide training sessions for all operators; however, the inherent variability in individual skills and approaches remained. While blinding was maintained during outcome assessments, the potential for operator-related bias during the earlier stages of the study, such as patient recruitment and surgical procedures, cannot be completely ruled out. This could introduce a systematic error that may impact the internal validity of the study results.

To address this potential bias, regular meetings were held among the operators to discuss and standardize procedures. Additionally, continuous monitoring and evaluation of operator performance were implemented throughout the study. The aim was to minimize any bias introduced by operator variability and enhance the overall consistency and reliability of the study findings.

Study size rationale

The study size was determined by a statistical power analysis, targeting a significance level (α) of 0.05 and an effect size of 0.5. The formula employed is the following:

$$n = (2 * (Z_{a2} + Z_p)^2 * o^2) \, IES^2$$

This analysis yielded a required sample size of 126 participants, with a power value of 0.97. This indicates a high probability of detecting differences within the samples, underscoring the robustness of the study design in ensuring adequate statistical power for reliable inference.

Quantitative variables (outcomes measures)

The investigation delved into three pivotal quantitative aspects: Implants Survival Rate, Surgical Complications, and Peri-implant Parameters (MBL and soft tissue parameters).

- Implants Survival Rate.

An implant that did not osseointegrate or whose osseointegration was compromised enough to result in bone loss and subsequent mobility that hindered its function as a prosthetic crown supporting was considered failed (32). The

assessment of implant survival rate was founded on monitoring instances of implant loss throughout the follow-up period. Subsequently, implant survival rates in CG and TG were scrutinized to ascertain potential disparities between these groups in terms of implant survival rates.

- Surgical complications.

Surgical complications such as alveolar nerve injuries, maxillary sinus issues, i.e., maxillary sinusitis following implant placement, edema, pain that cannot be managed with analgesics prescribed, bleeding, wound dehiscence, wound infection, suppuration, and abscessing were recorded during follow-up to compare the examined groups.

- Peri-implant parameters.

1. Marginal bone loss.

During each session, three blind operators (dentists) were involved in analyzing MBL values, one of whom performed the radiographs, the other the calibration, and the third the data collection.

Intra-oral radiographs were taken at implant placement, implant loading, 3, 6, 12 months, and then once a year for the following period. We employed calibrated software to analyze these images and assess marginal bone changes (DIGORA 2.5, Soredex, Tuusula, Finland). Calibration was performed for each image, referencing the known diameter of the implant at the most coronal portion of the implant neck.

The measurements included determining the linear distance between the most coronal point of bone-implant contact and the coronal margin of the implant neck on both the mesial and distal sides, with an accuracy of up to 0.1 mm. Subsequently, these measurements were averaged to calculate the overall average marginal bone changes for individual implants at the patient level. Further averaging was done at the group level.

2. Soft tissue parameters.

The parameters were assessed at the end of the follow-up period, i.e., 5 years after prosthetic loading. Two blind operators were involved, one clinically responsible for the measurements (dentist or dental hygienist) and the other for data collection. PSR, PI, BoP, and PPD were recorded.

A William probe was applied to measure PSR, PI, BoP, and PPD. The probing force applied was from 0.2 to 0.6 Newton. PSR involved the examination of six sites around each implant (distobuccal, mid-buccal, mesiobuccal, distolingual, mid-lingual, and mesiolingual) to assess the depth of the periodontal pocket and the presence of bleeding or calculus. According to the results, a code from 0 to 4 was assigned.

- Code 0: Healthy (no bleeding, no calculus, and pocket depth within normal limits);
- Code 1: Gingival bleeding (bleeding on probing, but no calculus or other signs of disease);
- Code 2: Calculus present (no bleeding, but calculus is detected);
- Code 3: 4-5mm pocket depth (indicating moderate peri-implant disease);
- Code 4: 6mm or deeper pocket depth (indicating severe peri-implant disease).

To measure PI, a probe was placed around each implant surface (buccal, lingual, mesial, and distal), and a score of 0 to 3 was assigned according to plaque amount. According to bleeding on probing, a zero value was assigned in the absence of bleeding and 1 if present.

PPD was obtained by inserting probing into the space between the implant and soft tissue, parallel to the implant axis, to measure the distance from the implant-abutment junction (IAJ) to the base of the gingival sulcus or pocket.

Statistical methods

Controlling for Confounding: in this study comparing HIV-infected patients under antiretroviral therapy (TG) with a control group of healthy patients (CG), robust strategies were employed to control for potential confounding factors. Covariate matching was conducted between TG and CG based on key demographic and clinical criteria, including age and gender. Propensity scores were calculated to ensure balance in observed covariates. Multivariate regression analysis employing multiple linear regression was then applied, incorporating these covariates to adjust for any residual confounding and enhance the accuracy of our comparisons. Such an operation relies on the checked assumptions of linearity, homoscedasticity, independence, and residual normality. These assumptions were checked visually with plots of the residuals, Durbin-Watson, and Shapiro-Wilk tests.

Examining Subgroups and Interactions: the analysis delved into subgroups and interactions to capture nuances in the data. Stratified analyses explored outcome variations within specific categories, such as implant type, loading protocols, and anatomical locations. Interaction terms were introduced into the statistical models, enabling the examination of whether the effects of group membership on outcomes differed based on distinct factors like age or smoking status. This approach allowed for a more nuanced understanding of the study findings.

Multiple imputation techniques were implemented, leveraging the capabilities of Python packages such as Pandas and SciPy.Stats. Addressing loss to follow-up: to mitigate the impact of potential loss to follow-up, sensitivity analyses were explicitly tailored to assess this concern. Alternative scenarios were considered, and subgroup analyses were performed for participants who completed the entire follow-up period. This approach allowed for a thorough evaluation of the potential biases introduced by attrition, ensuring the study's findings remained reliable.

RESULTS

Participants – descriptive data

At each stage of the study, 164 patients were considered potentially eligible and examined to confirm. According to exclusion criteria, the confirmed eligibility at baseline was 126 considering. Sample details at baseline and implant-prosthetic features in CG and TG are in the following table (Table I).

Table I. *Sample features at baseline, implant details, prosthetic loading and implant site in CG and TG.*

	CG	***TG***	*p-values*
Sample features			
Number patients	60	66	
Females	29	30	0.512
Males	31	36	0.572
Average age (range)	54.5 (28-81)	55 (32-78)	0.478
Smokers, alcohol intake	9	11	0.128
Smokers, no alcohol intake	7	3	0.092
No smokers, alcohol intake	26	24	0.821
No smokers, no alcohol intake	12	23	0.073
Implants details			
Number implants	116	114	
K 3.3x9	7	9	0.215
K 3.3x11	4	3	0.633
K 3.3x13	12	26	0.072
K 3.8x9	12	5	0.042
K 3.8x11	10	24	0.065
K 3.8x13	14	6	0.066
TTi 3.3x9	13	10	0.318
TTi 3.3x11	14	11	0.598
TTi 3.3x13	6	9	0.798
TTi 3.8x9	5	0	0.472
TTi 3.8x11	17	7	0.029
TTi 3.8x13	2	19	0.033
Prosthetic loading and implants site			
Delayed posterior maxilla	17	21	0.433
Delayed anterior maxilla	11	9	0.173
Delayed posterior mandible	18	13	0.439
Delayed anterior mandible	15	19	0.44
Immediate posterior maxilla	12	7	0.111
Immediate anterior maxilla	16	17	0.839
Immediate posterior mandible	13	16	0.909
Immediate anterior mandible	14	27	0.277

Dropout

During the follow-up period, 3 CG and 5 TG patients were lost. Of the three CG patients, one died 3 years after implant placement, while the others were non-compliant with recall sessions one and four years after implant-prosthetic

rehabilitation, respectively. Of the five TG patients, two reported that they were transferring to another city, thus making themselves unavailable for the planned follow-ups since the definitive crown placement. The other three were non-compliant with recall sessions three, two, and four years after implant-prosthetic rehabilitation, respectively. Therefore, 57 patients in CG and 61 in TG were considered for the study. Details concerning CG patients not considered in the study are in the table below (Table II).

Table II. *Patient dropout details in CG.*

	Sex	Age	Smokers	Alcohol intake	Implant details
1	Female	65	yes	no	TTi 3.3x11; Delayed posterior mandible
					TTi 3.3x13; Immediate anterior mandible
2	Male	49	no	no	K 3.8x9; Delayed posterior maxilla
3	Male	56	no	no	TTi 3.8x9; Delayed posterior mandible

Details concerning CG patients not considered in the study are in the table below (Table III).

Table III. *Patient dropout details in TG.*

	Sex	Age	Smokers	Alcohol intake	Implant details
1	Male	71	no	no	K 3.8x9; Immediate anterior mandible
2	Female	58	no	no	TTi 3.8x9; Delayed posterior mandible
3	Female	74	no	yes	K 3.8x11; Immediate posterior maxilla
					K 3.8x11; Immediate anterior maxilla
4	Male	61	yes	yes	TTi 3.8x13; Delayed posterior mandible
5	Female	64	no	no	K 3.3x13; Delayed posterior maxilla

Outcome data - main results

Implants survival rate: implant failure details are in the following table (Table IV).

Table IV. *Implants failure details according to the fixture's features and patient information in CG and TG.*

		Implant details				*Patient information*			
	Group	*Site of placement*	*Line, diameter, length*	*Prosthetic loading*	*Failure time*	*Age*	*Gender*	*Smoking*	*Alcohol intake*
1	CG	Posterior maxilla	Line K, diameter 3.3 mm, lenght 13 mm	Immediate	2 months	61	Male	no	no
2	CG	Posterior mandible	Line TTi, diameter 3.8 mm, lenght 9 mm	Immediate	1 month	73	Male	< 10	no
3	CG	Posterior maxilla	Line K, diameter 3.3 mm, lenght 11 mm	Delayed	3 months	67	Female	no	yes
4	CG	Posterior mandible	Line K, diameter 3.8 mm, length 13 mm	Immediate	2 months	56	Female	> 10	yes
5	CG	Posterior maxilla	Line K, diameter 3.8 mm, length 11 mm	Delayed	3 years	69	Male	> 10	yes
6	CG	Anterior maxilla	Line Tti, diameter 3.3 mm, length 11 mm	Immediate	5 years	75	Female	< 10	no
1	TG	Posterior mandible	Line TTi, diameter 3.8 mm, lenght 13 mm	Immediate	1 month	39	Female	> 10	yes
2	TG	Anterior maxilla	Line TTi, diameter 3.8 mm, lenght 9 mm	Immediate	3 months	76	Male	< 10	yes
3	TG	Posterior mandible	Line K, diameter 3.3 mm, lenght 11 mm	Delayed	2 months	59	Male	no	no

4	TG	Posterior mandible	Line K, diameter 3.3 mm, lenght 11 mm	Immediate	1 month	56	Female	no	yes
5	TG	Posterior maxilla	Line K, diameter 3.8 mm, lenght 11 mm	Delayed	4 years	72	Male	> 10	yes
6	TG	Anterior maxilla	Line TTi, diameter 3.3 mm, lenght 11 mm	Immediate	2 years	44	Male	< 10	no
7	TG	Posterior mandible	Line TTi, diameter 3.8 mm, lenght 11 mm	Immediate	1 year	66	Female	< 10	no
8	TG	Posterior maxilla	Line TTi, diameter 3.8 mm, lenght 9 mm	Delayed	5 years	71	Female	no	no
9	TG	Anterior mandible	Line TTi, diameter 3.3 mm, lenght 11 mm	Immediate	1 year	59	Male	> 10	yes
10	TG	Posterior maxilla	Line K, diameter 3.3 mm, lenght 13 mm	Delayed	2 years	79	Male	no	yes

Unadjusted Estimate: The unadjusted implant survival rate was 94% in the CG and 93% in the TG; Confounder-Adjusted Estimate: Adjusting for age, gender, and smoking status as potential confounders, the implant survival rate remained comparable between CG (94%) and TG (92%) with a 95% confidence interval (CI: 0.87, 1.01). No statistically significant differences were observed.

Surgical complications

The following table shows surgical complications in CG and TG (Table V).

Table V. *Surgical complications in CG and TG.*

	CG	***TG***
Alveolar nerve injuries	0	0
Maxillary sinus issues	0	0
Maxillary sinusitis	0	0
Edema	3	5
Pain	2	6
Bleeding	1	2
Wound dehiscence	1	0
Wound infection	0	1
Suppuration	1	1
Abscessing	0	0

Unadjusted Estimate: The occurrence of surgical complications showed no statistical differences between CG and TG; Confounder-Adjusted Estimate: After adjusting for potential confounders, such as age, gender, and smoking status, the incidence of surgical complications remained comparable between CG and TG. No statistically significant differences were observed, with a 95% confidence interval (CI: 0.90, 1.05).

Peri-implant parameters

MBL values recorded are in the following table (Table VI).

Table VI. *MBL values recorded in CG and TG.*

	CG	**TG**
6 months	0.56 ± 0.75	0.64 ± 0.80
1 year	0.89 ± 0.94	0.86 ± 0.99
2 years	0.94 ± 1.01	0.97 ± 1.03
3 years	0.97 ± 1.00	0.99 ± 1.01
4 years	1.02 ± 1.02	1.02 ± 1.09
5 years	1.01 ± 1.02	1.02 ± 1.00

Unadjusted estimate: The unadjusted analysis revealed a statistically significant difference in MBL between the CG and TG. TG exhibited an overall higher marginal bone loss compared to CG; cofounder-adjusted estimate: accounting for age, gender, and smoking status as confounders, the difference in MBL remained statistically significant. TG continued to demonstrate higher marginal bone loss compared to CG, with a 95% confidence interval (CI: 1.15, 1.30).

Crude regression coefficients and p-values are in the following table (Table VII).

Table VII. *Crude Regression Coefficients and p-values.*

	Beta	**p-value**
Age	0.02	0.0039
Gender	0.12	0.0477
Smoking status	4.25	0.009
Alcohol intake	2.78	0.023

The following Table shows adjusted regression coefficients and p-values (Table VIII).

Table VIII. *Adjusted Regression Coefficients and p-values.*

	Beta	**p-value**
Age	0.015	0.0101
Gender	0.21	0.051
Smoking status	5.45	0.02
Alcohol intake	3.48	0.019

Soft tissue parameters

The following table shows soft tissue parameters in CG and TG (Table IX).

Table IX. *Soft tissue peri-implant parameters in CG and TG.*

	CG	***TG***
PSR		
CODE 1	31	19
CODE 2	19	29
CODE 3	6	7
CODE 4	1	6
PI		
0	7	5
1	23	17
2	19	29
3	8	10
BoP		
0	39	19
1	18	42
PPD (mm)		
5	49	34
6	7	19
7	1	8

Unadjusted estimate: Statistical differences were found between CG and TG in peri-implant soft tissue parameters. TG globally exhibited more unfavorable PPD, PI, BoP, and PSR values; confounder-adjusted estimate: upon adjusting for age, gender, and smoking status as confounders, the statistical differences in peri-implant soft tissue parameters persisted. TG continued to demonstrate more unfavorable PSR, PI, BoP, and PPD values compared to CG, with a 95% confidence interval (CI: 1.25, 1.40).

Crude regression coefficients and p-values are in the following table (Table X).

Table X. *Crude Regression Coefficients and p-values for soft tissue parameters.*

	PSR		**PI**		**BoP**		**PPD**	
	Beta	p-value	Beta	p-value	Beta	p-value	Beta	p-value
Age	0.05	0.027	0.03	0.003	0.07	0.008	0.6	0.012
Gender	0.08	0.013	0.25	0.015	0.5	0.025	0.4	0.035
Smoking status	1.8	0.009	2.5	0.001	2.2	0.001	1.5	0.001
Alcohol intake	1.4	0.001	1.9	0.008	1.9	0.004	1.2	0.004

The following Table shows adjusted regression coefficients and p-values (Table XI).

Table XI. *Adjusted Regression Coefficients and p-values for soft tissue parameters.*

	PSR		**PI**		**BoP**		**PPD**	
	Beta	p-value	Beta	p-value	Beta	p-value	Beta	p-value
Age	0.6	0.012	0.65	0.008	0.07	0.009	0.6	0.025
Gender	0.4	0.045	0.4	0.008	0.55	0.001	0.4	0.036
Smoking status	3.2	0.001	2.8	0.025	2.3	0.004	1.6	0.001
Alcohol intake	1.2	0.003	1.3	0.014	1.7	0.004	1.1	0.008

Survival analysis

Confidence intervals of the Kaplan-Meier method provide a measure of the uncertainty associated with the estimated survival function for each time frame analyzed. For instance, from these results for the control group, we can conclude that the survival probability at five years is between 88% and 97%, with a confidence level of 0.95 (Fig. 1).

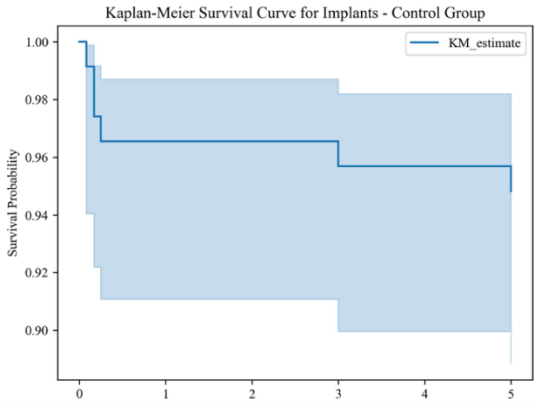

Fig. 1. *Kaplan-Meier Survival Curve for CG.*

For the test group, we observe that the survival probability at five years is between 84% and 95%, with a confidence level of 0.95, thus indicating a lower survival probability than the control group (Fig. 2).

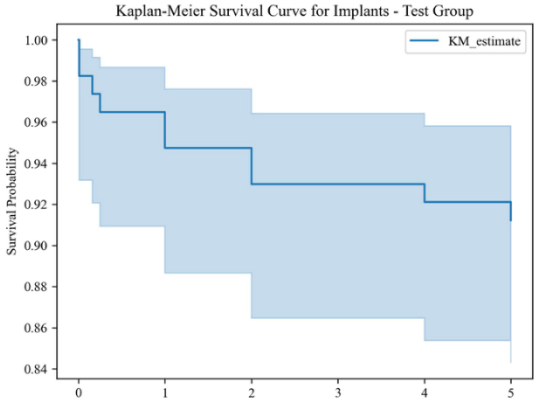

Fig. 2. *Kaplan-Meier Survival Curve for TG.*

The Cox proportional hazards model investigates the relationship between the survival time, event indicator, and covariates. The covariates here are age (covariate 1), loading type (covariate 2), smoking (covariate 3), alcohol consumption (covariate 4) and gender (covariate 5). The baseline hazard is handled non-parametrically using Breslow's method. In this case, the entire model is the traditional semi-parametric Cox model. Ties are handled using Efron's method (Table XII).

Table XII. *Efron's method results.*

	coef	Hazard Ratio	se(coef)	z	p	-log2(p)
Group	0.70	2.02	0.53	1.32	0.019	2.41
Age	0.09	1.10	0.03	3.54	<0.005	11.27
Immediate Loading	0.21	1.23	0.52	0.40	0.69	0.54
Smoking	1.62	5.04	0.53	3.06	<0.005	8.81
Alcohol	-0.38	0.69	0.54	-0.70	0.48	1.05
Sex	-0.37	0.69	0.54	-0.69	0.49	1.03

Analyzing coefficients associated with covariates, specifically cardiovascular treatments and smoking, reveals an elevation in the hazard rate connected with these covariates. Smoking stands out with the highest hazard ratio (5.05) and a low standard error of the coefficient (0.53), indicating a precise estimate with diminished variability. The second most impactful variable is group belonging, suggesting that test group members exhibit a higher risk of implant failure. The general sense from these results is that a higher risk of implant failure is associated with HIV disease and, in particular, smoking. The robustness of covariate results is further substantiated by notably low p-values associated with both covariates, reinforcing the reliability and statistical robustness of our conclusions.

Upon examination of summary statistics derived from the Cox proportional hazards model, which includes concordance, partial Akaike Information Criterion (AIC), log-likelihood ratio test, and the negative base-2 logarithm of the p-value corresponding to the log-likelihood ratio test, our analysis suggests that the model demonstrates good predictive performance. It effectively captures underlying data patterns and exhibits enhanced predictive capacity due to the incorporation of covariates when compared with a null model. All p-values linked to the log-likelihood ratio tests are consistently below 0.001, highlighting their statistical significance. The Cox Survival Model evaluation is in the following table (Table XIII).

Table XIII. *Cox Survival Model evaluation.*

Concordance	**0.82**
Partial AIC	157.47
log-likelihood ratio test	27.48 on 6 df
-log2(p) of ll-ratio test	13.05

DISCUSSION

The aim of this prospective longitudinal study was to compare, at five years follow-up, HIV-infected patients under ART with a control group of healthy patients concerning implant survival rate, surgical complications (first outcomes), and peri-implant parameters (secondary outcomes). The study aimed to compare implant survival rates, surgical complications, marginal bone loss, and peri-implant soft tissue parameters in HIV-positive patients receiving antiretroviral therapy (TG) and healthy individuals (CG). Unadjusted estimates indicated no statistically significant differences in implant survival rates and surgical complications between CG and TG. However, TG showed a statistically significantly higher marginal bone loss and unfavorable peri-implant soft tissue parameters than CG.

A contextual examination of our findings in light of the existing literature reveals both concordances and divergences. In parallel with our outcomes, Krennmair et al.'s prospective clinical study involving healthy and HIV-infected subjects on ART disclosed no statistically significant differences in implant survival rates between the two cohorts, fortifying the robustness of our observations (33).

Oliveira and colleagues, exploring a 12-month post-loading period in HIV-positive patients, align with our assertion that dental implant placement remains a viable treatment option for this patient demographic, substantiating the longevity of our observed implant survival rates (34). The congruence between our findings and Stevenson et al.'s study, emphasizing the absence of disparities in short-term implant success rates between HIV-positive and non-HIV subjects, collectively underscores the resilience of implant therapy in HIV-positive individuals (35).

Our observations echo the sentiment of Achong et al.'s case report, affirming that implant surgery doesn't pose an increased risk for HIV-positive patients, reinforcing the reliability of our unadjusted implant survival rate estimates (36). However, the nuanced interplay of variables exemplifies the contradictions observed in marginal bone loss and peri-implant soft tissue parameters compared to certain studies.

In contrast to our investigation, the systematic review conducted by Cruz et al. reported peri-implant bone loss among HIV patients that resembled levels observed in their healthy counterparts. This discrepancy is underscored by our comprehensive review of dental implants in HIV-positive patients, which included six studies comprising a total of 821 implants. Our analysis demonstrated promising outcomes for HIV-positive patients with controlled risk factors, with mean implant survival rates of 94.53% at the implant level and 94.76% at the patient level, challenging the notion of comparable peri-implant bone loss (37).

Moreover, Capparè et al.'s prospective clinical study, integrated into the broader context of our research, provided valuable insights by revealing no significant correlation between serological parameters and marginal bone levels. Their study, involving edentulous patients requiring implant prosthetic restoration, adds a layer of complexity to our understanding of these interrelationships. The study enrolled 24 patients, placing 116 implants using the 'All-on-four' protocol, and reported an implant survival rate of 91.37%. Notably, the 7-year radiographic evaluation indicated peri-implant crestal bone loss of 1.91mm for upright maxillary implants and 1.79mm for tilted maxillary implants. In the mandible, the mean peri-implant crestal bone loss was 1.54mm for upright implants and 1.5mm for tilted implants, further enriching the discourse on factors influencing implant outcomes in HIV-positive individuals (38).

Notably, our study did not uncover statistically significant differences in surgical complications between TG and CG, aligning with the findings of studies such as Stevenson et al. and Achong et al. This suggests that, despite the immunocompromised status associated with HIV infection and the influence of antiretroviral therapy, the occurrence of surgical complications in implant procedures remains comparable between HIV-positive and healthy individuals (35,36).

The study has several limitations that warrant consideration. Firstly, the potential for bias exists due to the inclusion of smokers and alcohol users in the study, as these factors can influence implant outcomes. Secondly, the sample size may impact the generalizability of the findings.

Concerning the impact of smoking and alcohol intake in implant-prosthetic rehabilitations, in a study led by Gherlone et al. (39), the focus was on investigating the correlation between implant success, CD4+ lymphocyte counts in HIV-positive patients, smoking habits, and oral hygiene levels. The study incorporated 68 patients and a total of 194 endosseous implants, all followed by loading times of 90 days for the upper maxilla and 60 days for the mandible. Patients with substantial smoking habits exhibited a statistically significant increase in implant failure, primarily attributable to peri-implant diseases, the presence of pus, and pain during compression.

In a study conducted by Patton et al. (40), participants were categorized into two groups based on alcohol consumption habits. The research identified alcohol consumption as a substantial risk factor for implant failure. Among

individuals who reported regular alcohol consumption, there was a notable correlation with an increase in bleeding on probing (BoP), signifying a heightened risk of implant failure. Specifically, the study reported that instances of implant failure were observed in a certain percentage of participants who regularly consumed alcohol. For example, the data indicated a 12% incidence of implant failure in the alcohol-consuming group, while only a 3% incidence was observed in the abstaining group. These percentages underscore the quantitative impact of alcohol consumption on the risk of implant failure. Moreover, the investigation conducted a meticulous comparison between HIV-positive and healthy individuals. Strikingly, no statistically discernible difference was found in the impact of alcohol consumption on implant outcomes between these distinct cohorts. Notably, participants who refrained from alcohol consumption demonstrated improved outcomes in terms of implant success. The study reported specific percentages, such as an 85% success rate among non-alcohol consumers compared to a 60% success rate among alcohol consumers.

Interpretation

In cautiously interpreting the results, the observed similarities in implant survival rates and surgical complications between TG and CG align with certain previous studies, reinforcing the resilience of implant therapy in HIV-positive individuals. However, the heightened marginal bone loss and unfavorable soft tissue parameters in TG contrast with some existing literature (20). This, again, confirms the absolute necessity of preventing inflammation and performing a hygienic maintenance protocol that reduces the peri-implant bacterial load (41, 42).

Discussing the generalizability of our study results requires recognition of the specific patient populations included, such as smokers and alcohol users. The findings may be more applicable to similar populations and settings. However, caution is warranted when extending the results to broader populations. Future research with larger, more diverse samples and consideration of various confounding factors will contribute to enhancing the external validity of the study results. Overall, our study adds valuable insights to the evolving understanding of implant outcomes in HIV-positive individuals but should be considered within the context of its specific limitations and characteristics.

CONCLUSIONS

Within the limitations of the present study, HIV-infected patients on ART may be equal to healthy subjects in implant survival rates and surgical complications; however, peri-implant hard and soft tissue parameters appear to be more impaired in diseased patients than in healthy ones. Further clinical studies may be necessary to confirm the obtained results.

Conflict of interest

The authors declare no conflict of interest.

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Cohort Study

DENTAL IMPLANTS IN PATIENTS DIAGNOSED WITH DEPRESSION AND TAKING SEROTONIN REUPTAKE INHIBITOR THERAPY (SSRI) VS HEALTHY PATIENTS: A 3-YEAR FOLLOW-UP PROSPECTIVE SINGLE COHORT STUDY

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KEYWORDS: *dental implants, depression, serotonin reuptake inhibitor, SSRI, systemic diseases*

ABSTRACT

The objective of this prospective longitudinal study was to compare, at three years follow-up, patients suffering from depression and taking Selective Serotonin Reuptake Inhibitors (SSRIs) (Test Group = TG) with a control group of healthy patients (Control Group = CG) concerning implants survival rate, surgical complications (first outcomes) and peri-implant parameters (secondary outcomes). The study included individuals with single edentulism requiring implant-prosthetic rehabilitation. Eligible participants were either healthy (CG) or diagnosed with depression and receiving SSRIs (TG). Single dental implants were placed, and patients were included in a three-year follow-up program. Implant survival rate, surgical complications, and peri-implant parameters (marginal bone loss and soft tissue parameters) were evaluated. Fifty-four patients in CG, unchanged from baseline, and 53 in TG were considered, respectively. Implant survival rate was 94.44% in CG and 94.34% in TG. The only case of wound infection was observed at surgical wound dehiscence 14 days after surgery. One case of suppuration was reported 14 months after prosthetic loading. No statistically significant differences were found between groups concerning implant survival rate and surgical complications. The analysis of marginal bone loss and soft-tissue peri-implant parameters between CG and TG revealed statistically significant variances, with a p-value below 0.05. Within the limitations of the present study, although the impact of serotonin reuptake inhibitors on dental implants may be significant concerning peri-implant parameters, no statistically significant differences were found in implant survival rate and surgical complications.

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INTRODUCTION

In recent years, dental implants have revolutionized restorative dentistry, offering an effective long-term solution to replace missing teeth with natural-looking and functional dentures (1, 2). The increasing demand for dental implants has drawn attention to the critical importance of considering the general health and medical history of patients when planning surgical implant procedures. It is becoming increasingly clear that systemic pathologies may significantly influence the short- and long-term success of implant-prosthetic rehabilitations (3-5).

Although removable prostheses still represent a viable therapeutic alternative, osseointegrated implants supporting fixed prostheses could be considered the gold standard (6, 7).

An emerging area of interest within this context is the intricate relationship between depression, serotonin reuptake inhibitor (SSRI) therapy, and dental implants. Depression, a pervasive mental health condition affecting millions globally, often necessitates pharmacological intervention, with selective serotonin reuptake inhibitors (SSRIs) being a primary choice of medication (6-8). Despite the demonstrated effectiveness of SSRIs in managing depression and anxiety, there is a growing awareness of the potential impact these medications may have on oral health and the outcomes of dental implant procedures, prompting collaboration and exploration of this intersection within both dental and psychiatric communities (9, 10).

Dental implants, acknowledged for their success in providing a reliable and long-term solution for missing teeth, require a nuanced consideration of various factors to ensure optimal results (11-13). Among these considerations, the potential implications of SSRIs on the implant procedure and its subsequent success are of paramount importance, spanning aspects such as bleeding risk, bone healing and osseointegration, implant failure, and the psychological well-being of the patient (14, 15).

An intriguing point of concern is the increased risk of bleeding associated with SSRIs. This elevated risk is attributed to serotonin's multifaceted role, extending beyond its functions in the brain to include regulation of platelet function and blood clotting. By inhibiting the reuptake of serotonin, SSRIs may interfere with platelet activity, potentially resulting in an increased tendency for bleeding during and after the implant procedure (16, 17).

Beyond bleeding risks, SSRIs have been implicated in influencing bone metabolism, a crucial factor in the success of dental implants. Osteoblasts and osteoclasts, key players in bone remodeling, are impacted by SSRIs, potentially affecting the delicate balance necessary for the osseointegration process. Changes in bone metabolism have the potential to influence the long-term stability and success of dental implants, raising questions about the need for tailored approaches in patients undergoing SSRIs (18).

However, the impact of SSRIs extends beyond the physiological realm to the psychological aspects of patients. Depression and anxiety can significantly influence a patient's motivation and commitment to dental care, potentially compromising oral health and implant success. Recognizing and addressing these mental health considerations becomes imperative, emphasizing the importance of managing the emotional well-being of patients throughout the implant treatment process (19).

The aim of this prospective longitudinal study was to compare, at three years follow-up, patients suffering from depression and taking SSRIs (Test Group = TG) with a control group of healthy patients (Control Group = CG) concerning implants survival rate, surgical complications (first outcomes) and peri-implant parameters (secondary outcomes).

The null hypothesis was that there were no statistically significant differences between the examined groups ($p>0.05$) concerning the investigated clinical outcomes.

MATERIALS AND METHODS

The current prospective clinical study adopted a comparative design to systematically investigate the impact of depression and serotonin reuptake inhibitors (SSRIs) on dental implant outcomes. The study involved the categorization of participants into two distinct groups: CG, comprising healthy individuals, and TG, consisting of patients suffering from depression and undergoing treatment with SSRIs.

The methodology and reporting of this study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology for Clinical Trials (STROBE-CT) guidelines (STROBE-CT Guidelines).

The recruitment of participants occurred at the Department of Dentistry, San Raffaele Hospital, Milan, Italy, over a period spanning from January to December 2019. The procedures performed on enrolled patients adhered to the ethical standards set by institutional and/or national research committees and the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. The study received approval from the ethics committee, with the assigned approval number being CE/INT/10/2015.

Participants

Eligibility criteria for inclusion in the study encompassed individuals suffering from single edentulism, necessitating implant-prosthetic rehabilitation. Specifically, only healthy patients or those diagnosed with depression and receiving SSRIs without concomitant psychiatric or systemic disorders were considered eligible.

Exclusion criteria comprised smokers (20), absolute contraindications to implant-prosthetic rehabilitation (21, 22), those not requiring fixed rehabilitation, individuals needing bone grafting or sinus lift procedures, and those unable to comply with follow-up checks and hygienic maintenance sessions.

To ensure the comparability of the study groups, the sample was meticulously divided into two categories: healthy patients (GC) and patients suffering from depression receiving serotonin reuptake inhibitors (GT). Matching criteria, if applicable, were transparently defined, and the study provided details regarding the number of exposed and unexposed individuals in both groups. This matching process aimed to enhance the internal validity of the study, allowing for a more significant comparison of outcomes between the two groups.

Implant-prosthetic protocol

Pre-surgical protocol

For diagnostic purposes, all patients were submitted to objective examination, first level (intraoral radiographs and orthopantomography) and, when needed, second level radiographic investigations (Cone Beam CT) to assess residual bone height and width and to evaluate position, length, and diameter of implant fixtures (23). Surgical procedures were carried out under local anesthesia, employing an opticain solution with 1:80,000 adrenaline (AstraZeneca, Milan, Italy).

Surgical procedure

The initial crestal incision was strategically inclined towards the palatal side to ensure uniform coverage of the keratinized mucosa on both sides of the surgical flap (24, 25). Vertical release incisions on the distal and mesial aspects exposed the underlying bone crest, allowing for a carefully elevated full-thickness flap.

The procedure involved the use of a lanceolate drill to penetrate the cortical bone, which was succeeded by a pilot drill with a 2.00 mm diameter to create an implant insertion pathway and verify the implant direction. Progressive diameter drills were sequentially employed until reaching the final implant diameter.

Intentional over-preparation vertically and slight under-preparation transversely were employed to enhance the primary mechanical stability of the implants (26). In incomplete implant seating, a manual screwdriver was used to position the implant neck at the bone level. Two types of implants were utilized, TTi and K line (Winsix, Ancona, Italy), featuring a Micro Rough Surface achieved through sandblasting.

The primary distinction between the two implant lines, characterized by internal connection, lies in their macromorphology: TT implants possess a tapering conical implant body, while K implants have a conical shape. TT implants, with a strongly tapered apical region, were applied in cases of lower bone density (typical of the upper jaw). In contrast, K implants were chosen in cases of a prevalence of cortical bone tissue, predominantly in the mandible and anterior sectors.

The implant design, length, and diameter selection were guided by a morphological evaluation of the residual bone ridge identified through Cone Beam CT scans. Implants were submerged, and suturing was performed using 3-0 non-resorbable sutures (Vicryl, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA). Intra-oral X-rays were taken to verify the accurate positioning of the implants.

Post-surgical protocol

Following the surgical procedure, each patient was provided with a prescription for antibiotic therapy (amoxicillin and clavulanic acid or clarithromycin in cases of allergies; 1 g every 12 hours for 6 days, starting the day before surgery) and analgesic therapy as required. Patients were instructed to perform mouth rinses with a solution containing 0.2% chlorhexidine digluconate twice daily for ten days. Sutures were removed one week after the surgical intervention.

Prosthetic protocol

In instances where an insertion torque of 25 Newtons or greater was attained, immediate implant loading was implemented (27, 28). Preliminary alginate impressions and simultaneous relining of temporary acrylic restorations were executed. For cases not meeting the criteria for immediate loading, a custom-made resin removable partial denture was supplied during the healing phase, with implants exposed approximately four months post-surgery. Healing screws replaced cap screws, pick-up impressions were taken, and provisional crowns were fitted for each patient.

Provisional resin (Fermit, Ivoclar Vivadent, Naturno, Italy) was utilized to seal screw access holes. Following thorough assessments of the provisional devices around four months later, they were substituted with either a metal-ceramic or stratified zirconia implant-supported final crown. The selection was based on anatomical location, aesthetic factors, and patient preferences.

The definitive impression, employing the pick-up technique with a customized spoon after delivering the definitive screw-retained crown, utilized polyether (Impregum Penta, 3M Italia, Pioltello, Italy) as the impression material. A metal test with radiographic control was conducted to ensure a precise fit between the metal framework and implants.

Follow-up

Follow-up visits were conducted 1 week post-surgery, at 3 and 6 months, and annually in the following years. Professional oral hygiene appointments were scheduled every 4 months after the surgical-prosthetic procedure (29, 30). Each patient was placed in a professional oral hygiene program that would allow for limiting complications, preventing inflammation, and monitoring and interception of any complications (31-33).

Clinical outcomes

The investigation delved into three crucial quantitative facets: implant survival rate, surgical complications, and peri-implant parameters (specifically, marginal bone loss and soft tissue parameters).

1. *Implants survival rate*

Any implant that did not achieve osseointegration or experienced compromised osseointegration resulting in bone loss and subsequent mobility, impeding its role as prosthetic crown support, was deemed a failure (34, 35). The evaluation of the implant survival rate was grounded in vigilant monitoring of instances of implant loss throughout the follow-up period. Subsequently, the implant survival rates in both the Control Group (CG) and Test Group (TG) underwent scrutiny to identify potential variances concerning implant survival rates.

2. *Surgical complications*

Surgical complications, such as alveolar nerve injuries, maxillary sinus issues (e.g., maxillary sinusitis post-implant placement), edema, pain resistant to prescribed analgesics, bleeding, wound dehiscence, wound infection, suppuration, and abscessing (36, 37) were meticulously documented during follow-up for comparative analysis between the examined groups.

3. *Peri-implant parameters*
    a. Marginal bone loss (MBL). During each session, three blind operators, all dentists, were engaged in the assessment of marginal bone loss values. Their roles were divided, with one operator responsible for capturing radiographs, another for calibration, and the third for data collection. Intra-oral radiographs were taken at specific milestones: implant placement, implant loading, 3, 6, 12 months, and annually after that. The analysis of these images and the evaluation of marginal bone changes were conducted using calibrated software (DIGORA 2.5, Soredex, Tuusula, Finland). Calibration was performed individually for each image, referencing the known diameter of the implant at its most coronal portion. The measurements involved determining the linear distance between the most coronal point of bone-implant contact and the coronal margin of the implant neck on both the mesial and distal sides, with a precision of up to 0.01 mm. Subsequently, these measurements were averaged to derive the overall average marginal bone changes for individual implants at the patient level. Further averaging was then carried out at the group level.
    b. Soft tissue parameters. After the 3-year follow-up period post-prosthetic loading, a comprehensive assessment of parameters was conducted. Two blind operators played distinct roles: a dentist or dental hygienist was responsible for clinical measurements, while the other focused on meticulous data collection. Various indices, including Periodontal Screening and Recording (PSR), Plaque Index (PI), Bleeding on Probing (BoP), and Peri-implant Probing Depth (PPD), were recorded. The evaluation involved the application of a William probe for measuring PSR, PI, BoP, and PPD.

4. *PSR*

Six sites were systematically examined around each implant (disto-buccal, mid-buccal, mesio-buccal, disto-lingual, mid-lingual, and mesio-lingual). This assessment considered the depth of the periodontal pocket and the presence of bleeding or calculus. Based on the findings, a code ranging from 0 to 4 was assigned, with interpretations as follows:

- Code 0: healthy (no bleeding, no calculus, and pocket depth within normal limits);
- Code 1: gingival bleeding (bleeding on probing, but no calculus or other signs of disease);
- Code 2: calculus present (no bleeding, but calculus is detected);
- Code 3: 4-5mm pocket depth (indicating moderate peri-implant disease);

- Code 4: 6mm or deeper pocket depth (indicating severe peri-implant disease).

5. *Plaque Index (PI)* measurement involved the probing of each implant surface (buccal, lingual, mesial, and distal), with scores ranging from 0 to 3 based on plaque amount;
6. *Bleeding on Probing (BoP)* was dichotomously assessed, with a value of zero indicating the absence of bleeding and 1 signifying its presence;
7. *The Peri-implant Probing Depth (PPD)* was assessed by gently inserting a probing instrument into the gap between the implant and the adjacent soft tissue. This probing was carried out parallel to the implant axis, measuring the distance from the implant-abutment junction (IAJ) to the gingival sulcus or pocket base.

Statistical analysis

Statistical analysis was performed utilizing Python 3.8.5, employing the Math, SciPy, and Pandas packages. Based on the sample distribution, variance, and experimental configuration, parametric independent samples t-tests, Pearson's Chi-Square tests, or z-tests were employed to assess differences between groups. Evaluation of the evolution of implant survival and associated risk factors over time involved Kaplan-Meier and Cox hazard analyses. Hypothesis tests regarding inter-group differences considered patients as analysis units, while survival analysis and hypothesis tests related to implant failure regarded implants as analysis units.

All analyses established significance at p-values<0.05, and the statistical examinations adhered to a 95% significance level. The study size was determined by a statistical power analysis utilizing a t-test for two independent samples. A significance level (α) of 0.05 and a power (1-β) of 0.80 were targeted, representing a widely accepted balance between Type I and Type II errors. The calculation of the required sample size for a two-sample t-test was executed using the formula:

$$\mathbf{n = 2(\sigma^2)\ (Z_{\alpha/2} + Z_{\beta})^2/\delta^2}$$

where σ is the estimated standard deviation, $Z_{\alpha/2}$ and Z_{β} are critical values for the chosen significance level and power, and delta is the effect size.

We performed a sensitivity analysis on the effect size employed in the power analysis. The required sample size for an effect size of 0.8 was established at 32, while for an effect size of 0.5, the necessary sample size rose to 72.

RESULTS

Participants – descriptive data

According to inclusion and exclusion criteria, 109 patients were considered eligible. The sample was divided into two groups: 54 healthy patients (Control Group = CG) and 55 patients suffering from depression and taking SSRIs (Test Group = TG). Sample details at baseline in CG and TG are in the following table (Table I).

Table I. *Sample features at baseline in CG and TG.*

Sample features	*CG*	*TG*
Number patients	54	55
Females	29	28
Males	25	27
Average age (range)	52.5 (31-74)	52.5 (29-76)

Dropout

During the follow-up period, 0 CG and 2 TG patients were lost. Of the two TG patients, one reported that he was transferring to another city, thus making themselves unavailable for the planned follow-ups since the placement of the definitive crown; the other was non-compliant with recall sessions since the beginning of the second-year follow-up. Therefore, for the purposes of the study, 54 patients in CG, unchanged from baseline, and 53 in TG were considered, respectively. All patients observed adhered to the scheduled follow-up and hygiene maintenance sessions.

Outcome data –main results

Sample failures, implant details, prosthetic loading, and implant sites are in the following table (Table II).

Table II. *Sample failures, implant details, prosthetic loading, and implant sites in CG and TG.*

	CG	*TG*
Sample features		
Number patients	54	53
Females	29	26
Males	25	27
Average age (range)	52.5 (31-74)	52.5 (29-76)
Implants details		
Number implants	54	53
K 3.3x9	7	3
K 3.3x11	4	6
K 3.3x13	6	2
K 3.8x9	1	4
K 3.8x11	3	6
K 3.8x13	8	7
TTi 3.3x9	1	2
TTi 3.3x11	4	4
TTi 3.3x13	6	3
TTi 3.8x9	4	5
TTi 3.8x11	3	7
TTi 3.8x13	7	4
Prosthetic loading and implant site		
Delayed posterior maxilla	11	13
Delayed anterior maxilla	3	1
Delayed posterior mandible	8	11
Delayed anterior mandible	1	3
Immediate posterior maxilla	3	4
Immediate anterior maxilla	9	10
Immediate posterior mandible	7	5
Immediate anterior mandible	12	6

Implant survival rate

At three years of follow-up, a total of five implants were lost, of which two in CG and three in TG. Implant survival rate was 94.44% in CG and 94.34% in TG. The following table (Table III) provides details of failed implants.

Table III. *Implant failure details in CG and TG.*

	CG		*TG*		
	Patient 1	Patient 2	Patient 1	Patient 2	Patient 3
Age	57	44	61	52	39
Gender	Female	Female	Female	Male	Female
Implant details	K 3.8x9	TTi 3.8x13	TTi 3.8x11	TTi 3.8x11	K 3.8x13
Implant site	Posterior maxilla	Anterior mandible	Posterior maxilla	Posterior mandible	Anterior maxilla
Prosthetic loading	Immediate	Immediate	Delayed	Delayed	Immediate
Implant loss timing	6 months	26 months	5 months	14 months	28 months

The comparison between CG and TG revealed no statistically significant differences in the survival rates of implants, as evidenced by a p-value exceeding 0.05. The absence of a significant contrast between the two groups at a 95% confidence level suggests that the differences observed are not substantial enough to warrant the rejection of the null hypothesis. Consequently, it is appropriate to conclude that, at a statistically significant level, the two groups should not be regarded as different concerning implant survival rate.

Surgical complications

Surgical complications are reported in the following figure (Fig. 1).

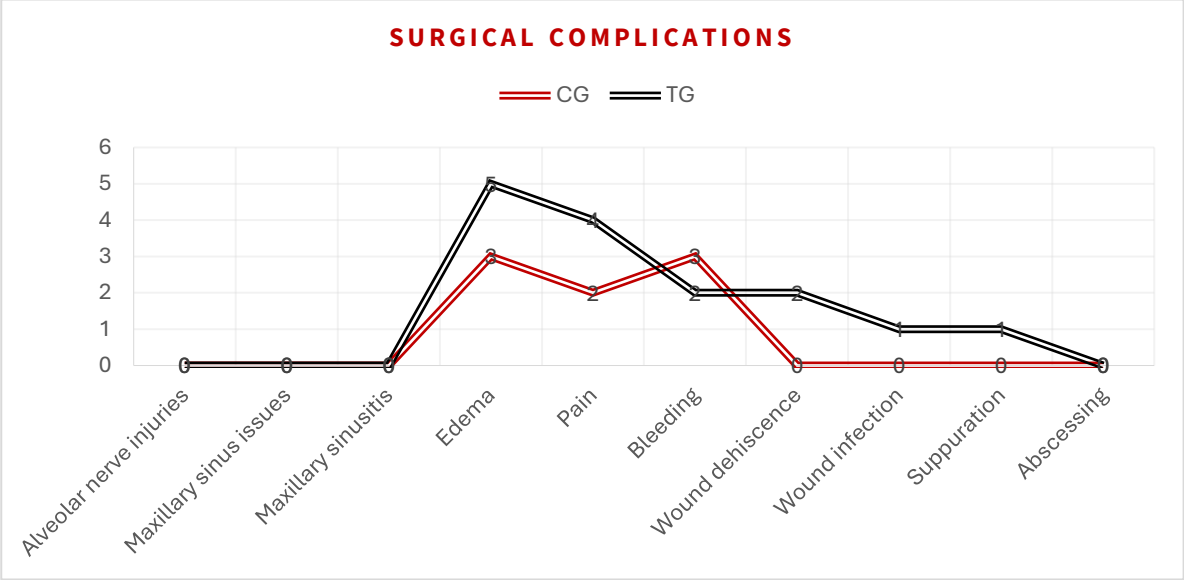

Fig. 1. *Surgical complications in CG and TG.*

There were no alveolar nerve injuries, maxillary sinus issues, sinusitis, or abscessing in either CG or TG. All the cases of edema, pain, and bleeding reported in the table occurred within ten days after the surgical procedure was performed. The only case of wound infection was observed at surgical wound dehiscence 14 days after surgery. One case of suppuration was reported 14 months after prosthetic loading.

Examining surgical complications between CG and TG yielded no statistically significant differences, as indicated by a p-value exceeding 0.05. The lack of a noteworthy divergence between the two groups at a 95% confidence level implies that the observed distinctions are not significant enough to justify rejecting the null hypothesis. Therefore, from a statistically significant standpoint, the two groups could be considered comparable concerning surgical complications.

Peri-implant parameters

The average ± the standard deviation of dental implants' marginal bone loss values in each group was measured and provided in the following table (Table IV).

Table IV. *MBL values at 6 months, 1, 2, and 3 years in CG and TG.*

MBL	*CG*	*TG*
6 months	0.5 mm ± 0.2 mm	0.8 mm ± 0.3 mm
1 year	1.0 mm ± 0.4 mm	1.2 mm ± 0.5 mm
2 years	1.5 mm ± 0.6 mm	1.8 mm ± 0.7 mm
3 years	2.0 mm ± 0.8 mm	2.5 mm ± 1.0 mm

The analysis of marginal bone loss between CG and TG revealed statistically significant variances, with a p-value below 0.05. The divergence between the two groups at a 95% confidence level implies that the observed differences are significant enough to justify the rejection of the null hypothesis. From a statistically significant perspective, it could be concluded that the two groups should be considered dissimilar concerning marginal bone loss. Specifically, TG showed a higher marginal bone loss level than CG.

Soft tissue parameters

The number of patients in CG and TG was divided according to soft-tissue peri-implant parameters at the end of the follow-up period (Fig. 2).

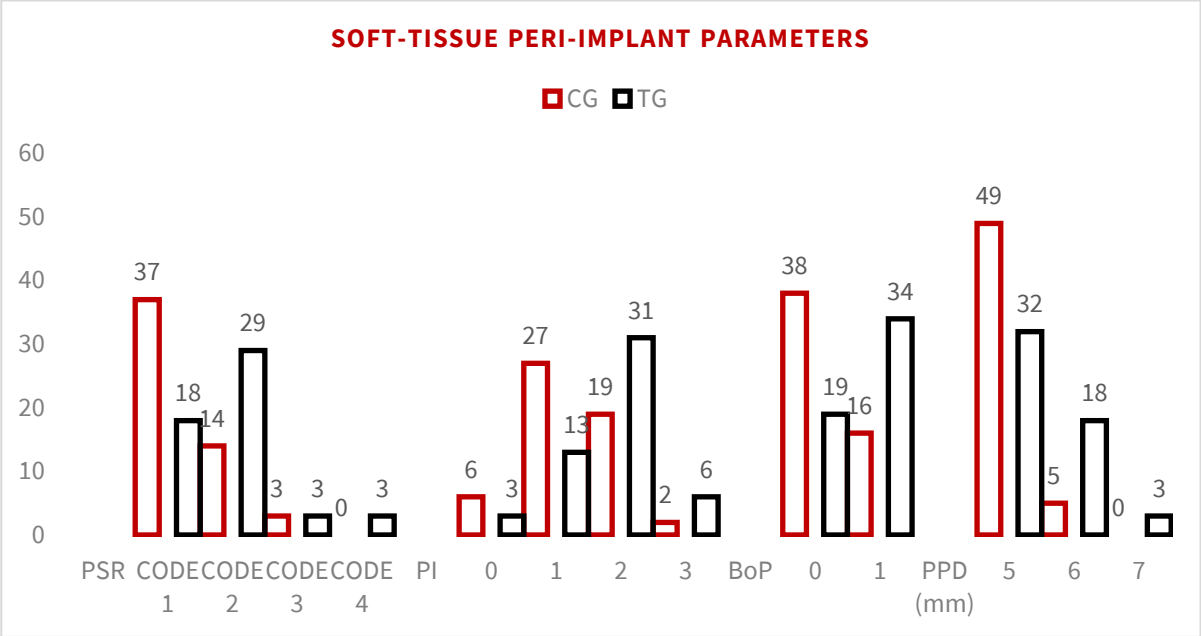

Fig. 2. *Soft-tissue peri-implant parameters in CG and TG.*

Examining soft-tissue peri-implant parameters between CG and TG unveiled statistically significant variances, as evidenced by a p-value below 0.05. The observed differences between the two groups at a 95% confidence level are substantial enough to warrant the rejection of the null hypothesis. Consequently, from a statistically significant perspective, one may infer that the two groups should be regarded as dissimilar regarding soft-tissue peri-implant parameters. More specifically, the TG exhibited less favorable soft-tissue peri-implant parameters than CG.

Survival analysis

To evaluate the progression of implant survival and identify temporal risk factors, we conducted Kaplan-Meier and Cox hazard analyses. The outcomes of the Kaplan-Meier analysis are presented in the subsequent table for visual reference (Table V).

Table V. *Kaplan-Meier survival rate confidence intervals CG.*

CG	KM estimate - lower percentile (0.95)	KM estimate - upper percentile (0.95)
6 months	0.9448	0.9964
1 year	0.9359	0.9931
3 years	0.9174	0.9851

Based on the provided values in the previous table, it can be inferred that the true survival probability for the test group at seven years lies within the range of 91% to 98%, with a confidence level of 95%. Additionally, for the test group, the true survival probability at three years falls within the interval of 92% to 99%, with a confidence level of 95%. Results for TG are shown in the following table (Table VI).

Table VI. *Kaplan-Meier survival rates' confidence intervals TG.*

TG	KM estimate - lower percentile (0.95)	KM estimate - upper percentile (0.95)
6 months	0.9465	0.9985
1 year	0.9380	0.9965
3 years	0.9285	0.9928

The study employed the Cox Proportional Hazards model to explore the association between survival time, implant failure, and various covariates. Specifically, the covariate of interest was the use of serotonin reuptake inhibitors. The baseline hazard was addressed in a non-parametric manner, utilizing Breslow's method. The overall model adhered to the conventional semi-parametric Cox model. Efron's method was applied to address tied event times.

Examining the coefficients associated with the covariate, particularly the use of SSRIs, reveals no significant increase in the hazard rate connected with these covariates. The low standard error of the coefficient (0.91) suggests a more precise estimate with reduced variability. The overall result from these findings indicates that there is no heightened risk of implant failure in patients taking SSRIs.

DISCUSSION

This prospective longitudinal study aimed to compare patients diagnosed with depression and taking SSRIs (TG) with healthy patients (CG) concerning implant survival rate, surgical complications, and peri-implant parameters at a three-year follow-up. Implant survival rate, surgical complications, marginal bone loss, and peri-implant parameters were considered in the study.

No statistically significant differences were found in implant survival rates between the two groups. These results are in contrast with other studies. Karen Rodríguez-Pena et al. found that individuals affected by depression and taking SSRIs had a lower dental implant survival rate at 90 months follow-up as compared to those who were not taking them. In their study, the hazard ratio (HR) was 4.53 ($p<0001$) (39). Even Wu and colleagues showed that SSRI treatment increases the risk of dental implant failure (hazard ratio=6.28; $p=0.03$) (40). Other studies also suggest an increased rate of dental implant failure in patients taking SSRIs (34, 39).

No statistically significant differences were found between the CG and TG regarding surgical complications. After the surgical procedure, no signs of alveolar nerve injuries, maxillary sinus issues, sinusitis, or abscess in CG or TG were noticed after the surgical procedure. Within ten days after the implant placement, edema, pain, and bleeding were reported by a few members of both groups. In the TG, one case of wound infection was observed at surgical wound dehiscence 14 days after surgery, and one case of suppuration was reported 14 months after prosthetic loading. These results agree with Karen Rodríguez-Pena and colleagues' retrospective clinical study: after placing 573 dental implants in 170 patients, only one patient taking SSRIs experienced pain, leading to implant failure (39).

Our study showed that the examination of marginal bone loss revealed statically significant differences between the CG and TG. Over the six-month, one-year, two-year, and three-year follow-ups, the TG showed higher marginal bone loss than the CG. This research suggests that SSRI medication and depression may affect the process of bone remodeling surrounding dental implants, which may affect the durability and long-term efficacy of the implants. These observations align with Deepa's clinical study involving 352 patients and 680 dental implants. It found that patients undergoing SSRI treatment exhibited a significantly higher level of marginal bone loss than non-users (38). Likewise, a cohort study by Wu and colleagues reported that SSRIs may reduce bone mass by preventing bone remodeling processes brought on by mechanical loading. (40). Indeed, it has been confirmed that serotonin (5-hydroxytryptamine (5-HT)) receptors on osteoblasts and osteoclasts appear to be activated by SSRIs through specific pathways, which control the effect of SSRIs on bone production and resorption. Both in vivo and in vitro studies suggest that SSRIs are detrimental to bone at therapeutic doses, which are used to treat depression in modern clinical practice (40, 41).

Another focus of our study was placed on the analysis of soft-tissue peri-implant parameters, which include Periodontal Screening and Recording (PSR), Plaque Index (PI), Bleeding on Probing (BoP), and Peri-implant Probing Depth (PPD). Statistically significant differences between the CG and TG were found. The TG exhibited less favorable soft-tissue peri-implant parameters compared to the CG. These findings emphasize the importance of oral hygiene procedures to prevent periodontal and peri-implant disease progression. Indeed, ALHarthi et al. reported that the patients taking SSRIs show healthy periodontal and peri-implant tissue statuses when dental hygiene is rigorously adhered to (42).

Given that chronic stress and related conditions, such as depression and anxiety, are currently considered 'risk indicators' for peri-implant disease (43), due to the possible interaction between stress and periodontium/periosteum (44), it is crucial to pay particular attention to these patients.

Even if this study sheds light on the potential impact of SSRI usage on dental implant outcomes and gives valuable insights, there are many limitations. The main limitation is the small sample size, limiting the generalizability of the findings. In addition, the study setting, the Dental School Department of Dentistry IRCCS San Raffaele Hospital, Milan, may not represent diverse populations. Hence, the specific geographic area might influence treatment outcomes and oral health behaviors. This is a 3-year follow-up prospective single cohort study; thus, it may not involve long-term complications or possible changes in dental implant outcomes that could occur over a longer time.

The study only included individuals suffering from single edentulism, necessitating implant-prosthetic rehabilitation, no-smokers, and those without concomitant psychiatric or systemic disorders. Therefore, the results found may not apply to a broader population. Smoking habits could have represented a possible variable: a significantly increased risk of dental implant failure is associated with smoking habits (45).

In this study, we did not consider the degree of depression of the patient, which may predict the implant success rate (46), the dosage of SSRIs, which may impact dental implant outcomes differently, and other classes of antidepressant medications. Nevertheless, all the implant placements for the patients included in this study were performed by a single surgeon, thus minimizing potential bias by operator-relator factors, such as experience.

Despite its many limitations, this study is relevant for the clinician because it adds insights into the association between dental implant outcomes and SSRIs: the study highlighted potential concerns regarding marginal bone loss and soft-tissue peri-implant parameters in the depressed group.

CONCLUSIONS

Within the limitations of the present study, although the impact of serotonin reuptake inhibitors on dental implants may be significant concerning peri-implant parameters, no statistically significant differences were found in implant survival rate and surgical complications.

Furthermore, the intricate interplay of factors influencing implant outcomes necessitates further research with larger cohorts to provide a more comprehensive understanding of the potential impact of SSRIs on dental implant success.

Conflict of interest

The authors declare no conflict of interest.

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Case Report

EARLY IMPLANT INSERTED IN A RECONSTRUCTED SITE WITH XENOGRAFT, HYALURONIC ACID, AND POLYNUCLEOTIDES IN NON-SYNDROMIC AGENESIS: HISTOMORPHOMETRY AND FOLLOW-UP

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ABSTRACT

The present clinical case aims to investigate how a mixture of polynucleotides and hyaluronic acid in gel form, combined with bovine-derived heterologous material, can expedite the process of bone neoformation suitable for implant placement. In this case, the biomaterials are covered with a resorbable membrane and stabilization pins to protect the grafted material. A patient with severe, non-syndromic multiple dental agenesis is described. After five months, implant placement was performed. Following a core drilling biopsy at the implant insertion site, histomorphometric investigations were conducted to assess the maturation status of the regenerated bone site. After 6 months of implant healing, prosthetic procedures were performed, followed by a subsequent radiographic follow-up. Upon return, the regenerated bone appeared well vascularized before implant placement and provided adequate primary stability.

KEYWORDS: *bone regeneration, hyaluronic acid, atrophy, polynucleotides, bone augmentation*

INTRODUCTION

Nowadays, bone regeneration remains one of the elective treatments to ensure a good three-dimensional anatomical situation of the implant site (1).

Indeed, it is now known that following dental extractions, significant bone remodeling of the alveolar process occurs massively within the first six months in both vertical and horizontal dimensions, within a range of 11-22% depending on the invasive and traumatic tooth extraction (2, 3).

Regenerative procedures are necessary to ensure the correct three-dimensional dimension of the perimplant bone tissue and to minimize perimplant resorption (4, 5). Different biomaterials are commonly used for regenerative maneuvers, including graft materials acting as scaffolds and membranes, maintaining space in the regenerating site, and stabilizing the inserted graft. The materials used as bone substitutes are of heterologous origin but are often mixed with autologous bone particulate, thus combining osteoinductive and osteoconductive properties. Moreover, the presence of morphogenetic proteins and growth factors induces and accelerates the processes of bone neoformation (6-8).

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The combined use of materials such as polynucleotides and hyaluronic acid (PNs-HA) in the form of gel seems to promote bone regeneration in horizontal alveolar defects and all the biological processes that characterize tissue regeneration (9-12).

CASE REPORT

The presence of multiple non-syndromic agenesis resulted in significant oligodontia. Agenesis is characterized by significant bone deficits, making implant treatment impossible without preliminary bone regenerative procedures.

The absence of dental elements has resulted over time in a bone deficit, especially in the horizontal component of the alveolar process. This situation is frequently described in the literature (13) (Fig. 1).

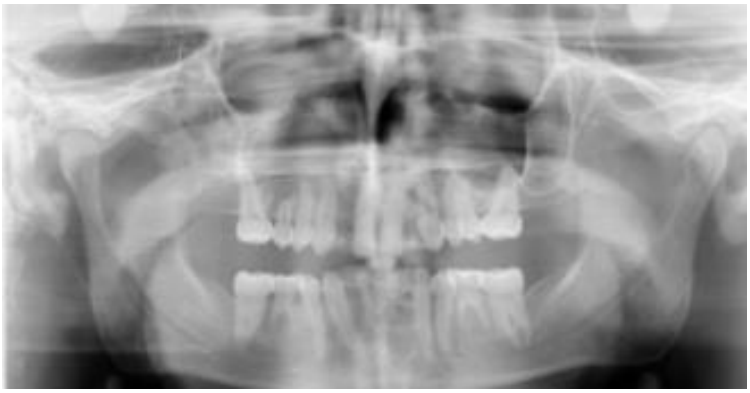


Fig. 1. *OPT X-ray showing multiple agenesis.*

The patient's decision to treat agenesis in the lower frontal group led to a preliminary study through diagnostic wax-ups to plan the implant placement following the construction of a surgical template (Fig. 2).

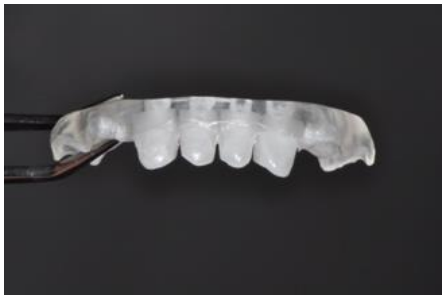


Fig. 2. *Surgical template for implant placement.*

The radiographic examination performed with Cone Beam Computer Tomography (CBCT) confirmed the need to regenerate the bone tissue in the lower frontal area to enable implant placement. The bone regeneration procedure was performed using a mixture of polynucleotides and hyaluronic acid in addition to a heterologous bovine-derived and autologous bone harvested from the surgical site.

Clinical presentation

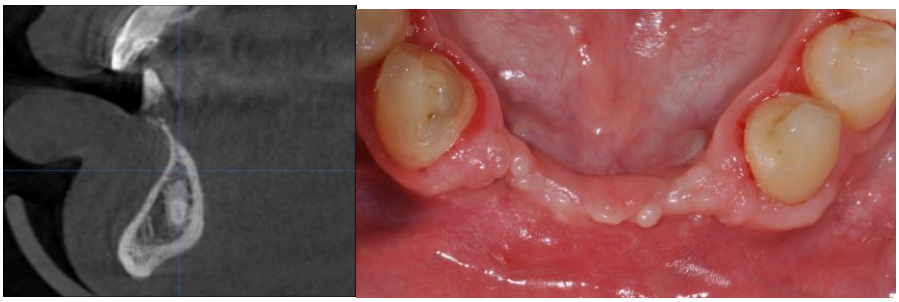
The patient came with a partial intercalated edentulism in the lower frontal area. The treatment plan, established in agreement with the patient, focused on the lower area. The patient had a temporary prosthesis placed a few years earlier at another facility.

Following the radiographic examination (Cone Beam CT), the surgical procedure that was established involved a staged implant approach, with implant surgery performed after bone regeneration.

According to the literature, dental agenesis results in bone loss, especially in the horizontal dimension of the edentulous site. In this case, the defect correction was performed using deproteinized bovine bone (Bio-Oss, Geistlich Pharma, Switzerland), autologous bone harvested from the surgical site, and a mixture of polynucleotides and hyaluronic acid (Regenfast, Officina Biofarmaceutica Mastelli Srl, Sanremo, Italy), subsequently covered with a resorbable collagen membrane (Biogide, Geistlich Pharma, Switzerland). The use of the mixture of polynucleotides and hyaluronic acid in gel form appears to boost tissue regeneration, reducing clinical time (14-17).

After the necessary period for bone integration, implants were placed. Preparation of the regenerated ite involved a 2 mm bone biopsy, the same diameter as the initial drill of the implant surgical kit. Subsequently, the implant preparation site was completed with the remaining drills of larger diameter for implant insertion. The need to start with the frontal group is due to the patient losing the deciduous teeth that supported the lower fixed prosthesis following a traumatic event.

In the initial analysis, a CBCT scan was performed to assess bone thickness. After evaluating the CBCT, the bone reconstruction procedure was scheduled as the thicknesses were unsuitable for implant insertion (Fig. 3).



a b

Fig. 3. ***A****): Parasagittal section of horizontal bone atrophy;* ***B****): intraoral view of bone resorption.*

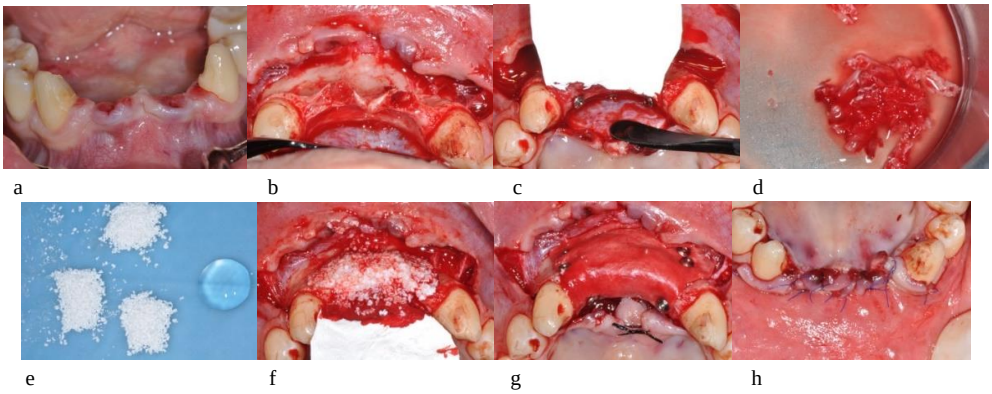
Surgical technique

Following local anesthesia with articaine with adrenaline 1:100.000 (Septanest, Saint-Maur-des-Fossés Cedex, France), a trapezoidal flap was performed with a mid-crestal incision and two distal release incisions adjacent to elements 33-43. Once the alveolar process was exposed with a full-thickness flap and after removing residual fibrous tissue, the clinical picture of severe loss of the horizontal component became evident. At this point, shaping and adaptation of the resorbable membrane to the surgical site were carried out, with fixation of the membrane using pins in the lingual area (Fig. 4a-c).

The grafting material was harvested using a safe scraper from the autologous bone portion in the mental symphysis area (Fig. 4a-d). The hyaluronic acid and polynucleotide gel was mixed with deproteinized bovine bone in a 1:3 ratio (Fig. 4e), following the manufacturer's instructions, adding the biomaterial to the biogel gradually to hydrate the granules progressively, without creating a non-homogeneous solid mass. Once the graft was inserted into the defect, the membrane is adapted vestibularly, putting it under tension and securing it with pins according to the technique described by Urban and colleagues (Fig. 4f-4g) (18-21).

An attentive periosteal release facilitated proper flap passivation for the correct horizontal mattress and interrupted sutures. Subsequently, a resin Maryland-type structure was placed as a provisional prosthesis during the healing period (Fig. 4h).

The supportive pharmacological treatment included antibiotic therapy with 2 grams of amoxicillin per day starting from the day before surgery, appropriate wound care and cleansing with chlorhexidine-based rinses (22-24), and pain management with as-needed nonsteroidal anti-inflammatory drugs (600mg Ibuprofen).



a b c d

e f g h

Fig. 4. ***A****): frontal view of the surgical site with loss of deciduous elements;* ***B****): skeletonization of the surgical site using a mucoperiosteal flap;* ***C****): lingual fixation of the membrane;* ***D****): autologous bone harvested with safe scrapers;* ***E****): adequate preparation in ratio of 3:1 between gel and deproteinized bone;* ***F****): graft adapted to the defect once mixed;* ***G****): membrane fixed vestibularly with fixation pins;* ***H****): suturing and passive adaptation of the flap.*

After 5 months of bone regeneration, a CBCT scan was performed to plan the implant placement and analyze the bone reconstruction. Radiographic images revealed an increase in the horizontal portion, allowing for implant insertion (Fig. 5).

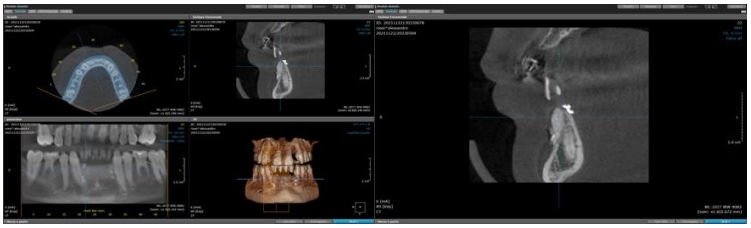


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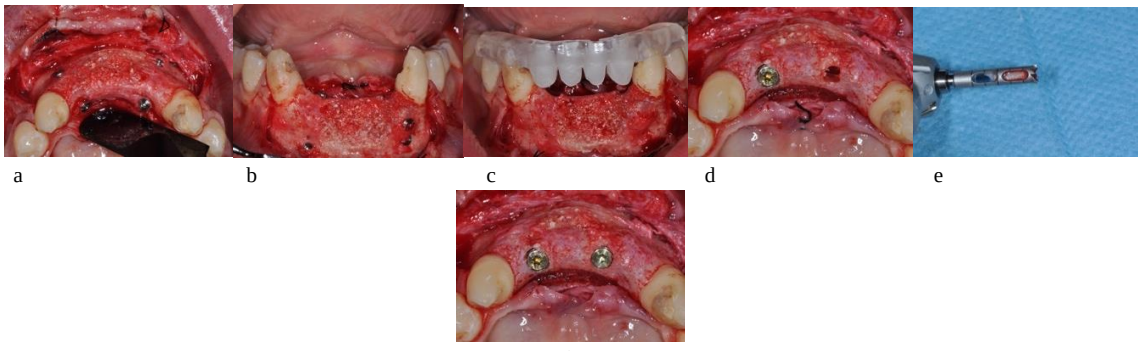
Fig. 5. ***A)****: CBCT Image;* ***B)****: the sagittal section shows evident regeneration of the horizontal dimension.*

The planning of the implant sites was carried out according to prosthetic requirements (23). The selected implants (Neodent®, Straumann Group, Switzerland), sized 3.5x11.5, were placed at 31 and 41. The implant surgery procedure included local anesthetic infiltration (1:100,000 Septanest, Saint-Maur-des-Fossés Cedex France), a crestal incision, and release incisions distal to elements 33-43. Once the full-thickness flap was detached, the reconstructed area was visible, allowing for the removal of the stabilization pins placed during the bone regeneration procedure.

With the aid of the surgical template, implants were inserted in positions 32-41 (Fig. 6c). The final prosthetic design included a cantilever element in position 42. This choice was determined by studying radiographic images that highlighted an excessive mesialization of the root of element 43. Placing the implant in position 42 would have caused conflicts with the root of element 43. While preparing the implant site in position 41, a biopsy was performed using a trephine bur for subsequent histomorphometric analysis of the regenerated bone. Subsequent steps dictated by the surgical insertion protocol involved the correct placement of implants in positions 32-41. After implant placement, the flap was sutured with interrupted stitches. The same pharmacological support therapy prescribed at the time of bone grafting months earlier was done again.



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f

Fig. 6. ***A)****: healing of graft at 5 months, occlusal view;* ***B)****: frontal view of graft healing at 5 months;* ***C)****: surgical template for implant placement;* ***D)****: excision with a 2mm trephine bur in position 41;* ***E)****: histological biopsy;* ***F)****: implants inserted.*

Prosthetic rehabilitation

Approximately 30 days after healing, healing screws were placed, and an impression was taken for the fabrication of provisional crowns (26-28). Fifteen days after tissue healing, temporaries were modeled and prepared according to the concepts expressed in the BOPT technique, as described by Loi and colleagues, regarding convergent prosthetic shapes and the adaptation of soft tissues to these structures (Fig. 7) (29).

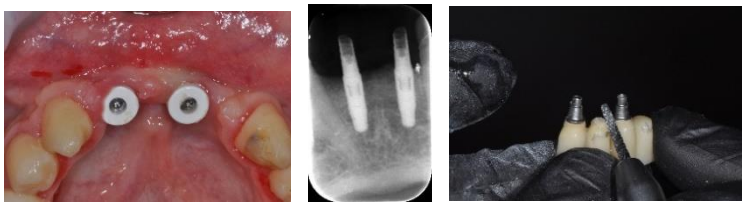

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Fig. 7. ***A****): healing screws placement after implants osteointegration;* ***B****): radiographic control during provisional crowns placement;* ***C****): preparation of provisional crowns according to the Loi technique.*

After 45 days, there was evidence of tissue healing around the provisional crown, a suitable situation for the preparation of the final crown. Once the provisional crown was removed, the good amount of keratinized mucosa around the implant was evidently ready to receive the permanent one (Fig. 8).

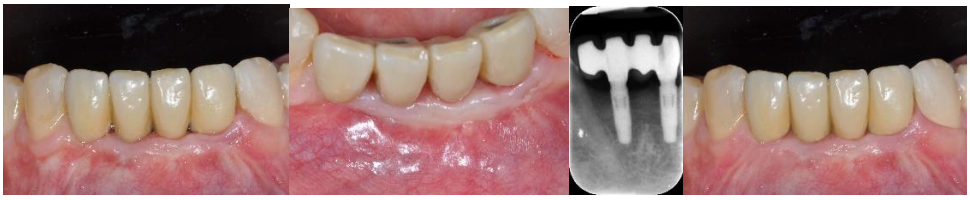

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Fig. 8. ***A****): provisional crowns placement after the healing period;* ***B****): detail of the evident increase in keratinized mucosa at the time of placement of the definitive prosthesis after 6 months;* ***C****): radiographic control after 6 months from placement of provisional crowns with definitive one;* ***D****): definitive crowns placement.*

Tissue processing

Immediately after harvesting, bone samples were immersion fixed in 4% formalin/0.1M phosphate buffer saline (pH 7.4) and processed for histological analysis without prior decalcification. Employing the technique elucidated by Donath & Breuner (1982), the biopsy specimens were systematically dehydrated in ascending concentrations of ethanol (ranging from 70% to 100%), infiltrated under agitation and vacuum, and embedded in Kulzer Technovit 7200 VLC (Bio-Optica, Milano, Italy). Subsequently, each block underwent longitudinal sectioning via a diamond saw (Micromet Remet, Bologna, Italy). The two central sections were grounded, polished to a final thickness of 90 µm, and stained with hematoxylin and eosin (H&E). Each section was viewed and photographed at different magnifications: 500x, 200x, 100x, 20x, and 10x (Fisherbrand Serie AX-500, Fisher Scientific, Milan, Italy). Immunohistochemistry was performed for KP-1 (Ventana, mouse), actin (Ventana, mouse, clone 1A4), and SATB2 (Santa Cruz, mouse, clone G-11).

The CBCT scans unveiled newly formed radiopaque hard tissue seamlessly integrated with the surrounding bone, devoid of any indications of radiolucent fibrous encapsulation. This augmented bone volume facilitated the precise placement of implants in alignment with prosthetic requirements, ensuring optimal primary stability. Therefore, five months after implant surgery, the radiographic images demonstrated excellent healing of inserted implants (Fig. 9). Therefore, planning the second surgical phase and the subsequent prosthetic procedure were carried out.

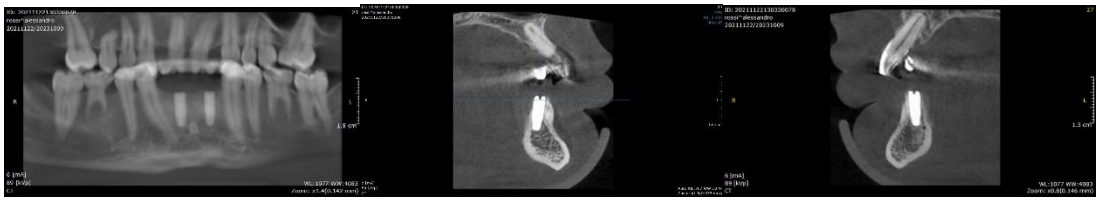

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Fig. 9. ***A****): CBCT, frontal view: implants inserted in the regenerated site;* ***B, C****): CBCT sagittal view: clear increase in bone thickness.*

The clinical image shows a surgical site with a reduction in keratinized mucosa (Fig. 10a). The reopening surgery of the implant was planned with a free gingival graft (Fig. 10b) harvested from the palate to increase the height of the keratinized mucosa (24, 25).

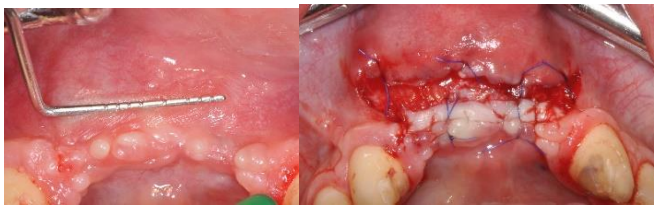

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Fig. 10. ***A****): Evidence of the surgical site with poor keratinized mucosa;* ***B****): Free gingival strip graft inserted in the surgical site and sutured with interrupted stitches onto the periosteum.*

No supplementary regenerative procedures were required concurrent with implant insertion, underscoring the favorable outcomes in localized volume augmentation. Indeed, the newly formed tissue exhibited tactile resistance, showing a good level of bone density from a macroscopic perspective.

RESULTS

Histological analysis

At low magnification, lamellar bone represented about 60% of the entire tissue volume (star), the inorganic bone matrix about 25% (arrows), and the remaining 15% interstitial spaces. (dashed arrow) (Fig. 11).

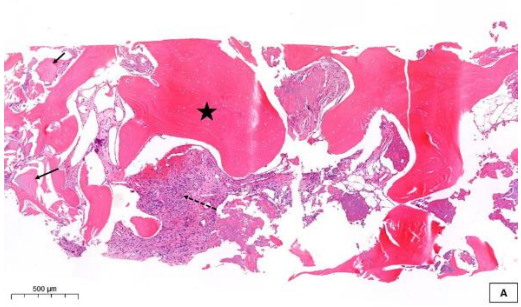

Fig. 11. *hematoxylin and eosin, Bar=500 µm*.

At higher magnification, osteoblast-like cells were easily found beneath lamellar bone fragments (arrows), with very few cells with histologic features of osteoclasts (circle) (Fig. 12).

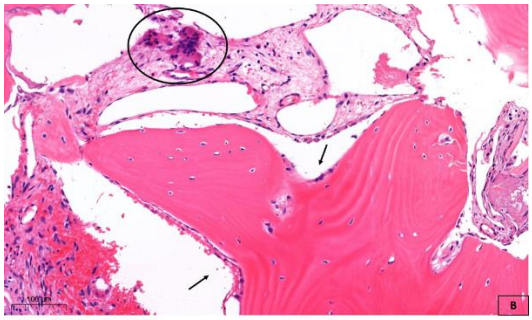

Fig. 12. *Hematoxylin and eosin, Bar=100 µm.*

Interstitial spaces comprised vessels, fibrosis, a great amount of fibroblasts, and myofibroblasts with their spindle appearance and few lymphocytes and monocytes (Fig. 13).

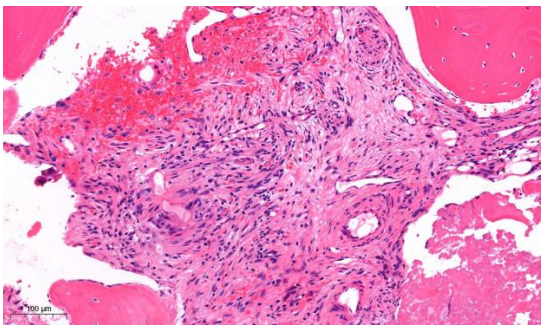

Fig. 13. *hematoxylin and eosin, Bar=100 µm.*

Immunohistochemistry for SATB2, CD68, and actin was performed to highlight these different components of the sample.

SATB2 (Special AT-rich sequence-binding protein 2) has a role in osteoblast differentiation and osteogenesis, whereas actin identifies pericytes, smooth muscle cells, and myofibroblasts. In the sample, numerous myofibroblasts positive for actin were also positive for SATB2 (circles) (Fig. 14).

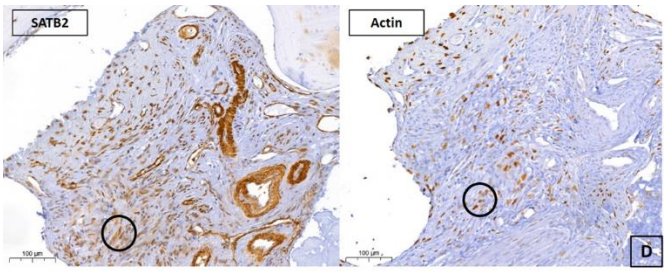

Fig. 14. *SATB2 and Actin IHC, Bar=100 µm*.

CD68 is a lysosomal marker identifying histiocytes/macrophages and monocytic cells, highlighting inflammatory components. Few macrophages were found in interstitial spaces (circles) (Fig. 15).

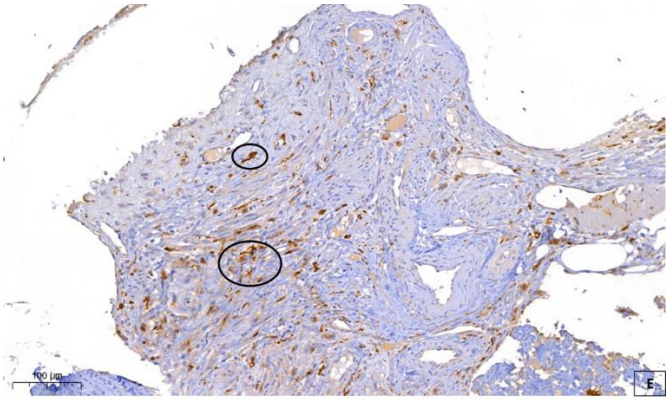

Fig. 15. *CD68 IHC, Bar= 100µm.*

DISCUSSION

In this patient, correct execution of the guided bone regenerative technique led to hard tissue augmentation, which allowed subsequent insertion of standardized osseointegrated implants in a position where, because of the marked atrophy, the presence of important anatomical structures would have made the preparation of the implant area impossible. Moreover, the use of a mixture of hyaluronic acid and polynucleotides, in addition to autologous and heterologous bone, appears to facilitate the handling of bone grafts, improve osseointegration characteristics and promote bone regeneration and repair (30, 31). As confirmed by histomorphometric analysis, the use of these biomaterials has a boosting effect on

tissue healing. With this surgical technique, a good functional outcome can be obtained by inserting standard-size implants and manufactured prosthetic products with adequate implant crown ratios in adduction to achieve a more pleasing rehabilitative solution.

Hard tissue augmentation was carried out in combination with gingival plastic surgery in which a free epithelial-connective graft was used; this resulted in a remarkable increase in the band of peri-implant keratinized gingiva leading to an objective improvement in rehabilitation esthetics and easier maintenance of soft tissue health thanks to simplified oral hygiene (32-37).

CONCLUSIONS

We can, therefore, conclude that the techniques used for tissue regeneration have allowed for implant placement in cases of severe atrophies, achieving soft tissue architecture suitable for ensuring adequate resistance to the peri-implant complex and a satisfying aesthetic outcome.

Conflict of interest

The authors declare no conflicts of interest.

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Retrospective Clinical Study

OSSEOINTEGRATED DENTAL IMPLANTS SUPPORTING FIXED PROSTHESIS IN PATIENTS WITH SYSTEMIC DISEASES: A 7-YEAR RETROSPECTIVE CLINICAL STUDY FOLLOW-UP

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ABSTRACT

The aim of this retrospective clinical study was to evaluate predictability and implants survival rate (first outcome) and marginal bone loss (second outcome) in implant-prosthetic rehabilitation in patients with systemic diseases as diabetes and cardiovascular diseases (hypertension, arrhythmias, cardiomyopathy and valvular insufficiency or stenosis). The sample of 104 participants was divided into two groups according to degree of edentulousness, single or partial. The first group included patients requiring single implant-prosthetic rehabilitations, the second group requiring multiple implant-prosthetic rehabilitations. A total of 298 teeth were extracted. Three months later, 197 dental implants were placed in the edentulous sites and loaded according to the deferred method. The predictability of the treatment, and thus implant survival, was assessed by periodic clinical and radiographic checks at 7 years follow-up. Marginal bone levels were assessed by comparing intraoral X-ray measurements. Any intra- and post-surgical complications was recorded. Within the limits of this study, implant-prosthetic rehabilitation in patients with systemic diseases could be safely applied in both the patient's health and in relation to implant survival rate and marginal bone loss.

KEYWORDS: *systemic diseases, dental implants, diabetes, hypertension, cardiovascular diseases*

INTRODUCTION

The increase in the average age leads to an increase in the occurrence of several systemic diseases as metabolic disorders, cardiovascular disorders, bone pathology and neoplasms (1, 2). At the same time, in dentistry, with the increase in the average age, the rehabilitation of partial or total edentulism may be increasingly required (3).

Although removable prostheses still represent a viable therapeutic alternative, osseointegrated implants supporting fixed prostheses could be considered the gold standard. As reported by several authors, the 10-year implant survival rate is approximately 96-98% (4-7). However, implant success, both immediate and long-term, could be conditioned by several local risk factors such as tissue inflammation, vascular changes and the different composition of resident oral bacterial species, which could occur in case of smoking, poor oral hygiene, systemic diseases and associated medications (8-10).

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The level of control of systemic diseases, rather than the presence of such disorders, is the most important consideration for the success and survival of implant therapy; the real contraindication to implant placement in elderly patients could be considered acute or decompensated diseases. In addition, many studies have reported a significant success rate in patients with systemic diseases, such as HIV-positive patients (11-14).

In fixed rehabilitation planning, patient's medical history could be a prerequisite to identify several risks factor for implants failure and complications (15). Uncompensated diseases as diabetes, cardiovascular disorders, or drug-related alterations could interfere with osseointegration process (14-16). Diabetes mellitus is a group of metabolic disorders which have in common the hyperglycemia as result of defective insulin secretion or activity or both (17).

While type I diabetes is an autoimmune disease characterized by an absolute insulin deficiency due to destruction of pancreatic ß-cells and affects approximately 5-10% of the population, tending to occur at a young age (18), type II is caused by the association between a peripheral resistance to insulin action and an inadequate secretory response of pancreatic ß-cells ("relative insulin deficiency") and accounts for many late-onset diabetes cases (19). The main manifestations in the oral cavity could be microangiopathy, altered immune response and changes in salivary composition (20, 21).

While this pathology reflects directly on the oral cavity, cardiac and/or vascular pathologies as hypertension, arrhythmias, cardiomyopathies and valvular insufficiencies or stenoses, and related medications, could require several measures on surgical approach as anesthesia with vasoconstrictor (22), antibiotic prophylaxis (23) and/or possible discontinuation, in agreement with the treating physician, of drug therapy (24).

The aim of this retrospective clinical study was to evaluate and compare the predictability and rate of implant survival (first outcome), marginal bone loss (second outcome) in implant-prosthetic rehabilitations performed in patients with systemic diseases such as diabetes and cardiovascular diseases such as hypertension, arrhythmias, cardiomyopathy and valvular insufficiency or stenosis.

MATERIALS AND METHODS

Patient selection

This retrospective study was performed at Department of Dentistry, San Raffaele Hospital, Milan, Italy. The ethics committee approval number is 190/INT/2021. The investigation was conducted according to the Helsinki Declaration. STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (http://www.strobe-statement.org/) were followed (25).

During the period from January 2012 to November 2019 patients with single edentulism or partial posterior edentulous maxilla or mandible [Appel-gate-Kennedy Class I or II (26)] or severe impairment of one or more teeth in posterior jaws, were consecutively enrolled for this study.

The eligibility criteria were as follows: age > eighteen years old, single or partial edentulism in mandible or maxilla or with severe impairment of one or more teeth requiring extraction, residual bone height equal or greater than 9 millimeters, diabetes treated with drugs, cardiac diseases treated with drugs or surgery, hypertension compensated by drugs, home hygiene maintenance ability, participation in follow-up visits and hygiene maintenance sessions.

The exclusion criteria could be summarized as follows: age < eighteen years old, residual bone height requiring placement of short or ultra-short dental implants or augmentation procedures e.g. sinus lift or bone grafts, severe cognitive impairment (dementia), immunosuppression, uncontrolled systemic diseases, diseases other than diabetes or hypertension or cardiac pathologies (patients with more than one of these conditions were also excluded), patients taking biphosphonates; smokers' patients, radiation therapy of head and neck within 5 years, parafunctional habits (bruxism, clenching), inadequate bone volume to straight implants placement, inability to maintain obligation to implant treatment and maintenance, inability or reluctance to provide informed consent, depression, psychiatric problems or unrealistic expectations, drug abusers, participation in other trials or non-compliance with control recalls and/or hygiene maintenance programme.

Before treatment, every patient was clinically and radiographically examined with a Panoramic radiography. Intra-oral X-rays were taken, if necessary, to assess the compromised teeth more accurately. The sample was divided into two groups according to degree of edentulousness, whether single (Group A) or partial (Group B). The first group included patients requiring single implant-prosthetic rehabilitations, and the second group requiring multiple implant-prosthetic rehabilitations. The sample was then subdivided by systemic disease category (type II diabetes, hypertension, and heart disease) to evaluate and compare implant survival rate and marginal bone loss between groups.

A written informed consent for implant-prosthetic rehabilitation was obtained from all patients prior to the beginning of the study and the local ethical committee approved the study; professional oral hygiene was provided before surgery.

Surgical protocol

Before the prosthetic rehabilitation treatment, mouth rinse with hydrogen peroxide, iodine, povidone, and chlorhexidine is recommended to reduce the existing bacterial load (27, 28). After clinical and radiographic evaluation, compromised teeth were extracted after antibiotic prophylaxis (2 gr. amoxicillin or 2 gr. clindamycin in allergic patients) and local infiltrations of opticain solution (AstraZeneca, Milan, Italy).

The procedure was performed as atraumatically as possible, avoiding the use of instruments with direct action on the bone tissue unless the tooth was ankylosed. Where necessary, multiple roots were dissected. Following surgical curettage, fibrin sponges were placed in the post-extraction socket. Vycril 3.0 sutures were employed to flaps adaptation.

Antibiotic (amoxicillin and clavulanic acid 1 g or clarithromycin 1 gr in case of allergy, twice daily for 7 days after surgery) and analgesic therapy (non-steroidal anti-inflammatory drugs, as needed), combined with chlorhexidine 0.20 mouth rinses were prescribed to all patients. In the absence of any complications, patients were seen after one week for a check visit and suture removal. After three months, bone healing, implant diameter, and length were evaluated with intra-oral X-rays and, if necessary, a Cone Beam Computed Tomography as a II level examination.

Surgery was performed under anesthesia induced by local infiltrations of opticain solution with adrenaline 1:80.000 (AstraZeneca, Milan, Italy). The first incision was made on the top of the alveolar crest and shifted to the palatal side to obtain the same level of keratinized mucosa on both flaps' sides. Then, distal and mesial vertical release incisions were performed to expose the underlying bone crest. A full-thickness flap was elevated to preserve anatomical subperiosteal structures. Anatomical structures, such as the piriform aperture, maxillary sinus, chin nerve, and midline, were defined with a sterile pensile as a reference for dental implant position. A lanceolate drill was employed to perforate cortical bone. A pilot drill of ø 2.00 was applied to create an implant way insertion and to define fixture's setting. A positioning pin was plugged in to verify implant location and emergence. Progressive diameter drills were employed up to the final fixture's diameter. The site was over-prepared vertically and sub-prepared transversely to promote the primary mechanical stability. A manual screwer was applied when incomplete seating of the implant occurred. The implant neck was aimed to be positioned at bone level. Flap adaptation and suturing were performed with 3-0 non-resorbable sutures (Vicryl, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA). Intra-oral X-rays were performed to assess the correct implant positioning. Antibiotic therapy (amoxicillin and clavulanic acid 1 g or clarithromycin 1 gr in case of allergy, twice daily for 7 days after surgery) and analgesic therapy (non-steroidal anti-inflammatory drugs, as needed) were prescribed for each patient. Mouth rinsing with a chlorhexidine digluconate-containing solution (0.12% or 0.2%) was recommended twice daily for 10 days. One week after surgical procedure, sutures were removed.

Prosthetic protocol

All the implants were covered for about 4 months. In the anterior region, for aesthetic reasons, a removable partial denture made of resin, obtained from preliminary alginate impressions and connected to the adjacent teeth with clasps, was delivered to the patient in the pre-reopening period. After about 4 months from the surgical procedure, the reopening was performed, and cap screws were replaced with healing screws. The provisional prosthesis was delivered to each patient. Screw access holes were covered with provisional resin (Fermit, Ivoclar Vivadent, Naturno, Bolzano, Italy) and the appropriate evaluation checks of the device was performed. After another four months, the provisional prosthesis was replaced with a metal-ceramic or stratified zirconia implant-supported final prosthesis (29). The material was chosen according to anatomical area and aesthetic and economic patients' needs. Metal-ceramic was preferred in the posterior regions, while zirconia was used in the anterior areas to improve the aesthetic result (30, 31).

The definitive impression was taken using the pick-up technique with an individual spoon. The transfers were first splinted with dental floss and resin, then separated to reduce the shrinkage error of the material and fixed together again. A polyether (Impregum Penta, 3M Italia, Pioltello, Italy) was used as impression material. The metal test with radiographic control was then conducted to assess the fit between the metal framework and the implants. The metal beam waxed up if the structure fits without tension and passively.

Follow-up

Follow-up visits were performed one week after surgery, at 3 and 6 months, and then once a year for the next 7 years. Each patient was placed in a professional oral hygiene program that would allow for limiting complications, preventing inflammation, and monitoring and interception of any complications.

1. *Implant survival rate.* The implant survival rate was defined as the absence of signs of peri-implantitis, implant mobility, radiolucent areas around fixtures, mucosal suppuration, or pain, as well as when implant removal is required during the follow-up period.
2. *Marginal bone loss.* Digital phosphor intra-oral radiography was performed for each patient using the parallel cone technique three months after tooth extraction, immediately after implant placement, at 3, 6 and 12 months and once

a year throughout the follow-up period. Measurements were taken only after image calibration to assess marginal bone trends. The Digora 2.5 software (Soredex, Tuusula, Finland) was used as the analysis platform, making use of the specific measurement tool contained therein.

As a first step, the calibration (pixels/mm) of the instrument was performed using the implant diameter of the investigation site as a known unit. Subsequently, any variations in the height of the peri-implant marginal bone with respect to the most coronal part of the implant fixture and the point of contact between the implant fixture and the marginal crest were measured. To evaluate the bone trend, a line passing over the shoulder of the implant was considered as a reference point for measurement from which a straight line was drawn parallel to the long axis of the implant to the most coronal point where the bone came into contact with the fixture both mesially and distally. In relation to the calibration, the software automatically provided the distance between the two points measured in millimeters. To reduce human error, this measurement was taken by three blind operators, and the average of the three measurements was considered. Subsequently, to calculate the marginal bone level, a mesial measurement was taken, a distal measurement was taken, and then the average of the mesial, distal, and the average between the two values of a single implant site (MBL, marginal bone level) was calculated, as reported in the "results" section. The obtained results were then statistically evaluated.

Statistical analysis

The statistical analysis was performed using SPSS for Windows release 18.0 (SPSS Inc., Chicago, IL, USA). Data were analyzed at the patient level and are reported as mean ± standard deviation (SD). Pearson's correlation coefficient was used to compare the implant survival rate between groups A and B, i.e., single and multiple implants.

The pairwise test of between-subject effects was applied to compare the implant survival rate between the different diseases.

Student's t-test at a significance level of $p < 0.05$ was applied to compare marginal bone loss between group A and group B and between pathologies. Analysis of variance was used to analyze changes in bone level over time. All statistical comparisons were conducted at the .05 level of significance. The null hypothesis was that the groups had no differences in mean marginal bone changes.

RESULTS

One hundred forty-six patients (69 males and 77 females) with single or partial edentulism in the mandible or maxilla or severe impairment of one or more teeth requiring extraction were enrolled. The mean age was 53 years (range: 32-74).

As a result of the division of the patients according to the category of edentulism, single or partial, 95 patients were placed in Group A and 51 in Group B.

Two hundred ninety-eight compromised teeth were extracted, and after the healing period, 197 implants were placed in the posterior maxilla or mandible. In the case of single edentulism, each missing unit was replaced by an implant; in case of partial edentulism, if two contiguous teeth were missing, two implants were placed to replace them; if three were missing, a three-unit restoration supported by two implants with a middle cantilever was made, for a total of 2 fixtures for each patient.

Implant survival rate

Implants number, length and diameter are summarized in Table I.

Table I. *Number, diameter, and length of dental implants classified by group.*

Number, diameter and length of dental implants classified by group				
		length 9 mm	length 11 mm	length 13 mm
Group A n=95	diameter 3.3 mm	14		2
	diameter 3.8 mm	29	34	3
Group B n=102	diameter 3.3 mm	2	3	1
	diameter 3.8 mm	16	21	3

The early failure occurs in 3 implants of Group A and 2 of Group B, providing a global implant survival rate of 97.44%. Implant failure details are summarized in Table II.

Table II. *Implant failures by the time of failure (early or late) and implant survival rate.*

	Number of implants	Early failure	Late failure	Implant survival rate
Group A	95	3	0	96.84%
Group B	102	2	0	98.04%
Global results	197	5	0	97.44%

The sample was further divided according to patients' diseases. Of 95 patients in Group A, 29 had hypertension, 32 type II diabetes and 34 heart disease. Of Group B, 19 patients suffered from hypertension, 18 from type II diabetes and 14 from heart disease (Table III).

Table III. *Sample division according with systemic diseases.*

No Patients			
	Group A	**Group B**	**Global results**
Hypertension	29	19	48
Type II Diabetes	32	18	50
Heart Diseases	34	14	48

The number of dental implants for each group, including implant survival rate, was assessed, considering hypertension, diabetes, and heart disease.

The early failure occurs in 2 implants of the hypertension group and 3 of the type II diabetes group, providing an implant survival rate of 97.01% in patients with hypertension, 95.59% in type II diabetes, and 100% in heart diseases. Any late failure was recorded. Implants failure details were summarized in Table IV and V.

Table IV. *Number of implants according with type of edentulism and systemic diseases.*

	No of implants	Hypertension	Diabetes	Heart Diseases
Group A	95	29	32	34
Group B	102	38	36	28
Global results	197	67	68	62

Table V. *Implants failure details according with systemic diseases.*

	No implants	Early Failure	Late Failure	Implants survival rate
Hypertension	67	2	0	97.01%
Type II Diabetes	68	3	0	95.59%
Heart Diseases	72	0	0	100%

In regards to implant survival rate, any statistically significant difference was found between single and multiple implants (Group A and Group B) rehabilitation or between systemic diseases (hypertension, type II diabetes, heart diseases).

Marginal bone loss

Marginal bone loss was assessed at 6 months, 12 months and once a year during the follow-up period (7 years). The assessment was performed according to type of rehabilitation, single or partial (Table VI), and based on considered systemic diseases (hypertension, type II diabetes and heart disease) (Table VII).

Table VI. *Average marginal bone loss by type of rehabilitation (single or partial).*

	Group A	Group B

6 months (mm)	0.58 ± 0.73	0.64 ± 0.53
1 year (mm)	0.80± 0.84	0.82 ± 0.94
2 years (mm)	0.86 ± 0.74	0.83 ± 0.63
3 years (mm)	0.87 ± 0.98	0.91 ± 0.75
4 years (mm)	0.91 ± 1.03	1.01 ± 1.03
5 years (mm)	0.96 ± 1.00	1.04 ± 0.88
6 years (mm)	1.04 ± 1.07	1.12 ± 0.67
7 years (mm)	1.07 ± 1.00	1.13 ± 0.90

Table VII. *Average marginal bone loss according with systemic diseases.*

	Hypertension	**Type II Diabetes**	**Cardiac Diseaes**
6 months (mm)	0.56 ± 0.71	0.64 ± 0.55	0.62 ± 0.75
1 year (mm)	0.76 ± 0.81	0.84 ± 0.96	0.80 ± 0.83
2 years (mm)	0.83 ± 0.72	0.84 ± 0.65	0.82 ± 0.76
3 years (mm)	0.85 ± 0.96	0.92 ± 0.75	0.87 ± 0.95
4 years (mm)	0.91 ± 1.03	1.02 ± 1.05	0.92 ± 1.01
5 years (mm)	0.93 ± 1.01	1.03 ± 0.87	0.94 ± 1.01
6 years (mm)	1.02 ± 1.03	1.10 ± 0.71	1.04 ± 1.08
7 years (mm)	1.08 ± 1.00	1.15 ± 1.02	1.10 ± 1.01

In regards to marginal bone loss, no statistically significant difference was found between single and multiple implants (Group A and Group B) rehabilitation or between systemic diseases (hypertension, type II diabetes, heart diseases).

DISCUSSION

The placement of osseointegrated implants to support fixed prostheses in patients with systemic diseases is an increasingly common practice with favourable short- and long-term results (32, 33).

As reported by Tawil G et al. in their prospective clinical study performed on 45 patients with type 2 diabetes, in which 255 implants placed following the classical protocol or following advanced protocols (sinus floor elevation, immediate loading and guided bone generation) were analysed, the patients were divided into two groups: a group of patients with controlled type 2 diabetes (group A) and a group of control patients (control group). The implant survival rate was 97.2% in group A and 98.8% in the control group. While the marginal bone level was 0.41+/- 0.58 mm and 0.49 +/- 0.64 mm in the group (33).

Similar results were obtained by Eskow et al. (34), Fiorellini et al. (35), and Alruhaim et al. (36). emphasizing the predictability of implant rehabilitation in patients with well-controlled type 2 diabetes and optimal hemoglobin A1c levels.

Regarding type 1 diabetes, however, as reported by Farzard et al. in a retrospective clinical study, 136 implants were placed in 782 patients, 36% of whom had type 1 diabetes mellitus. The implant survival rate was 96.3% of the total, with no statistically significant differences in marginal bone level between the diabetic and the control group (37).

The main manifestations of diabetes in the oral cavity could be microangiopathy due to the thickening of the basal membrane of the capillaries, the consequent deficit in blood perfusion and leukocyte migration, which makes the tissues more susceptible to microbial aggression, the reduction in the chemotactic activity of neutrophils and the phagocytic activity of macrophages, which could be responsible for the altered response of periodontal tissues to bacterial plaque and the impaired salivary composition (38 - 40). These factors could affect both the osseointegration of the implant and its long-term survival, predisposing the patient to peri-implantitis (41). In addition, poor oral hygiene and cofactors such as smoking could increase the patient's predisposition to implant failure (42).

In relation to cardiac disease, Nobre Mde et al. performed a retrospective clinical study of patients with systemic and cardiovascular disease (cardiovascular disease, arrhythmia, hypertension, atrial fibrillation, bypass, and pacemaker surgery). The patients were divided into two groups (CVD = patients with coexisting cardiovascular diseases and non-CVD = patients without coexisting cardiovascular diseases). A total of 352 implants were analysed, the implant survival rate was 97.4% in the non-CVD group compared to 100% in the CVD group (non-significant difference between the groups; P = 0.359) while the marginal bone level at 1 and 5 years was 0.95 mm and 1.52 mm in the CVD group and 0.78

mm and 1.54 for the non-CVD group with no significant differences between the groups at 1 year (P = 0.979) and 5 years (P = 0.300) (43). Similar results were obtained by Marchio V. et al. and Neves J et al. in subsequent studies (44, 45).

As reported by several studies, medications taken by patients with cardiovascular disease could influence the surgical procedure (46, 47). Antihypertensive therapies may cause drug interactions with vasoconstrictors associated with anesthesia. The same disease or drug therapies with antiplatelet agents create a modest risk of bleeding after surgery (48). Oral anticoagulants, which together with heparin and antiplatelet agents form the basis of pharmacological treatment of thrombotic and thromboembolic disease, may promote intra-operative and post-operative bleeding (49).

In addition, the administration of some antibiotics such as tetracyclines, erythromycin, sulphonamides and metronidazole and some analgesics such as aspirin and NSAIDs could potentiate the effect of anticoagulant therapies, altering platelet function and thus worsening bleeding diathesis (50).

CONCLUSIONS

Within the limitation of this study, according with obtained results, it could be stated that patients affected by the systemic pathologies considered in the study, if monitored over time, scheduling continuous and periodic check-ups and if instructed to maintain correct oral hygiene at home, present a satisfactory implant survival rate. As far as diabetic patients are concerned, it is essential, from a biological point of view to interface with their endocrinologist and keep the glycemic index under control; while patients with heart problems, coagulation problems and hypertension should interface with their cardiologist to keep the disease under control. It is therefore the duty of the dentist to ensure, before starting any kind of surgical intervention, that he/she liaises with the physician expert in treating this type of diseases.

In conclusion, implant rehabilitation in patients with systemic diseases does not worsen the patient's general health conditions such as the osseointegration of patients is not compromised. Further long-term prospective clinical trials are needed to confirm these results.

Conflict of interest

The authors declare no conflict of interest.

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Review

DENTAL MANAGEMENT OF PATIENTS AFFECTED BY BRUGADA SYNDROME: NARRATIVE REVIEW

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ABSTRACT

Brugada syndrome (BrS), a condition associated with life-threatening arrhythmias, demands meticulous consideration in dental management. This narrative review aims to provide clinicians with comprehensive insights into the dental implications of BrS, facilitating the implementation of appropriate procedures for affected patients. A thorough search across electronic databases, including Cochrane Oral Health Group Specialized Register, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, PubMed, EMBASE, and Google Scholar, identified pertinent articles. Inclusion criteria comprised randomized controlled trials, prospective/retrospective studies, observational studies, case reports, narrative, and systematic reviews. Before dental procedures, clinicians must exercise caution regarding potential triggers for arrhythmic events in BrS patients, encompassing fever, nausea, vomiting, dental anxiety, postoperative pain, and drug interactions. The implementation of recommended measures throughout the perioperative process is crucial to minimize the risk of significant complications. Adherence to established protocols before, during, and after oral surgery procedures is imperative for patient safety. Despite limited evidence, dental treatments for BrS patients can be considered safe with regular monitoring, avoidance of unsafe drugs, and efforts to minimize patient anxiety. A meticulous medical history is indispensable to mitigate risks of complications and navigate potential medico-legal implications. In conclusion, a cautious approach, adherence to guidelines, and continuous monitoring contribute to the safe provision of dental care for individuals affected by BrS.

KEYWORDS: *oral surgery, Brugada syndrome, BrS, dentistry, local anesthetics, dental anxiety, conscious sedation, complications*

INTRODUCTION

Brugada syndrome (BrS) is a rare genetic heart condition associated with an increased risk of ventricular fibrillation and sudden cardiac death (SDC). It takes its name from Spanish cardiologists Pedro and Josep Brugada, who first described it in 1992 (1).

BrS overall is quite rare: the worldwide prevalence is approximately 3 to 5 per 10,000 people and occurs 8 to 10 times more frequently in males than in females. It is related to mutations in genes that control the flow of sodium ions in

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the heart. The most common gene involved is SCN5A, which codes for the alpha-subunit of the cardiac sodium channel. These mutations could impair the electrical activity of the normal heart, resulting in a distinctive pattern on the electrocardiogram (ECG) (2). Indeed, diagnosis is based on the combination of ECG patterns and clinical presentation. The ECG can display three different patterns:

- type 1 presents a 2 mm coved ST segment or J point elevation, followed by a negative T wave;
- type 2 shows a saddleback appearance of the T wave with at least 1 mm elevation of the ST segment or 2 mm elevation of the J point, followed by a positive or biphasic T wave;
- type 3 can be either coved or saddleback in appearance with more than 1 mm of the ST-segment elevation (3).

The clinical criteria used to diagnose BrS include the following:

- data from family history (e.g., sudden cardiac death in family members under 45 years of age or ECG with a type 1 pattern at any age);
- ventricular arrhythmias, such as ventricular fibrillation or polymorphic ventricular tachycardia;
- symptoms of arrhythmias (syncope, seizures, fainting, convulsions, and gasping breathing) (3, 4).

When both a type 1 Brugada pattern and at least one of the clinical criteria are present, a diagnosis of BrS is considered definitive. On the other hand, the combination of type 2 or type 3 ECG patterns with at least one clinical criterion suggests BrS (3).

The ECG alteration can occur independently and spontaneously or be induced by a specific drug test, which involves the injection of sodium channel-blocking drugs, such as ajmaline, flecainide, procainamide, or pilsicainide (5).

Diagnosed patients are asymptomatic (64%) or have a history of syncope (30%), while only a small proportion (6%) present a cardiac arrest. It is worth noting that between 61% and 80% of BrS patients with cardiac arrest were previously asymptomatic (6). Arrhythmic alterations often occur during rest, sleep, and enhanced vagal tone situations, such as large meals or alcohol intoxication (7).

Fever is one of the most relevant arrhythmic triggers: 4 to 6% of life-threatening dysrhythmias in BrS are associated with fever, according to data from the Survey on Dysrhythmic Events in BrS (SABRUS) registry (8). Fever seems especially dangerous in affected children, although most symptoms manifest in young adults, peaking around the third or fourth decade (9).

Treatment of BrS usually involves the implantation of an implantable cardioverter defibrillator (ICD), which may provide an electric shock to the heart if a life-threatening arrhythmia is detected. In some cases, drugs, such as sodium channel blockers (quinidine), could also be applied to prevent arrhythmias (2, 8). However, only on rare occasions, quinidine has proven to be effective, and many side effects have been detected, such as thrombocytopenia, allergic reaction, and aggravation of sinus node dysfunction. Education and lifestyle changes are fundamental for preventing arrhythmias: the patient's awareness of all potential risks that could induce malignant arrhythmias plays a key role in encouraging the patient to adopt a healthy lifestyle.

The most serious consequence for patients affected by BrS is sudden cardiac arrest. However, if detected early and well managed, BrS does not lead to death. When ICD is placed, the total mortality rate of patients with BrS has been 0% during a 10-year follow-up. This is why the ICD represents a viable treatment option to reduce the risk of sudden death.

What are the potential risks and implications if a patient with BrS needs dental treatments? To address this question, we examined all the possible risks associated with dental anxiety, local anesthetics, and drug interactions that may affect the electrical activity of the heart, thus increasing the risk of developing life-threatening arrhythmias during or after dental procedures.

This narrative review aims to provide clinicians with an overview of the dental implications of BrS so that they can adequately manage these patients who need dental procedures.

MATERIALS AND METHODS

Published literature was searched via electronic databases: Pubmed, Scopus, Science Direct, and Web of Science. The search words included ‘Brugada syndrome’, ‘dentistry, ‘oral surgery’, ‘local anesthetics’, ‘dental anxiety’, ‘conscious sedation’, and ‘complications’. These terms were used alone or searched with the aid of Boolean operators such as AND.

Inclusion criteria:

- randomized controlled trials (RCTs), prospective studies, retrospective studies, observational studies, narrative reviews, and systematic reviews;
- animal studies;

- articles published in English;
- time period: the articles considered in this review were published from 1992 (when Spanish cardiologists Pedro and Josep Brugada described it) until October 2023.

Exclusion criteria:

- articles published in languages other than English;
- articles that, after reading their title and abstract, did not fit in with the subject of interest of this paper.

The search was conducted independently by two reviewers, and the gathered titles and abstracts were collectively screened in detail. We identified 5003 papers from electronic databases and removed 4726 papers based on exclusion criteria and duplicates. Seventeen papers retrieved from reference lists were added to the review.

The full text of 294 articles was retrieved, assessed, and discussed by both reviewers for relevant findings for this review. Thirty-six papers were included in the review for analysis (Fig. 1).

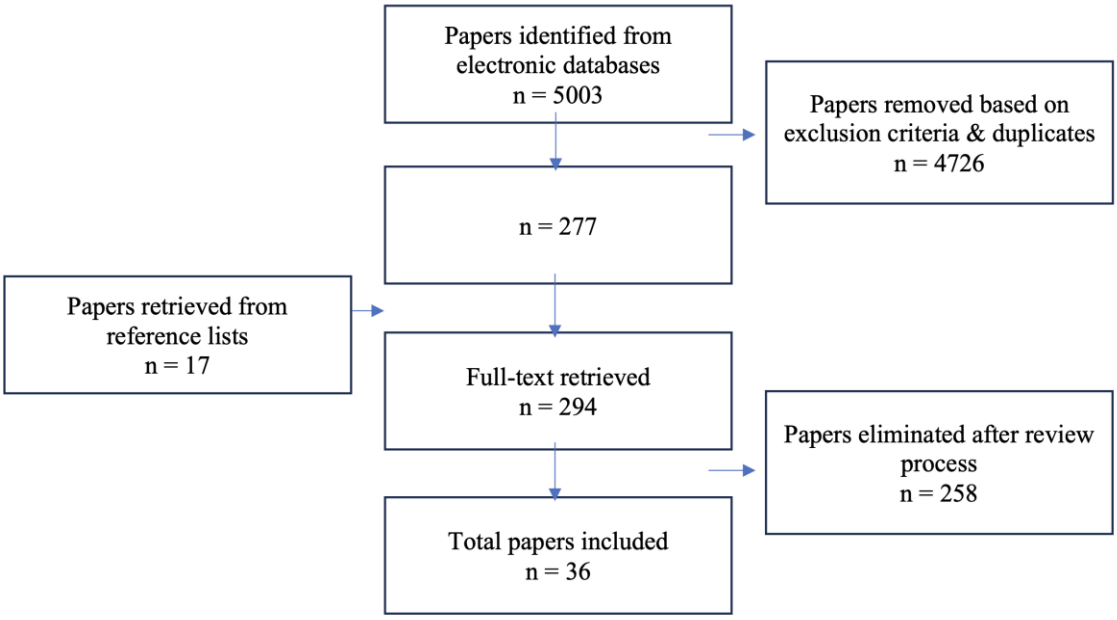

Fig. 1. *The methodology pathway for the literature search.*

RESULTS

Patients affected by BrS need to be correctly managed. Attention must be given to preoperative management, intraoperative monitoring, and postsurgical evaluation (10).

Firstly, a medical history evaluation and a consultation with the cardiologist are the first steps of any treatment plan. Before performing any procedure, dentists should also be careful about clinical triggers for arrhythmic events:

1. **Fever**. The electrocardiographic phenotype of BrS is influenced by the sodium channel ionic mechanisms, which depend on human body temperature.
2. **Nausea and vomiting**. Arai et al. reported that, in an electrophysiological study, when a 53-year-old patient who had 3 syncopal episodes over 6 months experienced severe nausea and vomiting, the ECG showed an increased elevation of the ST-segment and J-point. Thus, this alteration is supposed to have originated from the vagal stimulation associated with nausea and vomiting.
3. **Dental anxiety**. Dental anxiety is a common fear or phobia that some people experience when they think about going to the dentist or receiving dental treatments. It can range from mild nervousness to a severe fear that can prevent a person from seeking necessary dental care (11).

Some common causes of dental anxiety include fear of pain, fear of needles or injections, fear of loss of control or embarrassment, previous negative experiences with dental treatments, and general anxiety or phobias.

To assess dental anxiety, dentists should administer the Modified Dental Anxiety Scale (MDAS), ranging from 5 to 25 (low dental anxiety ranges from 5 to 9; moderate dental anxiety from 10 to 18; severe dental anxiety ranges from 19 to 25 (12).

Individuals with BrS with dental anxiety may have an increased risk of experiencing arrhythmias during dental procedures, which involve the stimulation of the vagus nerve (13). Therefore, BrS patients must inform their dentist and cardiologist about their condition before undergoing dental procedures (14).

Dental anxiety could make it difficult for individuals to undergo necessary dental procedures, which can lead to dental problems and potentially exacerbate systemic health conditions (15). Hence, individuals with BrS experiencing dental anxiety should consider seeking treatment to manage their anxiety and ensure proper dental care (16), which includes the following:

- *conscious sedation*: a form of sedation used in dentistry to help patients relax and manage anxiety during dental procedures. Several medications can be used for conscious sedation during dental procedures, including benzodiazepines, opioids, and nitrous oxide. However, the choice of medication depends on the patient's medical history and condition and the type and duration of the dental procedure. If conscious sedation is necessary for BrS patients, it is essential to closely monitor heart function and ECG–during and after dental procedures–to minimize the risk of arrhythmias (17).
- *non-pharmacological treatment*, such as cognitive-behavioral therapy or relaxation techniques, which do not carry the risk of arrhythmias associated with pharmacological interventions

First-line drugs to treat anxiety are selective serotonin reuptake inhibitors (SSRIs) (18). They are generally considered safe and effective for treating depression and anxiety, and they have fewer side effects than older antidepressant medications such as tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). Some SSRIs, such as paroxetine (Paxil), have been specifically studied for their effectiveness in treating dental anxiety (19). However, in BrS patients, SSRIs could have an impact on the electrical activity of the heart: they block the sodium channels in the heart, which can prolong the QT interval and increase the risk of arrhythmias in some individuals. This can be a major concern for BrS patients, as they already have an increased risk of arrhythmias due to their condition.

4. **Postoperative pain**. In the postoperative period, arrhythmias are more common. In particular, if the patient refers to pain, it may trigger BrS by increasing vagal tone (17). This makes pain management in the postsurgical period fundamental as it prevents the patient from becoming agitated and emotionally stressed (19)
5. **Drug interactions**: for BrS patients, while some drugs are safe, others should preferably be avoided because they are unsafe (Table I).

Table I. *Drug characteristics and safety for BrS patients.*

Name	Characteristic	Clinical use in dentistry	Safety	References regarding "safety" in BrS patients
Bupivacaine	Local anesthetic	Bupivacaine offers a rapid and deep anaesthesia to pulp, soft tissues, and bones. It is used in many dental treatments, such as tooth extractions, endodontic therapies, and dental surgery.	UNSAFE	(19- 23)
Procaine	Local anesthetic	In the past, procaine was the first choice for local anesthesia. However, currently newer local anesthetics like bupivacaine, lidocaine and mepivacaine have replaced procaine in clinical practice.	UNSAFE	(24-25)
Propofol	Anesthetic	Propofol is an intravenous hypnotic drug used for: - general anaesthesia - conscious sedation	UNSAFE SAFE	(19, 26-36)
Ketamine	Dissociative anesthetic with analgesic properties	- Using ketamine in combination with local anesthesia during the surgical removal of impacted mandibular third molars -Conscious sedation	PREFERABLY AVOIDED	(33)

Tramadol	Opioid, Analgesic	Tramadol's application in dentistry has limited indication in managing acute pain. It can be an alternative analgesic option when: - gastrointestinal side effects make the use of nonsteroidal anti-inflammatory drugs not recommended, - codeine/acetaminophen combination analgesics are either contraindicated or not tolerated	UNSAFE at high doses	(34)
Lidocaine	Local anesthetic	Lidocaine provides anaesthesia. Due to its better safety and effectiveness compared to other local anesthetics, it was quickly adopted	SAFE	(32, 35)
Midazolam	Benzodiazepine	Midazolam can be used for: - general anesthetic premedication; - conscious sedation; - treatment of seizures during dental procedures	SAFE	(32, 36)
Diazepam	Benzodiazepine	Conscious sedation	SAFE	(14)
Fentanyl	Opioid, analgesic	Conscious sedation	SAFE	(36)
Sevoflurane	Halogenated inhalational anesthetic	Conscious sedation	SAFE	(32, 36)
Nitrous oxide	Gas	Conscious sedation: nitrous oxide is used for its analgesic and anesthetic effects.	SAFE	(32 37)

The following drugs were analyzed:

Local anesthetics

Lidocaine

The studies performed by Theodotou et al. have demonstrated that using lidocaine as a local anesthetic in dental procedures for patients with BrS is safe (32).

Oliveira et al. conducted a crossover randomized, double-blind pilot trial to assess the safety of local dental anesthesia with lidocaine during dental procedures for individuals affected by BrS. They found that using 2% lidocaine without a vasoconstrictor and with 1:100,000 epinephrine during routine dental procedures was safe. No life-threatening arrhythmic events were observed, and no dynamic electrocardiographic changes occurred in BrS patients. Additionally, no significant differences were detected in anxiety measures and blood pressure values during the recording of these measurements with and without epinephrine (38).

In a case report conducted by Theodotou, 15 milligrams of lidocaine with epinephrine at a concentration of 1:100,000 were administered for dental treatment to a 55-year-old patient with BrS, who also had valvular heart disease and an implantable cardioverter-defibrillator (ICD). The treatment consisted of an abscess drainage and tooth extraction under general anesthesia. Neither intraoperative complications nor adverse cardiac events occurred (32).

Although Oliveira et al. and Theodotou et al. indicated the safety of using lidocaine as a local anesthetic for patients with BrS, Barajas-Martínez et al. reported a rare lidocaine-induced BrS ECG pattern caused by double missense mutations of the cardiac sodium channel in a patient affected by BrS (35).

Bupivacaine

In 1992, De la Coussaye and colleagues used high-resolution ventricular epicardial mapping to study the potential effects of bupivacaine at various concentrations (0.2, 0.5, 1.0, and 5.0 micrograms/ml) in 11 Langendorff-

perfused rabbit hearts. The results indicated that bupivacaine (at 5.0 micrograms/ml) induced ventricular dysrhythmias in 3 of 5 intact hearts. In 3 of 6 frozen hearts, bupivacaine (0.2 micrograms/ml) facilitated the induction of ventricular tachycardia by programmed electrical stimulation. Thus, the authors concluded that bupivacaine facilitated the occurrence of reentrant ventricular dysrhythmias in isolated rabbit hearts (22).

In 1994, Berman et al. stated that bupivacaine is more cardiotoxic than lidocaine and can induce fatal arrhythmias during either intravascular injection or accidental overdose. Studies conducted in adult guinea pig myocytes indicate that this toxicity is due to the stronger inhibition of sodium current by bupivacaine (23).

In their 2003 study, Phillips et al. observed that epidural bupivacaine produced the typical electrocardiographic changes associated with BrS (20). They also postulated that early diagnosis and the stop of the bupivacaine infusion might have prevented a fatal arrhythmia. Hence, the authors concluded that bupivacaine has the potential to induce severe arrhythmias in patients with BrS.

Vernooy et al., in their 2006 study, suggested that bupivacaine may trigger the electrocardiographic and arrhythmic manifestations of BrS in individuals with silent SCN5A mutations (21).

Procaine

According to Arumugam, procaine may unmask BrS and play a role in causing cardiac arrest (25). Hence, it must be avoided in patients with BrS.

Halogenated inhalational anesthetic

Sevoflurane

In case reports performed by Inamura and Theodotou, sevoflurane was administered in combination with propofol and fentanyl to patients with BrS for maintenance of anesthesia. Neither ECG changes nor arrhythmia were observed during surgeries (32, 36).

Other anesthetics

Propofol

Propofol administration, generally used for general anesthesia and conscious sedation, in patients with BrS, is debatable. Even if there is a lack of evidence for its feared arrhythmogenicity, the BrS cardiological society recommends avoiding its administration in patients with BrS due to propofol's sodium channel-blocking properties.

Even Robinson et al., in a study, concluded that prolonged high-dose propofol infusion in young patients is not safe as it may lead to serious arrhythmias (29).

However, other studies suggest that the use of propofol is safe and does not lead to arrhythmias. For instance, Flamée, in a retrospective cohort study, analyzed 135 BrS patients who underwent 304 anesthetic procedures receiving propofol. The patients showed no evidence of malignant arrhythmias or defibrillations (31).

Even Theodotou et al. (32) and Inamura et al. (36) stated in their case reports that neither adverse cardiac situations nor intraoperative complications developed using propofol.

Ketamine

Rollin et al. documented the case of a 31-year-old man who was referred for ketamine overdose and presented initially with a transient significant Brugada ECG pattern. According to the authors, in this case, Brugada-like ECG was likely induced by ketamine intoxication (33). For this reason, ketamine is preferably avoided in clinical use for patients with BrS.

Benzodiazepines

Benzodiazepines are a class of psychoactive drugs. They work by enhancing the activity of a neurotransmitter in the brain called gamma-aminobutyric acid (GABA), producing a calming effect, and reducing anxiety (39).

In dentistry, benzodiazepines are frequently administered, such as Midazolam (for general anesthetic premedication, conscious sedation, and treatment of seizures (39-41), while Diazepam is administered for conscious sedation. Both medications are safe for individuals with BrS.

Dell'Olio et al., in a patient with BrS, administered 8 mg of intravenous Diazepam for conscious sedation. The ECG did not show alterations during the perioperative and postoperative periods (14).

Other studies have demonstrated that using Midazolam in patients affected by BrS did not induce either Brugada ECG pattern or arrhythmic events (42-45).

For conscious sedation, benzodiazepines are preferred over subanesthetic dosages of general anesthetic drugs (e.g., ketamine and propofol) (46).

Opioids

Fentanyl

Commonly used in dentistry for conscious sedation. Inamura et al. administered fentanyl combined with propofol/sevoflurane to patients with BrS for maintenance of anesthesia and observed no ECG change or arrhythmia perioperatively (36).

Tramadol

Tramadol represents an alternative analgesic option when gastrointestinal side effects make the use of nonsteroidal anti-inflammatory drugs not recommended or codeine/acetaminophen combination analgesics are either contraindicated or not tolerated (44-46). In a 2010 case report, Cole and colleagues associated the Brugada ECG pattern with tramadol toxicity. Although usual doses of tramadol (serum tramadol therapeutic values 100-1,500 ng/mL) have not caused a Brugada ECG pattern, the very high serum level of tramadol in a patient (8,663 ng/mL) blocked voltage-dependent sodium channels, thus resulting in a Brugada ECG pattern. As the serum tramadol concentration decreased, the ECG findings resolved with time. Hence, tramadol must be avoided at high dosages (34).

Nitrous oxide

Known as "laughing gas," it is a commonly used sedative for dental procedures. It is a safe and effective option for many patients, as it produces a mild sedative effect and has a short duration of action. Nitrous oxide has not been shown to interfere with cardiac function, making it a safe medication for individuals with BrS (47).

Preoperative, perioperative, and postoperative management of oral surgery procedures for BrS patients

Preventive measures should be followed to prevent complications during oral surgery treatments for patients suffering from BrS. To ensure patient safety, the dentist needs to work in a secure environment. This is especially important because, in emergencies, responding promptly may effectively prevent the worst outcomes, such as patient death.

For these reasons, all the oral surgery procedures were conducted in a hospital setting so individuals with BrS could be accurately managed and the risk of a vasovagal syncope could be prevented.

A review of the published studies revealed several recommended measures for oral surgery procedures in patients suffering from BrS.

<u>Before starting an oral surgery procedure in the operating room, a dentist should:</u>

1. place the patient on an adjustable operating table, which could be easily reclined to perform cardiopulmonary resuscitation (CPR);
2. establish peripheral venous access. Normally, 500 mL of normal saline solution, 2 gr of amoxicillin as an antibiotic prophylaxis, and 1 gr of acetaminophen as an analgesic are administered for dental extractions;
3. apply an external biphasic defibrillator connected to defibrillator pads.

<u>During the procedure, the dentist needs to:</u>

1. administer anesthesia; some dentists chose to perform general anesthesia: Theodotou et al. (32) outlined the case of tooth extraction in a BrS patient while performing general anesthesia (induced by intravenous lidocaine, propofol and succinylcholine, maintained by sevoflurane with an oxygen/nitrous oxide gas mixture). Even Paradiso et al. (37) described the third molar extraction under general anesthesia (induced by intravenous rocuronium and propofol, maintained by a mixture of oxygen/nitrous oxide gas). Other dentists chose to perform local anesthesia with conscious sedation;
2. attach a 12-lead continuous ECG monitoring. BrS patients who undergo general anesthesia need continuous ECG monitoring in the intensive care unit within 24 hours after intervention because dysrhythmias may occur (1-3);
3. use an automatic sphygmomanometer to measure the patient's blood pressure every 5 minutes (31);
4. administer atropine and ephedrine to decrease vagal tone (if necessary);
5. administer isoproterenol to manage ST-segment elevation (if necessary for major dysrhythmic events).

After the dental procedure, the dentist must:

1. closely monitor and prevent postoperative fever, nausea, and vomiting because both temperature-dependent sodium channels and vagal stimulation have been shown to trigger BrS;
2. recommend postoperative ECG monitoring if:
   - general anesthesia is employed; an intensive care unit monitoring for 24 hours is recommended because relevant variations in the ST patterns in the V1 and V2 leads with 24-hour ECG monitoring have been detected in patients who received general anesthesia but were not associated with the incidence of arrhythmias;
   - local anesthesia is employed, and the ECG monitoring continues for 2 hours from the end of the dental procedure;
3. provide valid support in the postoperative period and being on call in case the patient feels something different can be very helpful in intercepting issues;
4. manage postoperative pain, which is generally achieved in all patients using acetaminophen (1000 mg tablets 3 per day): a safe drug for BrS patients who provides antipyretic effects;
5. recommend that the patient stay at home for 24 hours after the hospital discharge if diazepam is administered due to its long-lasting effect.

DISCUSSION

BrS is a disease that should not be underestimated because it may lead to life-threatening arrhythmia. Hence, dentists must conduct a thorough examination when they take the patient's medical history.

If the individual experiences symptoms of arrhythmias (syncope, seizures, fainting, convulsions, and gasping breathing) (8, 9) and has a family member who was affected by BrS (or had sudden cardiac death under 45 years of age) (7), the dentist should recommend a cardiological examination. If the individual has already been diagnosed with BrS by a cardiologist, the dentist should take all the possible precautions to avoid complications. For the effective and safe management of these patients, providing a dental treatment environment that minimizes stress as much as possible and avoids clinical triggers for arrhythmic events is crucial.

The triggers that could induce arrhythmias include fever (26), nausea and vomiting (27), dental anxiety (31), postoperative pain (42), and the avoidance of unsafe drugs (e.g., bupivacaine and procaine have been demonstrated to be unsafe, so their use is not tolerated (45-47).

Before, during, and after oral surgery procedures, dentists should follow the established guidelines to manage these patients accurately. Dentists should also collaborate with other figures, such as cardiologists and anesthesiologists, to assist BrS patients in a hospital setting; this is vital for the patient's safety and the outcome of the procedure.

For instance, Theodotou reported a case where a BrS patient with an ICD needed a tooth extraction. The dentist consulted the patient's cardiologist, who recommended turning off the patient's ICD and completing the procedure under general anesthesia in the operating room. Once the surgery was completed, the ICD had to turn on (32). The ICD was turned off because the surgery may have involved the use of electrocautery; thus, to prevent the risks of electromagnetic interference, the anti-tachycardia functions of ICD were deactivated during surgery if electrocautery had to be used during the surgery (31, 46).

Anesthesiologists are also key, as they help the dentist in a hospital setting in performing general anesthesia, local anesthesia, and conscious sedation with the right doses and techniques (21).

Another fundamental factor lies in the meticulous maintenance of professional oral hygiene, which reduces bacterial and viral load and preserves the patient from related risks (48-50).

If a thorough medical history is not performed, or it is inaccurate or incomplete, risks are likely possible. Therefore, the dentist may make several errors, leading to medico-legal implications. In an accusation of negligence by either the patient or the patient's relatives, the legal system relies primarily on documentary evidence (i.e., medical history). Therefore, improper record-keeping may result in a penalty.

CONCLUSIONS

Within the limited evidence, dental procedures for individuals suffering from BrS may be considered safe if the patient is monitored regularly, the unsafe drugs are avoided, and the patient's dental anxiety is reduced as much as possible. Hence, a thorough medical history must be obtained to reduce the risk of complications and potential medico-legal implications. More studies are needed to investigate this topic further.

Conflict of interest statement
The authors declare no conflict of interest.

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Evaluation Study

PERIODONTAL HEALTH COMPARED IN CHAMFER AND BIOLOGICALLY ORIENTED PREPARATION TECHNIQUE APPLIED TO AESTHETIC RESTORATION: PROSPECTIVE CLINICAL STUDY AT ONE-YEAR FOLLOW-UP

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ABSTRACT

The aim of this study was to compare prosthetic tooth preparation performed using the Chamfer and the Biologically Oriented Preparation Technique (B.O.P.T.) to analyze which of them performs better in maintaining the long-term health and trophism of the periodontal supporting tissues. From January 2020 to January 2022, patients requiring fixed tooth-supported rehabilitation in anterior regions were randomly selected for this clinical study, performed at the Department of Dentistry at San Raffaele Hospital, Milan, Italy. The sample was randomly divided into two categories: Group 1 (Chamfer preparation); Group 2 (B.O.P.T. preparation). Clinical periodontal measurements were taken to assess the health status of marginal tissues at time zero, i.e., at the time of preparation, at the time of provisional prostheses, and 12 months after time zero (after definitive prostheses had been fitted). Following the inclusion and exclusion criteria, eight patients were recruited, four of whom were treated with the Chamfer technique (Group 1) and the same number with B.O.P.T. (Group 2). Within the limitations of this study, based on the results obtained evaluating 12 months, it was concluded that no technique is significantly better and more predictable than the other about periodontal health status.

KEYWORDS: *B.O.P.T, chamfer, periodontal health, fixed prosthesis, periodontal index*

INTRODUCTION

Fixed prosthetic restorations allow the rehabilitation of the stomatognathic system, both for functional and aesthetic purposes, employing natural elements as supporting frameworks (1-3). Dental tissues do not have the regenerative capabilities found in most other areas of the human body. Hence, removing biological tissue for prosthetic purposes is irreversible and requires considerable attention and care to several details (4).

An ideal prosthetic preparation should allow the creation of a prosthetic restoration in continuity with the unprepared section of the tooth (5). The two key elements to ensure a fixed prosthetic restoration's long-term aesthetic and functional stability are the prosthetic margin and the precision of prosthetic abutment closure (6, 7). Together, they

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provide the finishing margin, i.e., the transition point between the intact part of the tooth and the most apical extension of the abutment preparation on which the prosthetic finishing is to be adapted (8, 9).

The purpose of the prosthetic margin is to create a precise seal that opposes bacterial infiltration. Failure to do so would promote bacterial plaque build-up, which, by penetrating the crown, would destroy the cement, resulting in secondary caries (10, 11). In addition, the aim of prosthetic finishing is to restore the correct prosthetic profile and, in aesthetic cases, to allow the execution of a correct and stable emergence over time (12, 13).

One of the main complications in fixed prostheses on natural teeth or dental implants encountered by clinicians is the unsatisfactory aesthetic result due to apical migration of the gingival margin (14). Furthermore, a critical requirement to be obtained before proceeding with tooth preparation is periodontal health, which may be successfully achieved through patient motivation for proper home and professional oral hygiene (15,16), scaling and root planning (17), periodontal surgery and laser therapy, in combination or not (18, 19), for the improvement of short-term clinical indices and in low-level modalities for the improvement of tissue healing and regeneration to provide a predictable result over time. Among the factors related to restorative procedures, one plays a crucial role: preparation technique and related finish line geometry (20).

The aim of this study is to compare teeth prosthetic preparation in aesthetic areas by applying the 'Chamfer' technique, commonly recognized as the most widely employed by clinicians (21), with the reinterpretation of the finishing technique proposed by Ribka et al. (22) and defined Biologically Oriented Preparation Technique (B.O.P.T) concerning their effect on periodontal health.

MATERIALS AND METHODS

Sample selection

From January 2020 to January 2022, patients requiring fixed tooth-supported rehabilitation in anterior regions were randomly selected for this clinical study, performed at the Department of Dentistry at San Raffaele Hospital, Milan, Italy. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethical committee approval number is CE/INT/10/2015.

Requirements for inclusion were fixed tooth-supported rehabilitations at anterior sectors, observance of the predetermined protocol with compliance towards the scheduled check-up visits, and professional oral hygiene sessions. Patients requiring tooth-supporting rehabilitation of posterior teeth and/or unable to adhere to protocol sittings were excluded.

a. Sample division

The sample was randomly divided into two categories: Group 1 (Chamfer preparation); Group 2 (B.O.P.T. preparation).

b. Clinical outcomes

According to the inclusion and exclusion criteria, once the patients had been selected and the treatment plan had been presented to them, clinical measurements were taken to assess the health status of marginal tissues at time zero, i.e., at the time of preparation, at the time of provisional prostheses and 12 months after time zero (after definitive prostheses had been fitted).

These measurements were performed with a periodontal probe applying a force of approximately 0.2/0.3 N at 6 reference points of each tooth element (mesio-vestibular, central-vestibular, disto-vestibular, mesio-lingual/palatal, central-lingual/palatal, disto-lingual/palatal). The clinical parameters considered during the survey were:

- presence or absence of plaque (PI);
- bleeding on probing (BoP), assessed as present if bleeding is evident within the 30s of probing or absent if no bleeding is noted within 30s of probing;
- presence or absence of suppuration (PUS);
- probing pocket depth (PPD) measured from the mucosal margin to the bottom of the probable pocket;
- recession (REC) measured from the mucosal margin to the margin of the restoration.

These parameters allowed a periodontal diagnosis and the presence or absence of inflammation and inflammation in the gingival tissues to be identified. Each patient was placed in a professional oral hygiene program that would allow for limiting complications, preventing inflammation, and monitoring and interception of any complications.

c. Statistical analysis

The researchers used Python 3.8.5 and several statistical packages (math, SciPy, and pandas) to perform statistical analyses on the recorded data. The specific tests depended on the sample distribution, variance, and experimental setup and included independent-sample parametric t-tests, Pearson's chi-square tests, and z-tests.

The researchers applied a significance level of $p < 0.05$ to determine whether the differences between the groups were statistically significant. The data were analyzed at an aggregate level, meaning they examined overall patterns and trends rather than individual data points.

To examine differences in periodontal parameters between Group 1 and Group 2, the researchers used Pearson's chi-square and z-tests. The null hypothesis was that there were statistically significant differences between the groups compared.

RESULTS

Following the inclusion and exclusion criteria, eight patients were recruited, four of whom were treated with the Chamfer technique (Group 1) and the same number with B.O.P.T. (Group 2). As a descriptive support of the procedures performed, clinical cases illustrating prosthetic procedures and the evaluation of periodontal parameters follow.

Clinical cases with Chamfer preparation (Group 1)

Case 1: Prosthetic preparation and rehabilitation with Chamfer technique of aesthetic sectors 16 to 14 and 34 to 44 (Fig. 1).

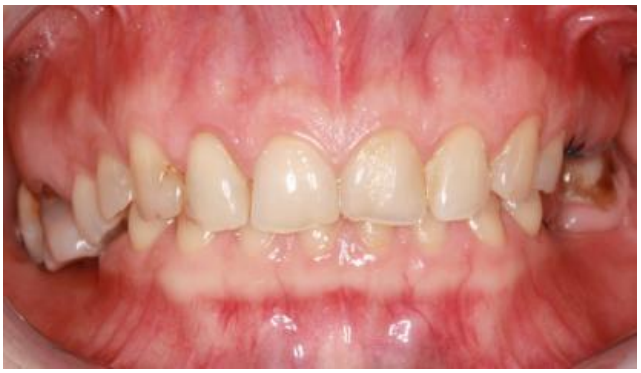


Fig. 1. *Patient's smile in maximum intercuspation before prosthetic treatment.*

The patient came intending to improve the aesthetics of a smile that has lost vertical height over time; the four incisors are markedly remodeled by the parafunctions that occurred during life, which significantly worsened the aesthetic and functional aspects (Fig. 2).

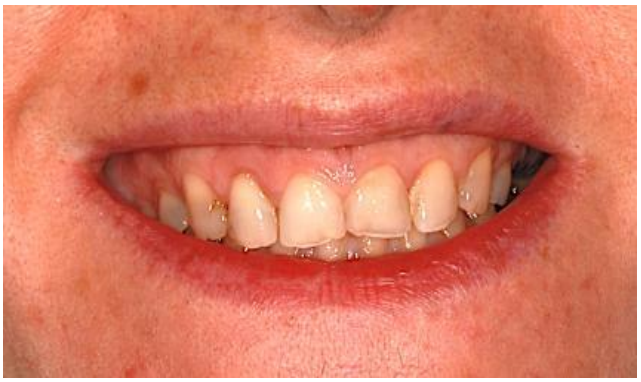


Fig. 2. *Natural smile of the patient in which aesthetic imperfections of the anterior sectors can be noted.*

Before the prosthetic rehabilitation treatment, mouth rinse with hydrogen peroxide, iodine, povidone, and chlorhexidine was recommended to reduce the existing bacterial load.

Before starting with the preparation of the dental elements, a periodontal chart was performed to compare recession (REC) and probing depth (PPD) before, during, and after the preparations and in the two subsequent moments of treatment. Subsequently, we proceeded first with the preparation of the dental elements (Fig. 3)

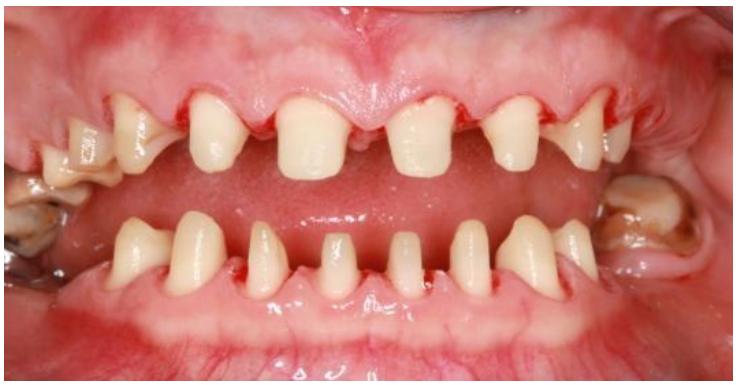


Fig. 3. *Prosthetic abutments at the end of preparation, Chamfer technique.*

Therefore, the prosthetics of the latter, with the temporary artifacts, should already try to replicate all the functions that must be present in the definitive ones (Fig. 4).

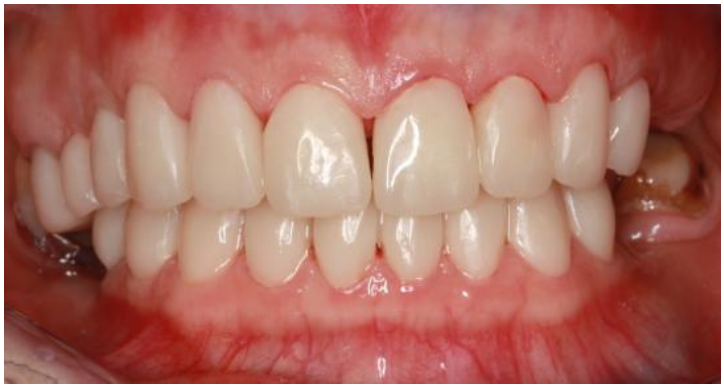


Fig. 4. *Temporary application.*

After 6 months, the periodontal parameters of our interest were resumed to verify the state of health and healing of the tissues with the application of temporaries. Finally, the definitive artifacts are applied, having functions and aesthetic characteristics obtained over time thanks to the temporaries and the changes that could be made to them (Fig. 5).

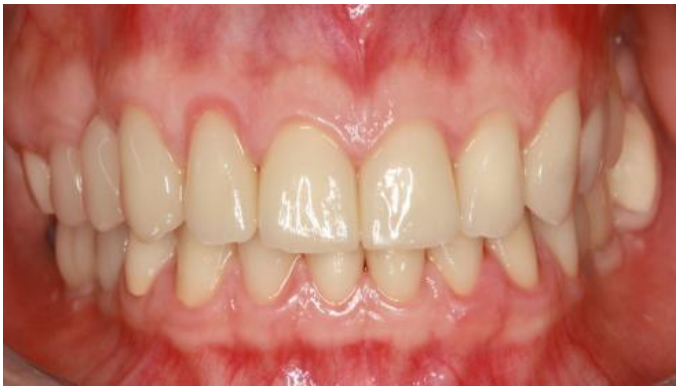


Fig. 5. *Final result. The smile is in maximum intercuspation after the application of the defined ones. You can see the restoration of a correct vertical height, also thanks to the insertion of implants and crowns in the posterior sectors and an improvement in the Spee line.*

It is very significant, as in clinical cases of this type, the psychological implications of the patient are fundamental and should never be underestimated. Through such important rehabilitation, it is possible to distort people's smiles and touch emotional aspects that will lead to a relationship of mutual gratitude and trust between doctor-patient, which is increasingly difficult to obtain today.

Clinical cases with B.O.P.T. preparation (Group 2)

Case 2: Prosthetic preparation and rehabilitation with B.O.P.T. elements 15 to 25 and 34 to 44 (Fig. 6).

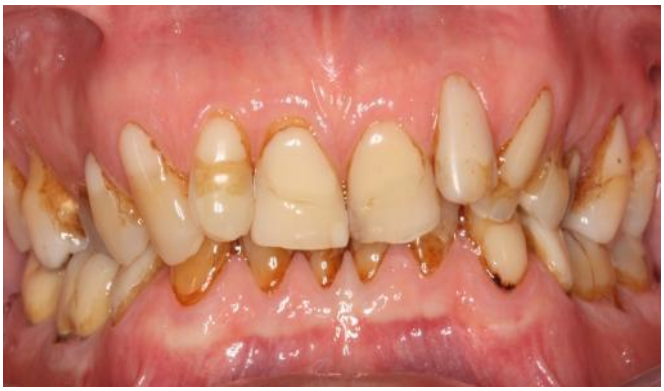


Fig. 6. *Smile in maximum intercuspation before starting the prosthetic treatment.*

It is emblematic, in clinical cases of this kind, how, during life, the chroma of a smile can be altered due to bad habits, or the inappropriate use of drugs can create permanent discoloration. In this case, the patient turns out to be a heavy smoker. This habit has been going on for many years now, which is why numerous discolorations both at the level of the upper and lower arches and both on the vestibular and interproximal sides can be easily noticed from a simple frontal view.

We then proceed with mapping the furrows, a fundamental step to know where and how much to deepen the preparation to end up inside the free gingiva. After obtaining a precise idea of the various probing depths, we proceeded to prepare the dental elements using the finishing drills (Fig. 7).

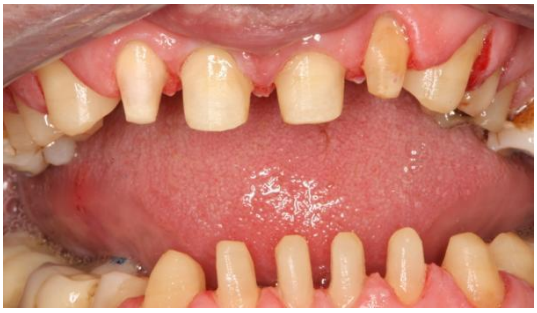


Fig. 7. *Preparation to finish 15 to 25 and 34 to 44.*

Immediately after the preparations, the temporaries were inserted, following the concepts that must then also be transmitted to the definitive ones: for example, the presence of the so-called "gull wings" which allow a moderate increase in the thickness of the marginal gingival tissue, which will follow the shapes and the anatomies that we have been able to give to our crowns and adapt them within the sulcus(Fig. 8).

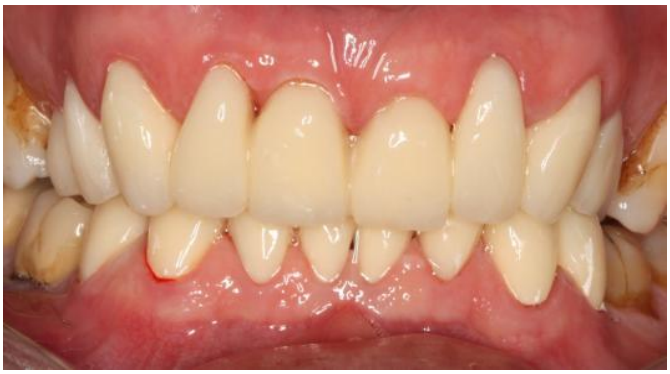


Fig. 8. *Smile in maximum intercuspidation with the temporaries inserted.*

As a final step, all the functional and adaptation information to the gingival tissues was transferred from the provisional to the definitive one, which simply must be more performing from an aesthetic point of view while maintaining everything that has been obtained in the previous months through use and changes made on the temporaries (Fig. 9, 10).

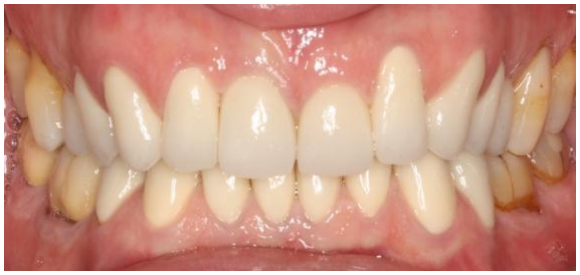


Fig. 9. *Result in maximum intercuspation after applying the definitive ones.*

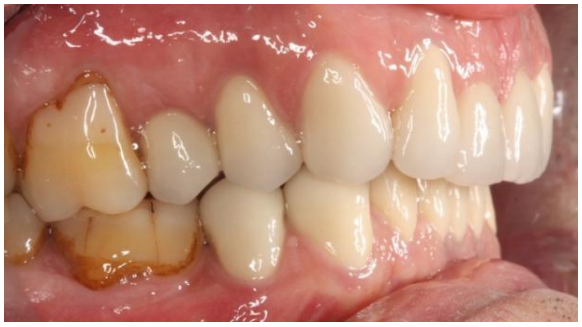


Fig. 10. *Lateral view of the final artifacts, in which you can appreciate the excellent periodontal health and the adaptation of the gingival margins on the crown profile.*

Finally, 12 months after the preparations, the last two periodontal records were drawn up to verify the change in the marginal periodontal tissues after 12 months.

All the values of the periodontal records of each patient have been reported, making a first major distinction in two sample groups: those who have undergone prosthetic treatment through chamfer preparation and those who have undergone prosthetic treatment through preparation to finish with B.O.P.T (Table I).

Table I. *Patient numbers are given according to Chamfer or B.O.P.T. preparation.*

Patient number	Technique Preparation
1	CHAMFER
2	CHAMFER
3	CHAMFER
4	CHAMFER
5	BOPT
6	BOPT
7	BOPT
8	BOPT

For each of these patients, a periodontal chart was drawn up with the values of recession (REC) and probing depth (PPD) in three distinct moments of the prosthetic treatment to verify the long-term adaptation and reaction of the marginal periodontal tissues in the aesthetic sectors. The second table shows the values of the dental elements before starting the prosthetic therapy, all those treated with the chamfer preparation or at the baseline in yellow and those with B.O.P.T. in green (Table II). The same thing was done for both preparations after 6 months (Table III).

Table II. *Values recorded before treatment.*

		Ms	Md	D	Ms	Md	D	Ms	Md	D	Ms	Md	D	
1	16	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	15	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	14	0	0	0	0	0	0	4	4	4	2	3	2	CHAMFER
1	13	0	0	0	0	0	0	3	4	4	2	3	2	CHAMFER
1	12	0	0	0	0	0	0	3	3	3	2	3	2	CHAMFER
1	11	0	0	0	0	0	0	3	2	3	2	3	2	CHAMFER
1	21	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	22	0	0	0	0	0	0	2	2	2	3	3	3	CHAMFER
1	23	0	0	0	0	0	0	2	3	2	2	3	2	CHAMFER
1	24	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	34	-2	0	0	0	0	0	2	2	2	3	2	0	CHAMFER
1	33	0	0	0	0	0	0	2	3	2	3	3	3	CHAMFER
1	32	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	31	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	41	0	0	0	0	0	0	3	3	3	2	2	2	CHAMFER
1	42	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	43	0	0	0	0	0	0	2	3	2	2	2	2	CHAMFER
1	44	0	0	0	0	0	0	2	3	2	3	3	3	CHAMFER
2	13	-2	-3	-2	-1	-1	-2	2	3	2	1	1	1	CHAMFER
2	12	-3	-2	-3	-1	-1	-1	3	2	3	2	1	0	CHAMFER
2	11	-2	-2	-2	-2	-2	-2	2	2	2	0	1	0	CHAMFER
2	21	-2	-3	-3	-1	-2	-1	2	3	3	1	1	1	CHAMFER
2	22	-2	-1	-2	-1	-1	-1	2	1	2	0	1	0	CHAMFER
2	23	-2	-1	-2	-1	-2	-1	2	1	2	1	2	1	CHAMFER
2	32	-2	-2	-2	0	-1	-1	2	2	2	1	0	1	CHAMFER
2	31	-3	-3	-3	-2	-2	-1	3	3	3	0	1	0	CHAMFER
2	41	-2	-2	-2	-2	-2	-2	2	2	2	1	1	1	CHAMFER
2	42	-1	-2	-1	-1	-1	-1	1	2	2	1	1	1	CHAMFER
3	13	-3	-3	-3	-1	-2	-1	4	2	2	0	0	0	CHAMFER
3	12	-2	-2	-2	-1	-2	-1	1	2	2	0	0	0	CHAMFER
3	11	-3	-2	-3	-2	-3	-2	2	3	4	0	0	0	CHAMFER
3	21	-3	-2	-3	0	-2	-3	2	2	2	0	0	0	CHAMFER
3	22	-3	-2	-3	-1	-2	-1	2	2	2	0	0	0	CHAMFER
3	23	-2	-2	-2	0	-1	-2	5	5	5	0	0	0	CHAMFER
4	12	-2	-2	-2	-2	-1	-2	2	2	2	2	1	2	CHAMFER
4	11	-2	-2	-2	-2	-2	-2	2	2	2	2	2	2	CHAMFER
4	21	-2	-3	-3	-2	-2	-2	2	3	3	2	2	2	CHAMFER
4	22	-2	-3	-2	-2	-2	-2	2	3	2	2	2	2	CHAMFER
5	15	0	-2	0	-1	-1	-1	0	2	0	0	0	0	BOPT
5	14	-3	-4	-3	-2	-2	-1	3	4	3	2	1	2	BOPT
5	13	-2	-3	-2	-1	-2	-1	2	3	2	2	3	1	BOPT
5	12	-2	-1	-2	-1	0	-2	2	1	2	1	2	2	BOPT
5	11	-1	-2	-3	-2	-2	-1	1	2	3	1	2	1	BOPT
5	21	-3	-2	-2	-2	-3	-3	3	2	2	2	2	3	BOPT
5	22	-3	-2	-3	-3	-1	-1	5	4	5	3	2	2	BOPT
5	23	-3	-2	-1	-2	-2	-2	3	2	1	3	2	1	BOPT
5	24	-2	-2	-3	-2	-2	-1	2	2	3	1	2	2	BOPT
5	25	0	0	0	0	0	0	0	0	0	0	0	0	BOPT
5	34	-1	-2	-3	-2	-2	-1	1	2	3	2	2	1	BOPT
5	33	-2	-1	-3	-2	-1	-2	2	1	3	2	1	2	BOPT
5	32	-2	-3	0	-1	-2	0	2	3	0	3	1	1	BOPT
5	31	-2	-3	-2	-2	-3	-3	2	5	2	2	3	4	BOPT
5	41	-3	-3	-2	-2	-2	-2	2	3	2	2	2	2	BOPT
5	42	-3	-3	-2	-3	-3	-2	3	3	2	3	2	2	BOPT
5	43	-2	-1	-2	-1	-1	-2	4	1	4	2	3	3	BOPT
5	44	-3	-2	-3	-2	-1	-2	5	4	5	3	3	4	BOPT
6	14	-3	-3	-3	-2	-1	-2	3	3	2	2	0	0	BOPT
6	13	-3	-2	-3	-1	-1	-2	3	2	3	0	0	0	BOPT
6	12	-2	-2	-2	-2	-2	-1	3	3	3	0	0	0	BOPT
6	11	-3	-2	-2	-1	-2	-1	3	2	3	0	0	0	BOPT
6	21	-2	-2	-2	-1	-1	-1	3	3	3	0	0	0	BOPT
6	22	-2	-2	-1	-1	-2	-1	3	2	3	0	0	0	BOPT
6	23	-2	-2	-2	0	-1	-2	3	3	2	0	0	0	BOPT
6	24	-2	-2	-3	-1	-2	-1	2	3	2	0	0	0	BOPT
7	14	-1	-2	-1	0	0	0	0	0	0	2	3	2	BOPT
7	13	-2	-2	-3	-2	-2	-3	0	0	0	0	0	0	BOPT
7	12	-3	-4	-3	-2	-2	-2	0	0	0	0	0	0	BOPT
7	11	-2	-1	-2	-2	-2	-2	0	0	0	0	0	0	BOPT
7	21	-3	-1	-3	-2	-2	-2	0	0	0	0	0	0	BOPT
7	22	-3	-1	-4	-2	-2	-2	0	0	0	0	0	0	BOPT
7	23	-2	-3	-2	-2	-2	-2	0	0	0	0	0	0	BOPT
7	24	-2	-2	-2	-2	-2	-3	0	0	0	0	0	0	BOPT
8	12	-3	-1	-3	-2	-1	-2	0	0	0	0	0	0	BOPT
8	11	-3	-2	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
8	21	-2	-2	-3	-2	-2	-3	0	0	0	0	0	0	BOPT
8	22	-3	-3	-2	-3	-3	-2	0	0	0	0	0	0	BOPT
8	32	-3	-3	-2	-1	-2	-1	5	5	3	0	0	0	BOPT
8	31	-2	-2	-1	-1	-1	-3	5	5	5	0	0	0	BOPT
8	41	-2	-3	0	0	-2	0	5	5	5	0	0	0	BOPT
8	42	-2	-2	-2	-2	-1	-2	7	6	6	0	0	0	BOPT

In the first column, the number corresponding to the patient was annotated, and in the second, the tooth treated. In the third and fourth columns, vestibular and palatal/lingual recession were entered, respectively. In the fifth and sixth columns, vestibular and palatal/lingual PPD were entered, respectively. In the last column, the type of preparation performed was described.

Table III. *Values were recorded 6 months after treatment.*

		Ms	Md	D	Ms	Md	D	Ms	Md	D	Ms	Md	D	
1	16	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	15	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	14	0	0	0	0	0	0	4	4	4	2	3	2	CHAMFER
1	13	0	0	0	0	0	0	3	4	4	2	3	2	CHAMFER
1	12	0	0	0	0	0	0	3	3	3	2	3	2	CHAMFER
1	11	0	0	0	0	0	0	3	2	3	2	3	2	CHAMFER
1	21	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	22	0	0	0	0	0	0	2	2	2	3	3	3	CHAMFER
1	23	0	0	0	0	0	0	2	3	2	2	3	2	CHAMFER
1	24	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	34	-2	0	0	0	0	0	2	2	2	3	2	0	CHAMFER
1	33	0	0	0	0	0	0	2	3	2	2	3	3	CHAMFER
1	32	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	31	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	41	0	0	0	0	0	0	3	3	3	2	2	2	CHAMFER
1	42	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	43	0	0	0	0	0	0	2	3	2	2	2	2	CHAMFER
1	44	0	0	0	0	0	0	2	3	2	3	3	3	CHAMFER
2	13	-2	-3	-2	-1	-1	-1	2	3	2	1	1	1	CHAMFER
2	12	-3	-2	-3	-1	-1	-1	3	2	3	2	1	0	CHAMFER
2	11	-1	-2	-1	-1	-1	-2	1	2	1	0	1	0	CHAMFER
2	21	-2	-3	-3	-1	-2	-1	2	3	3	1	1	1	CHAMFER
2	22	-2	-1	-2	-1	-1	-1	2	1	2	0	1	0	CHAMFER
2	23	-2	-1	-2	-1	-2	-1	2	1	2	1	2	1	CHAMFER
2	32	-2	-1	-1	0	-1	-1	2	1	1	1	0	1	CHAMFER
2	31	-3	-2	-2	-2	-2	-1	3	2	2	0	1	0	CHAMFER
2	41	-2	-2	-2	-2	-2	-2	2	2	2	1	1	1	CHAMFER
2	42	-2	-2	-1	-1	-1	-1	2	2	1	1	1	1	CHAMFER
3	13	-3	-3	-2	-1	-2	-1	4	2	2	0	0	0	CHAMFER
3	12	-2	-2	-1	-1	-2	-1	1	2	2	0	0	0	CHAMFER
3	11	-3	-2	-3	-2	-3	-2	2	3	4	0	0	0	CHAMFER
3	21	-2	-2	-3	0	-2	-3	2	2	2	0	0	0	CHAMFER
3	22	-2	-2	-3	-1	-2	-1	2	2	2	0	0	0	CHAMFER
3	23	-2	-2	-1	0	-1	-2	5	5	5	0	0	0	CHAMFER
4	12	-2	-1	-2	-2	-1	-2	2	1	2	2	1	2	CHAMFER
4	11	-2	-2	-2	-2	-2	-2	2	1	2	2	2	2	CHAMFER
4	21	-2	-2	-2	-2	-2	-2	2	2	2	2	2	2	CHAMFER
4	22	-2	-2	-2	-2	-2	-2	2	2	2	2	2	2	CHAMFER
5	15	0	-2	0	-1	-1	-1	0	2	0	0	0	0	BOPT
5	14	-2	-3	-3	-1	-2	-2	3	3	3	2	1	2	BOPT
5	13	-2	-3	-2	-1	-2	-1	2	3	2	2	3	1	BOPT
5	12	-2	-1	-2	-1	0	-2	2	1	2	1	2	2	BOPT
5	11	-1	-2	-3	-2	-2	-1	2	2	1	1	2	1	BOPT
5	21	-3	-2	-2	-2	-3	-3	2	2	2	2	2	2	BOPT
5	22	-2	-2	-2	-3	-1	-1	4	3	4	3	2	2	BOPT
5	23	-3	-2	-1	-2	-2	-2	3	2	1	2	2	1	BOPT
5	24	-2	-2	-2	-2	-2	-1	2	2	2	1	2	2	BOPT
5	25	0	0	0	0	0	0	0	0	0	0	0	0	BOPT
5	34	0	-1	0	-2	-2	-1	2	0	0	2	2	1	BOPT
5	33	0	-1	0	-2	-1	-2	3	3	2	2	1	2	BOPT
5	32	-1	-2	-1	-1	-2	0	3	3	3	3	1	1	BOPT
5	31	-1	-1	-1	-2	-2	-3	3	3	3	2	2	3	BOPT
5	41	-1	-1	0	-2	-2	-2	4	3	3	2	2	2	BOPT
5	42	-1	-2	-1	-2	-3	-2	3	4	3	3	2	2	BOPT
5	43	-1	-1	0	-1	-1	-2	0	3	4	2	3	3	BOPT
5	44	-1	-2	0	-2	-1	-2	0	0	0	3	2	4	BOPT
6	14	-3	-3	-3	-2	-1	-2	3	3	2	0	0	2	BOPT
6	13	-2	-1	-2	-1	-1	-2	3	2	2	0	0	0	BOPT
6	12	-1	-1	-2	-2	-2	-1	3	2	3	0	0	0	BOPT
6	11	-2	-1	-2	-1	-2	-1	2	2	3	0	0	0	BOPT
6	21	-2	-1	-1	-1	-1	-1	2	3	3	0	0	0	BOPT
6	22	-1	-2	-1	-1	-2	-1	2	2	3	0	0	0	BOPT
6	23	-1	-2	-1	0	-1	-2	2	3	2	0	0	0	BOPT
6	24	-1	-2	-2	-1	-2	-1	2	2	2	0	0	0	BOPT
7	14	-1	-1	-1	0	0	0	0	0	0	2	3	2	BOPT
7	13	-2	-2	-3	-2	-2	-3	0	0	0	0	0	0	BOPT
7	12	-3	-4	-3	-2	-2	-2	0	0	0	0	0	0	BOPT
7	11	-2	-1	-2	-2	-2	-2	0	0	0	0	0	0	BOPT
7	21	-3	-1	-3	-2	-2	-2	0	0	0	0	0	0	BOPT
7	22	-2	-1	-4	-2	-2	-2	0	0	0	0	0	0	BOPT
7	23	-1	-2	-1	-2	-2	-2	0	0	0	0	0	0	BOPT
7	24	-1	-1	-1	-2	-2	-3	0	0	0	0	0	0	BOPT
8	12	-3	-1	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
8	11	-3	-1	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
8	21	-1	-2	-2	-2	-2	-1	0	0	0	0	0	0	BOPT
8	22	-2	-3	-2	-2	-3	-2	0	0	0	0	0	0	BOPT
8	32	-1	-2	-1	-1	-2	-1	3	3	3	0	0	0	BOPT
8	31	-1	-2	-1	-1	-1	-3	3	4	3	0	0	0	BOPT
8	41	-1	-2	0	0	-2	0	3	4	3	0	0	0	BOPT
8	42	-1	-2	-1	-2	-1	-2	4	4	4	0	0	0	BOPT

And finally, an evaluation after 12 months from preparation execution (Table IV).

Table IV. *Values were recorded 12 months after treatment (at the end of the follow-up period).*

		Ms	Md	D	Ms	Md	D	Ms	Md	D	Ms	Md	D	
1	16	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	15	0	0	0	0	0	0	4	4	4	2	2	2	CHAMFER
1	14	0	0	0	0	0	0	4	4	4	2	3	2	CHAMFER
1	13	0	0	0	0	0	0	4	4	3	2	3	2	CHAMFER
1	12	0	0	0	0	0	0	3	3	3	2	3	2	CHAMFER
1	11	0	0	0	0	0	0	3	2	3	2	3	2	CHAMFER
1	21	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	22	0	0	0	0	0	0	2	2	2	3	3	3	CHAMFER
1	23	0	0	0	0	0	0	2	3	2	2	3	2	CHAMFER
1	24	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	34	-2	0	0	0	0	0	2	2	2	3	2	0	CHAMFER
1	33	0	0	0	0	0	0	2	3	2	2	3	3	CHAMFER
1	32	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	31	0	0	0	0	0	0	2	2	2	2	3	2	CHAMFER
1	41	0	0	0	0	0	0	3	3	3	2	2	2	CHAMFER
1	42	0	0	0	0	0	0	2	2	2	2	2	2	CHAMFER
1	43	0	0	0	0	0	0	2	3	2	2	2	2	CHAMFER
1	44	0	0	0	0	0	0	2	3	2	3	3	3	CHAMFER
2	13	-1	-2	-1	0	0	-1	1	2	1	0	1	1	CHAMFER
2	12	-2	-1	-2	0	-1	-1	2	1	2	0	1	1	CHAMFER
2	11	0	-1	0	-1	-1	-1	0	1	0	0	1	0	CHAMFER
2	21	-2	-1	-1	0	-1	-1	2	1	2	0	1	1	CHAMFER
2	22	-1	-1	-2	0	0	-1	2	1	2	0	1	0	CHAMFER
2	23	-2	-1	-2	-1	-1	-1	2	1	2	1	1	1	CHAMFER
2	32	-1	-1	-1	0	-1	-1	1	1	1	1	0	1	CHAMFER
2	31	-2	-1	-1	-2	-2	-1	2	1	1	0	1	0	CHAMFER
2	41	-1	-1	-1	-2	-2	-2	1	1	1	1	1	1	CHAMFER
2	42	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	CHAMFER
3	13	-2	-2	-2	-1	-2	-1	4	2	2	0	0	0	CHAMFER
3	12	-1	-1	-1	-1	-2	-1	1	2	2	0	0	0	CHAMFER
3	11	-2	-2	-2	-2	-3	-2	2	3	4	0	0	0	CHAMFER
3	21	-2	-1	-2	0	-2	-3	2	2	2	0	0	0	CHAMFER
3	22	-2	-1	-2	-1	-2	-1	2	2	2	0	0	0	CHAMFER
3	23	-1	-1	-1	0	-1	-2	5	5	5	0	0	0	CHAMFER
4	12	-2	-1	-2	-2	-1	-2	2	1	2	2	1	2	CHAMFER
4	11	-2	-1	-2	-2	-1	-2	2	1	2	2	2	2	CHAMFER
4	21	-1	-1	-1	-1	-1	-1	1	1	1	2	2	2	CHAMFER
4	22	-1	-2	-1	-1	-2	-1	1	2	1	2	2	2	CHAMFER
5	15	0	-2	0	-1	-1	-1	0	1	0	0	0	0	BOPT
5	14	-2	-2	-3	-1	-2	-2	2	3	2	2	1	2	BOPT
5	13	-2	-2	-2	-1	-1	-1	2	2	2	2	3	1	BOPT
5	12	-2	-1	-1	-1	0	-2	2	1	2	1	2	2	BOPT
5	11	-1	-2	-2	-2	-1	-1	1	2	2	1	2	1	BOPT
5	21	-2	-2	-1	-2	-2	-2	2	2	2	2	2	2	BOPT
5	22	-1	-1	-2	-2	-1	-1	3	2	3	3	2	2	BOPT
5	23	-2	-1	-1	-2	-1	-2	2	2	1	2	2	1	BOPT
5	24	-1	-1	-2	-2	-1	-1	2	2	2	1	2	2	BOPT
5	25	0	0	0	0	0	0	0	0	0	0	0	0	BOPT
5	34	0	-1	0	-1	-2	-1	2	0	0	2	2	1	BOPT
5	33	0	0	0	-1	-1	-2	2	2	2	2	1	2	BOPT
5	32	-1	-1	-1	-1	-1	0	3	2	2	3	1	1	BOPT
5	31	-1	-1	-1	-2	-1	-2	2	2	2	2	2	3	BOPT
5	41	-1	0	0	-1	-1	-1	3	3	3	2	2	2	BOPT
5	42	0	-1	-1	-1	-2	-2	1	2	3	3	2	2	BOPT
5	43	-1	-1	0	-1	-1	-2	2	2	0	2	3	3	BOPT
5	44	-1	-1	0	-2	-1	-2	0	0	0	3	2	4	BOPT
6	14	-3	-2	-3	-2	-1	-2	3	3	2	2	0	0	BOPT
6	13	-1	-1	-1	-1	-1	-2	3	2	2	0	0	0	BOPT
6	12	-1	-1	-1	-2	-2	-1	3	2	3	0	0	0	BOPT
6	11	-1	-1	-2	-1	-2	-1	2	2	3	0	0	0	BOPT
6	21	-1	-1	-1	-1	-1	-1	2	3	3	0	0	0	BOPT
6	22	-1	-1	-1	-1	-2	-1	2	2	3	0	0	0	BOPT
6	23	0	-1	-1	0	-1	-2	2	3	2	0	0	0	BOPT
6	24	0	-2	-2	-1	-2	-1	2	2	2	0	0	0	BOPT
7	14	-1	-1	-1	0	0	0	0	0	0	2	3	2	BOPT
7	13	-1	-2	-2	-2	-2	-3	0	0	0	0	0	0	BOPT
7	12	-2	-3	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
7	11	-1	-1	-1	-2	-1	-2	0	0	0	0	0	0	BOPT
7	21	-2	-1	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
7	22	-1	-1	-3	-2	-1	-2	0	0	0	0	0	0	BOPT
7	23	-1	-2	-1	-2	-1	-2	0	0	0	0	0	0	BOPT
7	24	-1	-1	-1	-2	-1	-2	0	0	0	0	0	0	BOPT
8	12	-2	-1	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
8	11	-2	-1	-2	-2	-1	-2	0	0	0	0	0	0	BOPT
8	21	-1	-2	-1	-2	-2	-1	0	0	0	0	0	0	BOPT
8	22	-1	-2	-1	-2	-3	-2	0	0	0	0	0	0	BOPT
8	32	-1	-1	-1	-1	-2	-1	2	2	2	0	0	0	BOPT
8	31	-1	-1	-1	0	-1	-2	2	3	2	0	0	0	BOPT
8	41	-1	-1	0	0	-2	0	2	2	3	0	0	0	BOPT
8	42	-1	-1	-1	-1	-1	-2	3	3	3	0	0	0	BOPT

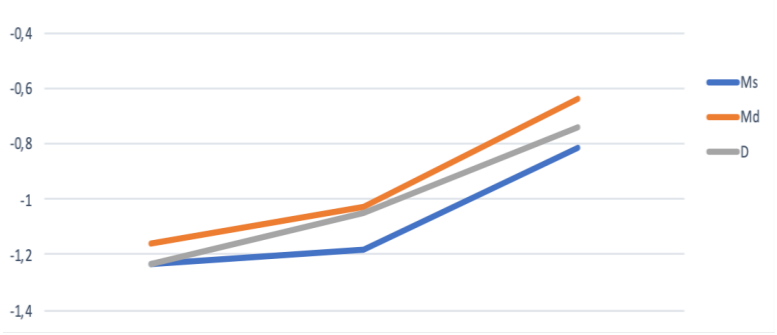
To give a value to the experimental study performed in vivo, a statistical analysis was carried out on the parameters taken into consideration clinically in the months in which the patients were treated and on which the various prosthetic steps were performed:

- first to prepare
- then for the immediate realization of the temporaries, which, for the purpose of their clinical usefulness, have been replaced by
- definitive prosthetic products

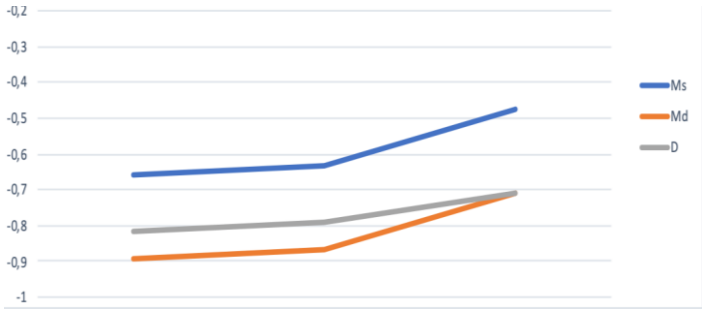
For each aspect that we have evaluated through the periodontal records, graphs have been produced that show us the changes, if any, of REC VESTIBULAR - REC PALATAL / LINGUAL - PPD VESTIBULAR - PPD PALATAL / LINGUAL for each site probed in each tooth over time:

- mesial
- medial
- distal

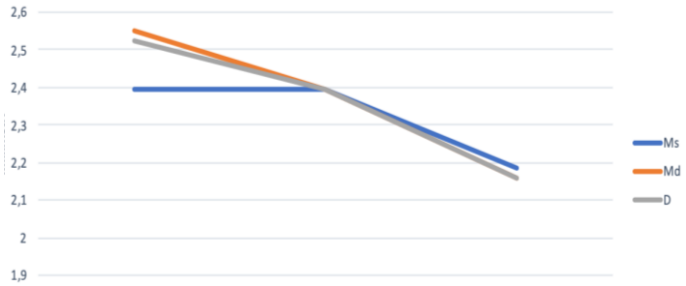
Statistical graphs on CHAMFER preparation
Graphs 1-8 show soft tissue remodeling over time.



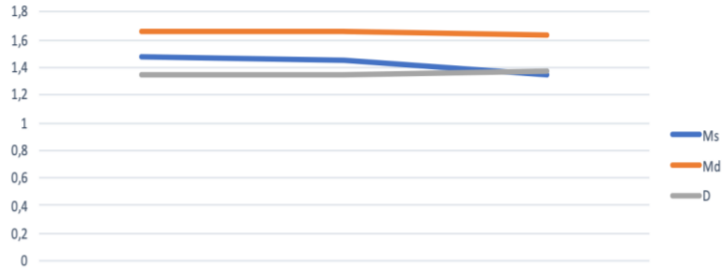
Graph 1. *Vestibular REC values were recorded before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*



Graph 2. *Palatal/lingual REC values were recorded before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*

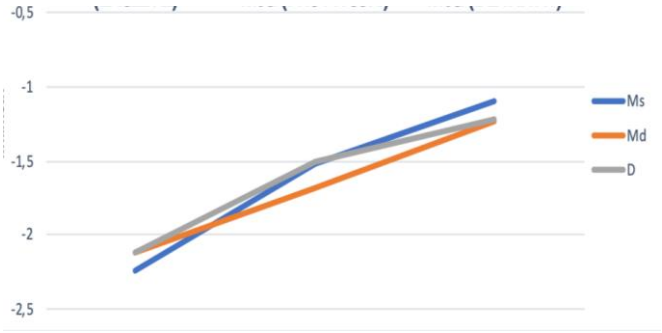


Graph 3. *The trend of the palatal and lingual PPD over time: before the procedure, after six months (with the provisional prosthesis), and at the end of the follow-up period (12 months) with the definitive prosthesis.*

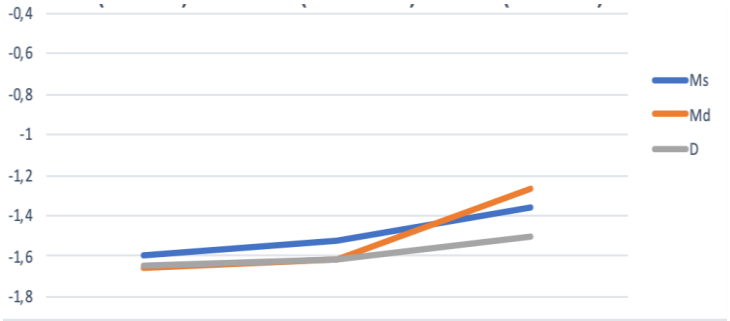


Graph 4. *Buccal PPD trend over time: before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*

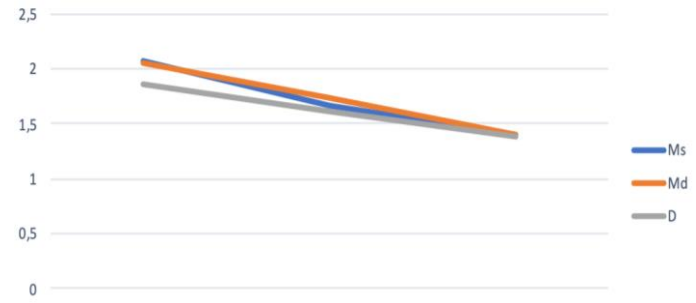
Statistical graphs on preparation to finish B.O.P.T.



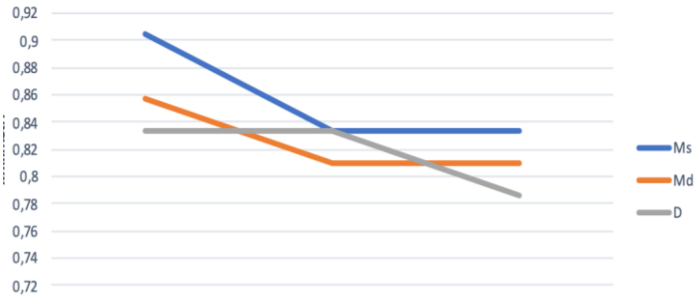
Graph 5. *Vestibular REC trend over time: before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*



Graph 6. *The trend of the palatal and lingual REC over time: before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*



Graph 7. *Vestibular PPD trend over time: before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*



Graph 8. *The trend of palatal and lingual PPD over time: before the procedure, after six months (with the provisional prosthesis) and at the end of the follow-up period (12 months) with the definitive prosthesis.*

Although the results from the clinical indices of the B.O.P.T. prepared teeth were clinically better than the control group (Chamfer preparation), no statistically significant differences were found between groups ($p>0.05$). The differences between the two groups at a 95% confidence level do not appear sufficiently significant to reject the null hypothesis. The two groups should be considered statistically not different.

DISCUSSION

The chamfer preparation accumulates numerous advantages of the other preparation techniques (23). It allows to obtain, in fact, a good marginal adaptation, having a net margin that is easily readable through the impression; minimum amount of tooth substance removed (problem encountered in the preparation at 90); net margin; good control of the position of the subgingival margin; good aesthetic result. The main indication of this type of preparation is full ceramic crowns in an area of considerable aesthetic value (24, 25). One of the biggest problems with all-ceramic restorations is their probable fracture against occlusal and lateral force (26).

A study conducted by Serra-Pastor et al. showed how the chamfer preparation could improve biomechanical performance, which may be due to the strong unity of the preparation margin itself (27, 28). Furthermore, the chamfer margin guarantees an adequate reduction of the thicknesses of the different restorative materials, especially in the fabrication of metal-ceramic restorations (29, 30).

Despite the advantages related to this technique, clinical execution is challenging (31, 32). For the preparation of a margin with the chamfer technique, the depth of the margin itself cannot exceed half the diameter of the drill used. Otherwise, the tip of the bur would create grooves, leaving an acute peripheral edge consisting only of enamel, which would be unsupported by dentin and easily fracture. Therefore, being able to use only half the diameter of the drill is very cumbersome and prevents its use in the interproximal spaces unless the adjacent tooth must also be prepared (33, 34).

The most common problem in fixed prosthetic restorations is the recession of the gingival margin, which can expose the finishing line of the dental prosthesis and which has been associated with the gingival phenotype (quality and quantity of keratinized gingival tissue), the iatrogenic effects of tooth preparation, chronic inflammation due to inadequate fit of the prosthetic margin and patient trauma (for example, traumatic tooth brushing).

The preparation of the tooth receiving the fixed prosthesis involves both the reduction of the tooth with diamond rotary instruments and the design of the finishing line (35). As reported by Schriwer et al., margin preparation with the BOPT technique could overcome these limitations (36). The criterion according to which it would be preferable to adopt

the BOPT technique concerns the creation of a new anatomical crown with a prosthetic emergence profile that simulates the shape of the natural tooth (37).

The BOPT technique allows to obtain a correction of the CEJ in unprepared teeth and the elimination of finishing lines in previously prepared teeth; the possibility of repositioning the prosthetic finishing line at different levels of the gingival sulcus at a depth of less than 0.5 to 1 mm, depending on the available biological width; the possibility of leveling the emergence profile and adapting it to the anatomy of the new cement-enamel prosthetic joint; the preservation of a greater dental structure; a more straightforward impression taking; the optimal restoration-tooth margin; and increased prosthetic retention due to the telescopic design of the prosthesis. Finally, it allows the gingiva to thicken and adapt to new shapes, leading to greater gingival stability in the medium and long term (38, 39). Compared to the chamfer preparation, with the BOPT technique, the finishing line is the margin itself of the prosthetic crown, and this margin can be modulated both in the provisional prosthetic and in the definitive one without affecting the "fitting" of the crown and the epithelial attachment.

Regarding periodontal support tissues, the BOPT technique allows to change the height of the gingival margin without any surgical intervention simply by modifying the emergence profile to make it more concave or more convex, which would allow the gums to thicken and adapt to the new shapes. In this way, it could be possible to obtain greater gingival stability in the medium and long term, improve the emergence profiles of the restorations, facilitate the maintenance of oral hygiene, and create a more natural appearance (40). The literature shows that, by adopting the BOPT technique, after one year, the risk of gingival recession can be considered negligible (41).

This is confirmed by a study by Galli et al., in which it is reported that the health of soft tissues can be maintained for a long time as the absence of a finishing line could favor an increase in the thickness of the keratinized gingiva margin, preventing the bacterial colonization and the consequent chronic inflammation leading to gingival recession (41, 42).

Although BOPT requires a greater learning curve, since the understanding of the localization of the margin of the restoration is not immediate due to the lack of a finishing line and the lack of experience in the execution of this technique by clinicians and technicians who could lead to causing accidental damage to the gingival sulcus (43), the results of our study confirm that the application of the method could represent a valid therapeutic alternative to chamfer.

CONCLUSIONS

Within the limitations of this study, based on the results obtained during the 12-month evaluation period, it was concluded that no technique is significantly better and more predictable than the other concerning periodontal health status.

Although there were better results in patients who were prepared with the B.O.P.T. technique, a correct clinical approach and careful case management at all stages of prosthetic rehabilitation do not promote one technique over the other. Further clinical studies may be necessary to confirm the obtained results.

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Retrospective Evaluation Study

FIVE-YEAR FOLLOW-UP STUDY ON FULL-ARCH IMPLANT-PROSTHETIC REHABILITATIONS: EVALUATION OF IMMEDIATE-LOAD PROCEDURES WITH DIGITAL PROTOCOLS

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ABSTRACT

The aim of this study was to evaluate, at a 5-year follow-up, full-arch implant-prosthetic rehabilitations. The main findings of the study revealed that immediate-load full-arch implant-prosthetic rehabilitations with digital protocols could represent an effective and predictable procedure to replace missing teeth. Patients with edentulousness of the maxilla, mandible, or both arches and/or impairment of the dental elements, such as those that required total restoration of one or both arches or insufficient residual bone height of the posterior sectors for the placement of traditional axial implants were ideal candidates for rehabilitation with the All-on-Four protocol or positioning of six axial dental implants supporting an immediate loading fixed prosthesis. The study also evaluated implant survival rate, the correlation between bone cortical thickness and width of keratinized gingiva (KG) and final prosthetic material, the correlation between bone cortical thickness and KG width and implant placement site (anterior or posterior), the correlation between bone cortical thickness and KG width and type of implant connection (external or internal), the correlation between peri-implant parameters and type of implant connection and patient satisfaction. Furthermore, in smoking patients, the correlation between bone cortical thickness and KG width associated with the number of cigarettes smoked per day was assessed.

KEYWORDS: *dental implants, immediate dental implant loading, implant-supported prosthesis dental, edentulous jaw*

INTRODUCTION

Immediate-loading dental implants could offer many advantages, including reduced treatment time, improved comfort, and increased patient satisfaction (1, 2). The combination of immediate loading and digital workflow offers several advantages, including improved accuracy, reduced treatment time, and increased patient satisfaction. Digital technology could also minimize the risk of errors and complications, leading to better treatment outcomes (3, 4).

Despite these many advantages, in the long term, even in implant-prosthetic rehabilitations performed with a digital workflow, complications may occur that negatively interfere with long-term follow-up (5). The most influential factors could be considered: bone cortical thickness, keratinized gingiva (KG) width, smoking, type of definitive

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prosthetic material used, and implant connection (internal or external) (6-8). Adequate cortical bone width is necessary for successful implant placement and osseointegration, which is the process by which the implant fuses with the surrounding bone (6).

Several factors could promote cortical bone resorption, such as age, hormonal imbalances, periodontal disease, trauma, and uncontrolled systemic diseases. In addition, improper implant placement or insufficient bone density may contribute to cortical bone resorption and implant failure (9-13).

The KG is the tough fibrous tissue that surrounds the teeth and forms a protective barrier between the teeth and the oral environment. In cases where the width around the fixtures is insufficient, the risk of implant failure increases, especially in areas where masticatory forces are greatest. In addition, insufficient KG may increase the risk of inflammation and infection around the implant due to the reduction of the protective barrier from the surrounding oral environment (14, 15). As for smoking (16), it may cause delayed healing or even implant failure, a reduction in bone density that may interfere with the osseointegration of dental implants, and the development of peri-implantitis (17, 18).

The choice of prosthetic materials, such as acrylic, ceramic, zirconia, and Polyether Ether Ketone (PEEK), in implant-prosthetic rehabilitation could be crucial for long-term success. Acrylic, valued for its slightness and malleability, may be the most appropriate choice for temporary prostheses as it is susceptible to wear; ceramic, having a high aesthetic impact, unlike zirconia, which is opaquer and, in this context, overlaps with PEEK, although less resistant, could be a viable alternative for definitive restorations (19, 20).

A crucial aspect influencing implant success is closely tied to the choice of implant-prosthetic connection, which directly impacts complications, encompassing variations such as tapered or screw-type connections that affect implant reliability, stability, masticatory force distribution, and the potential for long-term issues like loosening or microbial junctions, necessitating a specifical evaluation for optimal outcomes in implant rehabilitation (4).

The objective of this study was to evaluate, at a 5-year follow-up, full-arch implant-prosthetic rehabilitations concerning implant survival rate (first outcome) and correlation between bone cortical thickness (BCT) and width of KG and implant placement site (anterior or posterior), type of implant connection (internal or external), final prosthetic material and, in smoking patients, number of cigarettes smoked per day (secondary outcomes). The third outcome is a correlation between peri-implant parameters and implants 'connection (external connection *vs* internal Double Action Tight-DAT). As a final measure, patients' satisfaction was evaluated.

This report is written following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

MATERIALS AND METHODS

Patient selection

Between January and December 2018, a clinical trial was conducted at the Department of Dentistry, San Raffaele Hospital, Milan, Italy, involving the random selection of patients. Inclusion criteria encompassed individuals of all races and genders in good general health with satisfactory oral hygiene, physically and psychologically capable of undergoing implant-prosthetic rehabilitation (American Society of Anesthesiologists 1 and 2). Inclusion criteria extended to individuals with edentulous maxilla, mandible, or both arches or those experiencing dental impairments necessitating total restoration of one or both arches. Additionally, individuals with insufficient residual bone height in the posterior sectors for traditional axial implant placement are deemed ideal candidates for rehabilitation through the All-on-Four protocol or those possessing adequate overall residual bone height for placing six axial implants with immediate load prostheses.

The execution of all procedures involving human participants in this study adhered to the ethical standards established by the institutional and/or national research committee. The study conformed to the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. The approval number from the ethics committee is CE/INT/10/2015.

Implant-prosthetic protocol

Pre-surgical treatment

The diagnosis was performed clinically, using objective examination, and radiographically with Level I (Orthopantomography) and Level II (Cone Beam Computed Tomography), radiographic investigations to assess the level of impairment of the residual dental elements, morphology, and volume of the residual bone ridge, and to perform pre-surgical planning in each case.

All patients were given informed consent for the application of immediate loading and prosthetic rehabilitation procedures with digital workflow. Prior to surgery, all patients received a 2 g dose of Amoxicillin (Zimox, Pfizer Italia, Latina, Italy) one hour before the surgical procedure (19). The following figure represents an example of a clinical case treated with the described procedure (Fig. 1).

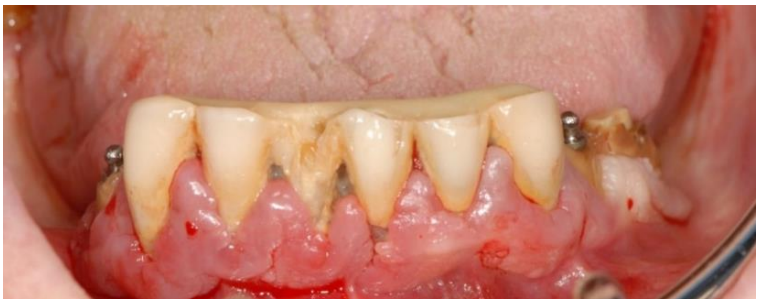

Fig. 1. *Pre-surgical clinical image.*

Surgical procedure

Anesthesia was induced through the local infiltration of lidocaine 20 mg/mL with 1:50,000 adrenaline (Ecocain, Molteni Dental, Florence, Italy). Incisions followed the alveolar ridge, extending bilaterally to expose the molar to the counter-lateral region of the residual bony ridge. Preserving KG on both margins of the horizontal incision facilitated suturing and ensured a biological seal at the soft tissue-implant interface. Surgical dissection, aligned with cleavage planes, proceeded at full thickness.

Implant sites adhered to manufacturer recommendations (Winsix typology TTx, BioSAF IN s.r.l, Ancona, Italy, and CSR implant system, Sweden & Martina, Due Carrare, Padova, Italy). Standard drills, guided by the palatal wall, prepared the implant sites, with the apical portion extending at least 4 mm beyond the apex. Post-preparation, implants (Winsix type TTx and CSR) were inserted, featuring a cylindrical body, tapered apex, and four cutting chambers for increased anti-rotational capacity, all crafted from grade 4 titanium (Fig. 2).

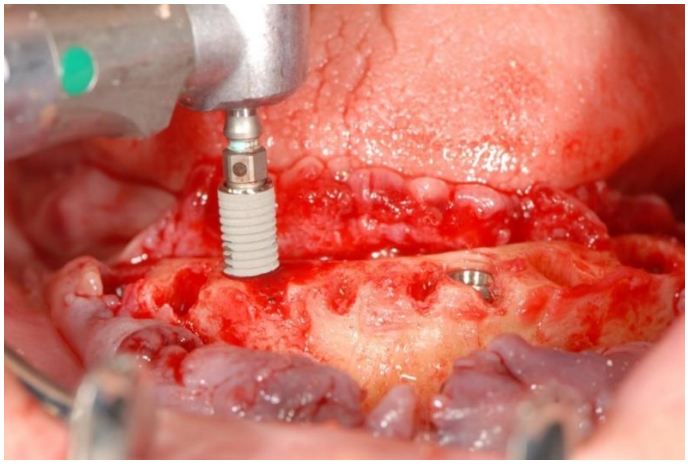

Fig 2. *Site preparation and implant placement.*

Based on posterior residual bone height, patients received 4 implants following the All-on-Four protocol or 6 axial implants (20).

Crestal leveling, if needed, utilized a "Bone scraper" for homogeneous subcrestal positioning, while bone recontouring occurred at inclined implant levels. The two anterior implants were axially positioned in cases of reduced bone density, and primary stability involved sub-preparation of implant sites. All implant elements achieved insertion with a minimum torque of 40 N-cm, placing the coronal margin apically 0.5 mm from the vestibular bone crest. Compensation for disparallelism, in the case of inclined implants, employed 17/30-degree pre-angled abutments to guide prosthetic screw access holes in occlusal or palatal positions (Fig. 3).

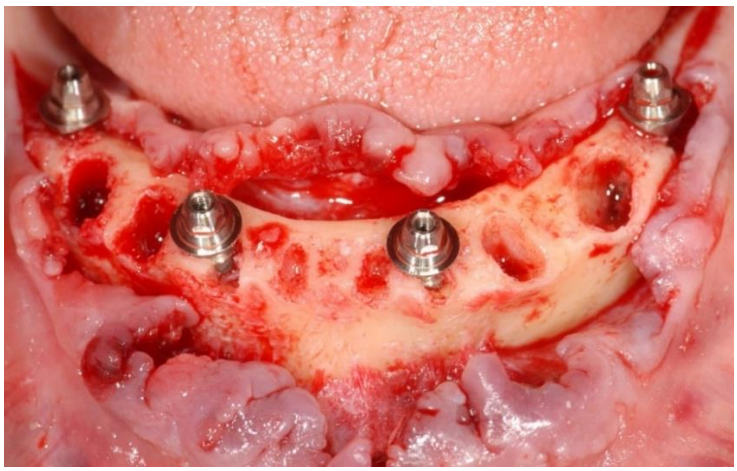

Fig. 3. *Abutment placement to offset disparallelism.*

Soft tissues underwent tension-free suturing with 3/0 resorbable thread sutures (Vicryl, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA).

Post-surgical treatment

Immediately post-surgery, patients were instructed to refrain from brushing to prevent traumatic effects. Prescriptions included non-steroidal anti-inflammatory drugs (Brufen 600 mg, Abbott Laboratories, Chicago, IL, USA), a 0.2% chlorhexidine digluconate mouthwash (Corsodyl, GlaxoSmithKline, Belgium) for a 2-week post-surgery period, and 1 g of Amoxicillin (Zimox, Pfizer Italia, Latina, Italy) to be taken twice daily for one week. Patients were advised to adopt a cold diet for the initial 24 hours after surgery, followed by a soft diet for the subsequent 2 months. Additionally, a follow-up orthopantomography was conducted (Fig. 4).

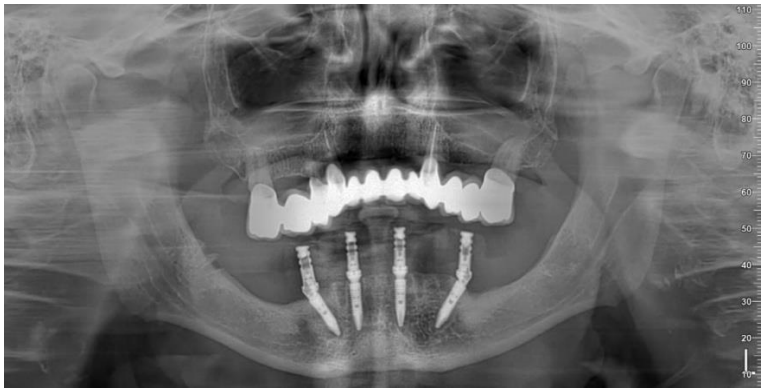

Fig. 4. *Post-surgical Orthopantomography.*

Each patient was placed in a professional oral hygiene program that would allow for both limiting complications, preventing inflammation, and monitoring and interception of any complications (21-24).

Provisional prosthetic rehabilitation

Preceding the surgical procedure, the vertical dimension of all patients was documented through facial landmarks. After surgery in both cohorts, provisional acrylic resin prostheses were directly relined in the patient's oral cavity using self-curing polyurethane resin (Voco, Fort Mill, SC, USA) (25, 26).

Within 24 hours, the prostheses were secured with a torque spanner at 15 N-cm. Verification and modification of static/dynamic occlusion and centric relation contacts were performed using a Bausch 40 μm articulating chart (Nashua, NH, USA). Centric and lateral contacts were confined to the intercanine area, ensuring the prosthesis's passivity. Lastly, a temporary material (Fermit, Ivoclar Vivadent, Naturno, Bolzano, Italy) was applied to cover the screw access holes.

Definitive prosthetic rehabilitation

After the completion of soft and hard tissue healing (4 months post-surgery), digital prosthetic procedures were initiated. The scan-body, serving as a replacement for traditional impression coping, was affixed using the same

methodology employed in conventional prosthetic techniques. The Carestream CS 3600 intraoral scanner (Version 3.1.0 Acquisition Software, Carestream Dental LLC, Atlanta, GA, USA) was uniformly utilized for all patients (27, 28). Employing the structured light principle, the Carestream system transformed the three-dimensional geometry of the dental arches into a virtual model (**Fig. 5**).

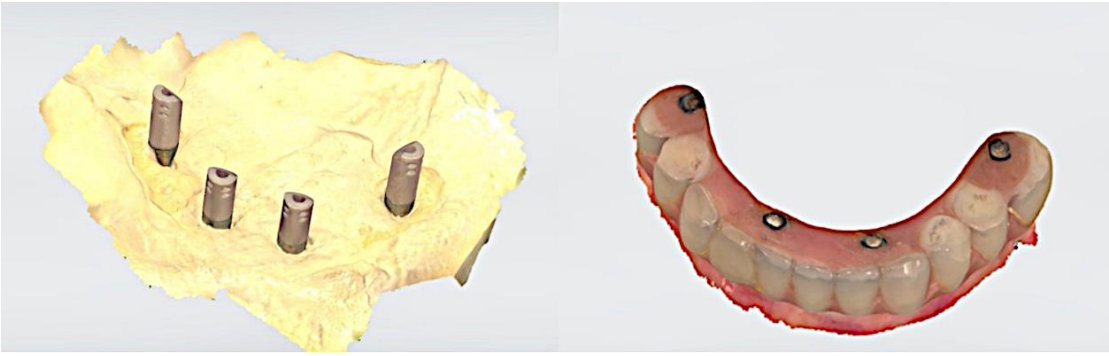

Fig. 5. *An example from the examined sample is a digital recording obtained through the Carestream digital system, which transforms the three-dimensional geometry of the dental arches into a virtual model.*

During the intraoral scanning process, the IOS light source was initially oriented parallel to the occlusal plane, starting from the distal implant elements on the left side and progressing towards the anterior implants on the contralateral quadrant (right side). The source was then repositioned behind the distal implants on the left side and tilted towards the palatal/lingual aspect. The occlusal plane was traversed towards the buccal aspect, and the scanner was moved from the starting point on the left side to the anterior implant on the right side, striving to maintain orthogonality to the occlusal plane. After this, the obtained image underwent meticulous analysis, and any incomplete areas were addressed through additional scanner passes. The same scanning sequence was replicated on the contralateral side.

Following the dental arch scans, the operator conducted a soft tissue scan and a scan of the provisional prosthesis with the analogs in place, ensuring alignment with each patient. The antagonist arch underwent a similar scanning process, followed by a scan capturing the buccal aspect of the patient's teeth in maximum intercuspation. The resulting 3D scans were exported in the standard tessellation format (.stl) (Fig. 6).

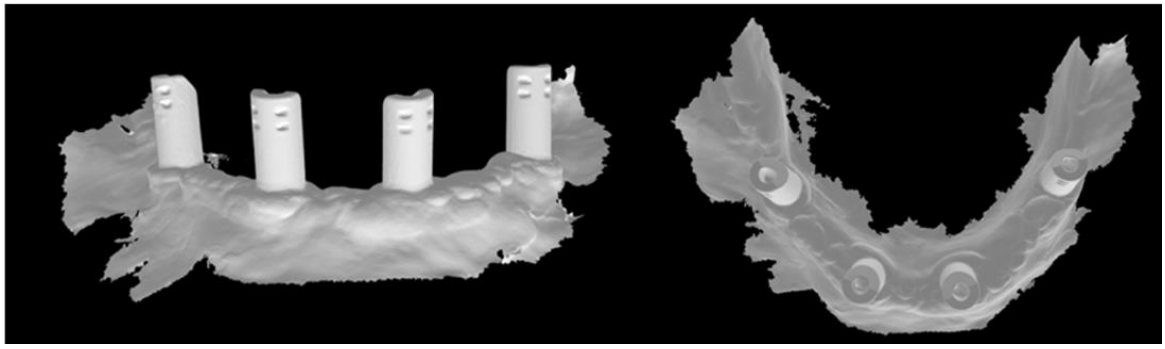

Fig. 6. *Example from the examined sample of standard tessellation format file analysis.*

The provisional prosthesis model, featuring implant analogs, was captured extraorally using a laboratory scanner (Neway, Open Technologies, Rezzato, Italy) to validate the precision and accuracy of the intraoral scan. When disparities emerged between the intraoral and extraoral scans, the restoration process deferred to the extraoral scan as a reference. All scans from the scanner underwent laboratory processing before being returned post-treatment. The virtual images underwent scrutiny for detail accuracy and the correct occlusal relationship.

The digital framework was generated using CAD software (Exocad Software, Darmstadt, Germany) upon completion of the virtual model with dental implants. Subsequently, the titanium framework was machined, concurrently using the prototype model to produce the final restoration (Fig. 7).

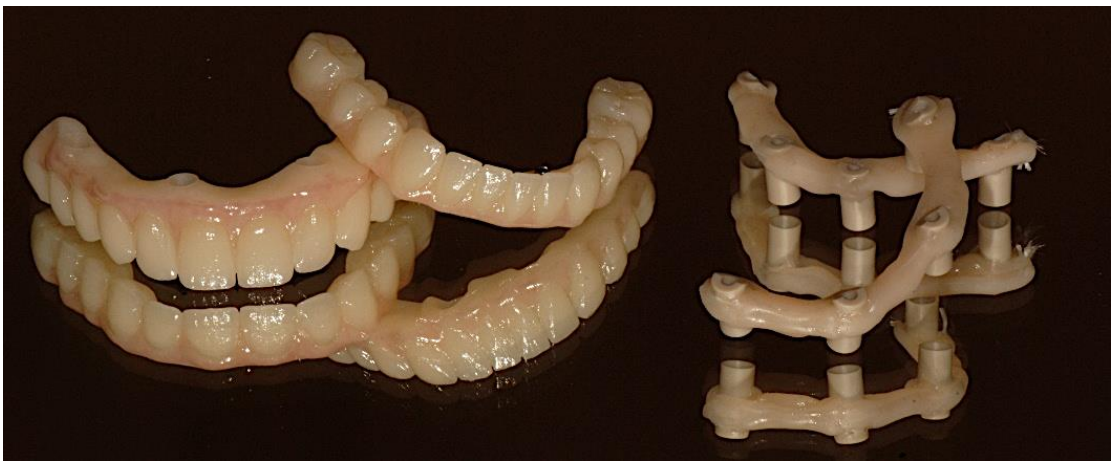

Fig. 7. *Aesthetic test and PEEK bar.*

The ultimate prosthesis, derived from the provisional prosthesis, incorporated meticulous attention to aesthetic, functional, and soft tissue details.

Following aesthetic evaluation, the prosthetic restoration reached its final form. Aesthetic tooth restoration material (Nacera Hybrid, Doceram Medical Ceramics GmbH, Dortmund, Germany) and soft tissue were added atop the mesostructure. Subsequently, the prosthesis was cemented with the titanium monostructure using a self-adhesive composite cement (RelyX Unicem, 3M, St. Paul, MN, USA).

All prostheses were affixed and secured onto the dental implants, and the Sheffield test was conducted to assess the framework's accuracy. An intraoral digital radiographic examination verified the marginal fit of the final prosthetic frameworks screwed onto the implants while articulating paper (Bausch Articulating Paper, Nashua, NH, USA) was employed to evaluate occlusion (29). Specifically, static occlusion involved central contacts across all masticatory units, while dynamic occlusion encompassed canine and premolar guidance. The screw access holes were covered with temporary resin (Fermit, Ivoclar Vivadent, Naturno, Bolzano, Italy). Impression technique results were analyzed based on the following criteria:

- accurate imprinting in the implant areas;
- absence of voids in the lingual, buccal, and occlusal regions;
- correct reproduction from the vestibule to the mucogingival junction. Impressions failing to meet these criteria were discarded, and the entire procedure was repeated.

Follow-up

Postoperative follow-up visits occurred at one week, three months, and six months after surgery, followed by annual visits for the subsequent five years. Professional oral hygiene sessions were conducted every four months post-surgery (30-32).

Clinical outcomes

Clinical outcomes were evaluated at a 5-year follow-up.

1. Implant Survival Rate. Implant survival was based on the number of implants lost during the follow-up period.
2. Correlation between bone cortical thickness (BCT), width of KG and implant placement site (anterior or posterior), type of implant connection (external connection *vs* internal Double Action Tight-DAT), final prosthetic material (layered ceramic zirconia *vs* cobalt chrome and acrylic resin) and, in smoking patients, number of cigarettes smoked per day.

The vestibular and lingual/palatal bone cortical thickness was evaluated through a three-dimensional cross-sectional examination, utilizing the intrinsic calibration and measurement tools within the employed software (MyRay v.10.1.0, Cefla s.c. Imola, Bologna, Italy). Horizontal bone thickness measurements, both vestibular and palatal, were determined at 1 - 3 - 5 mm apical to the implant neck. The measurements were independently performed by three operators, and the final value was derived by averaging the results obtained by each of the three operators (30, 31) (Fig. 8).

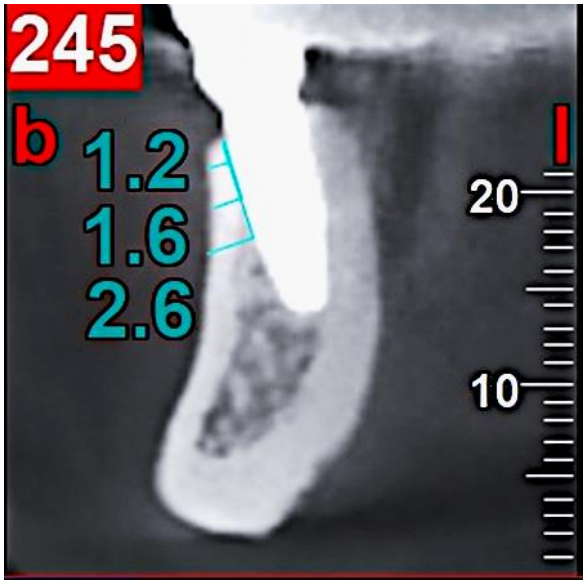

Fig. 8. *Measurement of horizontal bone thickness at 1 - 3 - 5 mm apical to the implant neck.*

Determining the width of KG around dental implants involves a meticulous process. A PCP UNC-15 millimeters periodontal probe (Hu Friedy, Chicago, IL) was employed to measure this parameter. The procedure begins by identifying key reference points—specifically, the mucogingival junction and the coronal margin of the free gingiva.

The clinician gently places the periodontal probe on the surface, ensuring a perpendicular orientation to the long axis of the implant. The measurement was then taken by carefully gauging the distance between the mucogingival junction and the coronal margin of the free gingiva. This value was recorded to the nearest millimeter. This process was repeated at multiple locations around the implant to enhance accuracy.

3. Correlation between peri-implant parameters and implants 'connection (external connection *vs* internal Double Action Tight-DAT).

The recorded peri-implant parameters encompassed the following metrics:

- modified Plaque Index (mPI): assessed on a scale where 0 indicates the absence of plaque and 1 denotes the presence of plaque;
- modified Bleeding Index (mBI): evaluated by observing bleeding during superficial probing at six sites, utilizing a scale where 0 signifies the absence of bleeding and 1 indicates the presence of bleeding;
- presence or absence of suppuration (PUS): identified by evaluating suppuration, with 0 denoting its absence and 1 indicating its presence;
- probing Depth (PD): measured at six points around the implant, reporting the maximum depth to the nearest millimeter for each analyzed area;
- recession (REC): quantified from the mucosa margin to the implant neck;
- KG width: gauged using a probe from the mucogingival junction to the coronal margin of the free gingiva.

All measurements were conducted employing a PCP UNC-15 millimeters periodontal probe (Hu Friedy, Chicago, IL), with a second clinician responsible for recording the data (32-34).

4. Degree of patient satisfaction

All patients were given a questionnaire with 12 questions, to which they had to give a score of 0 to 100 based on their experience (35). The questions are in the following figure (Fig. 9).

1. Are you satisfied with the treatment performed?
   (0 = very dissatisfied and 100 = very satisfied)
2. Are you satisfied with the functional result obtained?
   (0 = very dissatisfied and 100 = very satisfied)
3. Are you satisfied with the aesthetic result obtained?
   (0 = very dissatisfied and 100 = very satisfied)
4. Did you experience pain during which chairside surgical procedures?
   (0 = very painful and 100 = no pain)
5. Did you experience pain in the days following surgery?
   (0 = much pain and 100 = no pain)
6. Do you consider the time required for treatment to be justified?
   (0 = absolutely unjustified and 100 = absolutely justified)
7. Was the treatment carried out as planned?
   (0 = absolutely not and 100 = absolutely yes)
8. Did you develop bruxism (teeth grinding) problems as a result of the treatment?
   (0 = Absolutely Yes and 100 = Absolutely No)
9. Did you develop chewing problems as a result of the treatment?
   (0 = Absolutely Yes and 100 = Absolutely No)
10. Did you encounter any problems not listed above as a result of the treatment?
    (0 = Absolutely Yes and 100 = Absolutely No) If Yes please give a brief description:
11. Would you undergo treatment again?
    (0 = Absolutely No and 100 = Absolutely Yes)
12. Would you recommend this treatment to friends and relatives?
    (0 = Absolutely No and 100 = Absolutely Yes)

Fig. 9. *Questionnaire submitted to every patient to evaluate the degree of patient satisfaction.*

Statistical analysis

All data collected were statistically analyzed by SPSS software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

Depending on the sample distribution, variance, and experimental setup, we used the parametric t-test with independent samples, Pearson's chi-square test, or the z-test to test for differences between the groups. Across all analyses, p-values < 0.05 were considered significant. The statistical examination was conducted at a 95% significance level.

RESULTS

Patient selection

Based on the inclusion and exclusion criteria, 30 patients, 18 women and 12 men, undergoing implant-prosthetic rehabilitation performed with digital workflow were included in the study. The mean age of the subjects was 70.5, with a standard deviation of 8.53 (range: 60-81), with a total of 186 dental implants, 102 inserted in the upper jaw and 84 in the mandible.

Four patients were excluded; one refused to be included in the study, one died, and two did not comply with recall checks and hygiene maintenance sessions because they had moved to another location.

Implant survival rate

The 5-year implant survival rate for the implants examined in this study was 100%.

Correlation BCT and KG width and implant placement site (anterior or posterior)

Parametric t-tests with independent samples were employed to assess differences between posterior and anterior implants in terms of bone thickness and KG. The choice of the t-test was contingent upon the sample distribution, variance, and experimental design. The significance level was also set at 95%, and p-values less than 0.05 were considered indicative of statistical significance. The results of the analysis revealed no statistically significant differences in bone thickness and KG between posterior and anterior implants.

Correlation BCT and KG width and type of implant connection (external connection vs internal Double Action Tight-DAT)

To assess whether there were statistically significant differences in bone cortical thickness and KG width based on the type of implant connection (external hex connection *vs* DAT connection), parametric t-tests with independent samples were conducted. The results of the t-tests revealed no statistically significant differences in bone cortical thickness between implants with external hex connections and those with DAT connection ($p>0.05$). Similarly, there were no statistically significant differences in KG width between the two types of implant connections ($p>0.05$). The significance level for all analyses was set at 95%, and *p*-values less than 0.05 were considered indicative of statistical significance. Therefore, based on the statistical examinations, no significant variations were observed in either bone cortical thickness or KG width associated with the implant connection type.

Correlation BCT and KG width and final prosthetic material (layered ceramic zirconia vs cobalt chrome)

To examine potential differences in bone thickness and KG associated with different prosthesis materials (layered ceramic zirconia *vs* cobalt chrome and acrylic resin), a series of independent sample t-tests were conducted. The findings indicated a statistically significant difference in two parameters:

- Vestibular KG (mm): $t(60) = 2.398$, $p = 0.020$. This result suggests a higher vestibular KG (mm) for prostheses made of layered ceramic zirconia.
- Bone thickness at 5 mm: $t(60) = 2.512$, $p = 0.015$. This result indicates a greater bone thickness at 5 mm for prostheses composed of ceramic-layered zirconia.

The statistical tests were conducted with a significance level set at 95%, and *p*-values less than 0.05 were considered indicative of statistical significance. Therefore, based on the outcomes, the data suggest that prostheses made of layered ceramic zirconia exhibit a significant difference in terms of higher vestibular KG (mm) and greater bone thickness at 5 mm compared to those made of cobalt chrome and acrylic resin.

Correlation of BCT and KG width and the number of cigarettes smoked per day

Out of a total of 30 subjects, 6 were identified as cigarette smokers. Pearson's correlation test was employed to examine the relationship between the number of smoked cigarettes and various parameters. The results revealed a negative association between the number of smoked cigarettes and:

- Vestibular and lingual KG (mm): $r = -0.301$, $p = 0.018$; $r = -0.179$, $p = 0.165$
- Vestibular bone thickness at 1, 3, and 5 mm: $r = -0.166$, $p = 0.198$; $r = -0.397$, $p = 0.001$; $r = -0.478$, $p = 0.001$
- Lingual bone thickness at 1, 3, and 5 mm: $r = -0.266$, $p = 0.037$; $r = -0.280$, $p = 0.027$; $r = -0.086$, $p = 0.508$

These correlation coefficients and associated p-values were derived from the statistical analysis, suggesting that as the number of smoked cigarettes increases, there is a negative correlation with vestibular and lingual KG measurements and bone thickness at various locations. The significance level for all analyses was set at 95%, and *p*-values less than 0.05 were considered indicative of statistical significance.

Correlation between peri-implant parameters and implants 'connection (external connection vs internal Double Action Tight-DAT)

Out of the 186 examined implants, bacterial plaque was identified on 753 sites out of 1,116 (67.47%), while bleeding on probing was observed on 468 sites (41.93%). Despite the relatively high prevalence of bacterial plaque (67.47%) and bleeding on probing (41.93%), the average peri-implant surveys indicated values consistent with peri-implant tissue health. Specifically, among the 1,116 peri-implant sites evaluated, only 111 presented probing depths (PPD) of ≥5 mm, accounting for 9.95% of the total.

A series of t-tests were conducted to assess potential differences in probing depths (PPD) and recession (REC) based on the type of implant connection (external hex connection *vs* DAT connection). The statistical results indicated a significant difference in the following parameters:

- Mid-vestibular PPD (mm): $t(60) = 2.279$, $p = 0.026$, suggesting a higher mid-vestibular PPD (mm) for implants with an external hex connection.
- Mesio-vestibular PPD (mm): $t(60) = 2.619$, $p = 0.011$, indicating a higher mesio-vestibular PPD (mm) for implants with an external hex connection.
- Disto-lingual PPD (mm): $t(60) = 2.110$, $p = 0.039$, signifying a higher lingual PPD (mm) for implants with an external hex connection.

- Vestibular REC (mm): t (60) = 2.155, $p = 0.035$, revealing a higher vestibular REC (mm) for implants with an external hex connection.

These findings were derived from the statistical analysis, demonstrating significant differences in PPD and REC based on the type of implant connection. The significance level for all analyses was set at 95%, and *p*-values less than 0.05 were considered indicative of statistical significance.

We conducted a series of Chi-square tests to assess the association between implant connection types (external hex connection *vs* DAT connection) and peri-implant conditions. The results of these tests demonstrated a significant association between implant connection type and the following parameters:

- PI01 (Plaque Index at 01), Chi-square = 7.020, $p = 0.008$, indicating a higher presence of plaque for implants with DAT connection.
- PI01E (Plaque Index at 01 on the external aspect), Chi-square = 6.751, $p = 0.009$, suggesting a higher presence of plaque for implants with DAT connection.
- BoP01C (Bleeding on Probing at 01 on the mesio-vestibular aspect), Chi-square = 9.440, $p = 0.002$, indicating more bleeding for implants with DAT connection.
- BoP01D (Bleeding on Probing at 01 on the disto-vestibular aspect), Chi-square = 4.993, $p = 0.025$, signifying higher bleeding for implants with DAT connection.
- BoP01E (Bleeding on Probing at 01 on the external aspect), Chi-square = 6.972, $p = 0.008$, suggesting more bleeding for implants with DAT connection.
- BoP01C (Bleeding on Probing at 01 on the vestibular aspect), Chi-square = 9.440, $p = 0.002$, indicating higher bleeding for DAT-connected implants.

These findings, derived from Chi-square tests, underscore a statistically significant association between implant connection type, plaque presence, and bleeding on probing at various implant sites. The significance level for all analyses was set at 95%, and *p*-values less than 0.05 were considered indicative of statistical significance.

Degree of patient satisfaction

The questionnaire yielded a mean rating of 78.70, with a standard deviation of 30.60. The obtained results indicated high averages across various parameters. General satisfaction with the rehabilitation achieved was notably high, with a mean evaluation of 85 ± 29.41. Similarly, patients expressed elevated levels of satisfaction with the functional outcomes (mean evaluation 82 ± 30.59) and aesthetic results (mean evaluation 81 ± 29.81).

Only one patient reported a high level of pain during the surgical procedures, while post-operative pain exhibited the lowest mean value (mean evaluation 65 ± 30.74). Notably, patients expressed extreme satisfaction with the time required for both the surgical procedure and the delivery of the final artifact, deeming the time invested as entirely justified (85 ± 26.55).

All surveyed patients conveyed their willingness to undergo the treatment again if necessary in the future, with a mean evaluation of 80 ± 33.16. Furthermore, they expressed a strong inclination to recommend the treatment to friends and relatives, indicating a mean evaluation of 85 ± 32.01.

DISCUSSION

The 5-year implant survival rate for the implants examined in this study was 100%. The same result was obtained by Pera et al. in their retrospective clinical study at a 10-year follow-up in which they evaluated the implant survival rate of 49 patients who had undergone rehabilitation according to the All-on-Four protocol (36). As reported by several authors, immediately loaded full-arch rehabilitations could represent a valid therapeutic alternative in both the short and long term (37-39).

Regarding peri-implant parameters, despite the high percentage of sites where bacterial plaque (67.47%) and probing bleeding (41.93%) were detected, the average peri-implant values showed values compatible with healthy peri-implant tissues.

Contrasting results were obtained by Cercadillo-Ibarguren et al. in their retrospective clinical study in which they evaluated implant parameters of a total of 378 immediately loaded implants in 56 patients with a follow-up of 1 to 9 years, reporting a high incidence of peri-implant pathologies such as mucositis and peri-implantitis that affected 96.4% and 50% of patients, respectively (40).

Relative to this study, however, other authors considered the peri-implant parameters of immediately loaded full-arch implant-prosthetic rehabilitations compatible with the state of health. They analyzed 160 implants in 37 patients, and

it seems that the use of a screw-retained fixed prosthesis supported by four dental implants to rehabilitate edentulous jaws could be a valid treatment option in the short and medium term without peri-implant criticality (41, 42).

Regarding vestibular and lingual bone cortical thickness and KG width, a negative association was found in smoking patients between the number of cigarettes smoked and the following parameters: vestibular KG, vestibular bone cortical thickness at 3 and 5 millimeters, lingual bone cortical thickness at 1 and 3 millimeters. The results obtained emphasize previous studies by other authors on the role of smoking in implant and peri-implant parameters (43,44).

The same parameters were evaluated to see differences in bone thickness and KG due to the denture material (layered ceramic zirconia *vs* cobalt chrome and acrylic resin). The results revealed a significant difference only concerning buccal KG and cortical thickness at 5 millimeters, both of which are greater in zirconia prostheses, as also found in other studies in the literature, such as that of Mendez Caramês et al. in which 75 patients were analyzed with a follow-up of between 6 months and 5 years (45).

To test whether there were statistically significant differences in terms of bone cortical thickness and KG width due to the type of implant connection (external hex connection *vs* DAT connection), t-tests were conducted, the results of which revealed no statistically significant differences between the different implant connections. as stated in the paper by Laleman I. et al. (46).

In terms of PPD and REC due to implant connection type (external hex connection *vs* DAT connection), we conducted a series of t-tests. The test results revealed a significant difference, which was greater for implants with an external hex connection.

Despite the fact that the scientific literature still gives conflicting results as stated by several studies, such as the study by Tallarico et al. in which ninety patients (34 males and 56 females, aged between 24 and 81 years) and 243 inserted implants that were followed up for at least 5 years after prosthetic loading were analyzed, stating that smoking and tissue biotype are the most important variabilities associated with higher marginal bone loss and therefore higher PPD and REC (47, 48).

A series of Chi-square tests were performed to test whether there was an association between implant connection type (external hex connection *vs* DAT connection) and PI. The test results revealed a significant association between implant connection type and the presence of plaque and/or bleeding. Our study showed a higher presence of plaque and bleeding for implants with a DAT connection. This is a surprising finding, given that the scientific literature shows no papers concerning this possible correlation.

No difference in bone thickness and KG between posterior *vs* anterior implants was found when performing t-tests for independent samples, as stated by a systematic review of 2021 by Di Stefano et al., which considered about 970 papers in which it is preliminarily stated that it is not the implant positioning (anterior or posterior) that plays a key role in osseointegration but rather bone density and cortical bone thickness; moreover, the presence of a cortical layer, as well as its thickness, should be consciously considered as key factors in planning implant stability (49).

Finally, the aim of the authors of this paper was to find out what the real degree of patient satisfaction was. The questionnaire revealed that all patients showed high levels of general satisfaction with the rehabilitation performed (mean rating 85 ± 29.41) and high levels of satisfaction with the functional result obtained (mean rating 82 ± 30.59). Satisfaction with the aesthetic results obtained (mean evaluation 81 ± 29.81). These results are fully compatible with other papers in the scientific literature, such as the one by Gonçalves et al., in which they analyzed the satisfaction levels of 693 patients aged between 55 and 71 years about All-on-Four implant-retained prosthetic rehabilitation. This paper also showed that the degree of patient satisfaction was extremely high (50).

The study exhibits certain limitations that warrant consideration. Primarily, a noteworthy constraint lies in the relatively modest sample size of patients involved in the investigation. This restricted sample may affect the generalizability and external validity of the study's findings, as the outcomes may not fully represent the broader population.

Furthermore, the absence of digital planning for prosthetic reconstruction during the planning phase of implant positioning represents another notable limitation. The lack of a template in the surgical stage implies a potential compromise in precision and accuracy, which are crucial in implantology procedures. This deficiency may introduce variability and hinder the reproducibility of the surgical interventions.

Another limitation pertains to the omission of temporary reconstruction before the surgical procedure. The absence of interim prosthetic solutions may impact the assessment of functional and aesthetic outcomes and impede the monitoring of patient adaptation and satisfaction during the treatment process. Additionally, the study refrains from implementing immediate loading, which constitutes a further limitation. Immediate loading could provide insights into the early performance and stability of implants, offering a more comprehensive understanding of their functionality and success rates.

Despite these limitations, it is important to acknowledge the strengths of the study, particularly the detailed description of the protocol and the inclusion of various parameters. These strengths contribute to the transparency and replicability of the study.

CONCLUSIONS

Within the limitations of this study, considering the high implant survival rate and the average peri-implant surveys showing values compatible with peri-implant tissue health, clinical and radiographic results suggested that immediate-load full-arch implant-prosthetic rehabilitations with digital protocols could represent an effective and predictable procedure to replace missing teeth. However, smoking could be a risk factor, albeit in relation to the number of cigarettes smoked per day.

Concerning prosthetic materials, ceramic layered zirconia prostheses have shown increased vestibular KG and vestibular cortical thickness to 5 millimeters, suggesting that this material might be preferred to cobalt chrome and acrylic resin.

Hexagonal connections reported more PPD and RECs, while DAT internals reported more plaque accumulation and bleeding on probing; however, no statistically significant differences were found in terms of KG membrane and bone cortical thickness, which were also unaffected by the implant placement site (anterior or posterior).

The high degree of satisfaction from patients who underwent the procedure confirms the good acceptance and comfort achieved through this rehabilitation.

Conflict of interest statement

The authors declare no conflict of interest.

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