Clinical outcomes of dental implants placed in patients with and without a history of periodontitis. A 20-year prospective study

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Author contributions

A.R. collected, analyzed the data and led to the writing; C.M. performed the statistical analysis and contributed to the writing; J.C.I, G.E.S, analyzed the data and contributed to the writing; G.R. critically revised the manuscript; M.R. conceived the idea, performed the surgeries and critically revised the manuscript

Abstract

Aim: To present the 20-year clinical outcomes of tissue-level implants in partially edentulous patients previously treated for periodontitis and in periodontally healthy patients (PHP).

Material and Methods: The original population consisted of 149 partially edentulous patients consecutively enrolled in a private specialist practice and divided in 3 groups: PHP, moderately Periodontally Compromised Patients (mPCP) and severely PCP (sPCP). After successful completion of periodontal/implant therapy, patients were enrolled in an individualized Supportive Periodontal Care (SPC) program.

Results: Eighty-four patients reached the 20-year examination. During the observation time, 12 implants were removed due to biological complications, leading to an implant survival rate of 94.9% for PHP, 91.8% for mPCP, and 93.1% for mPCP. The final analysis included 169 implants. After 20 years, the odds ratio (OR) for implant loss in smokers non-compliant with SPC was 2.30 (95%CI 1.03-17.32, p=0.04) for the PHP group and 12.03 (95%CI 3.03-42.13, p=0.02) for the PCP group.

Conclusions: Tissue-level implants, placed following comprehensive periodontal therapy and SPC yield favourable long-term results. However, patients with a history of periodontitis and tobacco consumption non-compliant with SPC, are at higher risk of biological complications and implant loss.

INTRODUCTION

Over the past three decades the use of dental implants has radically changed the way to partially and totally rehabilitate edentulous patients, thus allowing clinicians to perform complex oral rehabilitations (Buser, Sennerby, & De Bruyn, 2017). In particular, if considering the wide body of evidence on the assessment of implant survival and success rates and peri-implant marginal bone level changes, the scientific interest has recently focused on long-term results, i.e. ≥10-year (Howe, Keys, & Richards, 2019)). Indeed, since dental implants are placed with the aim to restore missing teeth and last "forever", it is nowadays widely accepted that studies with a limited follow-up and reduced sample size provide limited clinical information. On the other hand, data reporting on implants placed many years apart (*i.e.* with at least 15-year follow-up) might not be representative of the contemporary situation and therefore, preclude from external validity (Astrand, Ahlqvist, Gunne, & Nilson, 2008; Mengel, Wendt, & Peleska, 2019). More specifically, due to the rapid development of implant surfaces and prosthetic materials and technologies, the results published with a follow-up up to 20 years seem to be relevant more for historical reasons rather than for their clinical utility (Chappuis et al., 2013; Donati, Ekestubbe, Lindhe, & Wennstrom, 2018). However, even-though sandblasted and acid-etched (SLA) implant surfaces have been used for the last 25 years, they are still present on the dental market. It seems therefore meaningful to monitor SLA implants in order to provide long-term clinical results, particularly in patients with a history of periodontitis representing a major risk factor for implant loss (Carra et al., 2021).

Hence, the aim of this study was to assess the 20-year clinical outcomes of SLA implants placed in a cohort of Periodontally Healthy Patients (PCP) compared to a group of Periodontally Compromised Patients (PCP) of both moderate and severe extent.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Ethics Committee (Nr.168/2021). The investigation was conducted according to the revised principles of the Helsinki Declaration (2013); all participants signed a written informed consent prior to entering the study. The trial was registered at http://ClinicalTrials.gov (NCT04983758) and reported according to the STROBE guidelines.

Study population

The original population consisted of 149 patients rehabilitated with 297 sandblasted large grit and acid-etched surface (SLA) dental implants (Straumann Group AG, Basel, Switzerland). Details of the treatment protocol have been described in a previous publication reporting on the 10-year outcomes (Roccuzzo, Bonino, Dalmasso, & Aglietta, 2014). In brief, 123 patients (mean age 50 years old; 17% smokers), attending the senior author investigator's private office (specialist periodontal practice, northwestern Italy) between December 1998 and September 2001 seeking for dental implant therapy were screened for inclusion in the study. From the original population, only individuals participating to all follow-up visits (10 and 20 years) were included in the present analysis.

The exclusion criteria were:

- edentulism;
- presence of an implant supported overdenture;
- mucosal diseases;
- alcohol and drug abuse;
- pregnant or lactating females;

- uncontrolled metabolic disorders;
- aggressive periodontitis according to Armitage 1999 (Armitage, 1999);
- inability or unwillingness to give informed consent.

Pre-treatment clinical examination

Socio-demographic characteristics, smoking status and medical history were collected during the initial visit and treatment planning. Moreover, subjects were clinically and radiographically monitored at baseline. Full mouth plaque score (FMPS), full mouth bleeding score (FMBS) and pocket depth (PD) were measured 4 sites per tooth for all teeth by means of a periodontal probe (XP23/UNC 15, Hu-Friedy, Chicago, USA), and rounded off to the nearest millimeter.

At baseline, 3 groups were identified based on periodontal status.

Patient without signs of periodontitis were classified as PHP (periodontally healthy patients). Patient with an initial diagnosis of periodontitis (PCP: periodontally compromised patients) received a score (S) on the basis of the number and depth of periodontal pockets according to the following formula:

S = Number of pockets (5-7mm) + 2 Number of pockets ($\geq$8 mm)

These patients were further divided in 2 groups:

1. Moderate PCP (mPCP): periodontally compromised patients with S $\leq$ 25
2. Severe PCP (sPCP): periodontally compromised patients with S > 25.

Periodontal therapy, implant therapy and prosthetic phase

After enrollment, all patients received appropriate initial therapy, consisting, depending on the cases, in motivation, oral hygiene instructions and scaling and root planing. Hopeless teeth were recorded and extracted. Periodontal surgery was performed as needed after re-

evaluation; when feasible, guided tissue regeneration was pursued. Individual treatment was thoroughly discussed with the patients and established according to their personal need and desire. No implant surgery was performed before optimal motivation and compliance from each single patient was achieved (FMPS ≤15%; FMBS ≤15%).

After completion of active periodontal therapy (APT), tissue-level SLA implants (Institut Straumann AG, Basel, Switzerland) were placed, under local anesthesia, by the same operator (MR), according to the manufacturer's instructions an using a standardized surgical procedure (Buser, von Arx, ten Bruggenkate, & Weingart, 2000). No bone augmentation procedures were performed. Following 6 to 12 weeks of non-submerged healing, abutment connection was carried and all patients were provided with cemented implant-supported fixed restorations (*i.e.* Single Unit Crown or Fixed Dental Prosthesis). Prosthesis delivery was considered as baseline (T0) and encompassed the collection of clinical and radiographical data.

Supportive periodontal/peri-implant care (SPC)

Patients were enrolled in an individualized Supportive Periodontal Care (SPC) program, including a continuous evaluation of the occurrence and the risk of disease progression.

Patients were recalled at various intervals for oral hygiene instructions, biofilm removal, and treatment of re-infected sites were performed whenever needed. If a patient expressed the desire not to attend follow-up examinations, they were classified as "drop-out". The diagnosis and treatment of peri-implant biological complications was performed according to Cumulative Interceptive Supportive Therapy (CIST) (Mombelli & Lang, 1998). The number of sites treated according to therapy modalities C and D (antibiotics and/or surgery) during the 20 years was also collected.

Clinical examinations

At the 10-year (T1) and 20-year (T2) follow-up examination, implant survival rate (*i.e.* presence of the implant in the oral cavity) was calculated. Moreover, an examiner (SG) with more than 15 years of experience as dental hygienist, blinded to the initial classification of the patients, recorded, for each treated implant probing depths (PD) measured at four sites (mesial, buccal, distal, and lingual) by means of a periodontal probe (XP23/UNC 15; Hu-Friedy). Measurements were rounded off to the nearest millimeter.

At the same implant sites, the presence of dental plaque (PI), bleeding on probing (BOP), and suppuration was recorded dichotomously.

At follow-up examinations, the following parameters were collected at patient-level:

- FMPS measured at four sites per tooth and implant and expressed as a percentage of examined sites;
- FMBS measured at four sites per tooth and implant and expressed as a percentage of examined sites;
- number of teeth lost during SPC;
- complete adhesion to the SPC (yes or no);
- deepest PD during the SPC;
- deepest PD at 10, 20-year follow-up;
- number of patients requiring, during SPC, either C or D therapy modality.

Statistical analysis

All analyses were performed with an *ad hoc* statistical software (STATA BE, version 17.1, StataCorp LP, Texas, USA) setting the level of significance at 5%. Continuous variables were presented as Mean ± Standard Deviation (SD), categorical variables were presented as number of observations (proportion, %). After verification of data distribution, parametric and non-parametric tests were used in order to perform intra and intergroup comparisons across groups and timepoints. Due to a significant difference between the three groups analyzed, variables were adjusted for patient's age. The survival rate was calculated overall, by group and in relation to adherence to SPC between baseline and 20 years, and between 10 and 20 years. Crude and adjusted odds ratios (OR) (95% Confidence Interval - 95% CI) for implant loss were calculated. The multilevel logistic regression models allowed for adjustment of tooth characteristics in the same subject. All computed *p*-values were two-tailed.

Results

Patient population

Details of the original population are shown in Table 1. Of the 123 patients included at the 10-year follow-up, 39 patients were lost at the 20-year follow-up: 16 died, 13 were not able to attend the final examination due to severe health problems or because they moved, and 10 refused the follow-up visit. Therefore, the population analyzed at the 20-year follow-up included 84 subjects and 169 implants (Table 1).

The final 20-year analysis was performed on 22 PHP, 29 mPCP and 33 sPCP subjects, corresponding to 39, 59 and 71 implants, respectively. PHP had a statistically significant lower mean age (63.36 ± 12.11 years) compared to both mPCP (70.6 ± 9.7) and sPCP (71.03 ± 7.76). The proportion of smokers was equally distributed across groups (Table 2).

The mean number of teeth lost during the SPC between 10 and 20 years was 0.27 ± 0.55 for PHP, 1.07 ± 1.23 for mPCP and 1.33 ± 1.29 for sPCP, respectively, with a statistically significant difference among the three groups (p<0.001) (Table 2).

At baseline, statistically significant differences were found among the three groups regarding both FMPS and FMBS (Table 3). Both parameters increased from PHP (27.36 ± 9.15 and 22.45 ± 9.72), to mPCP (37.47 ± 10.01 and 36.57 ± 13.52) up to sPCP (50.76 ± 23.94 and 48.97 ± 20.71). At the 20-year examination, both FMPS and FMBS decreased in all groups and the between-group analysis failed to show statistically significant differences (Table 3).

Clinical parameters at the 10 and 20-year follow-up (PD, BOP and PI at implant site)

Plaque around the tested implants was found at the 20-year examination as follows: 16.89 ± 29.59 % for PHP, 19.02 ± 29.68 % for mPCP and 25.75 ± 30.45 % for sPCP, while BOP was found to be 25 ± 22.05 %, 29.91 ± 28.35 % and 30.2 ± 27.01 %, respectively. BOP at implant site was comparable across groups and timepoints (p>0.05), while plaque was significantly lower in the PHP group compared to both PCP groups at 10 years (p=0.04). At the 20-year examination, no implants showed pus in the PHP and sPCP groups, while 2 implants presented pus in the mPCP group (Table 4).

CIST C/D and interventions during the SPC

At 20 years, the number of patients treated with CIST C/D was significantly lower in the PHP (33.3%) compared to the mPCP (48.28%) and sPCP (61.29%) groups, respectively (p=0.04) (Table 2). A significantly higher proportion of subjects underwent antibiotic therapy in the PHP (19.05%) and mPCP (31.03%) groups compared to surgery (4.76% *vs* 17.24%, respectively) (p=0.04). In the sPCP group, 8 subjects (25.81%) underwent antibiotic therapy and 10 subjects underwent surgery (32.26%).

Implant survival rate

The overall survival rate over 20 years was 93% (Table 6). In PHP, 2 implants were lost in patients non-compliant with SPC, resulting in a survival rate of 94.9%. Five implants were lost in the mPCP and sPCP groups, respectively, yielding a survival rate of 91.8% in the former and 93.1% in the latter group. No significant differences were found across groups (p>0.05).

Supportive Periodontal Care (SPC)

In the mPCP and sPCP groups, FMPS and FMBS were significantly lower in compliant *vs* non-compliant subjects ($p<0.05$) (Table 3). Moreover, the number of implants with at least one site with PD $\geq$ 6mm at 20 years was significantly higher in non-compliant compared to compliant subjects in the PHP (80% *vs* 23.53%, respectively) and sPCP groups (100% *vs* 41.66%, respectively), even though not statistically significantly in the mPCP group ($p=0.08$) (Table 5). After 20 years, a trend towards a higher survival rate in compliant *vs* non-compliant subjects was highlighted, even though it did not reach statistical significance ($p>0.05$).

Logistic regression models

Results of the crude and adjusted OR for implant loss are reported in Table 7. At 10 years, non-compliant subjects and those in the PCP groups had approximately 5 times higher odds of implant loss compared to compliant subjects and those in the PHP group, respectively (OR=5.63, 95% CI 1.31-70.42, $p=0.04$; OR=4.26, 95% CI 1.30-41.48, p=0.03). At 20 years, the odds of implant loss were almost 8 times higher in subjects non-compliant with SPC compared to compliant subjects, irrespective of their periodontal status at baseline (OR=7.65, 95% CI 1.48-39.38, $p=0.01$). Moreover at 20 years, in the PHP group, the combination of smoking and non-compliance with SPC led to an OR=2.30 (95% CI 1.03-17.32) of implant loss. In the PCP group, non-compliant and non-smoking subjects had an odds of implant loss of OR=5.93 (95% 1.05-33.67, $p=0.04$); in the same groups, the odds of implant loss doubled in non-compliant, smoking subjects (OR=12.03, 95% CI 3.03-42.13, $p=0.02$).

Discussion

Since the publication of the data from the first 10-year analysis (Roccuzzo et al., 2014), long-term results of implant therapy in patients with a history of periodontitis have received significant attention in the last years. Several studies, many of them with a retrospective or cross-sectional design, have been published on this topic (Smith, Knight, Al-Harthi, & Leichter, 2017).

Recently, a systematic review (Carra et al., 2021) investigated the effectiveness of implant-supported fixed partial denture (IS-FPD) in patients with history of periodontitis (HP) *vs* patients with no history of periodontitis (NHP). Seventeen articles (7 prospective and 10 retrospective) were selected, including the one regarding the 10-year data of the population of the present study (Roccuzzo et al., 2014). Pooled data analyses showed that overall implant survival was significantly higher in the NHP than in the HP group. This difference was noted when follow-up periods exceeded 5 years. The risk of peri-implantitis was higher in HP than NHP patients, whereas the mean marginal bone level change over time was not different between the groups. The authors concluded that in partially edentulous patients receiving IS-FPDs, a history of periodontitis is associated with poorer survival rate and higher risk of peri-implantitis during a 5-10-year period after implant loading.

The present investigation is, to the best of our knowledge, the first and only prospective study reporting on the 20-year results of dental implant treatment performed on a relatively large number of patients, recruited from a specialist private clinic. When evaluating long-term outcomes up to 20-years, it has to be underlined that the few available studies with data up to 20 years report on dental implants not commercially available anymore, hence resulting in a limited external validity (Chappuis et al., 2013; Donati et al., 2018; Jacobs et al., 2021). On the other hand, the present data set included SLA Tissue Level Implants which are nowadays widely used, providing unique evidence.

During the last three decades, the number of dental implants placed every year has increased dramatically (Misch, 2020) mainly due to the misleading assumption among clinicians that the prognosis of complex periodontal therapy may not compare favourably with the high levels of success of treatment with implants (Lang, 2019; Rasperini et al., 2014). Consequently, more and more teeth are extracted on the assumptions that implants perform better than periodontally compromised teeth and that their longevity is not affected by the individual's susceptibility to periodontitis (Lundgren, Rylander, & Laurell, 2008).

Actually, during the 20-year SPC, the mean number of teeth lost per patient, regardless of the clinician providing the treatment and the reason for the extraction, was 0.7 $\pm$ 1.0 for PHP, 1.3 $\pm$ 1.3 for moderate PCP and 1.9 $\pm$ 1.9 for severe PCP, with a significant difference between PHP and PCP. These results are confirmatory of those published with a 30-year follow-up by Axelsson and co-workers (Axelsson, Nystrom, & Lindhe, 2004): in both these unique cohorts, the mean number of tooth loss was < 1.

Overall, these results confirm that PCP patients, who are not completely enrolled in an appropriate SPC, tend to have more complications both around implants and teeth, and should not be treated on the assumption implants perform better than natural teeth. Furthermore, smoking seems to exacerbate the already deteriorating effect of non-compliance with SPC. These conclusions are similar to those reported by Pjetursson and co-workers (Pjetursson et al., 2012) n 70 patients with a follow-up ranging from 3 to 23 years (mean 7.9 years). The authors reported that the prevalence of peri-implantitis was lower in the group enrolled in a well-organized SPC program at the University. Conversely, the current study presents excellent results in terms of overall compliance for patients enrolled in an individually tailored SPC program in a private specialist setting.

Mir-Mari and co-workers (Mir-Mari, Mir-Orfila, Figueiredo, Valmaseda-Castellon, & Gay-Escoda, 2012) estimated the prevalence of peri-implantitis in private practice patients, enrolled in a periodontal maintenance program, between 12% and 22%, similarly to those published in University environment samples. Nevertheless, once again, the importance of SPC must be stressed, regardless of the fact that it takes place in a public or private setting. In the present study, 26 out of 149 (17.4%) patients were lost to follow-up and only 16 of these (10.7%) refused the visit for various personal reasons. These values should be considered positively in consideration of the long period of the follow-up and they are somehow similar to those reported by Cardaropoli & Gaveglio (Cardaropoli & Gaveglio, 2012).

The overall quality of SPC in the present investigation can be confirmed by the significant constant reduction of the FMPS and FMBS values both at the 10-year and 20-year follow-up. These changes are more pronounced in patients compliant with SPC compared to the ones not compliant with SPC. Ideally, patients undergoing a successful SPC should have similar low plaque scores regardless of the history for periodontitis. In these groups of patients, the 20-year FMPS, before the session of professional cleaning, were below the 25% threshold, *i.e.* respectively 19.4 $\pm$ 10.1% (PHP) *vs* 26 $\pm$ 14.5% (mPCP) *vs* 23.3 $\pm$ 17.3% (mPCP) with no difference among the groups.

During the entire 20-year follow-up period, only 12 implants had to be removed for biological complications. The calculated overall survival rate (*i.e.* 93%) therefore is similar to those reported in recent publications with such a follow-up (Donati et al., 2018; Jacobs et al., 2021) even-though it has to be underlined that these values were obtained from selected cohorts with smaller sample sizes (*i.e.* 32 and 10 patients, respectively).

Finally, antibiotic and/or surgical therapy was performed in 22.7% of cases in PHP, in 43.3% of cases mPCP and in 57.6% of cases in sPCP. In other words, in order to have a very elevated

long-term survival rate it is mandatory to monitor patients frequently, especially those who lost teeth due to periodontal disease, and to organize and promptly perform adjunctive additional treatments, whenever needed. Therefore, implant therapy cannot be simply proposed as “definitive”, but should be considered only as an important step in the comprehensive long-term treatment plan of patients.

The present study retains several limitations. First, the relative high number of drop-outs (31.7%) might have impacted on the final analysis, even though it has to be underlined that this value is much lower than the percentage of another recent 20-year publication (Donati et al., 2018). In particular, 16 out of 123 patients died, most of them for reasons connected to the elevated mean age. The fact that only 10 out of 123 patients refused to accept a visit must be considered a positive outcome, most likely as a result of the fact that the majority of them had received periodontal treatment before implant placement, in accordance with the results reported by Zeza and co-workers (Zeza et al., 2017). Second, with respect to the smoking status, it must be pointed out that patients’ self-reported data on their habit remains questionable. In addition, smoking status was assessed only at implant placement and, hence, it cannot be excluded that during the observation period patients’ habits might have changed, affecting periodontal/peri-implant conditions (Scott, Palmer, & Stapleton, 2001). Third, PCP were arbitrarily divided into two groups (moderate and severe) on the basis of the number and depth of periodontal pockets at the baseline examination. It is also worth mentioning that the classification of periodontitis was proposed in the context of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Tonetti, Greenwell, & Kornman, 2018), more than two decades after initiation of the present study.

Recently, Derks and co-workers (Derks et al., 2016), analyzing the effectiveness of implant therapy in a Swedish population sample demonstrated higher implant loss among smokers and

patients with an initial diagnosis of periodontitis, in accordance with the results of the present investigation. Moreover, the multilevel analysis revealed lower odds ratios for loss of tissue-level implants, which are of the same brand employed in the present study. According to these findings, the question of which implant surface and surgical protocol should be considered ideal is still open.

Conclusions

- Periodontally healthy patients who, after adequate implant therapy, are enrolled in a regular SPC program encounter very few biological complications, even long-term. Conversely, patients with a history of periodontitis, especially if smokers and non-compliant with an SPC program, are at higher risk of biological complications and implant loss.
- Considering the low number of teeth lost, the approach for strategic dental extractions and implant placement, based on the assumption the implants perform better than teeth, cannot find scientific support.
- Patients, especially those presenting risk factors, should be thoroughly informed, before implant placement, about the importance of SPC for long-term implant survival.
- Excellent values of long-term survival rate can be obtained even in PCP, if SPC is associated with a continuous evaluation of the risk of peri-implant diseases.
- PCP, even though placed in an adequate SPC program, may need further therapy for the treatment of long-term biological complications.

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Table 1. Number of patients attending the 10-year & the 20-year examination; number of implants examined and removed.

	Patients	Implants	Implants removed	Patients lost to follow-up
Baseline	149	297	-	-
10-year	123	246	6	26
20-year	84	169	9	39

List of reasons for drop-out between 10 and 20 years	
Death	16
Severe health problems	6
Moved	7
Refused to accept a visit	10
TOTAL	39

Table 2. Characteristics of patients who reached the 20-year examination. Mean number of teeth extracted and implants removed during the first 10-year of SPC and between 10 and 20 years of SPC.

	Patients	Age (years)	Smokers	Teeth extracted (0-10 y)	Teeth extracted (10-20 y)	Implants removed (0-10 y)	Implants removed (10-20y)	Patients treated with CIST C/D (0-10 y)	Patients treated with CIST C/D (10-20 y)
PHP	22 (26.20%)	63.36±12.11	4 (18.18%)	0.64±0.95	0.27±0.55	0	2 (5.13%)	5 (22.73%)	7 (33.33%)
mPCP	29 (34.52%)	70.6±9.70	4 (13.79%)	1.33±1.32	1.07±1.23	1 (1.67%)	3 (5.08%)	13 (43.33%)	14 (48.28%)
sPCP	33 (39.28%)	71.03±7.76	6 (18.18%)	1.97±2.13	1.33±1.29	2 (2.78%)	4 (5.63%)	19 (57.58%)	19 (61.29%)
Statistical difference between:									
All groups		*p=0.01*	*p*=0.87	*p=0.01*	*p=0.00*	*p*=0.61	*p*=0.94	*p=0.01*	*p=0.04*
PHP vs. mPCP		*p=0.00*		*p=0.03*	*p=0.00*			*p=0.04*	*p=0.04*
PHP vs. sPCP		*p=0.00*		*p=0.00*	*p=0.00*			*p=0.04*	*p=0.04*
mPCP vs. sPCP		*p*=0.46		*p*=0.15	*p*=0.18			*p*=0.07	*p*=0.06

Table 3. Clinical parameters at patient level at the 20-year examination (means ± SD).

	Baseline	10 y	20 y	Intragroup p-value	Mean difference (95% CI)			p-value BL vs 20 y
					Baseline -10y	20y -10 y	Baseline-20 y	
FMPS								
Overall	40.01±19.06[a]	24.69±14.49[b]	23.26±14.97[b]	*0.00*	-15.32±18.73[a,c]	-1.44±12.34[b]	-16.75±21.35[c]	*0.00*
PHP	27.36±9.15[a,A]	20.05±9.53[b]	19.41±10.06[b]	*0.00*	-7.32±10.40[A]	-0.64±8.65[A]	-7.95±11.79[A]	*0.00*
mPCP	37.47±10.01[a,B]	27.03±14.28[b]	26±14.49[b]	*0.00*	-10.43±14.51[A]	-1.03±15.76[B,C]	-11.46±14.84[A]	*0.00*
sPCP	50.76±23.94[a,C]	25.67±16.90[b]	23.33±17.33[b]	*0.00*	-25.09±22.23[B]	-2.33±11.14[C]	-27.42±26.62[B]	*0.00*
Intergroup p-value	*0.00*	0.27	0.30		*0.00*	*0.01*	*0.01*	
FMBS								
Overall	37.73±19.01[a]	22.62±14.54[b]	20.94±15.07[b]	*0.00*	-15.11±18.29[a,c]	-1.68±13.08[b]	-16.68±21.07[c]	*0.00*
PHP	22.45±9.72[a,A]	18±13.59[b,c,A]	17.27±13.30[c]	*0.00*	-4.45±14.77[A]	-0.73±8.94	-5.18±16.25[A]	*0.00*
mPCP	36.57±13.52[a,B]	25.27±13.34[b,B,C]	22.6±14.51[c]	*0.00*	-11.3±13.04[A]	-2.67±15.95	-13.97±15.39[A]	*0.00*
sPCP	48.97±20.71[a,B]	23.30±15.82[b,c,C]	21.88±16.64[c]	*0.00*	-25.67±19.34[B]	-1.42±12.85	-27.09±23.81[B]	*0.00*
Intergroup p-value	*0.00*	*0.04*	0.29		*0.00*	*0.01*	*0.00*	
FMPS and FMBS in relation to adherence to SPC								
FMPS								
PHP								
Adherent to SPC	28.58±8.74[a]	19.06±9.39[b]	17.01±8.37[b]	*0.00*	-9.53±6.58[a,c]	-2.06±8.54[b]	-11.58±8.47[c]	*0.00*
Non-adherent to SPC	23.2±10.28	23.4±10.26	27.6±11.89	0.29	0.2±17.41	4.2±7.95	4.4±13.97	0.12
p-value	0.39	0.45	0.06		*0.01*	0.11	*0.03*	
mPCP								
Adherent to SPC	32.76±5.75[a]	23.29±12.41[b]	18.64±10.11[b]	*0.00*	-9.47±14.17[a,c]	-4.65±12.28[b]	-14.12±12.22[c]	*0.00*
Non-adherent to SPC	43.62±11.21	31.92±15.55	35.62±13.95	0.09	-11.69±15.43[a,c]	3.69±18.88[b]	-8±17.62[c]	0.11
p-value	*0.01*	*0.04*	*0.00*		0.22	0.07	0.09	
sPCP								
Adherent to SPC	46.58±24.64[a]	18.71±8.99[b]	14.25±7.39[b]	*0.00*	-27.88±22.08[a,c]	-4.45±10.20[b]	-32.33±27.93[c]	*0.00*
Non-adherent to SPC	61.88±18.87	44.22±19.41	47.55±13.90	0.06	-17.66±22.14[a,c]	3.33±12.14[b]	-14.33±18.04[c]	0.08
p-value	0.12	*0.00*	*0.00*		0.12	0.09	0.05	
FMBS								
PHP								
Adherent to SPC	24.18±9.69[a]	16.35±10.37[b]	14.35±9.31[b]	*0.00*	-7.82±7.58	-2±9.25	-9.82±9.38	*0.00*
Non-adherent to SPC	16.6±8.05	23.6±22.13	27.2±20.55	0.09	7±26.53	3.6±6.88	10.6±25.13	0.13
p-value	0.12	0.09	0.11		*0.02*	0.12	*0.03*	
mPCP								
Adherent to SPC	32.06±6.79[a]	21.18±8.71[b]	15.06±8.45[b]	*0.00*	-8.88±10.32	-6.12±8.72	-15±9.08	*0.00*
Non-adherent to SPC	45.08±15.54	30.62±6.57	32.46±15.09	0.10	-14.46±15.81	1.85±21.78	-12.62±21.43	0.15
p-value	0.12	*0.04*	0.00		0.05	*0.04*	0.06	
sPCP								

Adherent to SPC	45.75±20.46[a]	17.33±7.19[b]	13.75±7.98[b]	*0.00*	-28.42±18.14[a,c]	-3.58±9.99[b]	-32±23.92[c]	*0.00*
Non-adherent to SPC	57.55±19.98	39.22±21.45	43.55±14.05	0.07	-18.33±21.61[a,c]	4.33±17.95[b]	-14±18.89[c]	0.07
p-value	0.17	*0.00*	*0.00*		*0.04*	0.11	*0.04*	

For each column, values sharing the same superscript upper-case letter are not different at the 5% level.
For each row, values sharing the same superscript lower-case letter are not different at the 5% level.

Table 4. Clinical parameters around the implants which reached the 20-year examination (means ± SD).

	Baseline	10 y	20 y	Intragroup p-value	Mean difference (95% CI) 20 y -10 y
Deepest PD (mm)					
Overall	-	4.59±1.34	4.29±1.38	*0.03*	-0.28±1.30
PHP	-	4.44±1.19^{A}	4±1.31^{A}	0.11	-0.41±1.44
mPCP	-	4.58±1.40^{B,C}	4.32±1.44^{B,C}	0.35	-0.21±1.28
sPCP	-	4.69±1.38^{C}	4.42±1.35^{C}	0.28	-0.26±1.25
Intergroup p-value	-	*0.00*	*0.00*		0.78
BOP at implant site (%)					
Overall	-	34.32±29.35	28.91±26.38	*0.02*	-4.69±29.83
PHP	-	33.25±27	25±22.05	0.18	-8.25±29.17
mPCP	-	34.72±31.15	29.91±28.35	0.44	-4.81±27.89
sPCP	-	34.51±29.38	30.2±27.01	0.48	-4.31±32.26
Intergroup p-value	-	0.68	0.73		0.83
PI at the implant site (%)					
Overall	-	29.14±28.96	24.83±28.25	0.16	
PHP	-	20.51±21.36^{A}	16.89±19.59	0.49	-3.62±31.21
mPCP	-	36.44±34.53^{B,C}	29.02±29.68	0.30	-7.42±26.73
sPCP	-	27.82±26.23^{C}	25.75±30.45	0.36	-2.07±31.76
Intergroup p-value	-	*0.04*	0.41		0.83
Pus at the implant site (%)					
Overall	-	12 (7.10%)	2 (1.25%)	0.11	-
PHP	-	0	0	-	-
mPCP	-	6 (10.17%)	2 (3.57%)	0.14	-
sPCP	-	6 (8.45%)	0	*0.00*	-
Intergroup p-value	-	0.11	0.17		-

For each column, values sharing the same superscript upper-case letter are not different at the 5% level.
For each row, values sharing the same superscript lower-case letter are not different at the 5% level.

Table 5. Clinical parameters at the 20-year follow-up in relation to adhesion to supportive periodontal therapy (SPC) in the three groups.

	Adhesion to SPC	Number of patients	PI (%)20y	BoP (%)20y	Deepest PD (mm)20y	Teeth lost during SPC (10y-20y)	No. patients treated with CIST C/D (10 y)	No. patients treated with CIST C/D (20 y)	Implants with at least a site with deepest PD>=6mm at 10 y	Implants with at least a site with deepest PD>=6mm at 20 y
PHP	*No*	5 (22.73%)	33.25±25.75	45.75±29.25	4.16±2.64	0.79±0.36	1 (20%)	2 (40%)	2 (40%)	4 (80%)
	Yes	17 (77.27%)	13.75±17.01	21.02±18.37	3.96±0.95	0.83±0.31	4 (23.53%)	5 (29.41%)	3 (17.65%)	4 (23.53%)
p-value			*0.02*	*0.01*	0.74	0.75	0.69	0.41	0.27	*0.04*
mPCP	*No*	13 (43.33%)	41.25±30.75	41.26±27.75	4.70±1.49	0.97±0.32	4 (30.77%)	8 (61.54%)	11 (84.61%)	10 (76.92%)
	Yes	17 (56.57%)	20.45±26	21.96±26.25	4.06±1.37	1.04±0.19	9 (52.94%)	6 (35.29%)	5 (29.41%)	6 (35.29%)
p-value			*0.01*	*0.01*	0.11	0.22	0.28	0.14	*0.02*	0.08
sPCP	*No*	9 (27.27%)	63.75±26.03	56.76±20.66	5.28±1.01	1.05±0.21	4 (44.44%)	3 (33.33%)	9 (100%)	9 (100%)
	Yes	24 (72.73%)	11.74±17.01	20.41±22.05	4.10±1.33	1.00±0.19	15 (62.5%)	16 (66.66%)	16 (66.66%)	10 (41.66%)
p-value			*0.00*	*0.00*	*0.00*	*0.04*	0.44	0.38	*0.04*	*0.04*

Table 6. 0-20 and 10-20 years survival rate, for each group and in relation to adherence to SPC.

	Implants placed	Implants lost	Survival rate (%)	*p*-value
Overall 0-20 years	172	12	93.0	
Group				
PHP	39	2	94.9	
Adhering to SPC	31	0	100	0.06
Not adhering to SPC	8	2	75	
mPCP	61	5	91.8	
Adhering to SPC	34	1	97.1	0.64
Not adhering to SPC	27	4	85.2	
sPCP	72	5	93.1	
Adhering to SPC	52	3	94.2	0.49
Not adhering to SPC	20	2	90	
Statistical difference between:				
All groups			*p*=0.29	
Overall 10-20 years	169	9	94.7	
Group				
PHP	39	2	94.9	
Adhering to SPC	31	0	100	0.06
Not adhering to SPC	8	2	75	
mPCP	59	3	94.9	
Adhering to SPC	34	1	97.1	0.65
Not adhering to SPC	25	2	92	
sPCP	71	4	94.4	
Adhering to SPC	51	2	96.1	0.59
Not adhering to SPC	20	2	90	
Statistical difference between:				
All groups			*p*=0.57	

Table 7. Odds Ratios (ORs) for implant loss at 10 and 20 years in relation to SPC adherence, smoking status and group.

Variable		ORs for implant loss							
		Crude ORs	95% CI		*p*-value*	Adjusted† ORs	95% CI		*p*-value*
			Lower	Upper			Lower	Upper	
10-year follow up									
Adherence to SPC									
	Yes	REF.			*0.02*	REF.			***0.04***
	No	4.46	1.08	50.31		5.63	1.31	70.42	
Smoking									
	No	REF.			0.23	REF.			0.71
	Yes	1.13	0.92	1.38		1.05	0.81	1.37	
Group									
	PHP	REF.			0.32	REF.			
	PCP	2.72	0.37	19.72		4.26	1.30	41.48	***0.03***
20-year follow up									
Adherence to SPC									
	Yes	REF.			*0.03*	REF.			***0.01***
	No	4.81	1.15	20.03		7.65	1.48	39.38	
Smoking									
	No	REF.			0.79	REF.			0.80
	Yes	1.03	0.85	1.24		3.03	0.82	5.30	
Group									
	PHP	REF.			0.95	REF.			0.53
	PCP	1.05	0.21	5.29		4.49	0.20	7.25	
Combination of SPC adherence and smoking status									
PHP									
	Adherent, non-smoker	REF.				REF.			
	Adherent, smoker	0.99	0.91	1.10	0.96	1.02	0.90	1.12	0.06
	Non-adherent, non-smoker	1.15	0.92	1.42	0.21	1.72	0.86	1.67	0.23
	Non-adherent, smoker	2.02	0.67	12.35	0.23	2.30	1.03	17.32	***0.04***
PCP									
	Adherent, non-smoker	REF.				REF.			
	Adherent, smoker	1.00	0.90	1.12	0.94	1.18	0.94	1.47	0.15

Non-adherent, non-smoker	5.41	0.92	31.72	0.06	5.93	1.05	33.67	***0.04***
Non-adherent, smoker	9.13	0.32	25.89	0.15	12.03	3.03	42.13	***0.02***

† Multilevel logistic regression model with implant loss at either 10 or 20 years follow up. Adjustments were made for: age, teeth missing at baseline, baseline FMPS and FMBS.