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Guided tissue regeneration combined with bone allograft in infrabony defects: Clinical outcomes and assessment of prognostic factors

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Abstract

Background: Clinical data on the outcomes of guided tissue regeneration (GTR) is scarce. The aim of this retrospective cohort study was to evaluate the outcomes after GTR, their stability and the survival of the treated teeth with periodontal infrabony defects.

Methods: Infrabony defects treated with GTR using a bioabsorbable membrane and a bone graft substitute with at least 1-year follow-up were included. Survival and regression analyses were conducted to evaluate the outcomes, their stability, and the retention of the teeth. The effect of recorded variables on clinical attachment gain (CAL) and tooth survival were assessed via Cox proportional-hazards models and multivariate generalized linear models.

Results: One hundred seventy-five treated defects were selected from a total of 641 charts. The average follow-up was 5.75 ± 4.6 years. At baseline, the mean CAL was 9.56 ± 1.93 mm with a mean pocket depth (PD) of 8.41 ± 1.42 mm. At the 1-year post-surgical recall, 3.55 ± 1.85 mm of CAL gain and 3.87 ± 1.87 mm PD reduction were observed ($P < 0.05$). The 5- and 10-year survival rates of the treated teeth were 85.0% and 72.7%, respectively. Baseline PD, smoking, and membrane exposure were significantly related to CAL gain, whereas baseline CAL, age, frequency in maintenance visits significantly affected tooth survival.

Conclusion: Within the limitations of this study, data suggests GTR is a good option for the treatment of infrabony defects because it can improve both tooth retention rate and overall clinical outcomes.

KEYWORDS
guided tissue regeneration, periodontitis, smoking, survival analysis

1 | INTRODUCTION

Periodontitis is a complex multifactorial disease that often leads to the formation of deep infrabony defects.[1] Their presence has been shown to increase the risk for the progression of periodontitis by more than 10 times.[2] The treatment of infrabony defects poses clinical challenges, making its presence one of the influential factors when determining the complexity of periodontal disease.[3] In order to address this concern, several approaches have been proposed for their treatment including scaling and root planing, open flap debridement, resective surgeries, and various periodontal regenerative therapies.[4]

Among the proposed regeneration procedures, evidence supports the use of guided tissue regeneration (GTR) that employed barrier membranes, and many studies have reported significant clinical attachment level (CAL) gain, pocket depth (PD) reduction, and bone fill with the usage of membranes.[5–9] Additionally, histologic evidence has confirmed the regeneration of new cementum, periodontal ligament and alveolar bone.[10,11] Moreover, the superiority of GTR outcomes over traditional flap surgeries in the treatment of infrabony defects has been well established.[6,9,12] Cortellini et al. in a 20-year follow-up of a randomized clinical trial, observed that treated sites with GTR showed better long-term stability of their clinical outcomes compared to sites that were treated with a modified Widman flap procedure. Interestingly, the authors found the differences between regenerative therapy and flap surgery more pronounced in the second decade of the observation.[13]

Nevertheless, patient related factors, defect morphology, and surgical techniques have all been reported to significantly impact the overall predictability of the GTR procedure.[8,14] In addition, most of the studies only assessed the short-term outcomes of GTR and have been performed on a very carefully selected pool of patients.[13,15,16]

Therefore, the aim of the present study was to investigate the clinical outcomes of GTR and assess potential prognostic factors that can affect the clinical outcomes and tooth survival.

2 | MATERIALS AND METHODS

2.1 | Study design

The current investigation was designed according to the principles presented in the Helsinki Declaration of 1975, as revised in 2000 for biomedical research involving human patients. The study was approved by the Institutional Review Board for Human Studies, School of Dentistry, University of Michigan, Ann Arbor, MI (HUM00154408) to be conducted at the Department of Periodontology within the same institution.

This retrospective cohort study selected all patients that had undergone treatment for infrabony defects with GTR at the School of Dentistry, University of Michigan, Ann Arbor, MI. All paper files and digital charts of patients treated with GTR were carefully scanned and analyzed by two independent and pre-calibrated investigators (JM, SB). At every stage, after examining the gathered data, in case of a disagreement, discussion was held by the two reviewers. If resolution was not possible, a third investigator (LT) was consulted to reach a consensus. This study was conducted by obtaining anonymized data and all personally identifiable patient information was removed; hence, there was no need for informed consent.

2.2 | Inclusion criteria

Patients that met the following inclusion criteria were included in this study:

1. A patient who had previously received GTR therapy for at least one infrabony defect with a probing depth (PD) of ≥6 mm.[17]
2. Before the GTR procedure, all individuals must have previously received a comprehensive periodontal treatment (including oral hygiene instructions, scaling/root planing, prophylaxis, etc.).
3. GTR procedures must have included the use of a bioabsorbable membrane in combination with a bone graft substitute.
4. Patient records must have had at least 1-year follow-up after GTR treatment.
5. Patient's charts should have contained complete clinical data including radiographs at baseline (pre-surgical stage) and at least 1-year after the surgical procedure.

2.3 | Exclusion criteria

Patients that had the following conditions were excluded from this study:

1. Patients without a post-surgical follow-up data reaching 12 months.
2. The use of barrier membranes for procedures other than GTR (sinus lift, guided bone regeneration, socket augmentation, etc.).
3. GTR procedures in furcation defects.
4. The sole use of bone graft without utilizing a barrier membrane, or the utilization of a membrane without placement of a bone graft.
5. Placement of a non-resorbable membrane.
6. A medically compromised patient or those taking medications that are known to interfere with the normal healing response process (e.g., bisphosphonates, anti-cancer therapy, etc.).

2.4 | Data collection and classification

The following information was obtained for all qualified individuals (1) patient related factors (such as age, gender, etc.), (2) medical history (including documentation of smoking, diabetes, other systemic, or local diseases), (3) location of the treated defect (mandible/maxilla), (4) related clinical parameters such as: PD, CAL, gingival recession (REC),

(5) flap design (envelope/papilla preservation), (6) occurrence of post-surgical complications (such as membrane exposure), (7) follow-up time (until tooth extraction or last maintenance appointment), (8) frequency of maintenance appointments throughout the entire follow-up, and (9) patient radiographs.

2.5 | Study outcomes

The study outcomes of the present project were three fold:

2.5.1 | Clinical outcomes of guided tissue regeneration

a. To assess the outcomes of the treatment, changes in the clinical parameters (PD, CAL, REC) were compared from baseline to the 1-year post-op/follow-up.
b. Additionally, the influence of other recorded variables was assessed on the CAL results.
c. Stability of the treatment results throughout the entire follow-up was assessed for all sites as previously performed in other studies.[18,19] Briefly, stability was defined for a treated site that maintained the 1-year post-surgical CAL throughout time, presenting with <2 mm of change. This was assessed with the Kaplan-Meier estimator.

2.5.2 | Survival

The survival of a treated tooth was assessed according to the Kaplan-Meier analysis. Additionally, the effect of the recorded variables on the treated sites was assessed for potential effect on tooth retention/survival.

2.5.3 | Assessment of the radiographic defect angle

Extracted baseline radiographs were used to measure the radiographic defect angle of the treated site,[20,21] by using a digital software.* The angle outlined by the bony defect wall and the root surface of the corresponding tooth was measured by using the criteria described by Bjorn et al. (1969)[22] and Schei et al. (1959).[23] Next, the effect of the width of the angle on tooth survival and post-surgical CAL gain was evaluated. All radiographic analyses were performed by two individual and calibrated examiners (JM, SB). In case of uncertainty or a substantial difference among the measurements, a third reviewer (LT) was consulted for reassessing the radiographs.

2.5.4 | Data management and statistical analysis

The extracted data were entered into pre-fabricated spread sheets by the same investigators. All analyses were performed by an author with expertise in biostatistics (SB) using Rstudio,† the survminer,[24] survival,[25,26] and ggplot2[27] packages. Descriptive statistics were used for presenting the retrieved data at baseline as means ± SD, and range. The treated defects served as the unit of analysis. The changes in clinical parameters from baseline to the 1-year outcome were assessed with dependent *t* tests. Mixed-effects Uni- and Multi-level Regression analyses were performed to identify prognostic factors for CAL gain. Kaplan-Meier survival probabilities were calculated and subsequently the curves were plotted. Multi-variate cox proportional hazzard models were used for assessing correlations between independent variables and tooth loss, accounting for the fact that an individual may have attributed to multiple treated infrabony defects (shared frailty was accounted for by including random effects). Step-wise regression analyses were performed using likelihood ratio tests, with variables presenting a p value of <0.05 in the initial univariate analysis. Exponentiated regression coefficients (Hazzard ratios) and corresponding 95% confidence intervals (CI) were produced, and a p value threshold of 0.05 was set for the statistical significance.

3 | RESULTS

3.1 | Study population

A total of 641 patient charts were retrieved and screened as a result of the initial search. Subsequently, 513 were excluded because of the following reasons: guided bone regeneration (121) or socket augmentation procedures (61), regenerative approaches performed with a non-resorbable membrane (94), with the use of membranes alone (6), or those treated solely with a bone graft material (16). Additionally, files with <1-year of follow-up (81), sinus augmentation procedures (28) and regeneration attempts in furcation defects (106) were also excluded, a flowchart diagram has been presented in supplementary Data S1 in online *Journal of Periodontology* to visualize the screening process.

As a result, a total of 128 patients (63 males and 65 females) with a mean age of 51.7 ± 13.88 (16 to 85 years), with 175 GTR-treated infrabony defects were included. In all GTR procedures, the combination of a collagen membrane with an allograft bone material was used. The bone grafts used were all allogenic in nature either Freeze-dried bone allograft‡ (in 38 defects), or Solvent-dehydrated bone allograft§ (in 137 defects). The membranes used were of two types, both collagenous in nature BioMend¶ in 128 defects, and Bio-Gide#

* Image J, the U.S. National Institutes of Health, Bethesda, MD.

† Rstudio Version 1.1.383, RStudio, Inc, Boston, MA.

‡ Salvin Dental Specialties, Charlotte, NC.

§ Puros, Zimmer Biomet, Carlsbad, CA.

¶ Zimmer Biomet, Carlsbad, CA.

Geistlich Pharma, Wolhusen, Switzerland.

TABLE 1 Characteristics of the included patients/defects at baseline

Characteristic	Frequency
Males (N, %)	63, 49.2%
Age	51.7 ± 13.9
Diabetics (N, %)	11, 8.6%
Smoker (N, %)	41, 32.0%
2017 World workshop[3]	
Stage 3 grade A periodontitis (N, %)	17,13.3%
Stage 3 grade B periodontitis (N, %)	46, 35.9%
Stage 3 grade C periodontitis (N, %)	27, 21.1%
Stage 4 grade A periodontitis (N, %)	10, 7.8%
Stage 4 grade B periodontitis (N, %)	13, 10.2%
Stage 4 grade C periodontitis (N, %)	15, 11.7%
Maxilla (N, %)	66, 37.7%
Mandible (N, %)	109, 62.3%
Endodontically treated (N, %)	14, 8%
Clinical attachment level (CAL [mm])	9.56 ± 1.93 mm
Pocket depth (PD [mm])	8.41 ± 1.42 mm
Recession (REC [mm])	1.21 ± 1.11 mm
Initial radiographic angle	36.86° ± 15.3°

Data are expressed as mean ± SD; or N, numbers, percentages.

in 47 cases. The mean follow-up for the selected cases was 5.75 ± 4.6 years. The average maintenance visits for patients was 2.2 (±1.1) times per year. Table 1 presents details on the characteristics of the included patients.

3.2 | Clinical outcomes of guided tissue regeneration

At baseline, 60.8% of sites presented with BOP, a mean PD of 8.41 ± 1.42 mm, REC of 1.21 ± 1.11 mm, and CAL of 9.56 ± 1.93 mm. At the 1-year post-surgical recall, the BOP dropped to 23.8%, a PD reduction of 3.87 ± 1.87 mm, an increase in recession of 0.35 ± 1.16 mm, and 3.55 ± 1.85 mm of CAL gain were observed, all of which were statistically significant.

An access flap with intrasulcular incision[13,28] was used in most of the surgical cases; however, a papilla preservation design was performed in 20 of the procedures (without statistically significant differences between the two). Vertical incisions were used in 38 surgeries to allow better access to the defect and the occurrence of a membrane exposure was noted in 22 of the cases.

Table 2 depicts the results of the regression models, exploring the effect of different variables on the gained CAL at 1-year post-surgery. Results from univariate analysis demonstrated that smoking (−1.01 [95% CI (−1.85, −0.16), P = 0.01]), post-surgery membrane exposure (−0.26 [95% CI (−0.50, −0.01), P = 0.02]), and wider initial radiographic angle (−0.02 [95% CI (−0.05, −0.002), P = 0.03]), were significantly related to a lower CAL, whereas an increase in initial PD (0.55 [95% CI (0.26, 0.85), P < 0.001]), and CAL (0.34 [95% CI (0.14, 0.55), P = 0.001]), were significant predictors for higher CAL gains. The negative effect of smoking on CAL gain was observed (CAL gain in smokers was 2.97 ± 2.06 mm versus 3.98 ± 1.90 mm in non-smokers).

Results from the multivariate analysis including the stated statistically significant variables demonstrated that, smoking (−0.91 [95% CI (−1.73, −0.07), P = 0.03]) and membrane exposure (−1.18 [95% CI (−2.28, −0.06), P = 0.03]), were associated with lower gains in CAL, whereas initial PD (0.57 [95% CI (0.16, 0.97), P = 0.006]), was positively correlated to higher CAL gains. Moreover, factors such as initial radiographic angle, and initial CAL did not prove to be statistical predictors from the model.

Last, gender, age, diabetes, placement of a vertical releasing incision during the surgery, and endodontic treatment, did not seem to impact the CAL gains (P > 0.05). Regarding the stability of the gained attachment levels, the Kaplan-Meier analysis showed that 70.4% ± 5.85% and 54.9% ± 7.26% of the treated sites remained stable at 5 and 10 years, respectively (supplementary Data S2 in online *Journal of Periodontology*).

3.3 | Survival analysis

Throughout the follow-up period 30 teeth in 27 patients were lost. The 5- and 10-year survival rates were 85.0% and 72.7%, respectively (76 treated teeth at the 5-year timepoint, and 21 at the 10-year timepoint). Figure 1 demonstrates the survival curves of the treated teeth, and the life table presented in Table 3 descriptively presents the number of followed and extracted teeth at every timepoint.

Univariate analysis demonstrated that smoking significantly affected the survival of the treated teeth (amounting to 21 of the total extractions). Visual representation comparing the survival curves of smokers versus non-smokers is presented in Figure 2. Frequency in maintenance visits was also found to have a significant impact on tooth survival (0.45 [95% CI (0.29, 0.67), P < 0.0001]). The average maintenance visits/year for the teeth that were extracted was 1.43 ± 0.90 whereas the mean number for the ones that remained was 2.39 ± 1.07 visit/year (P < 0.01).

Age, endodontic treatment, and membrane exposure were also significant factors associated with tooth loss. Nevertheless, factors such as gender, diabetes, flap design, presence of vertical incisions did not seem to be statistically correlated in the survival analysis.

When the significant factors from the univariate models were evaluated in a multi-variate cox proportional hazard model, it was shown that maintenance (0.34 [95% CI (0.20, 0.58), P < 0.001]), initial CAL (1.53 [95% CI (1.03, 2.28), P = 0.03]), and age (1.08 [95% CI (1.03, 1.14), P = 0.002]), were the most significant predictors affecting tooth survival (Table 4).

TABLE 2 Results of the regression models evaluating the effect of different variables on the clinical attachment levels of the treated defects at the 1-year recall

	Univariate analysis			Multivariate analysis			
Variable	**Estimate**	**95% CI**	***P* value**	**Estimate**	**SE**	**95% CI**	***P* value**
Gender (male)	−0.83	−1.67, 0.001	0.05				
Age	0.01	−0.01, 0.04	0.26				
Smoking	**−1.01**	**−1.85, −0.16**	**0.01**	**−0.91**	**0.41**	**−1.73, −0.07**	**0.03**
Diabetes	−0.18	−1.43, 1.07	0.77				
Membrane exposure	**−0.26**	**−0.50, −0.01**	**0.02**	**−1.18**	**0.55**	**−2.28,−0.06**	**0.03**
Endodontic treatment	−0.31	−1.91, 1.27	0.69				
Initial PD	**0.55**	**0.26, 0.85**	**<0.001**	**0.57**	**0.20**	**0.16, 0.97**	**0.006**
Initial CAL	**0.34**	**0.14, 0.55**	**0.001**	0.14	0.14	−0.13, 0.42	0.3
Flap design	0.55	−0.58, 1.69	0.33				
Vertical incision	−0.03	−1.04, 0.97	0.94				
Initial radiographic angle	**−0.02**	**−0.05, −0.002**	**0.03**	−0.01	0.01	−0.03, 0.01	0.26

Bold signifies statistical significance; CI, confidence intervals.

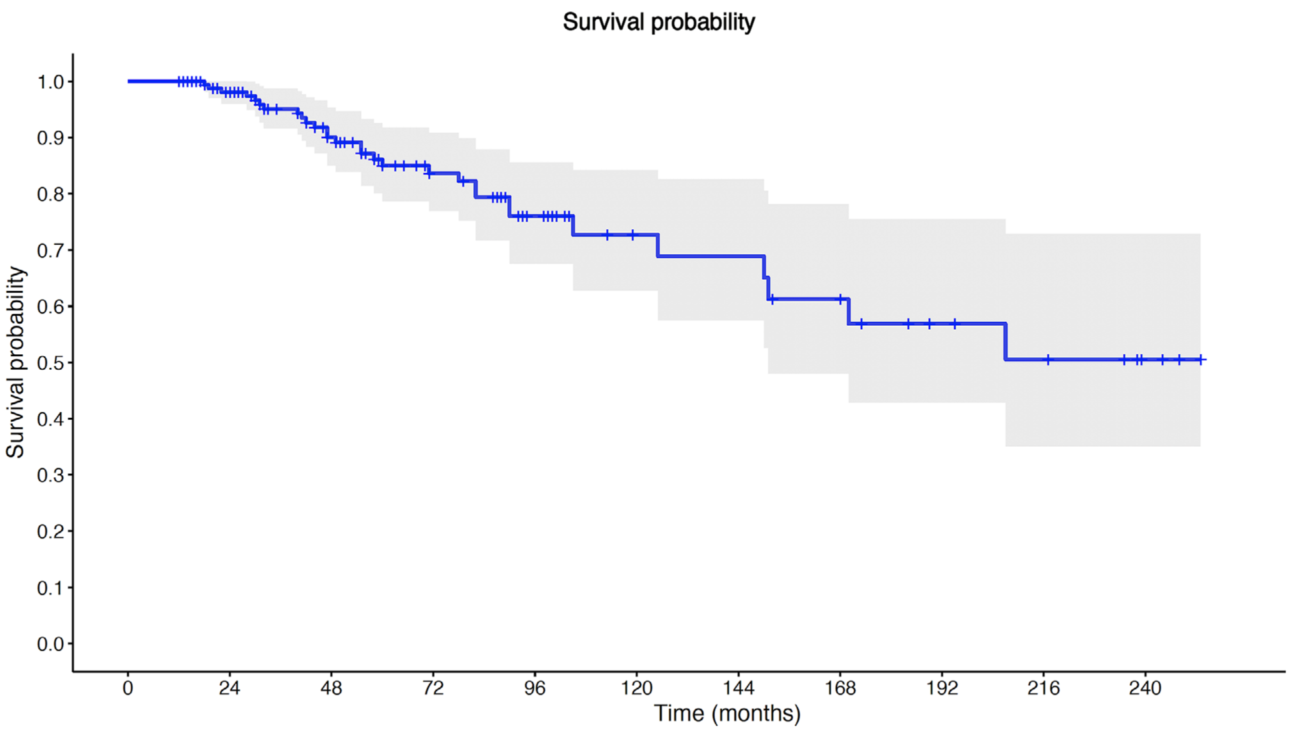

FIGURE 1 Kaplan-Meier survival curve for the entire follow-up period. Each event represents a tooth loss. The grayish hue represents the upper and lower limit of the 95% confidence bands

4 | Discussion

4.1 | Clinical outcomes after guided tissue regeneration

Results from this study showed 3.55 ± 1.85 mm gain of CAL and 3.87 ± 1.87 mm PD reduction 1-year following the GTR procedure. The gain in CAL observed at the 1-year recall are in line with previous studies. In fact, Kher et al. in a study evaluating the effect GTR using human allograft combined with a collagen membranes in infrabony defects found a mean CAL gain of 3.54 ± 0.36 mm one-year following the surgery.[29] Sculean et al., observed an average CAL gain of 4.07 ± 1.3 mm, 1 year after the GTR procedure using bovine bone xenograft in combination with a collagen membrane,[30] and 4.1 ± 0.9 mm using a composite bovine bone xenograft combined with a collagen membrane.[31]

When other treatment approaches were attempted for the treatment of infrabony defects, Nibali and colleagues found that minimally invasive non-surgical therapy achieved 3.0 mm

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TABLE 3 Life table descriptively summarizing the survival probabilities according to the Kaplan-Meier analysis. Survival estimations for the 5- and 10- year timepoints have been lightly shaded in grey

					95% Confidence Interval	
Time (months)	Number at risk	Number of event(s)	Survival	SE	Lower bound	Upper bound
0	175	0	0.1	—	—	—
18	159	1	0.994	0.00627	0.981	1.000
19	157	1	0.987	0.00887	0.970	1.000
22	152	1	0.981	0.01093	0.960	1.000
28	138	1	0.974	0.01296	0.949	1.000
30	131	1	0.966	0.01484	0.938	0.996
31	129	1	0.959	0.01651	0.927	0.992
32	125	1	0.951	0.01807	0.916	0.987
40	117	1	0.943	0.01966	0.905	0.982
41	114	1	0.935	0.02116	0.894	0.977
42	113	1	0.927	0.02253	0.883	0.972
44	108	1	0.918	0.02390	0.872	0.966
47	104	2	0.900	0.02650	0.850	0.954
49	101	1	0.891	0.02769	0.839	0.947
55	91	2	0.872	0.03035	0.814	0.933
58	81	1	0.861	0.03183	0.801	0.926
60	76	1	0.850	0.03337	0.787	0.918
71	63	1	0.836	0.03546	0.770	0.909
78	61	1	0.822	0.03743	0.752	0.899
82	58	2	0.794	0.04116	0.717	0.879
90	47	2	0.760	0.04583	0.676	0.856
105	23	1	0.727	0.05447	0.628	0.842
125	19	1	0.689	0.06365	0.575	0.826
150	18	1	0.651	0.07069	0.526	0.805
151	17	1	0.612	0.07619	0.480	0.782
170	14	1	0.569	0.08236	0.428	0.755
207	9	1	0.506	0.09438	0.351	0.729

CAL gain 1 year after treatment. However, the study included patients with a lower initial PD compared to the present study (7 mm versus 9.6 mm).[32] Whether deeper pockets such as the ones included in our study could be addressed with non-surgical therapies remains unknown.

Regarding the stability, it was observed that ≈70.4% and 54.9% of the treated sites remained stable after 5 and 10 years, respectively. In another retrospective study, with similar definition of stability, the authors reported a higher estimate of ≈80% and 70% after 5 and 10 years, respectively.[18] It can be speculated that their superior results in terms of stability of the CALs might be attributed to a more meticulous patient selection, the private practice setting, and the expertise of the surgeon.[13] In another publication, evaluating the 10-year results of a randomized clinical trial, Nickles and colleagues showed that three out of the 18 defects that remained 10 years after the GTR procedure were unstable. However, it should be noted that the mentioned study had a relative limited sample size compared to the present study.

4.2 | The effect of guided tissue regeneration on tooth survival

One of the goals of this study was to evaluate the survival of teeth treated with GTR.

We found that the 5- and 10-year survival rates of the treated teeth were 85.0% and 72.7%, respectively. Higher survival rates have been reported in the literature. In a 5-year study assessing the outcomes of GTR, only two out of 50 teeth were lost, none of which were attributed to the loss of the periodontal structure. This study included infrabony defects in a population which were 12% smokers and 86% attending at least one SPT visit per year.[33] Another study presenting the 10-year results after treatment of 38

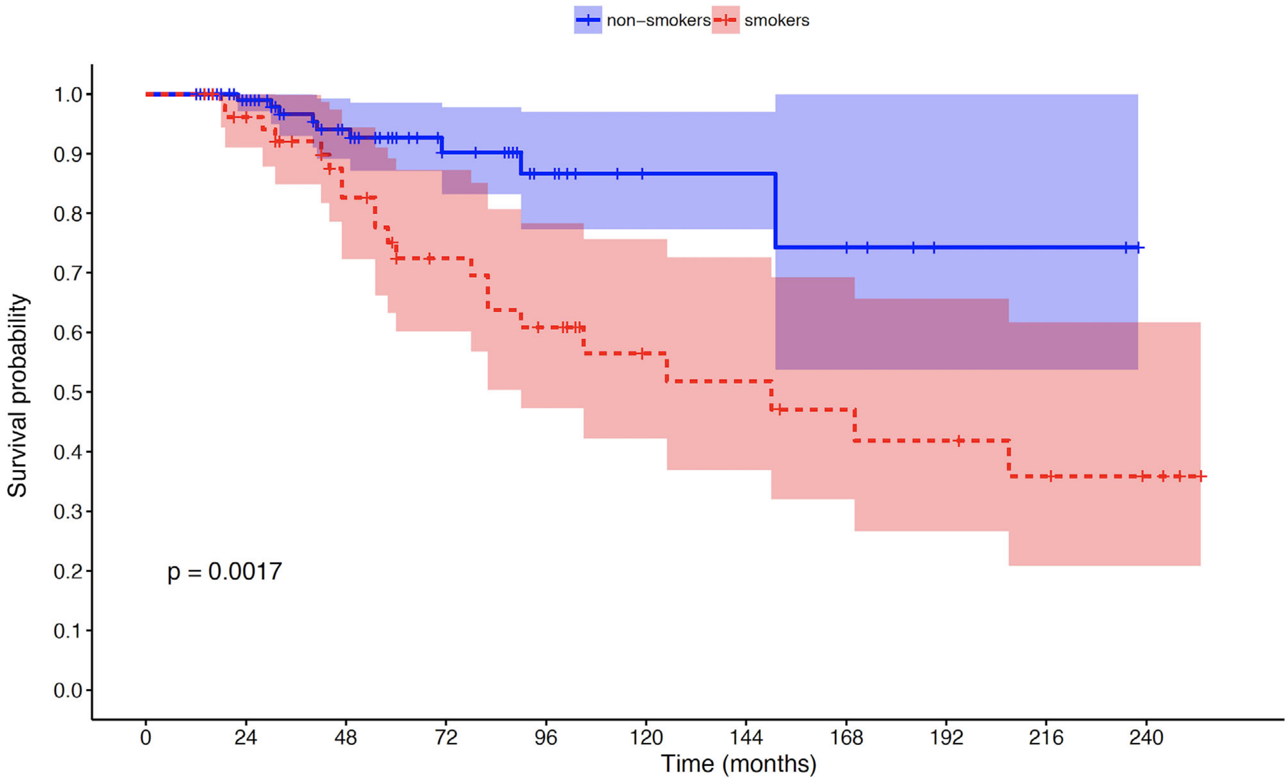

FIGURE 2 Kaplan-Meier survival curves displaying the comparison between smokers and non-smokers. Event = Tooth loss. Blue and red hues represent the upper and lower limit of the 95% confidence bands

TABLE 4 Results of the multilevel cox proportional hazard models evaluating the effect of different variables on the survival of the treated teeth

Variable	Univariate analysis			Multivariate analysis			
	HR	95% CI	*P* value	HR	SE	95% CI	*P* value
Gender (Male)	0.89	0.43, 1.85	0.77				
Age	**1.03**	**1.001, 1.063**	**0.04**	**1.08**	**0.03**	**1.03, 1.14**	**0.002**
Smoking	**3.36**	**1.52, 7.43**	**0.002**	1.75	0.50	0.65, 4.71	0.26
Diabetes	0.98	0.23, 4.15	0.98				
Membrane exposure	**3.31**	**1.51, 7.26**	**0.003**	1.76	0.52	0.63, 4.90	0.28
Maintenance/year	**0.45**	**0.29, 0.67**	**<0.001**	**0.34**	**0.26**	**0.20, 0.58**	**<0.001**
Endodontic treatment	**2.76**	**1.12, 6.82**	**0.03**	1.35	0.71	0.34, 5.42	0.67
Initial PD	**1.27**	**1.04, 1.56**	**0.019**	0.89	0.22	0.57, 1.38	0.60
Initial CAL	**1.28**	**1.07, 1.54**	**0.008**	**1.53**	**0.20**	**1.03, 2.28**	**0.03**
Flap design	0.30	0.04, 2.26	0.245				
Vertical incision	0.998	0.38, 2.63	0.99				
Initial radiographic angle	1.015	0.99, 1.05	0.25				

Bold signifies statistical significance; CI, confidence intervals; HR, hazard ratio.

patients with enamel matrix derivatives (EMD), GTR, a combination of EMD and GTR, and OFD, showed that none of the teeth treated with GTR or any other procedure were lost. Patients enrolled in this study were all non-smokers and attending a regular maintenance program consisting of four visits per year, including oral hygiene reinforcement and professional tooth cleaning.[34] Although the population enrolled in the current study consisted of 32% smokers and with patients showing variability in compliance with maintenance appointments. Our results showed that both smoking and maintenance were significantly associated with tooth loss. In fact, from the 30 teeth that were lost throughout the entire follow-up, 21 had been in patients that were smokers. Further, the extracted teeth belonged to individuals presenting with significantly less maintenance appointments/year (1.43 ± 0.90) than the ones that had retained their teeth (2.40 ± 1.07).

4.3 | Predictors for regenerative outcomes

In the pursuit of achieving improvement in results, predictability of clinical outcomes and higher survival rates for teeth treated with GTR, the identification of factors related to the patient, defect and surgical technique that potentially affect the result is imperative. In the present study, it was observed that higher levels of PD at baseline showed better results in terms of CAL gain. This is in line with several previous studies.[17,35] Teeth that presented with higher CAL at baseline had an increased risk of failure. A smoking habit was another factor that we found having a significantly negative effect on CAL gain. We observed that on average smokers had 1 mm less CAL gain when compared to non-smokers. Tonetti et al. were the first to assess the effect of smoking on periodontal regeneration following GTR in a retrospective study.[36] They found that smokers obtained significantly less CAL than non-smokers 1-year following GTR surgery in deep infrabony defects (2.1 ± 1.2 mm versus 5.2 ± 1.9 mm).[36] Later on, Stavropoulos and colleagues when identifying factors influencing GTR treatment outcomes found that patients that were smokers gain 1 mm less in CAL than nonsmokers (3.2 ± 1.4 in smokers and 4.3 ± 1.3 in non-smokers), and that smokers had seven times less chance of obtaining 4 mm CAL as compared to non-smokers.[37] Finally, Nickles et al., when comparing clinical outcomes of teeth with infrabony defects 10 years after OFD and GTR with a bioabsorbable barrier found that current smoking negatively impacts CAL gain.[38]

Another factor that affected the 1-year post-surgical outcomes was membrane exposure. This complication occurred in 22 cases and was associated with less favorable CAL gain. In line with these results, a systematic review and meta-analysis, reported that the mean CAL gain was statistically higher in the group that had not experienced membrane exposure compared to the ones which had.[14]

Periodontal maintenance was shown to be of utmost importance, as one of the very significant factors associated with tooth survival. Patients who had their teeth extracted presented on average with one less maintenance appointment per year than those who did not. In line with the literature, Weigel and colleagues in a 4-year study evaluating patients treated with GTR, showed that the number of recall visits highly affected the long-term outcomes.[39] Similarly, Cortellini et al. when evaluating 175 infrabony defects treated with GTR highlighted the importance of maintenance appointments by showing that patients who did not attend regular maintenance visits were more prone to tooth loss.[18] Indeed, periodontal maintenance has been shown to highly impact the outcome of regenerative therapy.[19,40]

We also found that that endodontic treatment did not affect CAL gain. This agrees with a study that evaluated GTR outcomes of non-vital, endodontically treated teeth.[41]

Finally, age was shown to be one of the most significant predictors affecting tooth survival. In line with these results, a study identifying prognostic factors relating to tooth survival including >200,000 subjects, found that the risk of losing to four teeth was associated with an increase in age.[42] Other studies have also highlighted upon the significance of age as a predictor of tooth loss.[43–45]

4.4 | Limitations

Among the limitations of our research are the retrospective nature of the study design and the lack of a control group. In addition, the infrabony component of the defect was not taken into consideration when evaluating the radiographic defect angle.[46] Our study includes many smoking patients. Nonetheless, this allowed us to focus on the impact of smoking on GTR outcomes. Finally, although the change in bleeding on probing provides a general idea about the oral hygiene of the patients,[47,48] full-mouth bleeding and local plaque scores were not available to evaluate the influence of oral hygiene status on the outcomes of GTR.

5 | CONCLUSION

Within the limitations of the present study, the following conclusions can be obtained: GTR with the use of a collagen membrane and bone graft is a viable treatment for the management of teeth with an infrabony defects. The treatment outcomes following the GTR procedure are significantly influenced by factors such as frequency of maintenance visits, smoking, occurrence of a post-surgical membrane exposure, and initial defect characteristics (pocket depth and clinical attachment level).

AUTHOR CONTRIBUTIONS

Jad Majzoub contributed to the conception and design of the work, drafted the work and revised it critically for important intellectual content, and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Shayan Barootchi contributed to the analysis of data for the work, drafted the work and revised it critically for important intellectual content, and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Lorenzo

Tavelli contributed to the conception and design of the work, drafted the work and revised it critically for important intellectual content, and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Chin-Wei Wang contributed to the interpretation of data for the work, revised the work critically for important intellectual content, and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Hsun-Liang Chan contributed to the interpretation of data for the work, revised the work critically for important intellectual content, and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Hom-Lay Wang contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data for the work; critical revision of the work for important intellectual content; final approval of the version to be published; and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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