

Erythritol airpolishing in the non-surgical treatment of peri-implantitis: A randomized controlled trial

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Abstract

Objectives: To compare erythritol air polishing with piezoelectric ultrasonic scaling in the non-surgical treatment of peri-implantitis.

Material and methods: Eighty patients ($n = 139$ implants) with peri-implantitis (probing pocket depth (PPD) ≥ 5 mm, marginal bone loss (MBL) ≥ 2 mm as compared to bone level at implant placement, bleeding, and/or suppuration on probing (BoP/SoP)) were randomly allocated to air polishing or ultrasonic treatment. The primary outcome was mean BoP (%) at 3 months after therapy (T3). Secondary outcomes were mean SoP (%), plaque score (Plq) (%), PPD (mm), MBL (mm), full mouth periodontal scores (FMPS) (%), levels of 8 classical periodontal pathogens, and treatment pain/discomfort (Visual Analog Scale, VAS). Patients who were considered successful at T3 were additionally assessed at 6, 9, and 12 months. Differences between both groups were analyzed using multilevel statistics.

Results: Three months after therapy, no significant difference in mean BoP (%) between the air polishing and ultrasonic therapy was found (crude analysis β (95% CI) -0.037 (-0.147 ; 0.073), $p = .380$). Neither secondary outcomes SoP (%), Plq (%), PPD (mm), MBL (mm), FMPS (%), and periodontal pathogens showed significant differences. Treatment pain/discomfort was low in both groups (VAS score airpolishing group 2.1 (± 1.9), ultrasonic 2.6 (± 1.9); $p = .222$). All successfully treated patients at T3 (18.4%) were still considered successful at 12-month follow-up.

Conclusions: Erythritol air polishing seems as effective as piezoelectric ultrasonic scaling in the non-surgical treatment of peri-implantitis, in terms of clinical, radiographical, and microbiological parameters. However, neither of the proposed therapies effectively resolved peri-implantitis. Hence, the majority of patients required further surgical treatment.

KEYWORDS

dental implant, intervention study, peri-implantitis, randomized controlled trial, ultrasonic therapy

Trial registry: www.trialregister.nl; identifier: NL8339

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1 | INTRODUCTION

Over the past decades, a variety of interventions, alone or in combination, has been investigated for the non-surgical treatment of peri-implantitis including, mechanical (e.g., carbon fiber/titanium curettes, glycine air polishing, and ultrasonic therapy), chemical (i.e., local or systemic antibiotics, and chlorhexidine irrigation), and light-mediated therapies (e.g., Er:YAG laser or photodynamic therapy) (Renvert et al., 2008; Renvert et al., 2011; Bassetti et al., 2014; Schwarz et al., 2015; Renvert et al., 2015; Mettreux et al., 2016; Wang et al., 2019). Despite these various treatment strategies, the most effective treatment option for treating peri-implantitis lesions in a non-surgical way remains unclear (Faggion et al., 2014; Renvert et al., 2019).

However, among the previously investigated interventions, the use of air polishing is considered a promising treatment method (Schwarz et al., 2015,2016). A myriad of in-vitro studies on air polishing has appeared in the recent literature showing positive results on implant surface cleaning efficacy and surface damage (Tastepe et al. 2012; Louropoulou et al., 2014; Moharrami et al., 2019). Clinically, air polishing has been scarcely investigated in the treatment of peri-implantitis (John et al., 2015; Renvert et al., 2011). Previous studies reported small sample sizes, different peri-implantitis case definitions, and the use of a single type of investigative powder (i.e., glycine). Although beneficial clinical results (i.e., reduction of BoP and PPD) were found, complete disease resolution (e.g., no pockets with a PPD >5 mm, with concomitant bleeding and/or suppuration on probing and absence of progressive marginal bone loss >0.5 mm) seemed difficult to achieve. Glycine air polishing could therefore not be appointed as favorable treatment method over others (i.e., plastic/titanium curettes, ultrasonic, or laser therapy).

Recently, a new air polishing powder, that is, erythritol, which is considered a sugar alcohol (similar to xylitol) and used as sugar substitute, has been introduced to the dental field. This powder is non-caloric, has a high gastrointestinal tolerance, and does not increase blood glucose or insulin levels (de Cock, 1999,2018). In vitro studies report that erythritol seems to be more effective in terms of cleaning efficacy compared to previously used powders (e.g., glycine and sodium bicarbonate) (Drago et al., 2014; Moharrami et al., 2019). Moreover, studies describe a more effective reduction in the bacterial biofilm and inhibition of post-treatment biofilm re-growth, improved cell attachment, cell viability, and proliferation of osteoblasts (Drago et al., 2017; Matthes et al., 2017; Mensi et al., 2018).

On the other hand, clinical periodontal maintenance studies on ultrasonic therapy report comparable clinical and microbiological effects to subgingival air polishing with erythritol powder (Müller et al., 2014). Ultrasonic therapy seems therefore another efficacious way to achieve infection control (Suvan et al., 2020). Compared to hand instrumentation, an ultrasonic device requires less effort and is less time-consuming which makes it a preferable cleaning method in day-to-day clinical practice. Ultrasonic therapy seemed able to

reduce clinical signs of inflammation (i.e., BoP) to a greater extent than carbon fiber/titanium curettes in the non-surgical treatment of peri-implantitis (Karring et al., 2005; Renvert et al., 2009). Yet, the effectiveness of both therapies (erythritol air polishing and ultrasonic scaling) in the non-surgical treatment of peri-implantitis has not been investigated in a randomized controlled trial.

Therefore, the current study was set up to test the hypothesis that air polishing with erythritol powder has the same effect as ultrasonic therapy on clinical, radiographical, and microbiological parameters in the non-surgical treatment of peri-implantitis. In addition, the aim was to evaluate the pain/discomfort of both therapies.

2 | MATERIALS AND METHODS

2.1 | Trial design

This two-armed, parallel, investigator-blinded randomized controlled trial was the first of a two-staged peri-implantitis treatment approach consisting of (a) a single non-surgical treatment and (b) a surgical follow-up treatment if signs of peri-implantitis persisted at the 3-month evaluation after the non-surgical treatment. Patients with a successful treatment outcome at the 3-month evaluation (i.e., probing pocket depth (PPD) <5 mm, no bleeding/suppuration on probing (BoP)/(SoP), and no progressive marginal bone loss (MBL)) were enrolled in a peri-implant maintenance program and were additionally assessed at 6, 9, and 12 months post-treatment. The study was approved by the Medical Ethical Committee of the University Medical Center Groningen (METc, UMCG with study number 2016/355) and registered in the Dutch national trial register (www.trialregister.nl) under number NL8339. The CONSORT guidelines for reporting a randomized controlled trial were followed (Schulz et al., 2010).

2.2 | Participants

2.2.1 | Eligibility criteria

Between September 2016 and August 2018, 100 patients were screened by one and the same researcher (D.H.) for eligibility. The last follow-up visit took place in November 2019. Eligible participants had at least one dental implant with clinical and radiographical signs of peri-implantitis, which was defined as follows: probing pocket depth (PPD) \geq 5 mm with concomitant bleeding and/or suppuration on probing (BoP/SoP) and progressive loss of marginal bone (MBL) \geq 2 mm, when compared to the baseline radiograph (after placement of the definitive restoration) ((de Waal et al., 2013). All the patients' eligible implants were included for clinical, radiographical, and microbiological assessment. A patient was excluded when one of the following criteria was met: a history of local head and neck radiotherapy, pregnancy, and/or lactation, uncontrolled diabetes mellitus (HbA1c > 7% or >53 mmol/mol), chronic bronchitis, and/

or asthma, use of antibiotics within 2 months before the baseline assessment, known allergy to chlorhexidine, long-term use of anti-inflammatory drugs, incapability of performing basal oral hygiene measures, implants with bone loss exceeding 2/3 of the length of the implant, implant mobility, and implants with no identifiable position for taking proper probing measurements. In addition, when the patient was subjected to a previous reconstructive or resective surgical treatment or previous non-surgical treatment of the peri-implantitis within the last 3 months, a patient was not included. Before participation, oral and written information about the study was provided. All the patients signed a written informed consent prior to enrollment.

2.2.2 | Setting and location

All patients were recruited consecutively from the patient population of the Center of Dentistry and Oral Hygiene and the Department of Oral and Maxillofacial Surgery of the University Medical Center Groningen in the Netherlands. This single-center study was performed at the Department of Oral and Maxillofacial Surgery of the University Medical Center Groningen.

2.3 | Intervention

One group of patients was treated once with an air polisher using erythritol-based powder (grain size 14 μm) containing 0.3% chlorhexidine (PLUS[®] powder, Electro Medical Systems (EMS), Nyon, Switzerland). The air powder was applied subgingivally through a hand piece with a plastic nozzle (settings device: Perio, max liquid pressure 5.0 bar and 75% air-powder pressure, ≈ 7 bar, as recommended by the manufacturer). The nozzle contained a trilateral powder-outlet and an apical water-only spray. The other group patients were treated once with the piezoelectric ultrasonic scaler with a Polyether Ether Ketone (PEEK)-coated plastic tip (PI instrument, EMS). Both interventions took place for 30 s per implant (5 s per site). Before subgingival decontamination, the implant surface was checked on hard deposits (i.e., calculus) and removed subsequently using hand instruments. The suprastructures remained fixed during the intervention and local anesthesia was used as needed. Both groups' treatments were preceded by a 30-s mouth rinse with 0.12% chlorhexidine +0.05% cetylpyridinium chloride without alcohol (Perio-aid[®], Dentaïd). Prior to peri-implant cleaning, but during the same session, a full mouth periodontal cleaning was applied using ultrasonic and/or hand instrumentation (EMS, Nyon, Switzerland/Hu-Friedy, Chicago, Illinois, US, scalers and currettes). Additionally, all patients received extensive oral hygiene instructions during the treatment appointment, including the use of an electric toothbrush and interdental brushes with the application of 0.12% chlorhexidine gel (PerioAid[®] gel, Dentaïd Benelux, Houten, the Netherlands). All treatments were performed by three experienced dental hygienists. Reinforcement of oral hygiene

instructions and supragingival cleaning of the included implant(s), using hand instrumentation, took place at 3, 6, 9, and 12 months (by the examiner, D.H.).

2.4 | Outcomes

2.4.1 | Primary outcome

The primary outcome was the mean percentage of peri-implant sites showing BoP at 3-month post-treatment.

2.4.2 | Secondary outcomes

The secondary outcome parameters were mean peri-implant SoP (%), Plq (%), PPD (mm), MBL (mm), mean full mouth periodontal BoP (%), SoP (%), Plq (%), PPD (mm), and the presence and levels of 8 classical periodontal bacterial species at the 3-month evaluation. In addition, the mid-buccal implant marginal soft tissue level between baseline and 3-month follow-up (i.e., recession (REC)) and the treatment pain/discomfort were assessed.

2.4.3 | Success criteria

The non-surgical therapy was considered successful at the 3-month evaluation when the implants demonstrated:

- Implant survival
- No pockets with a PPD ≥ 5 mm, with or without concomitant BoP and no SOP
- Absence of radiographically assessed progressive marginal bone loss

Clinical assessment

The clinical parameters were assessed at 6 sites per tooth and implant (e.g., mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual) using a Hu-Friedy PCPUNC156 periodontal probe and Shephaerds Hook Explorer EXS23. All assessments were carried out by one and the same examiner (D.H.) who was blinded regarding group allocation. The following clinical parameters were assessed binominally: BoP, visible presence of plaque and/or plaque on probing (Plq), SoP (1 = present or 0 = not present). Probing pocket depths were scored in absolute values to the nearest millimeter. To assess recession, a partial Vinyl Polysiloxane (VPS) impression (EXABITE[™] II NDS, GC America Inc., Alsip, Illinois, US) was made of the suprastructure at the implant site and buccally trimmed to half way down the suprastructure (as a fixed reference point). The distance from the mid-buccal marginal mucosa to the margin of the VPS mold was assessed using a periodontal probe. In the case of an overdenture attachment system,

the top of the suprastructure was taken as a fixed reference point. Peri-implant assessment took place at baseline, 3, 6, 9, and 12 months after therapy. Additional full mouth periodontal charts were made at baseline, 3, and 12 months.

Radiographical assessment

As approved by the Medical Ethical Committee, radiographs were taken at baseline, 3, and 12 months. To standardize the peri-apical radiographs and to assure perpendicularity (i.e., positioning of the film parallel to the long axis of the implant), the radiographs were taken using an individualized X-ray holder and paralleling technique (Planmeca Intra X-ray unit; Planmeca, Helsinki, Finland) (Meijndert et al., 2004). When it was not possible to position the X-ray holder peri-apically in fully edentulous patients (painful to the floor of the mouth, or no position in which reproducible images could be made), panoramic images were taken. Peri-implant bone loss was measured using the DICOM software (DicomWorks 1.5). Calibration of each radiograph took place on a 3-point reference scale using the known implant length and/or diameter. Bone level differences were calculated for the mesial and distal site of the implant. The outer points of the implant connection plateau were taken as reference to which the initial bone level was present (in bone level implants). Measurement corrections were made in the presence of a smooth transgingival segment of the implant (1-stage implant systems i.e., tissue level implants). In order to calculate the inter-observer and intra-observer agreement, radiographic images of ten randomly selected implants were examined twice by the same researcher (D.H.) and once by another researcher (H.M.), both of whom were blinded regarding group allocation. Subsequently, D.H. measured all the X-ray images.

Microbiological sampling

A biofilm sample from the peri-implant sulcus was obtained at baseline, 3, and 12 months using sterile paper points. Before sampling, supragingival plaque was mechanically removed. Samples were taken from four sites around the implant (mesiobuccal, distobuccal, mesiolingual, and distolingual). If a patient had more than one implant, sampling of the deepest pocket per implant took place. The samples collected from each patient were pooled in an empty vial. In dentate patients, bacterial samples were also taken from the site with the deepest probing pocket depth in each quadrant. If no deepened pockets were present, samples were taken from the mesiobuccal pockets of the teeth numbers 16, 26, 36, and 46. Outcome variables were the presence and numbers of the following putative periodontal pathogens; *Aggregatibacter actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg), *Prevotella intermedia* (Pi), *Tannerella forsythia* (Tf), *Fusobacterium nucleatum* (Fn), *Parvimonas micra* (Pm), *Treponema denticola* (Td), and *Filifactor alocis* (Fa). Microbial samples were sent to LabOral Diagnostics (Houten, the Netherlands) and analyzed using real time-PCR (quantitative polymerase chain reaction—qPCR).

Visual analog scale score

Immediately after the treatment, all patients scored the level of pain and discomfort they had experienced during both the peri-implant

therapy and periodontal cleaning using a Visual Analog Scale (VAS) ranging from 0 to 10.

2.5 | Sample size calculation

The sample size calculation for the present study was based on the total number of patients required for a two-staged trial design, so that enough patients from the non-surgical part would be available for the surgical part. Literature on sample size and a power calculation of multilevel analyses shows that at least 50 patients should be included for there to be a relevant statistic difference, since a total amount of less than 50 will lead to biased estimates of the second-level standard errors (Maas & Hox, 2005). Scherbaum and Ferreter (2009) pointed out the relationship of different levels in accordance to an adequate sample size and power. Translation of this relationship to our research protocol means a sample size (amount of patients) in combination with implants nested in patients. With a mean group size of 2 infected implants per patient and a minimum amount of 50 patients, it was estimated to detect a medium effect size with 80% power at a significance level of $\alpha = 0.05$. Since our study focused on clinically relevant effects, small effect sizes were less important and detection of medium effect sizes was supposed to be sufficient for our study.

According to the non-surgical peri-implantitis literature at the time of the study design, we estimated a 20% success rate for our non-surgical patient treatment phase (Muthukuru et al., 2012). Therefore, it was assumed that 80% of the patients would need surgical follow-up. To compensate for patient withdrawal and losses to follow-up (10%), a sample size of 80 patients (40 in the air polishing and 40 in ultrasonic therapy group) was used. This was an intentional slight overestimation in order to assure enough available participants for the surgical phase of the study.

2.6 | Randomization

Randomization was performed using sealed envelopes which contained a code ranging from AA to CZ alongside with a note saying either "air polishing" or "ultrasonic therapy." The dental hygienist performing the procedure opened the envelope, wrote down the code, read the note, and performed the procedure. A decoding list saying which code belongs to which procedure was kept sealed until data analysis. This way, the investigator did not know which procedure was performed.

2.7 | Statistical analysis

To analyze the difference in clinical and radiographical efficacy between both treatments, generalized linear mixed models (GLMMs) were used (IBM SPSS Statistical software, version 23.0. for Windows, Armonk, NY: IBM Corp). A three-level structure was chosen with

patient implant and time as level 1, 2, and 3, respectively. The patient was considered unit of analysis, whereas the implant the unit of observation. First, the T3 clinical and radiographical outcomes were analyzed while controlling for the corresponding baseline parameters BoP, SoP, Plq, PPD, and MBL (i.e., crude analysis). Then, the primary and secondary outcomes were analyzed while controlling for the baseline values and confounding effects (i.e., adjusted analysis). The following a priori defined confounders were used in the adjusted mixed model: history of periodontitis (dichotome), smoking, prosthetic design (nominal), and mean periodontal plaque level at T3 (linear). For skewed data (SoP and Plq), a gamma distribution was used. The full mouth periodontal outcomes, VAS scores, and mid-buccal recession were analyzed using an independent sampled *t* test. A paired sampled *t* test was applied to analyze differences in overall mean full mouth periodontal outcomes before and after therapy. The log-transformed mean peri-implant and periodontal microbiological outcomes were analyzed at T3 using a Mann-Whitney *U* test was used (for between group differences). The data collected at 6, 9, and 12 months (for successfully treated patients at 3-month evaluation) are presented with descriptive statistics.

3 | RESULTS

The flow of patients throughout the present study is depicted in Figure 1. The overall baseline patient and implant characteristics are shown in Table 1. Baseline characteristics of the successful subjects are described in Table 2. Patients, aged between 25–77 years (mean age 58 years, *SD* ± 12.3), were randomly allocated to receive air polishing (*n* = 39) or ultrasonic scaling (*n* = 40). Four patients (6 implants) were lost to follow-up between baseline, intervention, and 3-month evaluation (see Figure 1), yielding 76 patients with 133 implants, that is, 38 patients/63 implants in the airpolishing group and 38 patients/70 implants in the ultrasonic therapy group, available for analysis. Patients' baseline and 3-month follow-up clinical and radiographical outcomes are shown in Table 3. An overview of the successful patient outcomes (at baseline, T3, T6, T9, and T12) is presented in Table 4. Mixed model outcomes for the mean difference in BoP, SoP, Plq, PPD, and MBL between both groups at T3 are shown in Table 6. The log-transformed mean (*SD*) of the selected putative periodontal pathogens of the pooled peri-implantitis samples and pooled periodontal samples (in partial edentulous patients) is presented in Table 7. The number of patients with positive samples (%) before and after therapy is presented in Figure 2.

At 3-month evaluation, 14 patients (18%) showed a successful treatment outcome: 4 patients (5 implants) in the airpolishing group and 10 patients (18 implants) in the ultrasonic therapy group. Peri-implant assessment of these 14 patients took place at 6, 9, and 12 months follow-up. The distribution of sites with BoP in successful implants is shown in Table 5. The remaining 62 patients with an unsuccessful treatment outcome at the 3-month evaluation discontinued the current study but were invited to continue in a surgical follow-up protocol.

3.1 | Primary outcome

At 3-month evaluation, no statistical significant difference for mean BoP was found between air polishing ($49.8\% \pm 31.5$) and ultrasonic therapy ($48.1\% \pm 29.0$).

3.2 | Secondary outcomes

No significant differences between both groups at 3-month evaluation were found for the secondary clinical peri-implant parameters; SoP, Plq, and PPD, neither in the crude nor in the adjusted analysis, see Table 6. In addition, patients succeeded to lower mean levels of periodontal full mouth BoP and plaques scores (BoP reduced from $11.8\% \pm 10.5$ to $9.2\% \pm 7.0$ at T3, *p* = .032, plaque score reduced from $27.3\% (\pm 17.9)$ to $22.6 (\pm 16.8)$, *p* = .013, at T3) (see Table 3). No group differences were seen for mean marginal bone loss (at the mesial and/or distal site) or microbiological outcomes at 3-month evaluation (see Tables 3 and 7). Patients that showed more than 0.5-mm progressive bone loss at T3 all had probing pocket depths ≥ 5 mm. At baseline, the most frequent isolated species from the peri-implant pocket were Fn, Pm, and Tf (airpolishing group: 97.5%, 85%, and 80% and ultrasonic therapy group: 97.5%, 87.5%, and 70%, respectively). Three months after treatment, in both groups, almost unchanged levels for all periodontal bacterial species were found (see Table 7).

No difference in mean pain/discomfort level (VAS scores) was found between both groups. However, patients reported low VAS scores for both therapies (air polishing $2.1 (\pm 1.9)$, ultrasonic $2.6 (\pm 1.9)$, *p* = .222) as well as low periodontal pain/discomfort scores (VAS score air polishing $1.0 (\pm 1.1)$ versus ultrasonic $1.4 (\pm 1.5)$ respectively, *p* = .425). No significant difference in mid-buccal recession was found between both groups, but both groups showed a slight increase in recession (airpolishing group $7.2 \text{ mm} (\pm 2.0)$ to $7.4 \text{ mm} (\pm 2.0)$, ultrasonic therapy group $6.6 (\pm 1.8)$ to $6.7 \text{ mm} (\pm 1.9)$, *p* = .552). Treatment of both therapies went uneventful; no emphysema could be detected after airpolishing treatment or any adverse reaction to ultrasonic treatment was reported.

Within the successful subgroup, a continued reduction after 3 months of therapy was seen for peri-implant parameters BoP, Plq, PPD, and periodontal full mouth BoP and Plq. In addition, successful patients showed lower clinical scores at baseline (BoP, SoP, Plq, PPD, and MBL), a shorter implant time in function compared to the overall group and all successful patients were non-smokers. The majority of successfully treated implants at T3 showed 2 out of 6 sites with BoP, with none of the implants showing 5 or 6 out of 6 sites with BoP.

4 | DISCUSSION

4.1 | Key findings

This randomized controlled trial compared the clinical, radiographical, and microbiological outcomes of erythritol air polishing and

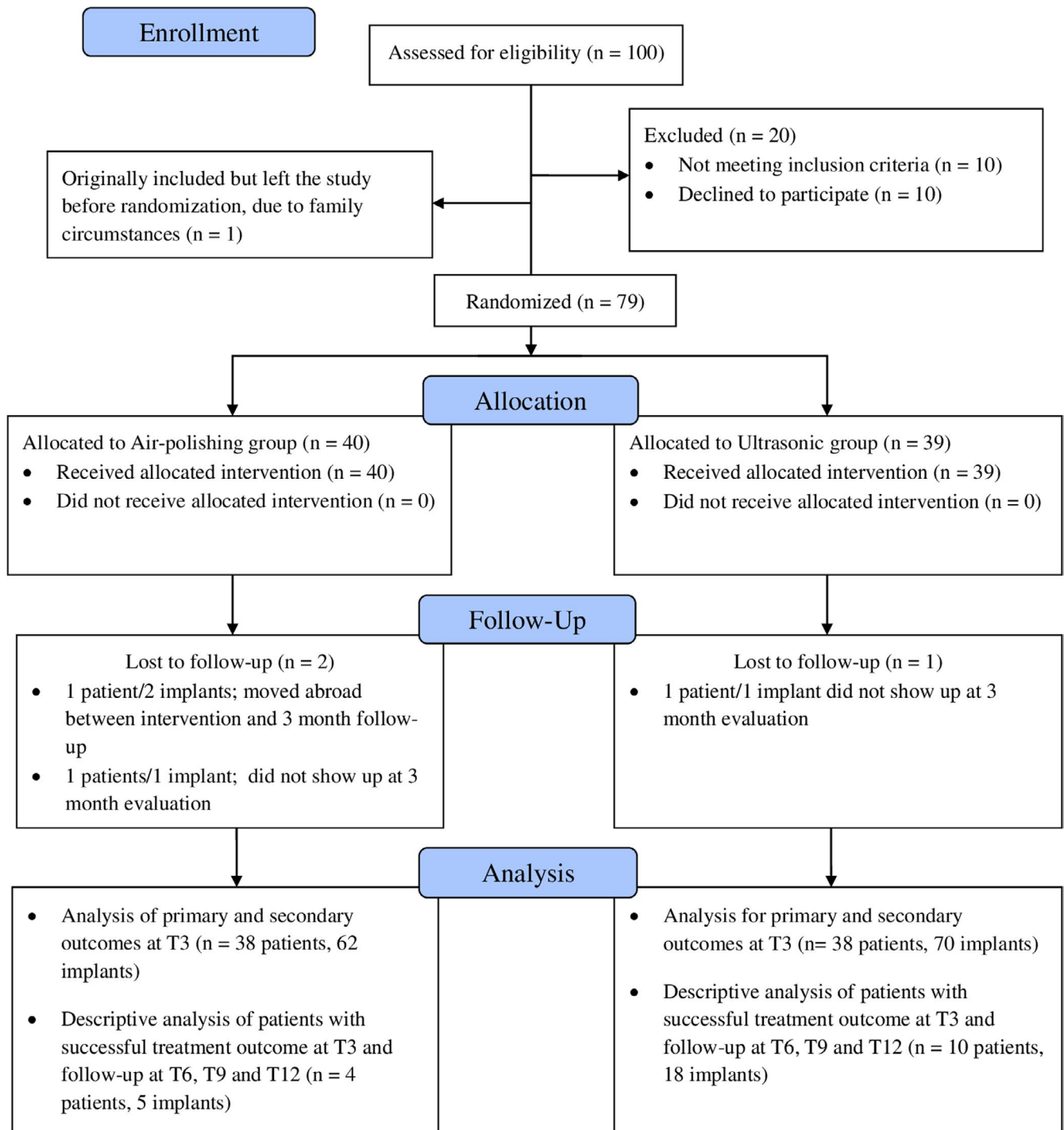


FIGURE 1 Flow diagram

piezoelectric ultrasonic scaling with a PEEK plastic tip in the non-surgical treatment of peri-implantitis. Three months after therapy, there was no significant difference between both therapies for the primary outcome mean BoP (%). Other clinical, radiographical, or microbiological parameters neither showed any difference between both groups. Therefore, in terms of our null-hypothesis, air polishing seems to be as effective as ultrasonic scaling in the reduction of inflammatory signs (BoP, SoP, Plq, and PPD). Both therapies, however,

resulted in limited success with most of the patients showing persistent signs of inflammation at 3-month follow-up. Interestingly, follow-up of successful patients showed gradual improvement of peri-implant parameters up to 12 months when supportive peri-implant therapy (supragingival instrumentation when plaque/calculus was visible) and oral self-care reinforcement were applied at 6 and 9 months. In addition, both therapies were considered minimally painful without one of both being significantly less painful.

TABLE 1 Baseline patient and implant characteristics

	Air polishing	Ultrasonic therapy
Patient characteristics		
Total number of patients	40	40
Age [years; mean (SD)]	62(8.9)	55(14.1)
Gender; F (female)/M (male)	15F/25M	20F/20M
Smoking; n subjects (%)		
Current	7 (17.5)	8 (20)
Never	26 (65)	23 (57.5)
Former	7 (17.5)	9 (22.5)
History of periodontitis; n subjects (%)		
Yes	17 (42.5)	10 (24)
No	23 (57.5)	30 (76)
Diabetes; n subjects (%)		
Yes (but controlled; HbA1c < 7% or <53 mmol/mol)	2 (5)	0 (0)
No	38 (95)	40 (100)
Parafunction (bruxism/clenching); n subjects (%)		
Yes	6 (15)	8 (20)
No	34 (85)	32 (80)
Dental status, n patients (%)		
Fully edentulous	10 (25)	9 (22.5)
Partially edentulous	30 (75)	31 (77.5)
Implant characteristics		
Total number of implants included	66	73
Total number of implants presenting peri-implantitis (range)	(1–6)	(1–6)
Time in function [years; mean (SD)]	8.6 (6.1)	9.7 (4.8)
Implant type; n implants (%)		
Nobel Biocare	25 (37.9)	35 (47.9)
Straumann	26 (39.4)	21 (28.8)
Biomet 3i	4 (6.1)	7 (9.6)
MegaGen	4 (6.1)	1 (1.4)
Astra Tech	2 (3.0)	2 (2.7)
Camlog	2 (3.0)	2 (2.7)
Other (Simpler,IMZ, Dentsply Friadent, Pitt-easy, Smeden-Martina, Triron Q)	3 (4.5)	5 (6.8)
Implant surface roughness (Sa)		
Minimally rough (turned, machined) ≥ 0.5 , < 1.0 μm	9 (13.6)	9 (12.3)
Moderately rough ≥ 1.0 , < 2.0 μm	56 (84.8)	59 (80.8)
Rough ≥ 2.0 μm	1 (1.5)	5 (6.8)
Type of restoration; n implants (%)		
Single crown	20 (30.3)	38 (52.1)
Fixed partial denture	23 (34.8)	12 (16.4)

(Continues)

TABLE 1 (Continued)

	Air polishing	Ultrasonic therapy
Overdenture	23 (34.8)	23 (31.5)
Screw- or cement-retained restoration; n implants (%)		
Screwed	47 (71.2)	52 (71.2)
Cemented	19 (28.8)	21 (28.8)
Implants placed in maxilla or mandible; n implants (%)		
Maxilla	36 (54.5)	46 (63.0)
Mandible	30 (45.5)	27 (37.0)
Implants placed anterior posterior; n implants (%)		
Anterior (central incisor to cuspid)	28 (42.4)	29 (39.7)
Posterior (premolar/molar)	38 (57.6)	44 (60.3)

4.2 | Comparison with relevant findings from other published studies

To date, no studies have evaluated erythritol air polishing as monotherapy for the non-surgical treatment of peri-implantitis. Only two previous studies report on a single non-surgical intervention in peri-implantitis patients with glycine airpolishing therapy (John et al., 2015; Renvert et al., 2011). When glycine powder air polishing was compared with mechanical debridement + local antiseptic therapy using chlorhexidine in a study by John and coworkers, a significant higher reduction in mean BoP scores at 3 months was found (BoP reduced from $99.0\% \pm 4.1$ to $57.8\% \pm 30.7$ in the airpolishing group and from $94.7\% \pm 13.7$ to $78.1\% \pm 30.0$ in the mechanical debridement group). Compared to the present study, glycine air polishing also seemed to result in a greater reduction of BoP. However, the study by John et al. included patients with as initial or moderate forms of peri-implantitis (probing pocket depths of ≥ 4 mm compared to ≥ 5 mm in our study and the loss of supporting bone as $\leq 30\%$ compared to ≥ 2 mm in our study), implying that implants with a less severe state of inflammation might have been studied. In addition, only non-smoking patients were included and a high risk of bias on several items was reported (e.g., allocation concealment, blinding of participants, and selective reporting) in the recent systematic review (Suárez-López Del Amo et al., 2016). Therefore, interpreting these results should be done cautiously.

In comparison with Renvert et al., no statistical differences in clinical parameters (BoP, SoP, Plq, and PPD) and bone level changes were found when glycine air polishing (Perioflow[®]) was compared to laser therapy (Er:YAG). Also, the range of pocket depth reduction in the present study was comparable to the reductions in the study by Renvert et al. (between 0.1 mm and 1 mm at 6 months in the majority of patients). Moreover, comparable changes in average marginal bone loss were found for air polishing (0.1 mm (± 0.8)) at 3 months. This despite the fact that suprastructures were removed,

TABLE 2 Characteristics of successfully versus unsuccessfully treated patients

	Successful	Unsuccessful
Patient characteristics		
Number of patients (%) / implants (%)	14 (18.4) / 23 (17.3)	62 (81.6) / 110 (82.7)
air polishing; n subjects (%) / n implants (%)	4 (28.6) / 5 (21.7)	34 (54.8) / 58 (52.7a)
ultrasonic therapy; n subjects (%) / n implants (%)	10 (71.4) / 18 (78.3)	28 (45.2) / 52 (47.3)
Age (years; mean (SD))	59.7 (12.0)	58.8 (12.0)
Gender; female (%) / male (%)	8 (57.1) / 6 (42.9)	26 (41.9) / 36 (58.1)
Smoking; n subjects (%)		
Current	0 (0)	13 (21.0)
Never	10 (71.4)	38 (61.3)
Former	4 (28.6)	11 (17.7)
History of periodontitis; n subjects (%) Yes / No	3 (21.4) / 11 (78.6)	22 (35.5) / 40 (64.5)
Diabetes; n subjects (%) Yes (but controlled) / No	0 (0) / 14 (100)	2 (3.2) / 60 (96.8)
Implant characteristics		
Time in function (years; mean (SD))	7.2 (4.0)	9.5 (5.6)
Jaw (upper/lower); n implants	12 (52.2) / 11 (47.8)	68 (61.8) / 42 (38.2)
Position (anterior/posterior); n implants	10 (43.5) / 13 (56.5)	45 (40.9) / 65 (59.1)
Edentulous (partial/fully); n patients	10 (71.4) / 4 (28.6)	48 (77.4) / 14 (22.6)
Screw/cement-retained; n implants	20 (87.0) / 3 (13.0)	75 (68.2) / 35 (31.8)
Single crown/ fixed partial denture (FPD) / overdenture; n implants	9 (15.5) / 8 (22.9) / 6 (13.0)	45 (40.9) / 27 (24.5) / 38 (34.5)
Implant surface roughness (Sa); n implants		
Minimally rough (turned, machined) ≥ 0.5 , $< 1.0 \mu\text{m}$	2 (8.7)	15 (13.6)
Moderately rough ≥ 1.0 , $< 2.0 \mu\text{m}$	19 (82.6)	91 (82.7)
Rough $\geq 2.0 \mu\text{m}$	2 (8.7)	4 (3.6)

TABLE 3 Clinical and radiographical peri-implant outcomes and periodontal full mouth scores

Outcomes ^a	N = 80 patients / 139 implants		Air polishing		Ultrasonic therapy		Overall	
			T0 (40 / 66)	T3 (38 / 63)	T0 (40 / 73)	T3 (38 / 70)	T0 (80 / 139)	T3 (76 / 133)
Peri-implant	mean BoP (%)	% of sites (SD)	58.1 (30.3)	49.8 (31.5)	56.2 (28.8)	48.1 (29.0)	57.1 (29.4)	48.9 (30.1)
		% of implants (n)	93.9 (62)	88.9 (56)	91.8 (67)	92.9 (65)	92.8 (129)	91.0 (121)
	mean SoP (%)	% of sites (SD)	15.4 (20.7)	13.0 (19.5)	14.4 (21.6)	13.3 (22.2)	14.9 (21.1)	13.2 (20.9)
		% of implants (n)	54.5 (36)	44.4 (28)	42.5 (31)	35.7 (25)	48.2 (67)	39.8 (53)
mean Plq (%)	% of sites (SD)	23.2 (33.2)	15.9 (30.7)	16.0 (22.1)	12.3 (23.2)	19.4 (28.1)	14.0 (27.0)	
	% of implants (n)	45.5 (30)	30.2 (19)	43.8 (32)	31.9 (22)	44.6 (62)	31.1 (41)	
PPD (mm)	mean (SD)	4.8 (1.2)	4.3 (1.3)	5.0 (1.5)	4.7 (1.8)	4.9 (1.4)	4.6 (1.6)	
Marginal bone loss (mm) ^b	mean (SD)	4.0 (1.9)	4.0 (1.8)	3.9 (1.8)	4.0 (1.8)	4.0 (1.8)	4.0 (1.8)	
Periodontal	Full mouth BoP (%)	mean (SD)	9.4 (7.0)	8.6 (6.4)	14.2 (12.9)	10.0 (7.7)	11.8 (10.5)	9.2 (7.0) ^c
		mean (SD)	2.7 (15.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.3 (10.7)	0.0 (0.0)
	Full mouth SoP (%)	mean (SD)	27.6 (18.3)	20.7 (16.5)	27.2 (17.9)	24.5 (17.1)	27.3 (17.9)	22.6 (16.8) ^c
		mean (SD)	2.1 (0.27)	2.1 (0.31)	2.0 (0.26)	1.9 (0.48)	2.1 (0.27)	2.0 (0.40)

^aMeasured on a 6 point scale.^bMeasured at the mesial and distal implant site.^cSignificant difference for within overall group analysis (paired sampled t test).

TABLE 4 Descriptive statistics of successful patients' (air polishing and ultrasonic therapy group combined) clinical and radiographical outcomes

Outcomes ^a	N = 14 patients / 23 implants		T0 (14/23)	T3 (14/23)	T6 (12/19)	T9 (14/23)	T12 (14/23)
Peri-implant	mean BoP (%)	site level (SD)	49.3 (23.8)	31.9 (16.6)	28.1 (20.8)	18.1 (18.7)	23.9 (20.0)
		implant level (n)	95.7 (22)	95.7 (22)	73.7 (14)	60.9 (14)	73.9 (17)
	mean SoP (%)	site level (SD)	6.5 (16.5)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
		implant level (n)	17.4 (4)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	mean Plq (%)	site level (SD)	17.4 (19.8)	15.9 (20.4)	12.3 (15.6)	12.3 (12.5)	12.2 (15.3)
		implant level (n)	52.2 (12)	52.2 (12)	52.6 (10)	56.5 (13)	47.8 (11)
	PPD (mm)	mean (SD)	4.0 (0.9)	3.2 (0.6)	3.1 (0.5)	3.0 (0.7)	2.9 (0.6)
	Marginal bone loss (mm) ^b	mean (SD)	3.0 (0.8)	2.9 (0.9)	NA	NA	3.0 (1.1)
Periodontal	N = 10 patients (partial edentulous)		T0	T3	T6	T9	T12
	Full mouth mean BoP (%)	patient level (SD)	14.6 (8.9)	9.9 (7.9)	NA	NA	9.4 (4.0)
	Full mouth mean SoP (%)	patient level (SD)	0.0 (0.0)	0.0 (0.0)	NA	NA	0.0 (0.0)
	Full mouth mean Plq (%)	patient level (SD)	33.5 (21.5)	31.3 (19.6)	NA	NA	21.9 (14.9)
	Full mouth mean PPD (mm)	patient level (SD)	2.0 (0.25)	2.0 (0.29)	NA	NA	2.0 (0.23)

^aMeasured on a 6 point scale.

^bMeasured at the mesial and distal site.

a sonic toothbrush was provided with a new brush head at the 3-month follow-up, and the treatment time was double as compared to our study (1 min vs. 30 s). Therefore, although it could be hypothesized that these measures might have led to a more effective removal of the peri-implant biofilm, it did not result in a better treatment outcome. Nevertheless, it might be reasonable to extend the subgingival treatment time and remove the suprastructure to secure a thoroughly cleaned peri-implant area, especially in more advanced lesions (Mensi et al., 2020).

None of the ultrasonic scaling studies in the current literature evaluated the same piezoelectric ultrasonic scaler with plastic PEEK tip in the non-surgical treatment of peri-implantitis. Two studies with a comparative study design, however, were found evaluating subgingival instrumentation using an ultrasonic device (Vector[®] system) (Karring et al., 2005; Renvert et al., 2009). That ultrasonic device showed to be more effective in the reduction of BoP when compared to carbon fiber curettes and titanium curettes, respectively. However, no significant differences between the groups in clinical improvements (i.e., BOP, PPD, and bone level changes) were found. In accordance, our study showed a similar limited clinical effect of ultrasonic debridement. Therefore, from the data in the present study, neither air polishing nor ultrasonic cleaning could be considered a superior therapy in terms of our primary outcome (i.e., mean BoP at T3).

Regarding the microbiological results in this study, comparable outcomes were found in two studies by Persson et al., 2010 and Persson et al., 2011. Both study showed no difference in bacterial

counts when using an air polishing, ultrasonic scaling, or laser therapy (Er:YAG), including no significant changes in bacterial load or in bacterial composition. Reduced bacterial counts of *P. aeruginosa*, *S. aureus*, and *S. anaerobius* were seen 1 month after the airpolishing therapy, but the bacterial counts did not decline further at the 6-month evaluation after air polishing and laser therapy. As compared to these studies, the limited clinical effect observed in the present study seems to be underlined by the unchanged levels of periodontal pathogens.

Success at 3 months after therapy was defined without BoP (%) being a discriminating factor. Rightly so, because if previously used success criteria would have been applied (e.g., criteria by Carcuac et al., 2016; Heitz-Mayfield & Mombelli, 2014), implants with PPD <5 with concomitant BoP would be considered unsuccessful. According to the current treatment protocol, patients subsequently would have been invited for a surgical follow-up. Looking at the gradual decline in clinical parameters (i.e., mean BoP, PPD) within the successful group of implants, it seemed that stable bone levels and absence of progression of disease could be attained in implants showing PPD <4 mm with the presence of BoP up to 12 months. Therefore, this study underlines that the sensitivity of BoP for the prediction of disease progression is quite low and that strict success criteria need to be cautiously interpreted and applied.

To decide which therapy could be considered preferable, next to the clinical, radiographical and microbiological parameters, treatment pain/discomfort of both therapies was assessed. In contrast to the periodontal literature, in which a low degree of discomfort for

erythritol air polishing was found compared to ultrasonic scaling, no difference in discomfort between both therapies in our study was found (Bühler et al., 2016). For both therapies, an equal low level of pain was reported. Therefore, neither this parameter seems to be a discriminating factor to decide which therapy to apply. However, it should be kept in mind that for airpolishing systems, the risk for emphysema may be increased in difficult to reach areas. Especially when it is needed to tilt the airpolishing nozzle. Moreover, air polishers are limited to the removal of attached biofilms whereas hard deposits should be removed by hand. Interestingly, as reported by the experienced dental hygienists in this study, access of the peri-implant pocket appeared more challenging using a thick nozzle compared to the lean ultrasonic tip. Hence, these factors may indicate to recommend a different decontamination method in specific cases.

At last, when baseline characteristics of the successful group of patients were compared with these of the unsuccessful ones, interesting differences regarding PPD (4.0 mm vs. 4.9 mm, respectively), MBL (3.0 mm vs. 4.0 mm, respectively), and time in function before therapy took place (7.2 vs. 9.5 year) were seen. Considering the success of these patients up to 12 months after therapy, these parameters might indicate the importance of early diagnosis and therefore early commencement of non-surgical therapy.

4.3 | Limitations

The following limitations should be addressed when interpreting the results of this study. First,

suprastructures were not removed during this study which might have led to inadequate peri-implant accessibility and inadequate clinical measurements. In addition, hampered access (e.g., due to overcontoured suprastructures) of the peri-implant

pocket could have complicated the insertion of the ultrasonic or airpolishing tip, and therefore led to an inadequate therapy effect.

Second, this study might lack a true control therapy. However, to date, no non-surgical intervention seems to be the gold standard in the treatment of peri-implantitis. As a means of non-surgical treatment, mechanical debridement of the implant surface is primarily recommended (Renvert et al., 2019). Therefore, a randomized study design in which two promising mechanical interventions were compared was chosen. This so, to analyze if the aforementioned treatment interventions could lead to appointing a superior standard therapy.

Third, the marginal bone level measurements were done on peri-apical radiographs as well as on panoramic pictures. In the latter case, a standardized angulation of the picture could not be secured. Therefore, the measurements on the overview X-ray pictures might

TABLE 5 Distribution of sites with BoP in implants with pocket depths <5 mm at 3, 6, 9, and 12 months

	T3 (N = 23)	T6 (N = 19)	T9 (N = 23)	T12 (N = 23)
Sites with BoP	N (%)	N (%)	N (%)	N (%)
0 out of 6	1 (4.3)	5 (26.3)	9 (39.1)	6 (26.1)
1 out of 6	7 (30.4)	2 (10.5)	6 (26.1)	6 (26.1)
2 out of 6	10 (43.5)	7 (36.8)	6 (26.1)	5 (21.7)
3 out of 6	3 (13.0)	4 (21.0)	1(4.3)	5 (21.7)
4 out of 6	2 (8.7)	1 (5.3)	1(4.3)	1 (4.3)
5 out of 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
6 out of 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: N = number of successfully treated implants.

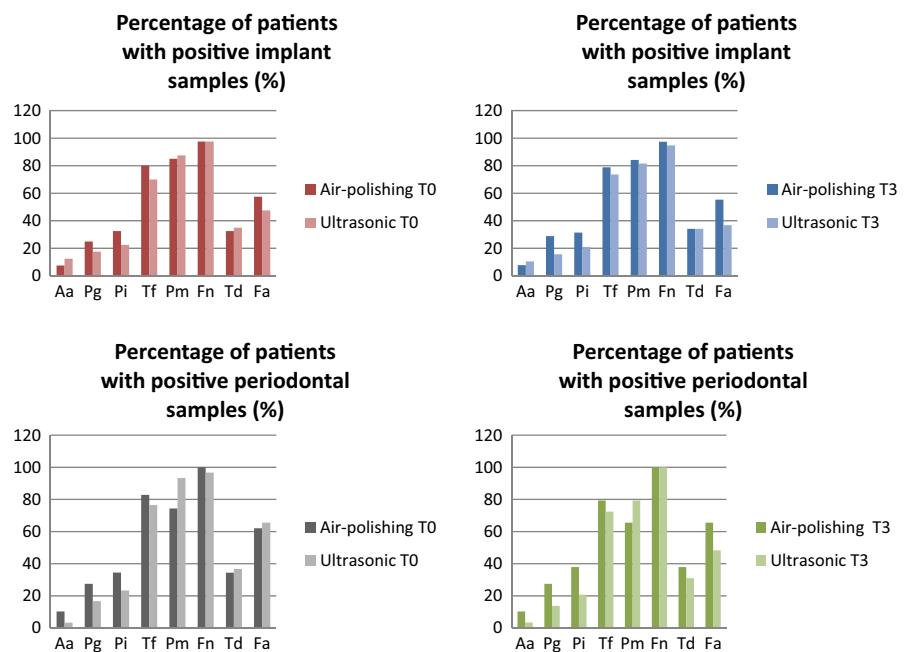


FIGURE 2 Number of patients in the airpolishing group and ultrasonic therapy group with positive pooled peri-implant and periodontal samples, before and 3 months after therapy

Outcome variable	Crude analysis ^c		Adjusted analysis ^d	
	β (95% CI)	p-value	β (95% CI)	p-value
Mean BoP ^a	-0.037 (-0.147; 0.073)	.380	-0.023 (-0.165; 0.119)	.746
Mean SoP ^b	0.048 (-0.048; 0.143)	.320	0.059 (-0.015; 0.134)	.114
Mean Plq ^b	0.034 (-0.103; 0.171)	.623	-0.009 (-0.154; 0.136)	.897
Mean PPD ^b	0.054 (-0.253; 0.361)	.728	0.140 (-0.249; 0.529)	.478
MBL ^a	0.126 (-0.370; 0.623)	.618	0.239 (-0.296; 0.775)	.380

^aNormal distributed data analyzed with linear model distribution.

^bNon-normal distributed data analyzed with gamma distribution.

^cAdjusted for baseline and time.

^dAdjusted for baseline, time, smoking, history of periodontitis, mean periodontal full mouth plaque score at T3, and type of suprastructure.

TABLE 6 Generalized linear mixed model outcomes for mean difference in BoP, SoP, Plq, PPD, and MBL between both groups at T3, using the ultrasonic therapy as reference arm

TABLE 7 Log-transformed mean (SD) of selected putative periodontal pathogens

Peri-implant outcome	Air polishing		Ultrasonic therapy	
	T0	T3	T0	T3
N = 40 (T0), N = 38 (T3)				
Aa	6.7 (0.9)	6.5 (0.8)	4.2 (1.5)	5.6 (1.1)
Pg	5.9 (2.5)	5.3 (1.8)	4.8 (2.3)	6.3 (1.6)
Pi	4.6 (1.9)	5.3 (1.0)	4.8 (2.0)	5.3 (1.3)
Tf	5.1 (1.3)	5.0 (1.1)	4.8 (1.2)	4.9 (1.1)
Pm	4.1 (1.0)	4.2 (1.0)	3.9 (1.2)	4.1 (1.0)
Fn	4.9 (0.9)	4.7 (0.9)	4.4 (1.3)	4.6 (1.0)
Td	4.7 (1.0)	3.9 (1.2)	4.7 (0.9)	4.9 (1.1)
Fa	5.2 (1.1)	5.0 (0.9)	4.4 (1.1)	4.7 (1.0)
Periodontal outcome				
N = 29 (T0), N = 29 (T3)				
Aa	4.7 (1.0)	3.9 (1.1)	4.9	6.6
Pg	4.3 (1.4)	3.7 (1.6)	4.5 (2.2)	5.1 (1.3)
Pi	4.6 (1.2)	4.4 (2.0)	4.2 (1.6)	4.5 (1.4)
Tf	4.1 (1.2)	4.2 (1.7)	3.9 (1.3)	4.1 (1.3)
Pm	3.6 (0.9)	3.8 (0.8)	3.5 (0.9)	3.8 (1.0)
Fn	4.1 (0.9)	4.1 (1.0)	3.8 (1.3)	4.1 (1.0)
Td	3.8 (0.9)	3.8 (1.5)	3.7 (0.9)	3.8 (1.0)
Fa	4.1 (1.2)	3.9 (1.3)	4.1 (0.9)	3.6 (1.4)

Note: Pooled patient peri-implantitis samples and periodontal samples (of partially edentulous) per group. *Aggregatibacter actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg), *Prevotella intermedia* (Pi), *Tannerella forsythia* (Tf), *Parvimonas micra* (Pm), *Fusobacterium nucleatum* (Fn), *Treponema denticola* (Td) and *Filifactor alocis* (Fa).

not have been as accurate for comparison purposes. However, given this study's outcomes, it seems unlikely that different bone levels would have been encountered when only peri-apical standardized pictures were used.

Lastly, the included patients showed large variations in implant characteristics (i.e., different implant brands, with different implant surfaces and suprastructures, placed in the anterior and posterior part of the mouth as well as in the lower and upper jaw), and

peri-implantitis disease severity (varying from mild to severe peri-implantitis). Although such a heterogeneous group of patients and implants might represent a true cross section of the society, it makes it very difficult to compare the effect of the therapies in specific subgroups of patients, for example, cases with mild versus severe peri-implantitis or smokers versus non-smokers. Future studies are needed to evaluate the effect of therapy in these specific groups of cases.

4.4 | A brief summary of clinical and research implications

Non-surgical peri-implantitis treatment using either air polishing or piezoelectric ultrasonic scaling seems to result in a reduction in clinical inflammatory outcomes up to the 3-month follow-up, however, without effectively arresting disease progression in the majority of cases. Therefore, our findings underline the limited effect of a single non-surgical intervention in the treatment of peri-implantitis.

Interestingly, in patients which show a positive outcome at 3 months after therapy, stable peri-implant health could be expected up to 12 months after therapy. A priori identification of potentially successful patients characteristics (i.e., specific clinical, implant, and patient characteristics) need to be further assessed in future studies.

Although the overall effect for non-surgical therapies seems limited, a non-surgical treatment phase per se seems imperative in the overall treatment approach since a small number of patients may benefit from a non-surgical treatment in such a way that no further surgical treatment is required. Additionally, the clinician can evaluate patient motivation and use this phase to educate patients about the disease process and modifying factors.

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CONFLICT OF INTEREST

All authors declare no conflict of interest. The study was self-funded by the authors and their institution.

AUTHOR CONTRIBUTIONS

Diederik Hentenaar: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (equal); Writing-original draft (lead). **Yvonne Catharina Maria De Waal:** Conceptualization (equal); Methodology (equal); Supervision (lead); Writing-original draft (supporting). **Roy Stewart:** Methodology (supporting). **Arie Jan van Winkelhoff:** Writing-original draft (supporting). **Henny J.A. JA Meijer:** Supervision (supporting); Writing-original draft (supporting). **Gerry M Raghoebar:** Supervision (lead); Writing-original draft (supporting).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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