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**Effect of two post-surgical cleansing protocols on early periodontal wound healing and cytokine levels following osseous resective surgery: a randomized controlled study.**

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## **ABSTRACT**

*Objectives:* The aim of this RCT study was to compare early wound healing and gingival crevicular fluid cytokine levels of patients treated with two different post-surgical cleansing protocols.

*Methods:* A total of 30 chronic periodontitis patients scheduled for osseous resective surgery with fiber retention technique was randomly assigned to follow one of two post-surgical protocols. Patients assigned to the test protocol (n = 15) were instructed to brush the surgical area with a sonic toothbrush starting the day after surgery in addition to 0.12% chlorhexidine (CHX) rinsing, while patients following the control protocol (n = 15) rinsed only with 0.12% CHX solution and resumed mechanical cleansing with a manual toothbrush on day 14 after surgery. Interleukin (IL)-1 $\beta$  and IL-8 levels were assessed before and 14 days post-operatively in gingival crevicular fluid. Patients were recalled on day 7, 14, 21, 28 after surgery for clinical assessment. Pain was self-reported by a visual analogue scale.

*Results:* Lower early wound healing scores, higher bacterial plaque reduction and milder inflammatory response were observed at the surgical sites in the test group on day 7, 14 and 28 when compared to the control group ( $P < 0.01$ ). The faster wound healing process was modulated by a statistically significant decrease in IL-1 $\beta$  and IL-8 levels on day 14 in the sonic group. The intensity of pain was similar between groups.

*Conclusions:* The introduction of sonic toothbrush on the first post-operative day as an adjunct of daily CHX rinsing would seem to accelerate early wound healing.

## **Introduction**

The inhibitory effect of bacterial contamination on post-surgical wound healing has been extensively documented.<sup>1,2</sup> In the presence of minimal plaque amounts, periodontal wounds appear to heal faster and with fewer complications than when greater amounts of plaque are allowed to accumulate.<sup>3,5</sup> In this context, post-surgical removal of newly formed biofilms plays a crucial role in the early healing phase and in successful long-term periodontal outcomes.<sup>6-8</sup> Extensive research has demonstrated the beneficial clinical effects of chemical control of supra-gingival plaque formation in any type of surgery, with chlorhexidine (CHX) being considered as the gold standard for this purpose.<sup>9-11</sup> In contrast, only a limited number of studies described timing, frequency and detailed technique of mechanical plaque removal during the first days after periodontal and implant flap surgery.<sup>11-16</sup> This is likely due to toothbrush trauma, and subsequent discomfort and sensitivity perceived by the patient in the surgical area. Several manual toothbrushes dedicated to post-surgical plaque control are currently available but unfortunately with poor scientific support.<sup>16,17</sup> Recently, a new generation of powered sonic toothbrushes has been introduced, and has been shown to have superior efficacy in plaque removal and in control of periodontal inflammation in comparison with manual toothbrushes.<sup>18,19</sup> The combination of hydrodynamic shear forces and waves of pressure in the liquids surrounding the teeth is capable of dislodging dental plaque in hard-to-reach areas such as interdental surfaces.<sup>20</sup> For these data, it is feasible to propose the use of a sonic toothbrush immediately after osseous resective surgery (ORS) to improve post-surgical plaque control and accelerate wound healing. In ORS procedures bone remodelling is combined with flap margin positioning at the level of bone crest to reestablish a physiologic scalloped bone morphology and soft tissue contour in a more apical position.<sup>21</sup> The interproximal areas are generally not covered by gingival tissue and heal by secondary

intention. Previous studies reported an incomplete epithelialization and inter-proximal fibrin deposits in about 50% of patients treated with ORS at 1-week follow-up.<sup>22,23</sup>

Surgical procedures trigger metabolic and immunologic reactions that lead to a rise in pro-inflammatory cytokines.<sup>24</sup> It has been demonstrated that evaluation of cytokine levels in wound fluids is a sensitive and specific assessment of inflammation.<sup>25</sup> Specifically, mediators such as interleukin (IL)-1 $\beta$  and IL-8 are crucial for postsurgical wound healing.<sup>24,26,27</sup> IL-1 $\beta$  induces periodontal inflammation, up regulates adhesion molecules on endothelial cells, stimulates chemokine production, and induces the expression of other mediators that amplify the inflammatory response.<sup>28,29</sup> IL-8 modulates functions of neutrophils, including transmigration, chemotaxis and antimicrobial activities.<sup>30</sup> Assessment of IL-1 $\beta$  and IL-8 GCF levels provides a more objective and accurate wound healing evaluation compared to clinical methods.<sup>31</sup>

Therefore, the goal of this study was to test the hypothesis that mechanical cleansing of the surgical area with a powered sonic toothbrush in addition to daily rinsing with CHX starting the day immediately after ORS can predictably enhance gingival wound healing as assessed by clinical parameters and cytokine levels compared with chemical plaque control alone for the first 2 weeks after surgery and manual toothbrushing for the other 2 weeks.

## **Material and methods**

### ***Experimental design and study population***

This article is reported according to the CONSORT statement. The study was a parallel, single-centre, randomized, controlled clinical trial designed to assess the impact of a new post-surgical protocol for home plaque removal on early wound healing, clinical and biochemical parameters in comparison with conventional post-operative care protocol. It was conducted at the University of Turin, C.I.R. Dental School, Department of Surgical Sciences, from February 2017 to January 2018. The protocol complied with the rules of the Declaration of Helsinki of 1975, as revised in 2002 and was approved by the Institutional Ethics Committee of the "AOU Città della Salute e della Scienza, Turin, Italy (protocol approval no 0017928). The purpose and procedures were fully explained to all participants before

enrolment in the study and written informed consent was obtained from all those wishing to participate.

Patients were consecutively enrolled in the study from among patients with a diagnosis of severe chronic periodontitis<sup>32</sup> (Stage III based on the current classification<sup>33</sup>) when the following inclusion criteria were met: 1) completion of etiological treatment at least 3 months prior to screening; 2) a full mouth plaque score (FMPS) and full mouth bleeding score (FMBS) < 20% at the time of enrolment; 3) need for ORS determined on the basis of residual pockets in posterior sextants with  $\geq 5$  mm probing depth (PD) associated with radiographic intrabony component  $\leq 3$  mm<sup>21</sup> and persisting bleeding on probing (BoP); 4) no history of periodontal surgical treatment on the involved teeth.

Exclusion criteria were: 1) contraindications for periodontal surgery; 2) systemic diseases that could influence the outcome of the therapy; 3) medications affecting periodontal status or periodontal inflammation in the previous 6 months; 4) pregnancy or lactation; 5) smoking > 10 cigarettes/day.

### ***Sample Size and Randomization***

The difference between the two post-surgical care protocols in the soft tissue healing at 14 days as assessed by a modification of the Early Wound-Healing Index (EHI)<sup>34</sup> was set as the primary outcome. A sample size of 12 patients per group was calculated to detect at the 14-day follow-up a minimum difference of 0.5 in EHI between the groups with an expected standard deviation of 0.4, an alpha error of 0.05, and an 80% power. However, taking into account the possibility of dropouts, 15 patients per group were recruited.

Each patient was given a number and was randomly assigned to one of the two post-surgical cleansing regimens by a computer-generated table. To conceal assignment, opaque envelopes assigned to the patients were opened at the completion of the surgery. The investigator and the statistician were masked to the experimental procedure.

### ***Surgical procedures and post-surgical protocols for plaque control***

All surgical interventions were performed by the same clinician (ZS). The surgical technique was the same for each operation and consisted of the apically positioned flap plus ORS with

fiber retention technique according to Carnevale.<sup>35</sup> Bone remodeling was carried out using diamond-round burs and chisels to reshape positive bone architecture. Flaps were secured at the level of the alveolar crest. Patients were prescribed ibuprofen 600 mg to be taken immediately after surgery and every 12 hours for 5 days.

At the completion of the surgical session the sealed envelope was opened and the patient assigned to follow one of two post-operative protocols. Patients assigned to the sonic toothbrushing post-surgical cleansing protocol (test group) were instructed to brush teeth including the surgical area with a sonic toothbrush (Sonicare FlexCare Platinum, Philips Oral Healthcare Inc., Bothell, WA, USA) with sensitive head (Gum care mode) starting the day after surgery for 4 weeks and to rinse with a 0.12% CHX solution with antidiscoloration system (Curasept, Curadent Healthcare srl, Saronno, Va, Italy) two times a day for 60 seconds for the first 14 days. Patients following the conventional post-surgical cleansing protocol (control group) were instructed to avoid brushing in the surgical area and to rinse with a 0.12% CHX solution with antidiscoloration system two times a day for 14 days. At day 14 post-surgery they were advised to discontinue CHX rinsing and were allowed to resume mechanical plaque control using a manual soft-bristle toothbrush (GUM Technique Post Operation 317, Sunstar Saronno, Va, Italy) for another 14 days.

The total brushing time was set at 2 minutes twice a day, and patients were instructed to gently brush for 30 seconds teeth in the surgical area. They were also advised to brush all teeth not included in the treated area with toothpaste without sodium lauryl sulfate (Elmex®, GABA®, Lörrach, Germany). The same dental hygienist (GC) delivered brushing instructions and post-operative care.

Seven days after surgery sutures were removed. During the first operative month a weekly professional debridement with rubber cups and CHX gel 0.20% was performed on teeth in the surgical area along with interdental cleaning with super floss. The patients's oral hygiene standards were reviewed and oral hygiene procedures were reinforced.

### ***Clinical Examination***

All the study participants received at baseline a periodontal examination performed by a



calibrated and masked clinician (MB). The periodontal parameters were assessed at six sites per tooth in the surgically treated sextant by means of 1-mm marked periodontal probe (PCP UNC15, Hu-Friedy, Chicago, IL, USA). Clinical parameters assessed were presence/absence of plaque (PI), presence/absence of BoP, gingival index (GI),<sup>36</sup> PD, gingival recession (Rec), CAL and keratinized tissue width (KT, only on 3 sites at the buccal aspect). The percentage of sites with PI and BoP was also measured in the whole mouth and expressed as FMPS and FMBS, respectively. At 7, 14, 21 and 28 days after surgery EHI<sup>34</sup>, PI, and GI were measured again. EHI was modified in the following scale in order to comply with the wound healing phases following osseous resective procedures: (1) complete flap re-epithelialization, no fibrin line in interproximal area and no red line along the gingival margin; (2) complete re-epithelialization and fibrin line in the interproximal area; (3) complete flap re-epithelialization, fibrin clot in the interproximal area; (4) incomplete flap re-epithelialization and partial necrosis; (5) incomplete flap re-epithelialization and complete necrosis. Intraexaminer agreement for EHI recordings was assessed on 10 nonstudy sextants involved in ORS surgeries. The Kendall  $\tau$  coefficient was 0.96.

### ***Patient-centered outcomes***

Patients were asked to score pain intensity on a horizontal visual analog scale (VAS) 10-cm long (0 = no pain, 10 = extreme pain) at 7, 14, 21 and 28 days after surgery. Each evaluation form consists of three lines, one for each postoperative week.

### ***GCF and PWF collection***

In each subject of both groups, fluid samples were collected from the tooth with the deepest intrabony defect in the sextant. The area was isolated with cotton after removing the supragingival plaque and the gingival tissues were gently dried with air syringe. Gingival crevicular fluid (GCF) was collected immediately prior to the surgical treatment (baseline) and periodontal wound fluid (PWF) 14 days after surgery by means of paper strips (PerioPaper Strips, Oraflow Inc., Plainview, NY, USA) inserted into the site and left in place for 30 seconds. Strips contaminated by bleeding were discarded. The amount of collected fluid was measured using an electronic volume quantification unit (Periotron 8000, Oraflow Inc.,

Plainview, NY, USA), calibrated with distilled water.<sup>37</sup> The strips were placed into coded sealed Eppendorf tubes containing sterile phosphate-buffered saline. After 1 hour at room temperature, the strips were removed, and the eluates centrifuged at 6.000 x g for 5 minutes to remove plaque and cellular elements. The supernatant was stored at -80°C until further analysis.

### ***IL-1 $\beta$ and IL-8 assay***

Biochemical analyses were performed by a blinded examiner (MM) at the Department of Clinical and Biological Sciences, University of Turin (Italy). Commercially available enzyme-linked immunosorbent assay (ELISA) kits (Invitrogen CA, USA) were used to detect IL-1 $\beta$  and IL-8 levels in 50  $\mu$ l aliquots of GCF/PWF sample according to the manufacturer's instructions. Each sample and standard was run as duplicates within the same plate and the intensity of the color was measured by absorbance at 450 nm using a microplate reader (Wallac 1420, PerkinElmer, Finland). Concentrations of the cytokines were determined from the standard curve and expressed as pg/mL. The detection levels of the assays were 1 pg/ml for IL-1 $\beta$  and <5.0 pg/mL for IL-8.

### ***Statistical analysis***

A statistical software program (SPSS for Mac, SPSS version 24.0, IBM Corporation, Armonk, NY, USA) was used for data analysis. Data were first examined for normality by the Kolmogorov-Smirnov test and if the data did not achieve normality analyses were performed using non-parametric methods. Descriptive statistics were performed using mean  $\pm$  standard deviation (SD) for quantitative variables and frequencies and percentage for qualitative variables.

Pairwise comparisons between the treatment groups were performed using the Student's *t*-test for unpaired samples for quantitative variables with normal distribution (FMPS, PD, CAL, KT), the Mann-Whitney *U*-test for those with non Gaussian distribution (FMBS, BoP, PI, GI, EHI, VAS scores, IL-1 $\beta$  and IL-8) and the Chi-square test for qualitative variables.

Within-group differences in clinical and biochemical parameters were analysed by the

Wilcoxon signed-rank test (IL-1 $\beta$  and IL-8) or the Friedman's test (PI, GI, BoP, EHI, VAS scores). Multiple comparisons were conducted with post-hoc tests. The significance level for all analyses was set at 5%.

## Results

The flow chart of the study is presented in Fig. 1. Forty-eight chronic periodontitis patients were consecutively screened for enrollment. Twelve patients did not meet the inclusion criteria and six patients refused the surgical intervention. Thirty subjects were consecutively enrolled and randomized in the test (n = 15, 5 males and 10 females aged 37 to 68 years, mean age 47.9  $\pm$  8.8 years) and control group (n = 15, 7 males and 8 females aged 34 to 76 years, mean age 49.0  $\pm$  12.8 years). The two groups were balanced for age ( $P = 0.791$ ) and gender distribution ( $P = 0.256$ ).

Surgical procedures were performed between June and November 2017. Each patient provided a posterior sextant for the ORS procedure. Fifteen posterior sextants (6 maxillary and 7 mandibular) were assigned to follow the sonic toothbrushing cleansing protocol, while 15 (7 maxillary and 6 maxillary) the conventional post-operative protocol. The frequency of sextants on the left and right jaw side was similar between groups. All follow-up visits were completed in January 2018. No data points were missing for analysis.

Clinical variables are presented in Tables 1 to 3. At baseline, no statistically significant differences ( $P > 0.05$ ) were observed between test and control sextants (Table 1). No adverse events were registered during the early healing period. FMPS and FMBS remained below 20% through the study as summarized in Table 2.

When considering teeth involved in the surgical procedure (Table 3) the percentage of BoP positive sites decreased 28 days after therapy in both groups ( $P < 0.001$ ). Statistically significant differences between the two post-surgical cleansing protocols were observed. Lower EHI scores at weeks 1 and 2 characterized the surgical sites in the patients using the sonic toothbrush when compared to controls. This difference in the wound healing profile was accompanied by less bacterial plaque accumulation (PI) at the same time points and by a significantly decrease of gingival inflammation degree (GI) at week 2 in the sonic group. The

profile of the pro-inflammatory mediators at baseline and week 2 is shown in the Table 4. A statistically significant decrease in IL-1 $\beta$  and IL-8 levels was observed in the sonic group. Anyway, the intergroup analysis did not show any statistically significant differences between groups ( $P > 0.05$ ).

When control patients resumed mechanical plaque control, the differences remained statistically significant only at week 3 in favor of the sonic group (Table 3). At the end of week 4 an optimal wound closure was observed in the surgical sites of both cleansing groups.

Data from patient perception about the early healing phase is reported in Table 5. None of the patients reported intraoperative pain at the end of the surgery. Based on a horizontal VAS, it was observed that the pain/discomfort experienced after surgery was statistically similar between groups ( $P > 0.05$ ) and decreased progressively during the first 4 post-operative weeks. At week 4 pains was no longer reported.

### ***Discussion***

Although the role of patient-performed oral hygiene measures on wound healing process and periodontal treatment outcomes has been widely reported, a specific post-surgical plaque control protocol is still lacking.<sup>3-7</sup> The general routine is to replace the mechanical cleansing procedures by a chemical plaque control with CHX solution during the first 2-6 weeks post-surgery depending on the type of surgical intervention.<sup>21,38</sup> The suspension of mechanical plaque control measures after periodontal regeneration procedures is finalized to guarantee blood clot stability and to not disturb the maturing newly formed connective tissue.<sup>39</sup> Following conservative and osseous resective surgeries it could be advised the early introduction of a mechanical cleaning process provided that it does not result in any local adverse event and does not cause patient discomfort.

In the present randomized controlled trial an oral hygiene post-surgical protocol consisting of the use of sonic toothbrush from the first post-operative day in combination with daily CHX rinsing resulted in faster wound healing and lower biofilm formation rate but comparable patient acceptance when compared to the conventional post-operative care protocol following ORS.<sup>21-23,34</sup> In the control group the reintroduction of the extra-soft manual toothbrush at the

surgical sites was done after 2 weeks so that plaque control was guaranteed only by rinsing with 0.12% CHX twice a day during the first 2 weeks after ORS.

Past investigations have shown the anti-plaque and anti-inflammatory benefits of sonic powered toothbrushes relative to manual toothbrushes for managing gingivitis and periodontitis.<sup>40-42</sup> Brushing-induced turbulence has been shown to drive fluid dynamic forces into the more inaccessible areas of the oral cavity, particularly in the inter-proximal spaces, resulting in an effective biofilm removal in these areas.<sup>43</sup> Of note, ORS intervention modifies soft tissue morphology by apically positioning the flap margin to the level of the bony crest both interproximally as well as facial/lingually with consequent higher crown length and larger interdental spaces at posterior sextants. This makes it more difficult to effectively clean the exposed root surfaces during the initial healing phase using CHX mouthwashes alone. During the first 14 days after surgery a significant 20% additional reduction in plaque accumulation in the operated areas was found for subjects using the sonic brush in combination with CHX mouthrinse. This was accompanied by a different pattern in the early postoperative healing phase. The healing after regenerative procedures and flap surgeries has been addressed in previous clinical studies by using the EHI.<sup>15,44</sup> This index was designed to monitor periodontal wound healing by primary intention.<sup>34</sup> Following ORS for elimination of bony defects and repositioning of the soft tissue flaps to the level of the alveolar bone, healing occurs by secondary wound closure in the interdental surgical area. Considering the lack in the literature of wound indexes assessing healing by secondary intention, we modified the EHI to comply with the soft tissue healing process in the first operative weeks after ORS. After 14 days about 86.7% of surgical areas in the sonic group displayed EHI of 1 or 2 compared with 40% of surgical sites in the control group. At week 4 an optimal wound closure was observed in both groups. It has been previously reported that when oral disinfection is guaranteed a good level of healing is achieved around 4 weeks following flap surgery.<sup>12</sup>

Previous investigations proposed the use of soft bristle toothbrushes alone or in combination with chemical plaque control for post-surgical maintenance care. Heitz et al.<sup>12</sup>, O'Neil et al<sup>13</sup>

and Montevicchi et al.<sup>16</sup> proposed the reintroduction of an extra-soft toothbrush on day 3 after periodontal flap and implant surgery and reported similar wound healing outcomes over a 4-week experimental period when compared with chemical plaque control only<sup>12,13</sup> or with the use of a conventional manual toothbrush<sup>16</sup>. It is important to point out that the decision to restart the use of the control toothbrush depended on the patient's perception of discomfort and was between 3 and 14 days after surgery.<sup>16</sup> This might have impacted on the study results. Laugish et al. observed a similar healing profile after 2-week rinsing period with a 0.05% CHX/extract herbal combination mouthrinse or a 0.1% CHX solution as adjunct to mechanical plaque control with a soft toothbrush starting on the third day after surgery.<sup>15</sup>

The introduction of mechanical cleaning on day 3 is based on the frailty of the healing tissue involved in an initial inflammatory process during the first postoperative days.<sup>12</sup> However, some authors reintroduced mechanical cleansing on the same day of the surgical intervention or the day after surgery, but they did not report any detail on the brush and the technique.<sup>11,14</sup> In the present study patients started brushing the day after surgery. It has been clearly established that the daily use of a power toothbrush reduces brushing force and the incidence of gingival bleeding because of gum damage.<sup>45,46</sup> An *in vitro* study demonstrated that sonic toothbrushes could remove 56-73% from enamel specimens at a distance of 3 mm between the dental surface and the bristles.<sup>20</sup>

The present findings would support the safety of power toothbrushes.<sup>47</sup> No adverse events were observed and no differences were found at 3-month examination in periodontal clinical outcomes between test and control group. Pain at toothbrushing application was generally reported till day 14 but pain intensity was comparable or lower than that from surgical areas where toothbrushing was not applied. In addition, pain perception decreased fast in both groups and on day 28 was not longer reported. These data are consistent with those previously published on patient perception after ORS procedures with and without fiber retention technique under standard post-operative care protocol.<sup>22,23</sup>

Clinical findings were supported by biochemical analysis. Since it is known that the total amount of cytokines varies based on the volume of GCF, the concentration instead of the

total amount was considered.<sup>48</sup> For the present study, IL-1 $\beta$  and IL-8 were chosen as two pro-inflammatory cytokines involved in early inflammatory processes related to wound healing.<sup>24,25</sup> IL-1 $\beta$  induces periodontal inflammation and controls the extracellular matrix degradation activity of the plasminogen activator system during inflammation and wound healing.<sup>28</sup> Overproduction of IL-1 $\beta$  induces periodontal tissue destruction and inflammation, while local application of inhibitors of IL-1 $\beta$  may promote periodontal wound healing and regeneration.<sup>29</sup> IL-8 modulates the activity and function of neutrophils, and regulates neutrophil-related tissue damage.<sup>30</sup>

In the present study, statistically significant differences in IL-1 $\beta$  and IL-8 levels between baseline and week 2 were observed only in the test group. It was reported that surgical wound healing in a site with plaque accumulation results in prolonged production of IL-1, which may be a reflection of the extent of tissue trauma and delayed wound healing.<sup>49</sup> Due to the large variations among individuals, the present analysis could not demonstrate any statistically significant differences in the effect of the two post-surgical cleansing protocols on the cytokine levels. In specific anatomic conditions (e.g. incipient or early furcation involvement) the enhanced wound healing process coupled with the lower expression of cytokines may be beneficial to reduce the postsurgical intensity of the host-mediated inflammatory response and the osteoblastic activity following ORS.<sup>50</sup>

The present study has some limitations. A split-mouth study would be more indicated to control confounding covariates and compare patient-related outcomes between test and control procedures. However, repeated instructions and motivations could hide the clinical differences between the two cleansing protocols. Second, several other biological mediators are involved in the wound healing process and should be studied to better understand the different phases of healing.

## **Conclusion**

This is the first study examining the effectiveness of a sonic toothbrush to mechanically remove bacterial plaque from posterior sextants immediately following ORS. Clinical and

biochemical findings suggest accelerated wound healing and reduced inflammation following mechanical cleansing of the surgical area compared with conventional post-operative care protocols. However, future studies are needed to confirm the present results.

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#### **Clinical relevance**

**Scientific rationale for study:** Although the role of patient-performed oral hygiene measures on wound healing process and periodontal treatment outcomes has been widely reported, a specific post-surgical plaque control protocol is still lacking.

**Principal findings:** Clinical inflammatory indices and gingival crevicular levels of inflammatory cytokines suggest accelerated wound healing following mechanical cleansing with sonic toothbrush of sextants treated with osseous resective surgery (ORS) compared with chemical plaque control alone.

**Practical implications:** Due to their safety and comfort, sonic-powered toothbrushing may be used for plaque control starting the first post-operative day following ORS.



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**Table 1. Comparison of baseline clinical characteristics of sextants treated with osseous resective surgery (mean ± SD) in the two experimental groups.**

	<b>Sonic toothbrushing post-surgical cleansing protocol (n = 15) Mean ± SD</b>	<b>Conventional post-surgical cleansing protocol (n =15) Mean ± SD</b>	<b>Differences between groups*</b>
<b>BOP (%)</b>	23.0 ± 13.9	21.9 ± 12.1	NS
<b>PD (mm)</b>	3.5 ± 0.4	3.4 ± 0.4	NS
<b>Rec (mm)</b>	1.0 ± 0.7	1.0 ± 0.9	NS
<b>CAL (mm)</b>	4.5 ± 1.0	4.4 ± 0.8	NS
<b>KT (mm)</b>	5.2 ± 0.7	5.3 ± 1.2	NS

*BOP* percentage of sites with bleeding on probing, *PD* probing depth, *Rec* gingival recession, *CAL* clinical attachment level, *KT* keratinized tissue width, *NS* difference between groups is not statistically significant ( $P > 0.05$ ).

\*Student's unpaired *t*-test or Mann-Whitney *U*-test.

**Table 2. FMPS and FMBS over the experimental period.**

	<b>Sonic toothbrushing post-surgical cleansing protocol (n = 15)</b>		<b>Conventional post-surgical cleansing protocol (n =15)</b>		<b>Differences between groups*</b>
	<b>Mean ± SD</b>	<b>Range</b>	<b>Mean ± SD</b>	<b>Range</b>	
<b>FMPS (%)</b>					
<i>baseline</i>	15.8 ± 3.1	13 -19	16.7 ± 3.4	8 - 19	NS
<i>28 days</i>	14.5 ± 3.9 <sup>a</sup>	9 - 18	15.8 ± 4.2 <sup>a</sup>	6 - 19	NS
<b>FMBS (%)</b>					
<i>baseline</i>	12.2 ± 4.4	5 – 18	13.3 ± 3.9	7 – 19	NS
<i>28 days</i>	10.7 ± 4.5 <sup>a</sup>	4 – 19	11.4 ± 2.5 <sup>a</sup>	8 – 17	NS

FMPS full-mouth plaque score, FMBS full-mouth bleeding score.

<sup>a</sup> $P > 0.05$ ,  $P$ -values represent changes from baseline (paired t-test or Wilcoxon test).

\*Student's unpaired  $t$ -test or Mann-Whitney  $U$ -test.

**Table 3. Clinical variables during the early wound healing phase of sextants treated with osseous resective surgery.**

	Sonic toothbrushing post-surgical cleansing protocol (n = 15)		Conventional post-surgical cleansing protocol (n = 15)		Differences between groups*
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	
<b>BoP (%)</b>					
baseline	23.0 $\pm$ 13.9	11 - 50	21.9 $\pm$ 12.1	8- 50	NS
28 days	9.3 $\pm$ 9.4 <sup>a</sup>	0 - 25	7.0 $\pm$ 9.3 <sup>a</sup>	0 - 20	NS
<b>EHI</b>					
7 days	3.3 $\pm$ 0.6 <sup>b</sup>	2 - 4	3.8 $\pm$ 0.4 <sup>b</sup>	3 - 4	0.009
14 days	1.8 $\pm$ 0.5	1 - 3	2.7 $\pm$ 0.7	2 - 4	0.006
21 days	1.1 $\pm$ 0.3 <sup>d</sup>	1 - 2	1.5 $\pm$ 0.5 <sup>c</sup>	1 - 3	0.010
28 days	1.0 $\pm$ 0.0 <sup>d</sup>	1	1.0 $\pm$ 0.0 <sup>d</sup>	1	NS
<b>PI (%)</b>					
baseline	28.4 $\pm$ 12.0 <sup>b</sup>	11 - 56	24.7 $\pm$ 20.4 <sup>b</sup>	14 - 67	NS
7 days	41.7 $\pm$ 15.7 <sup>c</sup>	11 - 61	69.7 $\pm$ 27.5 <sup>d</sup>	33 - 100	0.006
14 days	36.3 $\pm$ 16.2	15 - 67	66.7 $\pm$ 22.4 <sup>c</sup>	13 - 100	0.003
21 days	32.5 $\pm$ 17.7	6 - 61	59.6 $\pm$ 22.2 <sup>c</sup>	22 - 100	0.002
28 days	28.5 $\pm$ 15.3	11 - 67	39.9 $\pm$ 28.2 <sup>c</sup>	10 - 89	NS
<b>GI</b>					
baseline	0.6 $\pm$ 0.5 <sup>b</sup>	0 - 2	0.5 $\pm$ 0.4 <sup>b</sup>	0 - 1.6	NS
7 days	1.2 $\pm$ 1.0 <sup>c</sup>	0.2 - 3	1.4 $\pm$ 0.6 <sup>d</sup>	0.1 - 2	NS
14 days	0.3 $\pm$ 0.2	0 - 0.7	0.8 $\pm$ 0.6	0.2 - 2	0.018
21 days	0.1 $\pm$ 0.1 <sup>c</sup>	0 - 0.3	0.7 $\pm$ 0.4	0 - 1.6	0.004
28 days	0.2 $\pm$ 0.2	0 - 0.6	0.3 $\pm$ 0.2 <sup>d</sup>	0 - 0.7	NS

EHI early wound healing index, PI percentage of sites with bacterial plaque in the treated sextant, GI Gingival index, BoP percentage of sites with bleeding on probing in the treated sextant, NS difference between groups is not statistically significant ( $P > 0.05$ ).

<sup>a</sup> $P < 0.001$ ,  $P$ -values represent changes from baseline (Wilcoxon test).

<sup>b</sup> $P < 0.001$ ,  $P$ -values represent changes among the time points (Friedman's test).

<sup>c</sup> $P < 0.01$ ,  $P$ -values represent longitudinal changes from baseline (Dunn test).

<sup>d</sup> $P < 0.001$ ,  $P$ -values represent longitudinal changes from baseline (Dunn test).

\*Mann-Whitney  $U$ -test.

**Table 4. GCF/PWF cytokine concentration during early wound healing.**

	Sonic toothbrushing post-surgical cleansing protocol (n = 15)		Conventional post-surgical cleansing protocol (n = 15)		<i>Differences between groups*</i>
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
<b>IL-1β (pg/ml)</b>					
<i>baseline</i>	1.5 ± 1.1	1.1 (0.6 – 4.4)	1.2 ± 0.7	1.1 (0.6 – 3.7)	NS
<i>14 days</i>	0.9 ± 0.3 <sup>a</sup>	0.8 (0.5 – 2.2)	1.1 ± 0.5	0.9 (0.5 – 2.4)	NS
<b>IL-8 (pg/ml)</b>					
<i>baseline</i>	25.7 ± 22.7	18.7 (7.6 – 57.4)	21.1 ± 23.9	15.2 (6.2 – 60.7)	NS
<i>14 days</i>	15.2 ± 9.4 <sup>b</sup>	13.2 (3.2 – 42.7)	16.7 ± 13.4	14.00 (4.2 – 45.1)	NS

GCF gingival crevicular fluid, PWF periodontal wound fluid, IL-1β Interleukin-1 β, IL-8 interleukin-8, SD standard deviation, NS difference between groups is not statistically significant, P > 0.05.

<sup>a</sup> Significantly different from baseline, P < 0.01 (Wilcoxon test).

<sup>b</sup> Significantly different from baseline, P < 0.001 (Wilcoxon test).

\*Mann-Whitney U-test.

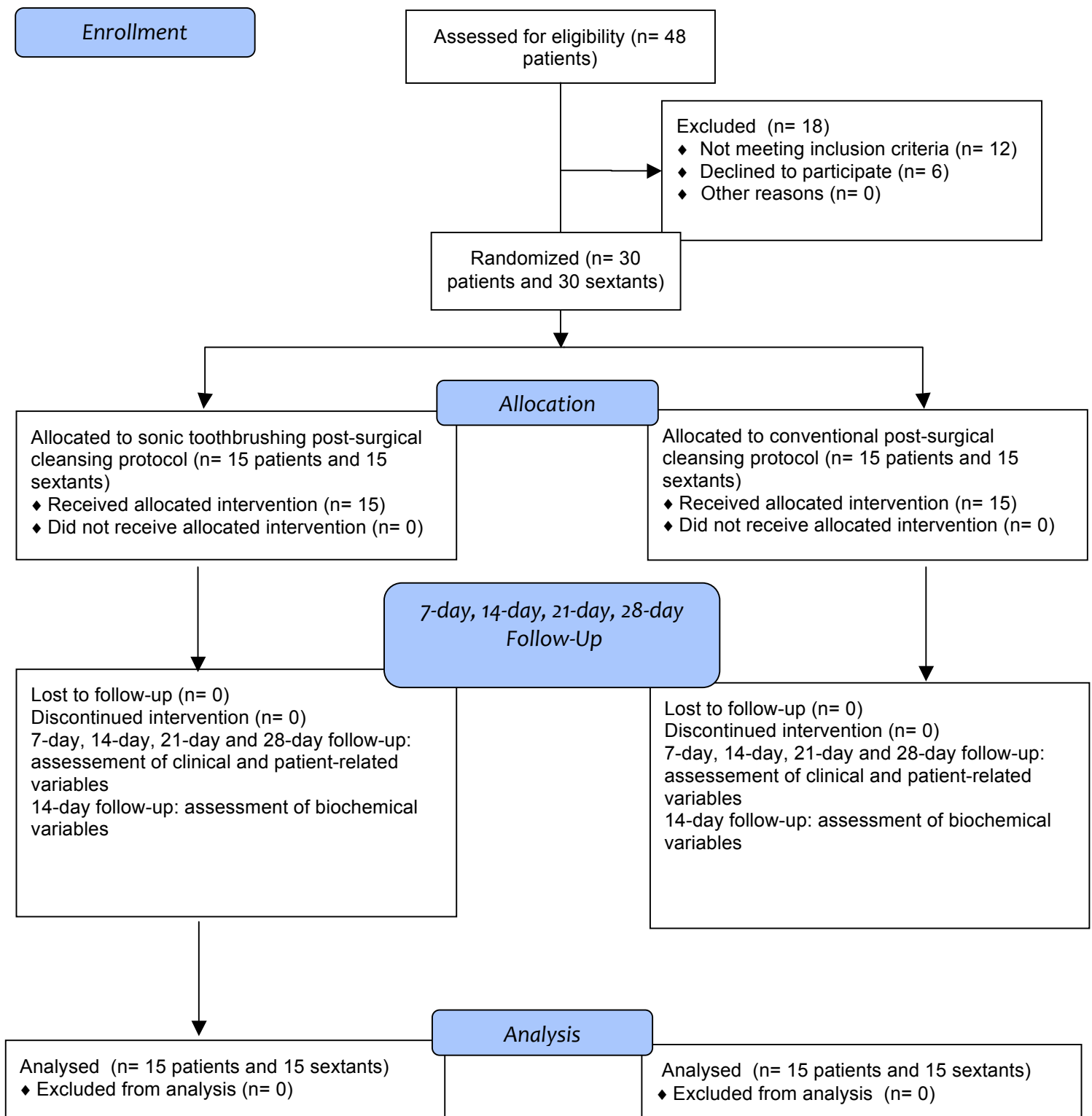


**Table 5. Patient experience in terms of post-operative pain (VAS units).**

	Sonic toothbrushing post-surgical cleansing protocol (n = 15)		Conventional post-surgical care protocol (n =15)		<i>Differences between groups*</i>
	Mean $\pm$ SD	Median (range)	Mean $\pm$ SD	Median (range)	
<b>7 days</b>	4.1 $\pm$ 2.3	4.9 (1.0 - 7.9)	4.8 $\pm$ 3.1	5.2 (1.0 - 10.0)	NS
<b>14 days</b>	1.3 $\pm$ 1.6	1.0 (0 -5.2)	1.9 $\pm$ 2.0	1.1 (0 -7.3)	NS
<b>21 days</b>	0.3 $\pm$ 0.7	0 (0 – 2)	0.3 $\pm$ 0.6	0 (0 – 2.2)	NS
<b>28 days</b>	0	0 (0)	0	0 (0)	NA

VAS *units* visual analogue scale units (with 0=no pain and 10=unbearable pain), NS difference between groups is not statistically significant ( $P > 0.05$ ), NA not applicable.

\*Mann-Whitney *U*-test.



**Fig. 1** Consort diagram showing the study design.