The Evaluation of Enamel Matrix Derivative on the Bone Regenerative Potential of the Dental Implant with the Transcrestal Sinus Floor Elevation Approach: A Randomized, Parallel CBCT Study

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Purpose: To evaluate the clinical and radiographic results of simultaneous implant placement using transcrestal sinus floor elevation (TSFE) with and without enamel matrix derivative (EMD) application. ***Materials and Methods:*** Twenty-four patients were randomly assigned into two groups: The EMD+TSFE group (n = 13 patients, 20 implants) received TSFE with EMD application, and the TSFE group (n = 11 patients, 20 implants) received TSFE without EMD application. The patients were recalled at 3 (T3) and 12 (T12) months postsurgery. The residual bone height (RBH), implant protrusion length (IPL), peri-implant sinus bone level (SBL), endo-sinus bone gain (ESBG), and implant stability (ISQ) were measured. Multivariate regressions were performed for the groups. ***Results:*** At T3, the ESBG was 3.72 ± 0.85 mm in the EMD+TSFE group and 3.10 ± 0.05 mm in the TSFE group, and there were statistically significant differences ($P < .05$). However, there were no statistically significant differences in ESBG at T12 between the groups ($P > .05$). ISQ values did not show a statistical difference between the groups at T1 and T3, but at T3 in the TSFE+EMD group, there was a statistical increase in the intragroup evaluation compared to the TSFE group. ***Conclusions:*** The use of EMD in TSFE procedures is effective in new bone formation at the apical part of the implant during the early healing period, but in the long term, no significant difference was shown between cases in which EMD was or was not used in terms of new bone formation and primary and secondary stabilization. *Int J Oral Maxillofac Implants 2024;39:615–624. doi: 10.11607/jomi.10506*

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Implant surgery has become a challenge due to insufficient bone height in the posterior alveolar region. For this reason, different surgical techniques have been presented in the literature to reduce healing times for maxillary sinus elevation, accelerate healing, and improve patient-reported outcomes.[1–3]

Transalveolar sinus floor elevation (TSFE) is a quite reliable method, considering the augmentation of the bone under the sinus membrane as well as enabling the administering of graft materials, which improves the primary implant stability that contributes to bone regeneration.[4] Adequate bone formation in the apical implant region is crucial for implant stabilization and protection of the maxillary sinus in TSFE operations.[5] Therefore, to increase apical new bone formation, different grafts and biologic adjunct materials have been applied after the osteotomy in TSFE operations.[6] In short-implant applications, plasma-rich growth factor was applied together with TSFE, and predictable results were achieved.[6] Recent preclinical and clinical studies showed that growth factors have positive effects on hard and soft tissue regeneration.[7,8] A recent meta-analysis reported that bone graft application increased the risk of sinus membrane perforation, and a higher rate of endo-sinus bone gain (ESBG) occurred in cases where the graft was applied, but this was not statistically significant; thus there are controversial results in the literature regarding the application of biologic adjunct materials and biomaterials in TSFE operations.[9] One study reported that in cases where an apical graft was placed along with TSFE, the size of the graft decreased, and a decrease in the apical newly formed bone occurred with remodeling.[10]

Bioactive agents or *bioactive factors* are so named because they are natural mediators of tissue repair that can elicit a response from a living tissue, organism, or cell, such as osteoblast differentiation, angiogenesis,

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matrix mitosis, or hydroxyapatite formation.[11] Growth factors, enamel matrix derivatives (EMDs), and autologous platelet concentrates are such bioactive factors.[12]

EMD has demonstrated relevant benefits for both hard and soft tissues and is used for regenerative purposes; amelogenins, the major components of EMD, are a group of hydrophobic proteins that account for approximately 95% of the total protein content.[13] Some studies have suggested that EMD can also stimulate the proliferation and mineralization of preosteoblasts and plays an essential role in the cell differentiation necessary for periodontal regeneration[14,15]; other studies have pointed out that EMD also reduces the differentiation of osteoblasts.[16] EMD has previously been investigated as a potential biomaterial for improving bone regeneration in implant-associated defects.[17] Additionally, EMD can increase the proliferation and differentiation of osteogenic cells on titanium surfaces.[18]

In the literature, the effect of using various biologic materials in the TSFE approach with grafted and nongrafted applications on the bone formation at the apical region of an immediately placed implant has been discussed. However, the effect of EMD with TSFE on apical bone formation and implant stabilization has not been evaluated.

This study hypothesizes that EMD will have no effect on radiographically evaluated new bone formation and stabilization when used in TSFE operations with simultaneously placed implants. The present study aimed to radiographically and clinically investigate the potential regenerative role of EMD in TSFE operations.

MATERIALS AND METHODS

Study Design and Eligibility Criteria

The proposed study is a prospective, single-center, randomized, parallel, single-blinded clinical trial. The study protocol was approved by the Institutional Review Board of Ankara University, Faculty of Dentistry, Turkey (July 27, 2016; decision no. 14/4). It was conducted in accordance with the Declarations of Helsinki and internationally accepted guidelines for RCTs, including the CONSORT statement. All patients were informed about the objectives and methods of the study and signed an informed consent form. The study was registered at ClinicalTrials.com (no. NCT05507047).

The study participants were selected from partially maxillary edentulous patients referred to Gazi University, Faculty of Dentistry, and Department of Periodontology. The research was started in 2017 and completed in 2020, the follow-up period was 1 year.

Inclusion criteria were as follows: age ≥ 18 years; partial edentulism in the maxillary posterior region for at least 4 months from tooth loss and requiring implant treatment; coronal bone thickness ≥ 4 mm for primary stabilization; residual bone height between 4 and 6 mm; systemic and local condition compatible with implant placement and sinus floor elevation; sound antagonist teeth; and willingness to provide informed consent and able to comply with the surgical protocol.

The patients were excluded if they met any of the following criteria: uncontrolled diabetes mellitus or other systemic disorders (eg, hepatitis, tuberculosis, AIDS); pregnancy; untreated periodontal disease; endodontic lesions or other oral disorders; smoking habit; acute or chronic rhinitis; sinusitis or sinus pathology; inadequate residual bone height/quality to achieve implant stability; previous implant treatment/failure or bone augmentation in the implant site; sinus perforation as confirmed via the Valsalva maneuver; and insufficient primary implant stability measured by resonance frequency analysis (RFA), shown as an implant stability quotient (ISQ) ≤ 37.

Study Groups and Randomization

According to study design, patients were treated by TSFE with or without EMD (Emdogain, Straumann) and simultaneous implant placement. Figure 1 shows the study process.

All patients were assigned to one the following two groups: *(1)* EMD+TSFE group (n = 20 implants, 13 patients): TSFE procedure with EMD (Emdogain), or *(2)* TSFE group (n = 20 implants, 11 patients): TSFE procedure without EMD material.

Patients were randomly assigned one of the groups using a specifically designed locked computer program (SPSS, version 23, IBM). Allocation concealment was implemented by a study examiner (S.T.), who received a sealed opaque envelope for each patient's treatment corresponding to their assigned treatment group. The examiner (A.U.C.) opened envelope before implant surgery and informed the periodontists.

Sample Size

The sample size was estimated from a previous study[19] using biologic material in simultaneous implant placement with sinus floor augmentation, assuming an alpha error of 5% and study power of 80% by means of changes in residual bone height (RBH) ranging from 1.5 to 6.0 mm (SD: 0.9 mm). Based on these results, the minimum sample size was calculated as 20 simultaneously dental implant placement in each group (G*Power for Windows, Heinrich Heine Universität Düsseldorf).

Surgical and Prosthetic Procedures

The surgical technique utilized was a modification of the original Summers technique.[20] All surgical procedures were performed by the same expert surgeon (D.O.). Surgery was performed under local anesthesia,

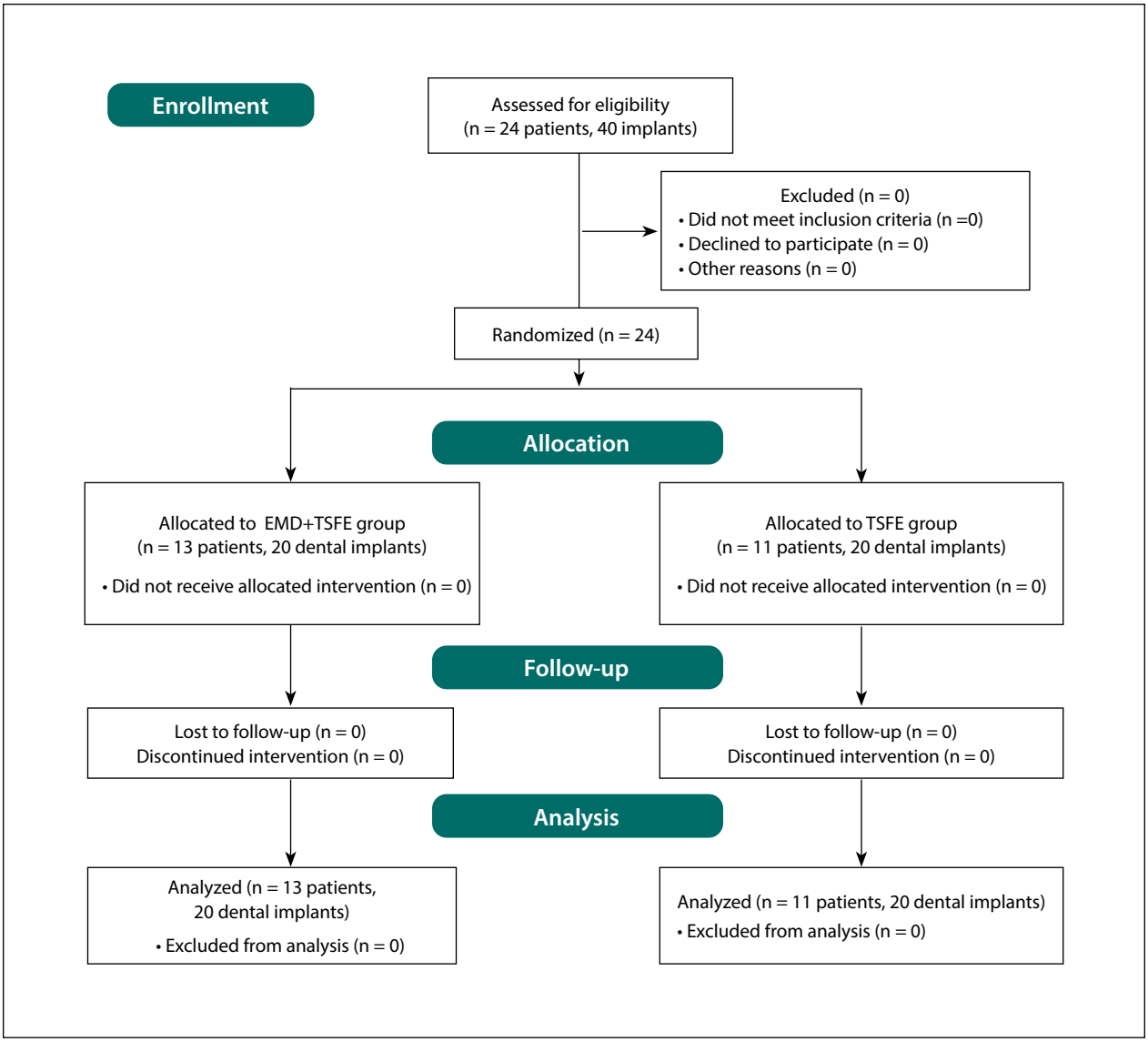

Fig 1 CONSORT study flowchart.

following a midcrestal incision, with mesial and distal releasing incisions extending well up into the buccal fold, and a full-thickness mucoperiosteal flap was raised. A pilot drill was used to a depth approximately 2 mm away from the sinus floor, according to the depth taken from CBCT scans. The maxillary sinus membrane elevation was achieved using osteotomes (Osteotome Kit, Straumann). In the EMD+TSFE group, 0.15 mL of EMD (Emdogain) was administered in the prepared implant sockets. In the TSFE group, no material was applied in the prepared implant sockets. Bone-level implants (Roxolid, Straumann) were placed simultaneously with TSFE at the crestal bone level and inserted at a speed of 15 rpm. After implant insertion, the mucoperiosteal flaps were repositioned and sutured to ensure primary and tension-free closure using 4-0 silk sutures, allowing transmucosal healing.

All patients were instructed to use antibiotics (including 1,000 mg amoxicillin/clavulanate; Augmentin, GlaxoSmithKline) twice daily for 7 days and to rinse twice a day with a chlorhexidine digluconate 0.12% mouthwash for 1 week. Anti-inflammatory drugs (Flurbiprofen, 100 mg) (Majezik, Sanovel) were also prescribed, twice a day for the first 2 days. Sutures were removed 7 days after implant surgery.

After 3 months of healing, each patient received transmucosal healing abutments for each implant system, which were screwed with a torque wrench calibrated at 35 Ncm, and prosthetic procedures were performed. Patients were recalled for follow-up sessions at 3 months (T3) and 12 months (T12) postoperative.

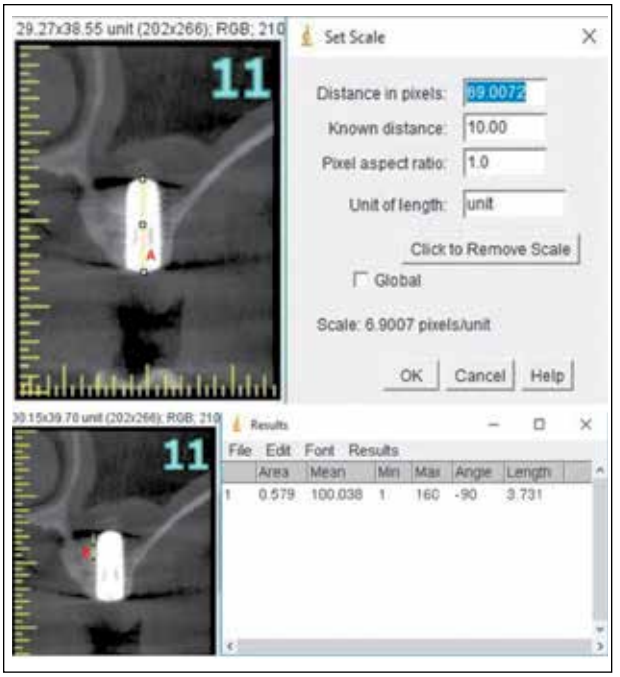

Fig 2 Measurements made with ImageJ: implant length *(top)* and IPL (*bottom*).

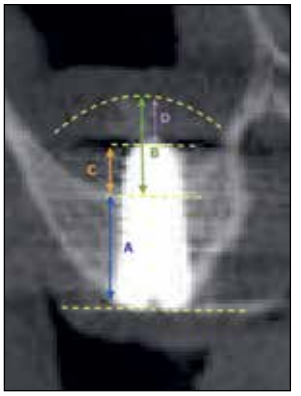

Fig 3 CBCT images at T3. A = RBH; B = PSBL; C = IPL; D = ESBG.

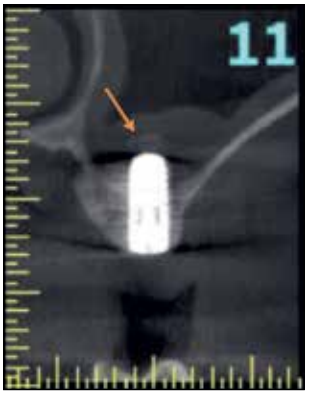

Fig 4 Bone gain (arrow) at the apical implant aspect after osteotomy.

Primary and Secondary Outcomes

The primary outcome was ESBG that newly formed in the sinus following TSFE operations. The secondary outcomes were RBH, implant stability, implant protrusion length into the sinus, and peri-implant sinus bone level.

Data Collection

Radiographic assessment

CBCT was performed using the Veraviewepocs 3D R100 (Morita) and analyzed with the Scion Image software (Scion). The scanning parameters were as follows: 60- to 80 kV-tube voltage, 1.0-mA tube current, 3.5-second scanning time, 0.125-mm voxel size, and 100-mm field of view (full arch). Radiographic assessment was conducted on CBCTs obtained at baseline (T0), immediately after operation (T1), and at the 3- and 12-month follow-ups (T3 and T12, respectively). Radiographic measurements were done by the same researcher (S.T.), who was blinded to the group allocation.

Radiographic assessments were performed as follows: The most distal/mesial point of the cementoenamel junction of the terminal tooth near the surgical area was used as the reference point. By measuring the distance between the vertical parallel line passing through the middle of the placed implant and the reference point, measurements were made on images at the same distance for each CBCT. All CBCT sagittal section scans were taken at 1-mm intervals, and radiographic measurements were completed using the CBCT images taken at T0, T1, T3, and T12. Using ImageJ software (National Institutes of Health), the ratio between the length of the placed implant and the implant length measured on CBCT scans was calculated (Fig 2).

The following parameters were recorded at the mesial and distal sides of each implant, then averaged to achieve one measurement (Figs 3 and 4).

- RBH: distance between the top of the alveolar bone crest and the maxillary sinus floor, coinciding with the center of the placed implant
- Implant protrusion length into the sinus (IPL)
- Peri-implant sinus bone level (PSBL): mean distance between the groove most coronal to the implant and the bone-to-implant connection most apical to the implant
- ESBG: new bone formation into the sinus following TSFE

RFA

Implant stability was measured by resonance frequency analysis (RFA) at T1 and T3. An Osstell Mentor appliance and a commercially available transducer (Type 4) adapted to Straumann implants were used for RFA. The transducer (Smartpeg) was kept perpendicular to the implant and was hand-screwed into the implant body, as recommended by the manufacturer. The Osstell Mentor made the measurements by transmitting electromagnetic waves from its probe to the bone and reflecting the waves from the bone to the device screen in response. The digital values acquired by this operation were recorded as the implant stability quotient (ISQ) values for each implant. During the measurement, the probe was applied in buccal, palatal, mesial, distal, and occlusal directions, and the mean ISQ value was recorded.

Statistical Analysis

Data analysis was performed using SPSS. All data were transferred to the Microsoft Excel file by one researcher (S.T.), and all information on patients and study groups were de-identified. Study groups were coded as 1 and 2 for blind statistical analysis. Kolmogorov-Smirnov test was used to test the normality of the distribution; all measurements were normally distributed. Paired-samples *t* test was used for within-group comparisons at each time point, and independent-samples *t* test was used for comparisons between groups. Variables affecting ISQ values at T1 and T3 and variables affecting ESBG at T12 were analyzed by modeling with multivariate regression analysis. For all tests, $P < .05$ was considered statistically significant.

Table 1 Intergroup Comparison of Radiographic Measurements at Different Time Intervals

	EMD+TSFE group	TSFE group	*P**
RBH–T0	4.82 ± 0.41 mm	5.33 ± 0.54 mm	.84
IPL–T1	4.85 ± 1.24 mm	4.74 ± 0.73 mm	.18
PSBL–T1	4.91 ± 0.45 mm	5.83 ± 1.18 mm	.17
PSBL–T3	8.62 ± 1.19 mm	8.93 ± 1.05 mm	.51
PSBL–T12	8.45 ± 1.25 mm	8.66 ± 0.92 mm	.65
ESBG–T3	3.72 ± 0.85 mm	3.10 ± 0.05 mm	.048
ESBG–T12	3.53 ± 0.99 mm	3.14 ± 1.29 mm	.408

Data are presented as mean ± SD.
*Independent *t* test. $P < .05$ is considered significant.

RESULTS

Demographic Data

A total of 24 patients (13 women, 11 men) were included, with 40 implants placed by TSFE with or without EMD in the posterior maxilla. The mean age was 47.2 ± 7.33 years in EMD+TSFE group and was 48 ± 11.31 years in TSFE group. No patient experienced implant loss or significant complications, including sinusitis symptoms. All wound healing was uneventful. All included implants were analyzed for the outcome measurement up to the maximum follow-up period (1 year).

Of the 20 implants included in the EMD+TSFE group, the diameters were as follows: 6 were 3.3 mm, 11 were 4.1 mm, and 3 were 4.8 mm. The implant lengths were as follows: 6 were 8 mm, 8 were 10 mm, and 6 were 12 mm. Of the 20 implants included in the TSFE group, the diameters were as follows: 4 were 3.3 mm, 13 were 4.1 mm, and 3 were 4.8 mm. The implant lengths were as follows: 3 were 8 mm, 11 were 10 mm, and 6 were 12 mm.

Outcomes of Radiographic Measurements

Intergroup comparisons

The mean RBH was 4.82 ± 0.41 mm and 5.33 ± 0.54 mm in EMD+TSFE and TSFE groups, respectively, at T0; there were no statistical differences between groups ($P = .84$). The IPL was 4.85 ± 1.24 mm and 4.74 ± 0.73 mm in the EMD+TSFE and TSFE groups, respectively, at T1; no statistically significant difference was observed between groups ($P = .18$, Table 1).

At T1, the mean PSBL was 4.91 ± 0.45 mm in the EMD+TSFE group and 5.83 ± 1.18 mm in the TSFE group. At T3, mean PSBL was 8.62 ± 1.19 mm in the EMD+TSFE group and 8.93 ± 1.05 mm in the TSFE group. At T12, mean PSBL was 8.45 ± 1.25 mm in the EMD+TSFE group and 8.66 ± 0.92 in the TSFE group. No statistically significant difference was found for the mean PSBL values between groups at T1, T3, or T12 ($P > .05$, see Table 1).

The mean ESBG was 3.72 ± 0.85 mm in the EMD+TSFE group and 3.10 ± 0.05 mm in the TSFE group at T3, and there was a statistically significant difference between the groups, with a higher ESBG value recorded in the EMD+TSFE group ($P < .05$). Mean ESBG was 3.53 ± 0.99 mm in the EMD+TSFE group and 3.14 ± 1.29 mm in the TSFE group at T12, and no statistically significant difference was found between groups ($P > .05$, see Table 1).

Intragroup comparisons

A statistically significant difference was found in intragroup PSBL values from T1 to T3 and from T1 to T12 in both EMD+TSFE and TSFE groups ($P < .05$). However, no statistically significant difference was found in PSBL intragroup evaluations from T3 to T12 in either group ($P > .05$, Table 2).

No statistically significant difference was obtained in the intragroup comparison of ESBG values from T3 to T12 ($P > .05$, see Table 2).

RFA outcomes

At T1, the mean ISQ values were 69.69 ± 6.07 and 72.6 ± 4.68 for the EMD+TSFE and TSFE groups, respectively. At T3, the mean ISQ values were 75.42 ± 4.56 and 74.54 ± 4.85 for the EMD+TSFE and TSFE groups, respectively. No significant differences were found between groups for the ISQ values at T0 and T3 ($P > .05$, Table 3).

When intragroup comparisons were evaluated, the mean ISQ values in the EMD+TSFE group were statistically significantly higher at T3 compared to T1 ($P = .000$ vs $P < .05$, respectively). For the mean ISQ values in the TSFE group, no statistically significant difference was found for intragroup comparisons ($P = .204$ [T1], $P = .653$ [T3]; see Table 3).

Table 2 Intragroup Comparison of Radiographic Measurements at Different Time Intervals

	EMD+TSFE group	TSFE group
PSBL T1–T3	.000	.000
PSBL T1–T12	.000	.000
PSBL T3–T12	.088	.268
ESBG T3–T12	.92	.254

Data are presented as *P* values (paired-samples *t* test). $P < .05$ is considered significant.

Table 3 Intragroup and Intergroup Comparisons of ISQ Values

	EMD+TSFE group	TSFE group	*P*[a]
ISQ-T1	69.69 ± 6.07	72.6 ± 4.68	.204
ISQ-T3	75.42 ± 4.56	74.54 ± 4.85	.653
P[b]	.000	0.156	

Data are presented as mean ± SD.
[a]Independent *t* test for intergroup comparisons. $P < .05$ is considered significant.
[b]Paired-samples *t* test for intragroup comparisons. $P < .05$ is considered significant.

Table 4 Regression Model for Parameters Influencing ISQ Values at T1 (ISQ-T1)

		Unstandardized coefficients		Standardized coefficients		
Model	Group	B	SE	Beta	*t*	*P**
Implant diameter	EMD+TSFE	—	—	—	–1.950	.234
	TSFE	5.595	1.772	0.442	3.158	.372
Implant length	EMD+TSFE	11.109	2.409	0.953	4.612	.181
	TSFE	3.769	2.798	0.874	1.347	.002
RBH-T0	EMD+TSFE	22.442	8.405	1.657	2.670	.107
	TSFE	1.590	1.976	0.174	0.805	.001
IPL-T1	EMD+TSFE	0.023	0.852	0.005	0.028	.268
	TSFE	–2.747	2.796	–0.398	–0.983	.001
PSBL-T1	EMD+TSFE	–8.534	7.306	–0.688	–1.168	.142
	TSFE	0.067	2.430	0.013	0.027	.978

SE = standard error.
*Multivariate regression analysis. $P < .05$ is considered significant.

Multivariate regression analysis

A regression model was created for the parameters affecting the ISQ values at T1, and the effects of implant diameter, implant length, RBH, IPL, and PSBL on the mean ISQ values at T1 were evaluated separately for both groups. RBH-T0, IPL-T1, PSBL-T1, and implant diameter and length had an effect on mean ISQ values. In the EMD+TSFE group, implant diameter, implant length, RBH, IPL, and PSBL had no effect on ISQ values individually. In the TSFE group, implant length, RBH, and PSBL does not effect on the ISQ values ($P < .05$), but implant diameter and IPL had an effect (< .001) on the mean ISQ value at T1 (Table 4).

A regression model was created for the parameters affecting the ISQ values at T3, and the effects of implant diameter, implant length, PSBL, and ESBG on the mean ISQ values were evaluated separately for both groups. Implant length, PSBL, and ESBG had an effect on mean ISQ-T3 values in the EMD+TSFE group ($P < .05$), but implant diameter had no effect. In the TSFE group, implant length and PSBL had an effect on mean ISQ-T3 values ($P < .05$), but implant diameter and ESBG had no effect (Table 5).

A regression model was created for the parameters affecting the ESBG values at T12, and the effects of implant diameter, implant length, RBH-T0, IPL-T1, ISQ-T1, and ISQ-T3 were evaluated separately for both groups. In the EMD+TSFE group, implant length and IPL-T1 had an effect on ESBG-T12 ($P < .05$), but implant diameter, RBH-T0, ISQ-T1, and ISQ-T3 had no effect. In the TSFE group, implant diameter, implant length, RBH-T0, IPL-T1, ISQ-T1, and ISQ-T3 had no effect on ESBG-T12 (Table 6).

DISCUSSION

This study aimed to evaluate the effect of EMD application on radiographic and clinical recovery in implants placed simultaneously with transcrestal sinus elevation. The hypothesis established at the beginning of the study (that EMD would have no effect) was rejected at short evaluation times but is accepted for long

Table 5 Regression Model for Parameters Influencing ISQ Values at T3 (ISQ-T3)

		Unstandardized coefficients		Standardized coefficients		
Model	Group	B	SE	Beta	*t*	*P**
Implant diameter	EMD+TSFE	3.611	2.068	0.398	1.746	.976
	TSFE	3.772	2.892	0.272	1.305	.743
Implant length	EMD+TSFE	−0.547	1.732	−0.188	−0.316	.013
	TSFE	−0.382	1.977	−0.081	−0.193	.028
PSBL-T3	EMD+TSFE	5.091	3.010	1.377	1.692	.005
	TSFE	3.574	2.167	0.714	1.649	.007
ESBG-T3	EMD+TSFE	−2.261	3.357	−0.451	−1.674	.000
	TSFE	0.347	2.297	0.035	0.151	.181

SE = standard error.
*Multivariate regression analysis. $P < .05$ is considered significant.

Table 6 Regression Model for Parameters Influencing ESBG Values at T12 (ESBG-T12)

		Unstandardized coefficients		Standardized coefficients		
Model	Group	B	SE	Beta	*t*	*P**
Implant diameter	EMD+TSFE	0.574	0.810	0.295	0.708	.933
	TSFE	−0.689	0.403	−0.428	−1.708	.230
Implant length	EMD+TSFE	0.981	1.654	1.569	0.593	.004
	TSFE	−0.441	0.277	−0.804	−1.593	.740
RBH-T0	EMD+TSFE	−0.719	2.218	−0.318	−0.324	.310
	TSFE	0.189	0.338	0.163	0.558	.743
IPL-T1	EMD+TSFE	−0.450	1.691	−0.579	−0.266	.002
	TSFE	0.685	0.264	0.780	2.591	.271
ISQ-T1	EMD+TSFE	−0.037	0.068	−0.222	−0.541	.663
	TSFE	−0.023	0.046	−0.181	−0.501	.271
ISQ-T3	EMD+TSFE	0.006	0.077	0.030	0.082	.260
	TSFE	0.075	0.026	0.651	2.897	.256

SE = standard error.
*Multivariate regression analysis. $P < .05$ is considered significant.

evaluation times for ESBG, the primary outcome. The present study showed that EMD contributed to bone formation (measured radiographically) during short-term healing, but EMD did not have a significant effect in the long term. To the present authors' knowledge, this is the first randomized clinical trial reporting the radiographic and clinical outcomes of EMD application with simultaneous implant placement in the extremely atrophic posterior maxilla (RBH < 6 mm) using TSFE operations.

In TSFE, many different materials and bioactive factors have been applied to increase primary stabilization and bone healing at the apical implant region, and successful results have been reported.[21] In a meta-analysis, when the TSFE with and without a graft were compared, the perforation rate increased when bone graft material was used, and the ESBG value was higher in cases where graft was applied[9]; however, there was no difference in terms of marginal bone loss and long-term survival rates.[9] A network meta-analysis reported that Emdogain application with a xenograft did not increase bone healing and regeneration in the lateral approach for maxillary sinus elevation.[22] One study evaluated the application of concentrated growth factor with hydrodynamic piezoelectric TSFE, and reported that the RBH value was 4.98 ± 2.8 mm and the total vertical bone height was 8.23 ± 2.88 mm, and the concentrated growth factor (CGF) was successful and predictable for

TSFE operations[23]; however, that study did not have a control group.[23] Another study on short implants applied plasma-rich growth factor together with different bone grafts in 15 of 58 short implants, and it was reported that short implants could be applied together with bioactive factors.[6] Further, one study compared cases with and without Bio-Oss use in the TSFE operation, and the ESBG value was obtained at a higher rate in grafted cases, but there was no statistically significant difference between those results and that of nongrafted cases.[24] A study evaluating the relationship between bone graft resorption and sinus width after lateral approach maxillary sinus augmentation, it was reported that vertical bone graft resorption occurring at the apical implant aspect was higher in the wide-sinus group.[25] In a study evaluating TSFE operations and maxillary sinus anatomy, it was reported that increasing the distance and angle between the implant and the lateral wall of the sinus floor was associated with decreased new bone formation.[26] Further, it has been reported that sinus membrane thickness is affected after lateral approach maxillary sinus augmentation operations: thin sinus membranes thicken, and thick sinus membranes become thinner.[27]

The present study determined that ESBG was statistically greater in EMD+TSFE patients at 3 months, but there was no difference between EMD+TSFE and TSFE groups at 12 months. For the intragroup evaluations of the change in ESBG between T3 and T12, there was a decrease in ESBG in the TSFE+EMD group, while there was a slight increase in the TSFE group. The initial increase and subsequent decrease in implant placement torque may be due to bone pressure due to EMD and related biologic effects, or it may be related to sinus membrane thickness and sinus width, but studies explaining the relationship between TSFE operations and sinus anatomy are limited in the literature. The most important limitation of the present study is that no correlation was made between ESBG and sinus anatomical structures.

One study reported that an IPL of 3 to 5 mm created a positive correlation with new bone formation in the treatment of 357 implants placed with the TSFE.[26] In an in vitro study conducted on titanium discs, it was reported that osteoblast-like cells caused a higher concentration of gene expression when EMD was applied on SLA surfaces compared to the control group.[28] In the present study, at the 12-month follow-up, implant length and IPL values were determined to have an effect on ESBG in the EMD+TSFE group, but there was no effect on ESBG in the TSFE group; this finding may be related to the higher gene expression of EMD on titanium surfaces. When the factors related to ESBG were evaluated, it was found that the IPL was related to the ESBG in the EMD+TSFE group. Although there was no difference between groups in IPL values, a statistically significant difference was found between ESBG values at T3, and this difference may be related to the IPL value; this is because the possibility of higher bone formation increases as the implant surface area increases. The limited number of included patients makes interpretation difficult, and thus further studies with a higher number of samples are needed.

Morris et al [29] found that implant diameter has no significant effect on the primary implant stability.Oppositely, Kim et al [30] showed that implant stability was related to a wide implant diameter creating larger bone-to-implant contact.One study has mentioned that the relationship between implant length, insertion depth, and ISQ values in short implants have positive correlation.[31] On the contrary, another study evaluated primary and secondary implant stabilization between short and standard implant groups and reported that ISQ values were not significantly different.[32] There are many confounding factors in the present study. Factors affecting ISQ-T1, ISQ-T3, and ESBG-T12 in each study group were evaluated with multivariate regression analysis. Although there were differences in implant diameter, it was shown that implant diameter did not affect ISQ-T1, ISQ-T3, and ESBG-T12, but implant length did affect ISQ-T3 values in both groups. For ISQ-T1, implant length was not found to be effective in the EMD group, which, although not statistically significant, could be associated with the lower IPL and higher RBH values in the TSFE group. Although there is no significant difference in ISQ values between the groups, within-group evaluations show a statistically significant increase between ISQ atT1 and T3. It can be said that EMD may be supportive for secondary stabilization in early bone healing, but it does not create a clinically or statistically significant difference compared to the non-EMD group. Additionally, when the factors affecting secondary stabilization were evaluated, it was found that implant length and PSBL had an effect in both groups.

Emdogain material contains amelogenin and propylene glycol alginate (PGA) as a carrier, and EMD also has antimicrobial properties due to its PGA carrier.[33,34] In one study, EMD containing a gel carrier and a liquid carrier was compared, and both showed increased cell proliferation of osteoblasts and increased expressions of BMP-2 and TGF-β1, with the liquid carrier providing a higher gene expression.[35] In another study, radiation was applied to experimental bone defects with high-resolution computed tomography at different time intervals, and it was reported that the radiation dose had no effect on the healing of bone defects.[36] In the present study, CBCT images were taken from the same machine with the same technical features in all cases. The effect of the amelogenin carrier and the radiation dose may be the confounding factors, but further studies

are needed to evaluate this. Applying a placebo-effect material with a PGA carrier without amelogenin in the present study could have blinded the surgeon and created a standard effect while evaluating the effect of the carrier on the sinus membrane and ESBG, and this is an important limitation of the study, as well as: sinus membrane thickening with EMD application, the effects on the sinus membrane during implant placement after EMD application, the effect of the Emdogain carrier, and the failure to evaluate factors related to the maxillary sinus anatomy. There is a need for long-term studies on the factors affecting new bone formation and the stabilization of the resulting bone.

CONCLUSIONS

EMD (Emdogain) application before implant placement in TSFE operations is effective for new bone formation at the apical implant aspect during a short healing period but is not effective for long healing periods. Additionally, EMD provided significant increased ISQ values for 3 months (short term), but there is no significant difference in primary and secondary stabilization compared to TSFE-only operations. There is a need for further studies with a higher number of control groups administered together with the carrier.

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