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Adjunctive effect of soft tissue grafting in the surgical treatment of peri-implantitis: clinical and radiographic outcomes from a preclinical canine experiment

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ABSTRACT

Purpose: The aim of this study was to clinically and radiographically investigate the effect of soft tissue grafting as an adjunct in the surgical treatment of ligature-induced peri-implantitis lesions in canines.

Methods: Seven Mongrel dogs received implant placements on both sides of the posterior mandible (3 fixtures per side). After inducing peri-implantitis via ligation with suture material, surgical treatment was performed on each implant according to randomly assigned groups: DI, implantoplasty only; DIB, implantoplasty followed by collagenated, deproteinized bovine bone mineral (DBBM-C) grafting; DIC, implantoplasty followed by autogenous connective tissue graft (CTG); DIV, implantoplasty followed by volume-stable collagen matrix (VCMX) grafting; DIBC, implantoplasty followed by DBBM-C grafting and CTG; and DIBV, implantoplasty followed by DBBM-C and VCMX grafting. Clinical and radiographic outcomes were evaluated. Composite treatment success was defined by the following criteria: absence of bleeding on probing at 12 weeks post-surgery; a reduction in probing depth (PD) or an increase of 1 mm or less in PD at 12 weeks post-surgery; and absence of additional bone loss ≥0.5 mm at 12 weeks post-surgery compared to radiographic baseline. Statistical significance was set at $P<0.05$.

Results: All groups exhibited clinical and radiographic improvement after surgery. Clinical parameters, radiographic bone levels, and mucosal thickness did not significantly differ among the groups. The DI and DIV groups demonstrated higher composite treatment success rates (71.4%) compared to the other 4 groups. Adjunctive soft tissue grafting resulted in fewer changes in peri-implant mucosa. The effect of hard tissue grafting on bone regeneration was minimal, and combining hard and soft tissue grafting did not yield better outcomes than implantoplasty alone.

Conclusions: The surgical treatment of peri-implantitis lesions remains challenging. Soft tissue grafting showed clinical benefits by reducing changes in the peri-implant mucosa. The effect of hard tissue grafting on bone regeneration was very limited.

Keywords: Animal research; Bone; Dental implants; Mucosa; Peri-implantitis; Surgical procedures

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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INTRODUCTION

Peri-implantitis is an inflammatory disease characterized by progressive resorption of the supporting bone [1,2]. Similar to periodontitis, dental plaque is recognized as the primary etiologic factor, and peri-implant mucositis—where inflammation is limited to the mucosa—typically precedes peri-implantitis, analogous to gingivitis preceding periodontitis [3]. Due to the high prevalence of peri-implantitis [4,5], numerous treatment modalities have been proposed to regenerate lost marginal bone and re-establish peri-implant health [6,7].

The effectiveness of both non-surgical and surgical treatments has been extensively investigated. While some studies reported successful outcomes following non-surgical treatments [8,9], several other studies concluded that complete resolution of peri-implantitis could not be achieved through non-surgical treatment alone [9,10]. Despite this inconsistency, surgical treatment generally provides higher predictability compared to non-surgical approaches. This improved predictability primarily results from better accessibility to the affected areas, overcoming limitations related to implant fixture topography, restoration design, and peri-implant defect morphology [6].

Various surgical treatments for peri-implantitis have been proposed [6]. All procedures typically begin with raising a mucoperiosteal flap, allowing direct access to the disease site and enabling decontamination of the affected implant surface [11]. This is generally followed by either a resective approach, such as osteotomy to establish a physiological bone contour and/or implantoplasty [11] or a regenerative approach, such as guided bone regeneration (GBR) or bone grafting [12]. Additionally, these 2 treatment modalities may be combined, such as performing implantoplasty on the supracrestal component along with a regenerative approach for the intraosseous component [13]. While considerable research over recent decades has addressed issues related to the hard tissue and fixture surface affected by peri-implantitis, relatively little attention has been devoted to enhancing the quality and quantity of peri-implant soft tissues.

Maintaining adequate thickness of the peri-implant mucosa around the abutment—both crestally and horizontally—and having a sufficient amount of keratinized tissue are essential for preserving marginal bone levels and preventing peri-implant disease [14]. However, only a few case reports have examined the efficacy of soft tissue augmentation during the surgical treatment of peri-implantitis [15,16]. This implies that augmenting the quantity of soft tissue around implants may potentially improve outcomes of surgical peri-implantitis treatments, whether used alone or in combination with other surgical methods, a perspective supported by a consensus report [17].

Therefore, the present preclinical study aimed to clinically and radiographically investigate the effect of adjunctive soft tissue grafting in the surgical treatment of ligature-induced peri-implantitis lesions in canines.

MATERIALS AND METHODS

Study design and ethical statement

This canine experiment was designed as a randomized controlled preclinical study. All experimental protocols, including animal selection and management, were approved by

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the Animal Care and Use Committee of Yonsei Medical Center, Seoul, South Korea (No. 2020-0032). The manuscript adheres to the ARRIVE guidelines.

Sample size determination

As no previous preclinical studies had simultaneously compared implantoplasty with hard and soft tissue grafting, the sample size calculation assumed that peri-implant probing pocket depth would be 2 mm shallower (standard deviation assumed as 1.2 mm) with soft tissue, hard tissue, or both types of grafting compared to implantoplasty alone. With a significance level (α) of 5% and a power (1–β) of 95%, 7 implants per group were determined necessary. To minimize animal use, 7 dogs were recruited, and a split-mouth experimental design was applied.

Experimental animals, housing, and husbandry

Seven healthy male Mongrel dogs aged 12–15 months, weighing 25–30 kg, with healthy periodontium and permanent dentition were included. Animals were housed under standard laboratory conditions, maintained at 15°C–20°C, and at humidity levels above 30%, with appropriate feeding.

Experimental procedure

The schematic flow of the experimental procedure is summarized in **Figure 1**.

Presurgical anaesthesia

All surgical procedures (extraction, implant placement, and peri-implantitis surgery) were conducted under general anaesthesia induced by inhalation of isoflurane (Forane, Choongwae Pharmaceutical, Seoul, Korea), intravenous injection of xylazine (0.5 mg/kg, Rompun, Bayer Healthcare LLC, Whippany, NJ, USA), and intramuscular injection of medetomidine (0.75 mg/kg, Tomidin, Provet Veterinary Products, Istanbul, Turkey), supplemented by local anaesthesia (2% lidocaine HCL with epinephrine 1:80,000, Kwang Myung Pharm, Seoul, Korea).

Tooth extraction and implant placement

The mandibular first to fourth premolars and the first molar were extracted bilaterally. After a 10-week healing period, full-thickness mucoperiosteal flaps were elevated bilaterally in the posterior mandible. Following sequential osteotomy, 3 titanium implants with sandblasted, large-grit, acid-etched (SLA) surfaces (ø 3.1 mm, length 9 mm; NR line,

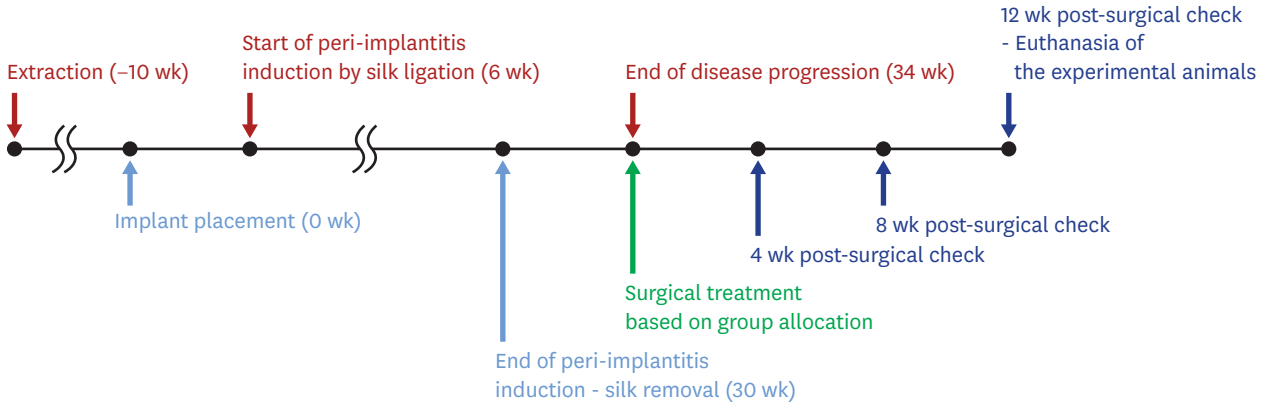

Figure 1. Timeline of the experimental protocol.

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Dentium, Suwon, Korea) were placed per side (6 implants per animal). Adjacent implants were consistently spaced 10 mm apart. Implant platforms were aligned at the lingual bone crest level, surrounded circumferentially by at least 2 mm of bone thickness on buccal and lingual aspects. Flaps were closed with 4-0 resorbable suture (Monosyn 4-0 Glyconate Monofilament, B. Braun, Melsungen, Germany), and healing abutments facilitated transmucosal healing.

The animals received antibiotics (enrofloxacin 5 mg/kg, Baytril, Bayer Korea, Seoul, Korea) and analgesics (ketorolac tromethamine 0.5 mg/kg, Keromin, Hana Pharm) daily for 5 days, with suture removal after 1 week. Dogs were given a soft diet for the duration due to the lack of prostheses. Oral hygiene was omitted for the first week but resumed every other day without anaesthesia thereafter.

Induction of peri-implantitis

Six weeks post-implant placement, peri-implantitis induction began with ligation of non-resorbable silk sutures (4-0 Permahand Black Silk Suture, Ethicon, NJ, USA) submarginally around healing abutments to provoke plaque-induced inflammation, following previously described methods [18]. Silk ligatures were replaced every 4 weeks for 24 weeks until circumferential bone loss reached 40% of initial support, assessed by standardized serial periapical radiographs [19]. After achieving the targeted bone loss, silk ligatures were removed, initiating a 4-week progression period maintained by plaque control as described above [18].

The disease induction process is summarized in **Figure 2**.

Surgical treatment of peri-implantitis

The surgical procedure is summarized in **Figure 3**.

1) Debridement and implantoplasty

After the 4-week progression period, surgical treatment commenced. Buccal and lingual mucoperiosteal flaps were raised, granulation tissue was thoroughly removed using titanium curettes, and circumferential defects were exposed. The following peri-implant defect dimensions (mm) were measured using a periodontal probe (UNC 15, Hu-Friedy Co., Chicago, IL, USA) (**Figure 2**):

- Suprabony height: linear distance from the bone crest to the implant platform
- Intrabony dimensions:
  - Depth: vertical distance from the intrabony defect base to the bone crest
  - Width: horizontal distance between the implant platform and the bone crest

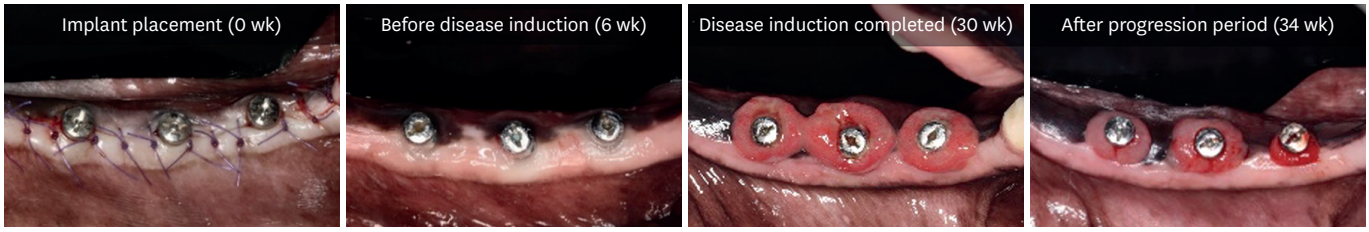

Figure 2. Clinical photographs of implant placement and peri-implantitis induction.

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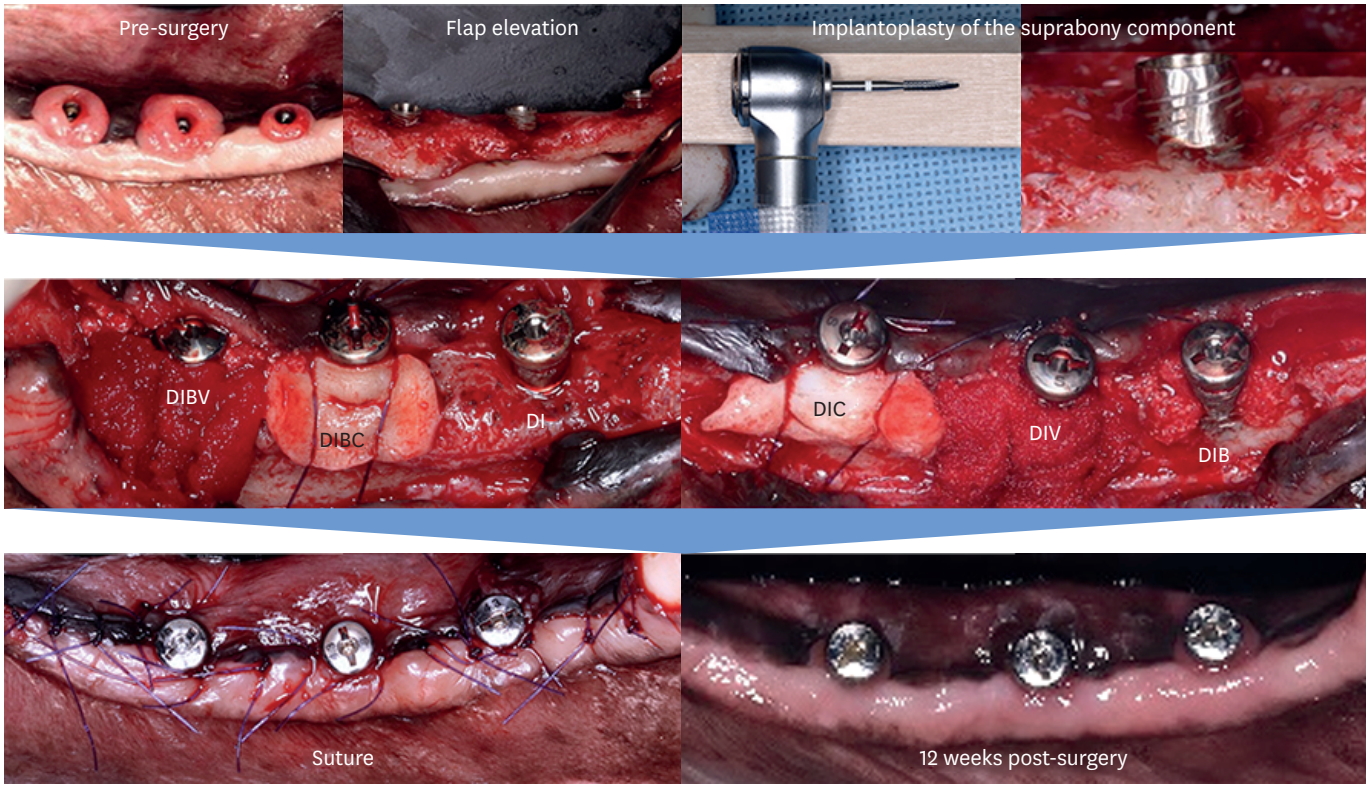

Figure 3. Clinical photographs summarizing the surgical procedures for peri-implantitis treatment. Groups are presented as follows: DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DI, the group receiving implantoplasty only; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting.

Measurements were taken mesially, buccally, distally, and lingually, averaging to yield representative implant values.

Non-mineralized deposits were removed from fixture surfaces using saline-soaked cotton balls, followed by sterile saline irrigation. Implantoplasty was performed using high-speed diamond burs and low-speed silicone points with irrigation to remove exposed threads and smooth surfaces.

2) Treatment of peri-implantitis defect according to the group allocation

After implantoplasty, implants were randomly assigned to 1 of the following 6 treatment modalities, using a split-mouth design with 3 groups on each side:

i. DI group: no grafting after implantoplasty of the supracrestally exposed implant surface
ii. DIB group: grafting of collagenated, deproteinized bovine bone mineral (DBBM-C; Bio-Oss Collagen, Geistlich Pharma, Wolhusen, Switzerland) after implantoplasty of the supracrestally exposed implant surface
iii. DIC group: grafting subepithelial connective tissue (SCTG) after implantoplasty of the supracrestally exposed implant surface
iv. DIV group: grafting volume-stable collagen matrix (VCMX; Fibro-Gide, Geistlich Pharma) after implantoplasty of the supracrestally exposed implant surface
v. DIBC group: grafting of DBBM-C (Bio-Oss Collagen, Geistlich Pharma) followed by SCTG after implantoplasty of the supracrestally exposed implant surface

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vi. DIBV group: grafting of DBBM-C (Bio-Oss Collagen, Geistlich Pharma) followed by grafting VCMX (Fibro-Gide, Geistlich Pharma) after implantoplasty of the supracrestally exposed implant surface

In the DIC and DIBC groups, autogenous connective tissue (6 mm coronally-apically, 10 mm mesio-distally, 2 mm thickness) was harvested from lingual keratinized mucosa of mandibular second molars. Soft tissue grafts (SCTG or VCMX) were placed buccally and secured with periosteal internal mattress sutures in respective groups. DBBM-C, hydrated with saline, was applied intrabony only (DIB, DIBC, and DIBV groups). Flaps were primarily closed with 6-0 resorbable sutures (Monosyn 6-0 Glyconate Monofilament; B. Braun), removed 1 week post-surgery. Animals underwent clinical assessments for 12 weeks postoperatively.

Euthanasia of the experimental animals

Animals were euthanized by intravenous administration of zolazepam and tiletamine (15 mg/kg, Zoletile 50, Virbac Animal Health, Westlake, TX, USA), combined with xylazine (4 mg/kg, Rompun, Bayer Healthcare LLC), followed by intravenous potassium chloride injection. Operative sites were dissected for radiographic analyses.

Clinical and radiographic measurements

All clinical and radiographic parameters were measured by a single examiner (Y.H.K.) who was blinded to the group assignments. Prior to the measurements, an intraclass correlation coefficient of 0.93 was confirmed at a calibration meeting.

Probing depth (PD), bleeding on probing (BOP), width of keratinized tissue (KTW) and level of the margo mucosae (MM)

PD (mm) of the peri-implant mucosal sulcus was measured using a UNC 15 periodontal probe (Hu-Friedy Co.) at 6 sites (mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual, and mesio-lingual). BOP was subsequently assessed at these same 6 sites (absence: 0; presence: 1). For each implant, the average PD of the 6 sites served as the representative PD value, while the total number of sites showing BOP (ranging from 0 to 6) was recorded.

The KTW (mm) was measured from the mucogingival junction to the coronal margin of keratinized mucosa. The level of the MM (mm) was measured from the implant shoulder to the mucosal margin. Both KTW and MM were assessed at the midpoint of the buccal side of each implant using the same periodontal probe.

These 4 clinical parameters (PD, BOP, KTW, and MM) were recorded at 4 different time points: immediately before surgery, and at 4, 8, and 12 weeks after surgery. The measurement methods for PD, KTW, and MM are illustrated schematically in **Figure 4A**.

Early wound-healing index (EHI)

The extent of wound closure was qualitatively assessed and recorded using the EHI, as proposed by a previous study [20] at 2 time points: 1 and 2 weeks after surgery. Each implant site received a score based on the extent of flap closure at the mesial and distal sides of the healing abutment:

- Score 1: complete wound closure without any fibrin line
- Score 2: complete wound closure with a fine fibrin line
- Score 3: complete wound closure with a fibrin clot

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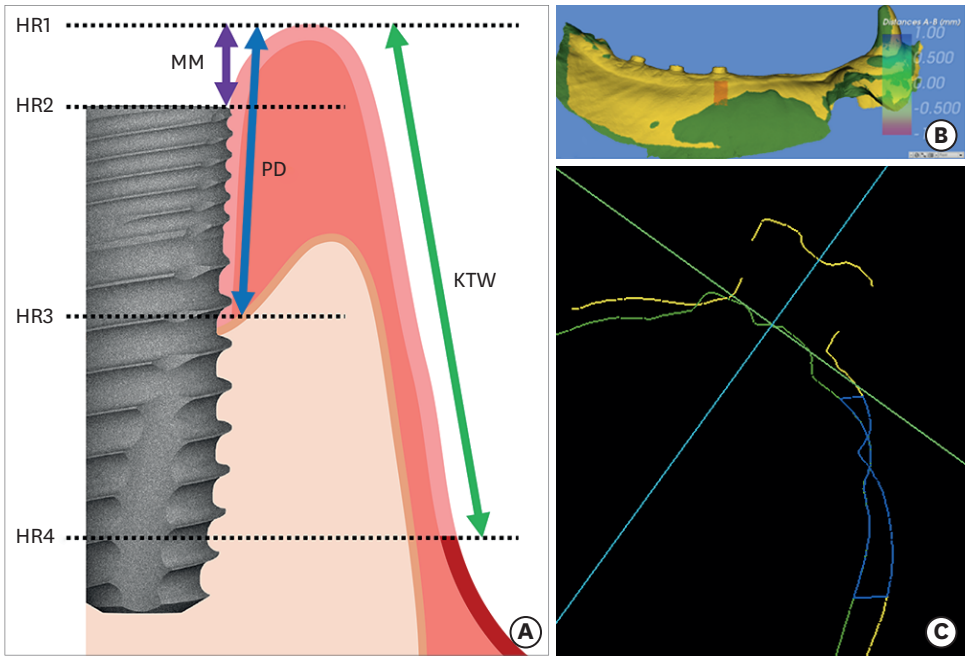

Figure 4. Schematic image of the measurements. (A) Measurement methods for PD, KTW, and MM. The black dotted lines indicate HR lines perpendicular to the long axis of the implant fixture: HR1 represents the mucosal margin, HR2 corresponds to the fixture platform, HR3 denotes the apical margin of the peri-implant mucosal sulcus, and HR4 indicates the mucogingival junction. The blue, green, and purple double-headed arrows indicate measurements of PD, KTW, and MM, respectively. (B) Measurement of peri-implant MT change over time, using intraoral scan data taken pre-disease induction (yellow) and at 12 weeks post-surgery (green). The ROI (orange) was defined on the pre-disease induction scan in the corono-apical dimension (from 1 mm apical to the mucosal margin to the mucogingival junction) and mesio-distally (matching the implant platform width). (C) Cross-sectional view sliced along the implant fixture's long axis, illustrating measurement of the gap between the 2 scan files. The MT difference within the ROI (outlined in blue) was calculated as the mean distance between scans.
HR: horizontal reference, MM: margo mucosae, PD: probing depth, KTW: width of keratinized tissue, MT: mucosal thickness, ROI: region of interest.

- Score 4: incomplete wound closure with partial mucosal necrosis
- Score 5: incomplete wound closure with complete mucosal necrosis

The average of the mesial and distal scores was used as a representative EHI value for each implant.

Modified plaque control record

The presence of dental plaque on each implant was visually assessed and recorded at 4 surfaces (mesial, buccal, distal, and lingual) according to the modified plaque control record [21] at 4, 8, and 12 weeks after surgery as follows:

- Score 0: the healing abutment surface is clean
- Score 1: the healing abutment surface appears clean, but plaque can be removed with a periodontal probe
- Score 2: plaque is visible along the mucosal margin around the healing abutment
- Score 3: the healing abutment surface is covered with abundant plaque

For each implant, the average score from the 4 surfaces was calculated as the representative multiplex polymerase chain reaction (mPCR) value.

Radiographic bone gain (RBG) after the treatment

Periapical radiographs taken at 2 time points—immediately before surgical intervention (prior to flap elevation) and at 12 weeks post-surgery—were used to estimate RBG. RBG was measured linearly from the implant shoulder to the most coronal point of bone-to-implant

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contact, parallel to the implant's long axis. Measurements were performed mesially and distally for each radiograph, and the average was used as the representative RBG value.

Profilometric analysis of peri-implant buccal mucosal thickness (MT) change

Optical impressions were obtained using an intraoral scanner (Trios 3, 3Shape, Copenhagen, Denmark) prior to disease induction and at 12 weeks after surgery. Scan data were extracted as stereolithographic files and superimposed using computer software (SMOP, Swissmeda, Zurich, Switzerland) to assess peri-implant MT changes over time, based on a previously described method [22]. The region of interest (ROI) was manually selected by the same examiner (Y.H.K.) on the pre-disease induction scan as follows: the apico-coronal dimension extended from the mucogingival junction to 1 mm apical to the mucosal margin, and the mesio-distal dimension corresponded to the implant platform width. Within the ROI, the mean distance (mm; calculated as the difference in volume [mm^3] divided by the ROI area [mm^2]) between pre-disease induction and 12 weeks post-surgery was measured, representing the MT change over time (**Figure 4B**).

Composite treatment success rate

Composite treatment success was assessed 12 weeks after surgery to determine whether the peri-implantitis was successfully treated according to the assigned surgical protocol. Treatment was considered successful if all of the following criteria were met:

- Absence of BOP at 12 weeks post-surgery
- Decrease in PD or increase in PD of 1 mm or less 12 weeks after surgery
- Absence of additional bone loss of 0.5 mm or more 12 weeks after surgery compared to radiographic baseline

The percentage of implants meeting these criteria was calculated as the composite treatment success rate (%).

Statistical analysis

All collected data were analysed statistically using SPSS software (version 23, IBM, Armonk, NY, USA). Normality of data was confirmed using the Shapiro-Wilk test ($P>0.05$), allowing parametric tests for subsequent analyses. Repeated-measures analysis of variance (ANOVA) was performed to compare EHI, KTW, MM, PD, BOP, and mPCR among groups. RBG and MT change among groups were compared using 1-way ANOVA, followed by a *post hoc* test as necessary. Within-group comparisons were made between the endpoint (12 weeks post-surgery) and baseline or relevant previous time points (pre-disease induction for KTW, pre-surgery for PD, BOP, MM, and RBG, and 4 weeks post-surgery for mPCR) using the paired t-test. Binary logistic regression analysis was used for intergroup comparisons of composite therapeutic outcomes, evaluating whether outcomes differed based on the presence or absence of bone grafting, soft tissue grafting (SCTG or VCMX), or both. Statistical significance was set at $P<0.05$.

RESULTS

All measurements are summarized in **Tables 1**-**5**. Serial radiographs obtained at different time points are presented in **Figure 5**. Changes in PD, BOP, KTW, MM, and RBG at 12 weeks post-surgery are illustrated in **Figure 6**.

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Table 1. Clinical measurements (PD, BOP, KTW, MM)

	Group	Pre-surgery	4 wk post-surgery	8 wk post-surgery	12 wk post-surgery	Temporal change over 12 wk[a]
PD (mm)	DI	6.4±0.3	2.4±0.8	3.9±1.0	**2.5±0.7**	−3.9±0.7
	DIB	6.5±0.3	2.4±0.7	4.2±0.6	**2.5±0.5**	−4.0±0.5
	DIC	6.3±0.3	2.7±0.7	4.0±0.9	**2.8±0.5**	−3.6±0.4
	DIV	6.4±0.4	3.1±0.4	4.5±0.6	**2.9±0.7**	−3.6±0.9
	DIBC	6.3±0.4	2.9±0.7	3.9±0.5	**2.8±1.0**	−3.5±1.1
	DIBV	6.4±0.2	2.8±0.7	4.5±0.6	**2.6±0.7**	−3.8±0.5
BOP	DI	1.0±0.0	0.6±0.2	0.4±0.5	**0.2±0.4**	−0.8±0.4
	DIB		0.7±0.4	0.4±0.5	**0.3±0.4**	−0.7±0.4
	DIC		0.7±0.2	0.6±0.5	**0.5±0.5**	−0.5±0.5
	DIV		0.6±0.2	0.6±0.4	**0.2±0.3**	−0.8±0.3
	DIBC		0.7±0.3	0.4±0.4	**0.3±0.3**	−0.7±0.3
	DIBV		0.5±0.2	0.4±0.4	**0.3±0.3**	−0.7±0.3
KTW (mm)	DI	4.5±0.7	3.8±1.1	3.9±1.0	3.7±0.9	−0.8±1.2
	DIB	5.1±1.7	4.1±0.6	4.2±0.6	4.2±0.7	−0.9±1.7
	DIC	4.4±1.3	4.1±0.8	4.0±0.9	4.1±1.1	−0.3±1.6
	DIV	4.7±0.8	4.3±0.7	4.5±0.6	4.7±0.7	0.0±1.0
	DIBC	4.4±1.0	3.9±0.7	3.9±0.5	4.3±0.9	−0.1±0.6
	DIBV	4.9±1.5	4.3±0.7	4.5±0.6	4.7±0.7	−0.2±1.6
MM (mm)	DI	4.0±0.6	0.9±0.4	0.9±0.3	**0.8±0.2**	−3.2±0.7
	DIB	4.2±0.5	0.8±0.4	0.9±0.4	**0.8±0.4**	−3.4±0.8
	DIC	3.7±0.5	1.4±0.5	1.4±0.4	**1.5±0.6**	−2.2±0.8
	DIV	3.9±0.5	1.4±0.6	1.3±0.6	**1.6±0.5**	−2.4±0.7
	DIBC	3.7±0.6	1.3±0.9	1.4±0.8	**1.6±0.8**	−2.1±1.3
	DIBV	4.1±0.7	1.1±0.7	1.1±0.8	**1.4±0.8**	−2.8±1.3

Values are presented as mean ± standard deviation.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.
Bold words are presented as statistical significance observed in the intragroup comparison between the following 2 time points, pre-surgery and 12 weeks post-surgery ($P<0.05$).
PD: probing depth, BOP: bleeding on probing, KTW: width of keratinized tissue, MM: margo mucosae.
[a]Positive values indicate an increase, while negative ones indicate a decrease.

Table 2. Clinical measurements (early wound healing index)

Group	1 wk post-surgery	2 wk post-surgery
DI	2.6±0.9	**1.6±0.6**
DIB	2.8±1.1	**1.6±0.5**
DIC	3.6±0.9	**1.9±0.2**
DIV	3.5±1.2	**1.9±0.5**
DIBC	2.8±0.8	**2.1±0.4**
DIBV	3.7±1.1	**2.1±0.2**

Values are presented as mean ± standard deviation.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.
Bold words are presented as statistical significance observed in the intragroup comparison between 1 week post-surgery and 2 weeks pot-surgery ($P<0.05$).

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Table 3. Clinical measurements (modified plaque control record)

Groups	4 wk post-surgery	8 wk post-surgery	12 wk post-surgery
DI	1.0±0.5	0.9±0.7	1.0±0.8
DIB	0.8±0.6	0.8±0.7	1.2±0.6
DIC	0.8±0.6	0.8±0.7	1.1±0.7
DIV	0.9±0.5	0.6±0.5	1.0±0.8
DIBC	0.8±0.6	0.9±0.7	1.1±0.7
DIBV	1.0±0.5	0.9±0.6	1.1±0.7

Values are presented as mean ± standard deviation.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.

Table 4. Radiographic bone level change

Groups	Pre-surgical radiographic bone level	12 wk post-surgical radiographic bone level	Radiographic bone gain over 12 wk
DI	3.0±0.3	**2.3±0.5**	0.7±0.7
DIB	3.1±0.4	**2.2±0.5**	0.9±0.5
DIC	3.3±0.4	2.6±1.1	0.8±0.9
DIV	3.3±0.3	**2.4±0.9**	1.0±1.0
DIBC	3.6±0.5	**2.7±0.4**	0.8±0.5
DIBV	3.3±0.3	**2.5±0.5**	0.8±0.7

Values are presented as mean ± standard deviation.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.
Bold words are presented as statistical significance observed in the intragroup comparison between pre-surgery and 12 weeks post-surgery ($P<0.05$).

Table 5. Peri-implant buccal MT change (mm)

Groups	Peri-implant buccal MT change[a] (pre-disease induction–12 wk post-surgery)
DI	−0.9±1.5
DIB	−0.6±1.0
DIC	0.1±1.2
DIV	−0.2±1.1
DIBC	0.4±1.4
DIBV	0.0±0.7

Values are presented as mean ± standard deviation.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.
MT: mucosal thickness.
[a]Positive values indicate a gain, while negative ones indicate a shrinkage.

Clinical findings and intrasurgical defect assessment

Overall, healing occurred uneventfully at all sites in all canines. All groups exhibited healing of the peri-implantitis lesions, albeit to varying extents.

All bone defects were classified as class IIIb according to the recently published classification [23], characterized by a combination of 2-wall (mesial and distal) intrabony defects along

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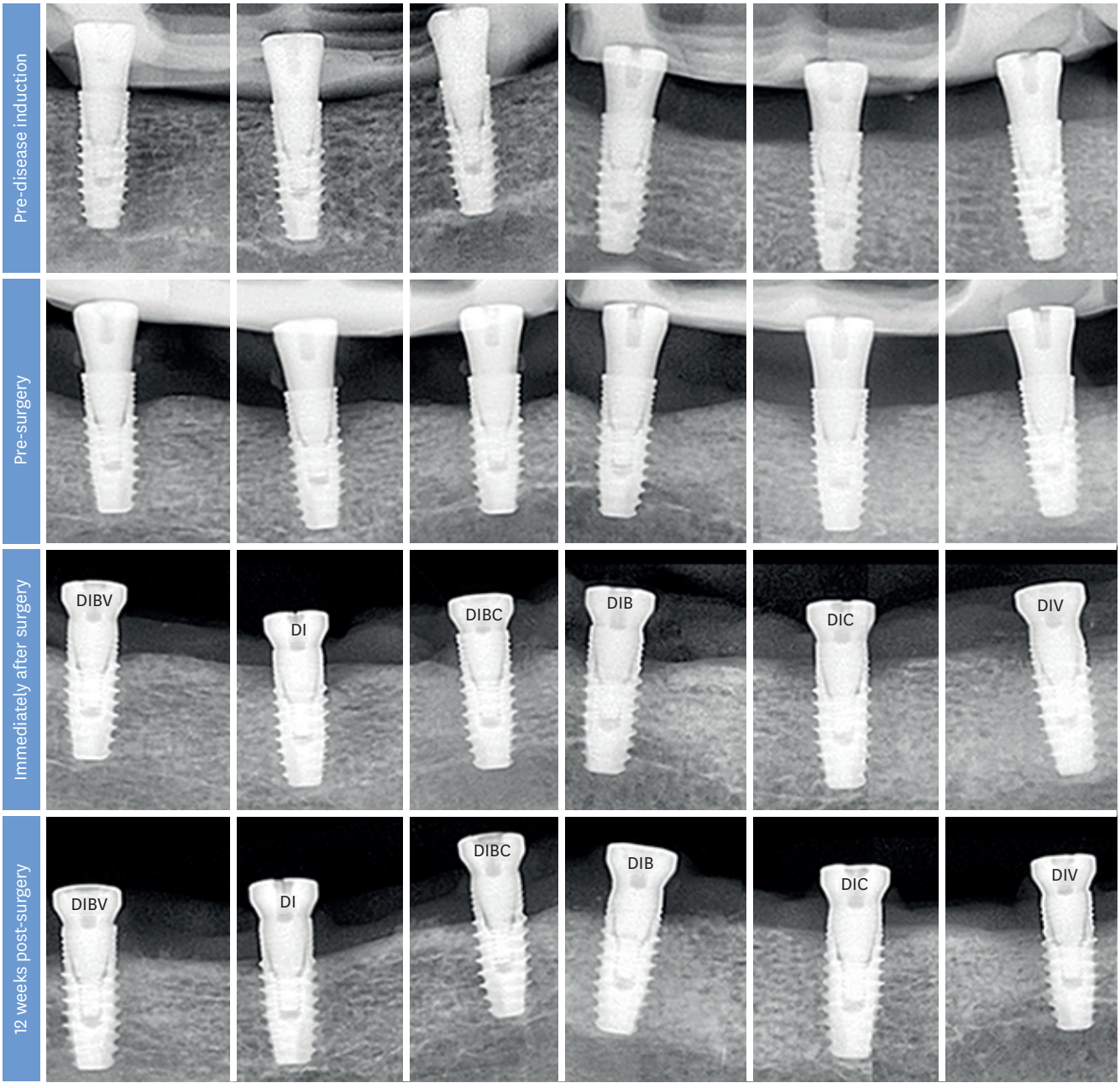

Figure 5. Periapical radiographs taken prior to disease induction, before surgery, immediately after surgery, and at 12 weeks post-surgery for each peri-implantitis treatment group.
Groups are presented as follows: DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting; DI, the group receiving implantoplasty only; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting.

with horizontal bone loss. Mean suprabony height, intrabony depth, and intrabony width ranged from 0.63 to 0.95 mm, 2.29 to 2.63 mm, and 1.38 to 1.96 mm, respectively; no statistically significant differences among groups were observed.

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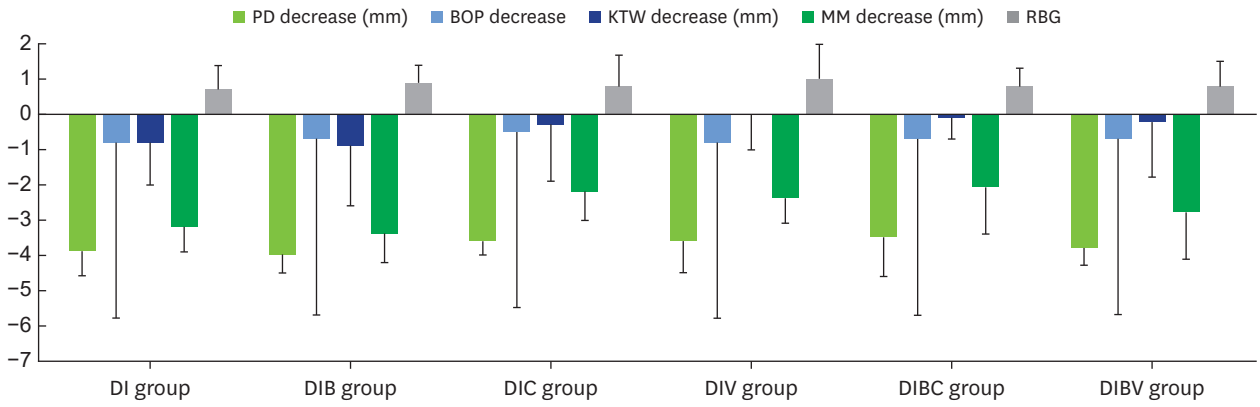

Figure 6. Temporal changes in PD, BOP, KTW, MM, and RBG over 12 weeks post-surgery.
Groups are presented as follows: DI, the group receiving implantoplasty only; DIB, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting; DIC, the group receiving implantoplasty followed by autogenous connective tissue graft; DIV, the group receiving implantoplasty followed by volume-stable collagen matrix grafting; DIBC, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral grafting and connective tissue graft; DIBV, the group receiving implantoplasty followed by collagenated, deproteinized bovine bone mineral and volume-stable collagen matrix grafting.
PD: probing depth, BOP: bleeding on probing, KTW: width of keratinized tissue, MM: margo mucosae, RBG: radiographic bone gain.

Effect of surgical debridement on probing depth, BOP, EHI, and modified plaque control record

Probing depth and BOP

Mean PD values exceeded 6 mm in all groups initially and decreased gradually by approximately 3 mm following surgery. At 12 weeks, PD values in all groups were significantly lower than pre-surgery measurements (P<0.05).

Before surgery, BOP was positive at every probing site in all groups. BOP values progressively decreased in all groups at 4 and 12 weeks (mean values: 20%–50%), demonstrating statistically significant differences compared to pre-surgery values (P<0.05).

EHI and modified plaque control record

EHI scores significantly decreased between 1 and 2 weeks post-surgery in all groups (P<0.05), with no significant differences noted among groups. Throughout the entire observation period, none of the groups achieved complete plaque removal. The mPCR values did not show substantial changes over time within each group, and no significant intergroup differences were observed (P>0.05).

Effect of hard tissue grafting-RBG following surgical treatment

Prior to surgery, mean marginal bone loss was ≥3 mm in all groups. At 12 weeks post-surgery, radiographic bone levels ranged from 2.2 to 2.7 mm, representing statistically significant improvements compared to pre-surgery levels (P<0.05) in all groups except the DIC group. The largest RBG was observed in the DIV group (1.0±1.0 mm), and the smallest in the DI group (0.7±0.7 mm). The data also demonstrated that adjunctive bone grafting (DIB, DIBC, and DIBV) had only a limited effect, resulting in no significant improvement in bone regeneration compared to groups without hard tissue grafting (DI, DIC, and DIV).

Effect of soft tissue grafting on KTW of the MM, and MT

A decrease in the KTW was observed in all groups at 4, 8, and 12 weeks after surgery compared to the pre-surgical values, except in the DIV group, where mean KTW remained unchanged from pre-surgery. Furthermore, KTW notably increased in the DIV and DIBV

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Table 6. Binary logistic regression analysis assessing whether hard or soft tissue grafting affected the achievement of composite treatment success

	B	Standard error	*P* value	Exp(B)
DBBM-C grafting conducted[a)]	−0.601	0.638	0.347	0.548
SCTG conducted[b)]	−0.895	0.786	0.255	0.409
VCMX grafting conducted[c)]	−0.307	0.785	0.696	0.736

DBBM-C: collagenated, deproteinized bovine bone mineral, SCTG: grafting subepithelial connective tissue, VCMX: volume-stable collagen matrix.
[a)]Reference: DBBM-C grafting not conducted.
[b)]Reference: SCTG not conducted.
[c)]Reference: VCMX grafting not conducted.

groups between 4 and 12 weeks post-surgery, achieving the greatest width (both groups 4.7±0.7 mm) at the final evaluation (12 weeks).

Swelling of the peri-implant mucosa was prominent before surgery but gradually decreased in all groups after surgical treatment. The change in the level of the MM between pre-surgery (mean range, 3.7–4.2 mm) and 12 weeks post-surgery (mean range, 0.8–1.6 mm) was statistically significant within each group ($P<0.05$). The smallest reduction in MM was observed in the DIC and DIV groups, suggesting a beneficial effect of adjunctive soft tissue grafting.

The mean change in peri-implant buccal MT, assessed from pre-disease induction to 12 weeks post-surgery, showed a decrease or minimal change in the DI (−0.9±1.5 mm), DIB (−0.6±1.0 mm), DIV (−0.2±1.1 mm), and DIBV (0.0±0.7 mm) groups. In contrast, a slight increase in MT was observed in the DIC (0.1±1.2 mm) and DIBC (0.4±1.4 mm) groups. However, intergroup comparisons revealed no statistically significant differences.

Composite treatment success rate

The highest composite treatment success rates were achieved in the DI and DIV groups, both reaching 71.4% (5 out of 7 implants). The DIB group showed an intermediate success rate of 57.1%, while the remaining 3 groups each demonstrated lower rates of 42.9%. Despite these differences, no statistically significant differences were found among the groups (**Table 6**).

DISCUSSION

The present preclinical experiment investigated the adjunctive effect of hard and/or soft tissue grafting in the surgical treatment of peri-implantitis lesions. The study primarily demonstrated that: i) composite treatment success was greatest in the DI and DIV groups; ii) soft tissue grafting was beneficial in preserving peri-implant soft tissue levels, characterized by a smaller reduction in KTW and greater stability of the level of the MM; iii) hard tissue grafting provided no additional benefit compared to approaches without bone regenerative procedures; and iv) combining hard and soft tissue grafting negatively impacted outcomes.

Regardless of the treatment modality, early wound healing was similar across all groups, and improvements in clinical and radiographic parameters occurred to a comparable extent. In terms of composite treatment success, treatment was most effective when the DI group or the DIV group was performed. Compared to more complex treatments involving GBR, these simpler approaches yielded superior clinical outcomes.

In the DI group, where intrabony defects were not grafted, the composite treatment success rate was highest at 71.4%, with the lowest mean PD and BOP values. Clinically and radiographically, both the DIC and DIV groups achieved outcomes similar to those of the DI group.

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These findings were somewhat unexpected, as no bone regeneration procedures were performed in the DI group. However, a previous preclinical experiment demonstrated the potential for successfully resolving peri-implantitis by cleaning contaminated implant surfaces without altering thread morphology [24]. In that same animal study, radiographic bone fill averaged 0.89 mm over 6 months with SLA-surfaced implants, similar to the mean outcome of 0.7 mm observed in the present study. Additionally, a clinical study previously reported improvements in PD and BOP values (mean decreases of 1.55 mm and 0.31, respectively) and RBG (mean gain of 0.31 mm) 6 months after open-flap debridement, despite the absence of adjunctive antibiotics [11].

One of the most common surgical approaches involves combined therapy, mechanically removing suprabony implant threads (implantoplasty) while preserving intrabony threads to encourage re-osseointegration [6]. Such an implantoplasty approach was employed in all 6 experimental groups in the present study.

Early data reported in clinical case studies were supported by findings from the present study, demonstrating the beneficial effects of soft tissue grafting in maintaining peri-implant mucosal levels as coronally as possible and limiting reductions in keratinized tissue, particularly when using a soft tissue substitute (VCMX).

When bone substitutes were grafted into intrabony defects, as done in the DIB, DIBC, and DIBV groups, several previous studies have reported successful bone regeneration. Roos-Jansåker et al. [25] demonstrated RBG exceeding 25%, along with reductions in PD and BOP values, over a 5-year follow-up period after grafting bovine-derived bone substitutes. Recent clinical studies similarly reported radiographic bone fill of more than 1 mm, accompanied by significant reductions in inflammatory signs when bone grafts were applied [26,27]. Consistent with these previous reports, the present study also observed reductions in PD and BOP values, alongside approximately 1 mm of RBG in all bone-grafted groups (DIB, DIBC, and DIBV).

Despite favourable outcomes regarding hard tissue regeneration, concerns remain regarding potential mucosal recession following resective and regenerative peri-implantitis treatment [6]. According to a recently published systematic review, resective procedures resulted in more pronounced mucosal recession compared to combined regenerative surgery [28]. Surprisingly, although combined resective and regenerative approaches effectively reduced PD and BOP values, they were more likely to cause soft tissue recession compared to regenerative procedures alone [28]. Several case series have suggested that adjunctive soft tissue grafting could help minimize or prevent such mucosal recession [15,29].

Although intergroup comparisons showed no statistical significance, soft tissue grafting nonetheless appeared beneficial in both the quantitative and qualitative aspects of peri-implant mucosa in the present study. Compared to the groups without soft tissue grafting (DI and DIB), the mucosal margin was positioned nearly twice as coronally in groups receiving either autogenous connective tissue grafting (DIC, DIBC) or soft tissue substitutes with VCMX (DIV, DIBV). This implies that soft tissue augmentation can effectively limit mucosal recession following surgical peri-implantitis therapy. Previous studies have also indicated that grafting autogenous tissue or soft tissue substitutes increases peri-implant keratinized mucosa, maintains marginal mucosal levels, and stabilizes marginal bone, although other parameters such as PD, BOP, and plaque index might not differ significantly from non-grafted sites [14,17,30]. The present study demonstrated similar findings; even though KTW

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and MM in the DI and DIB groups were slightly lower compared to the 4 soft-tissue-grafted groups, PD, BOP, and mPCR were comparable among all groups. The clinical improvements observed following soft tissue augmentation can be explained histologically by previous preclinical findings, which demonstrated improved buccolingual soft tissue thickness and an increased number of rete pegs between keratinized epithelium and underlying connective tissue following autogenous connective tissue or xenogeneic collagen matrix grafting [22,31].

Despite the absence of bone grafting, the RBG in the DIC and DIV groups was similar to that observed in bone-grafted groups (DIB, DIBC, DIBV), and even comparable to the DI group. This spontaneous bone fill might result from thorough debridement and effective decontamination of implant surfaces, subsequently covered by healthy keratinized peri-implant mucosa during post-surgical healing. Such spontaneous bone fill is supported by previous canine studies that showed the potential for spontaneous resolution of peri-implant bone defects without bone grafting, particularly when implant surfaces were hydrophilic and surrounded by healthy mucosa [32-34].

Numerous publications have compared the performance of VCMX to autogenous connective tissue grafts (CTGs), considered the gold standard for soft tissue augmentation around dental implants [35-40]. Some previous studies concluded that connective tissue grafting yielded superior outcomes for optimizing peri-implant ridge volume compared to VCMX [35,39,40]. Similarly, in the present study, the buccal tissue volume only increased in groups with autogenous connective tissue grafting (DIC and DIBC), while the other 4 groups showed no change (DIBV) or slight shrinkage (DI, DIB, DIV) between pre-disease induction and 12 weeks post-surgery. However, groups with VCMX grafting (DIV and DIBV) demonstrated less shrinkage than groups without soft tissue grafting (DI and DIB), showing only minor differences (mean range, 0.1–0.4 mm) compared to groups DIC and DIBC. It is well established that clinically acceptable outcomes can be achieved with VCMX [36,38]. Moreover, soft tissue substitutes like VCMX offer advantages over autogenous soft tissue grafting, including simplified surgical procedures, minimized invasiveness, and improved patient satisfaction [35-37]. Thus, the soft tissue substitute used in this preclinical study may represent a beneficial option for adjunctive treatment of peri-implantitis lesions.

The present study had several limitations. First, since the peri-implant defects induced by chronic plaque accumulation comprised both intrabony and supracrestal components, the extent of bone grafting was inherently limited, potentially creating a surgical environment less favourable for bone regeneration compared to soft tissue grafting. Second, all surgeries were performed using a transmucosal approach. Given the ongoing debate about the potential advantages of submerged versus non-submerged procedures, particularly regarding bone grafting [6], additional experimental groups with submerged graft materials during healing could have provided more comprehensive data. Third, although clinical and radiographic improvements were observed over time, the composite treatment success rates were moderate, ranging from 42.9% to 71.4%, and did not reach 100%. Difficulty in controlling animal behaviour and maintaining optimal oral hygiene throughout the post-surgical observation period likely contributed to persistent BOP at some sites at 12 weeks. This limitation could potentially be overcome in future clinical studies through improved plaque control managed cooperatively by clinicians and patients.

Within the limitations of this study, all tested surgical treatments resulted in both clinical and radiographic improvements. Adjunctive soft tissue grafting provided clinical benefits in

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peri-implant soft tissue parameters (less decrease in KTW, greater stability of MM levels, and MT), whereas hard tissue grafting demonstrated negligible additional benefits on clinical and radiographic outcomes.

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