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Periodontal healing following reconstructive surgery: effect of guided tissue regeneration using a bioresorbable barrier device when combined with autogenous bone grafting. A randomized-controlled trial 10-year follow-up

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Abstract

Objective: The objective of this 10-year randomized-controlled trial follow-up was to evaluate the stability of treatment outcomes following the implantation of autogenous bone graft with or without guided tissue regeneration (GTR) in the treatment of deep intra-bony periodontal defects.

Materials and Methods: Forty patients exhibiting deep intra-bony periodontal defects were included in a randomized-controlled trial evaluating the adjunctive effect of GTR to autogenous bone graft. Twenty-six of 39 patients completing the original study were available for follow-up 10 years post-treatment. The patients had been included in a structured maintenance programme and were evaluated using the criteria of the original study by the same investigators.

Results: Significant improvements in the probing depth and clinical attachment level were observed for both groups between baseline and 9 months. Whereas the autogenous bone graft+GTR group showed significant improvements in probing bone levels and increased gingival recession at 9 months, no significant differences were observed for the autogenous bone graft group. Nine-month within-group results were maintained throughout the 10-year follow-up. Nevertheless, between-group comparisons at 10 years showed that the autogenous bone graft+GTR group exhibited significantly greater probing depth reduction (mean ± SE: 4.2 ± 0.5 *versus* 2.7 ± 0.5 mm, $p = 0.023$) and probing bone-level gain (3.9 ± 0.8 *versus* 1.3 ± 0.9 mm, $p = 0.034$) than the autogenous bone graft group. Borderline significant differences between the autogenous bone graft+GTR and the autogenous bone graft groups were observed for clinical attachment level gain at 10 years (3.8 ± 0.5 *versus* 2.2 ± 0.7 mm, $p = 0.067$), whereas no significant differences were observed for gingival recession (0.7 ± 0.3 *versus* 0.6 ± 0.5 mm, $p > 0.05$).

Conclusions: The results of this randomized study suggest that statistically significant differences were found with the adjunct use of GTR to an autogenous bone graft at 10 years. Nevertheless, these results should be interpreted with caution in light of its clinical relevance and biological rationale. Importantly, resolution of deep intra-bony periodontal defects can be maintained in the presence of a structured maintenance programme emphasizing high oral hygiene standards.

Key words: autogenous bone graft; barrier membrane; guided tissue regeneration; long term; periodontal regeneration; polylactic acid; randomized-controlled trial

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Controversy remains regarding the preferred management of advanced stages of periodontal disease. Various approaches have been discussed relative to their merit and shortcomings in the treatment of intra-bony periodontal defects (Pagliaro et al. 2008). These include conservative treatments, such as scaling and root planing, open flap debridement and modified Widman procedures with and without bone contouring (Lang 2000), osseous resective surgery (Carnevale & Kaldahl 2000) and procedures aimed at regeneration of the periodontal attachment (Cortellini & Tonetti 2000, Rosen et al. 2000). Irrespective of the treatment approach, it appears to be important to consider the long-term value of the procedure relative to the prognosis or the survival, functionality and aesthetics of the teeth involved. In a retrospective study evaluating guided tissue regeneration (GTR) procedures in patients complying with a strict maintenance programme, it was concluded ''that tooth retention and clinical improvements following GTR treatment of intra-bony defects can be maintained long term in the great majority of cases and thus that regenerative periodontal treatment represents an important alternative for the management of severely compromised teeth'' (Cortellini & Tonetti 2004).

Clinical studies suggest that patients exhibiting high oral hygiene standards maintain their teeth in healthy conditions for long periods of time, perhaps even a lifetime (Axelsson et al. 2004). Also, teeth exhibiting severely advanced periodontal disease and exposed to treatment protocols emphasizing plaque control may be maintained healthy for the long term (Lindhe & Nyman 1984). In the absence of high oral hygiene standards, however, periodontal treatment achieves limited success (Nyman et al. 1977, Becker et al. 1984, Cortellini et al. 1996).

Long-term outcomes of a variety of regenerative periodontal procedures in various constellations for the treatment of intra-bony periodontal defects have been reported including GTR using resorbable and non-resorbable barriers, an enamel matrix derivative product, autogenous bone graft, bone biomaterials and occasionally gingival flap surgery without additions (Becker & Becker 1993, Cortellini et al. 1996, Cortellini & Tonetti 2004, Sculean et al. 2004, 2006, 2007, 2008, Stavropoulos & Karring 2004, 2005, Heden & Wennström 2006, Eickholz et al. 2007, Sakallioglu et al. 2007, Slotte et al. 2007, Orsini et al. 2008, Pretzl et al. 2008, 2009). It appears that significantly decreased gingival probing depths and improved clinical attachment and crestal bone levels might be expected following the treatment of deep intra-bony periodontal defects including gingival flap debridement and any of the additional protocols. Importantly, immediate effects of the treatments appear to be maintained over the long term. Recently, we reported the short-term effects of a protocol aimed at treating deep intra-bony periodontal defects using an autogenous bone graft harvested from an intra-oral source and combined with GTR (Nygaard-Østby et al. 2008). It was demonstrated that the autogenous bone graft and the combined treatment of autogenous bone graft + GTR resulted in improved periodontal conditions without remarkable differences between the treatment protocols. The objective of this randomized-controlled trial 10-year follow-up was to evaluate the stability of treatment outcomes following implantation of an autogenous bone graft with or without GTR in the treatment of deep intra-bony periodontal defects.

Conflict of interest and source of funding statement

The authors declare no conflict of interests.

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Materials and Methods

Study design and follow-up

The initial study used a randomized, double-blind, controlled, parallel clinical trial design. Patient enrolment occurred between July and October, 1997, in a private practice setting. Patients were followed for 9 months (Nygaard-Østby et al. 2008). Scoring was carried out between July and November, 1998. The present report considers the 10-year follow-up data collected from July to November, 2008 (Fig. 1).

Patients

For the original study, 40 systemically healthy patients (20 males/20 females; mean age 53 years; range 42–67 years; non-smokers), recruited from the patient pool of the principal investigator (PNØ), exhibiting chronic periodontitis with localized or generalized advanced loss of attachment including one or more periodontal defects with a probing depth >6 mm, were enrolled (Table 1) (Nygaard-Østby et al. 2008). Further inclusion criteria comprised the presence of an associated inter-proximal intra-bony defect with a depth (alveolar crest – fundus of defect) >4 mm as measured using a probe during surgery. Sites associated with root concavities/furrows or furcation defects were excluded. The patients had completed basic periodontal therapy including scaling, root planing and oral hygiene training at the time of enrolment approximately 3 weeks before surgeries. They all exhibited high oral hygiene standards at the initiation of the study. The study protocol followed the Declaration of Helsinki. Patients who agreed to participate signed an informed consent. Using a randomized-controlled parallel

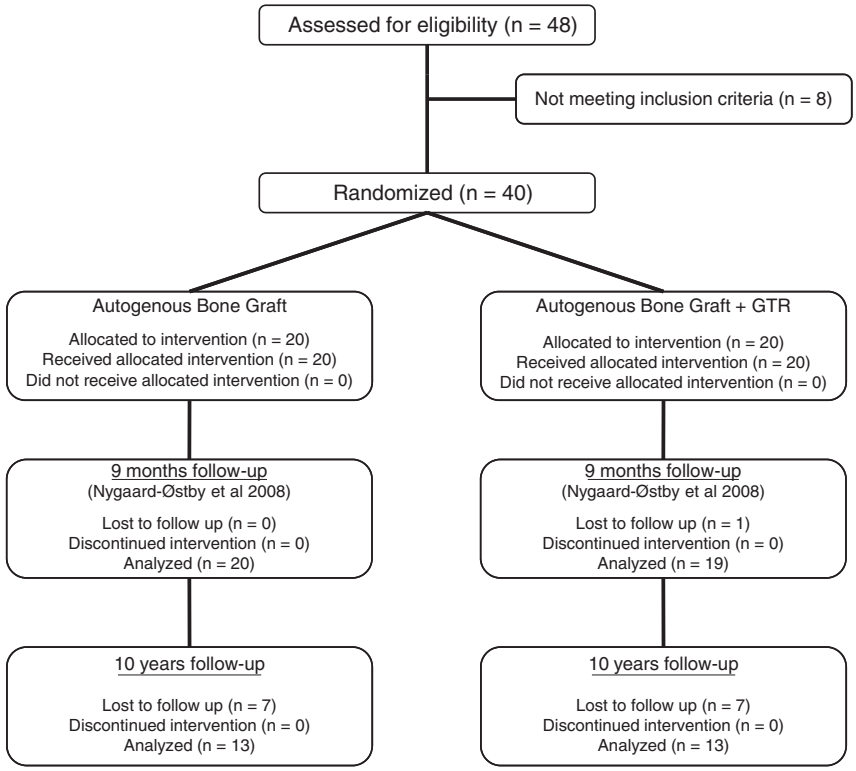

Fig. 1. Study-flow chart.

Table 1. Patient characteristics at baseline and at 10 years for patients completing the 10-year follow-up

	Autogenous bone graft		Autogenous bone graft+GTR	
	baseline	10 years	baseline	10 years
Age (mean years ± SE)	53.7 ± 1.4	63.1 ± 1.2	52.6 ± 1.5	63.2 ± 1.9
Males/females	11/9	8/5	9/11	6/7
Maxillary anterior/prem	8/8	5/5	9/5	7/1
Mandibular anterior/prem	3/1	3/0	4/2	4/1

GTR, guided tissue regeneration; prem, premolars.

group design, 20 patients received GTR combined with autogenous bone grafting and 20 patients received autogenous bone grafting solo (control). The patients were assigned to treatments using a computer-generated random code. Subject numbers were assigned at baseline in a consecutive order by the principal investigator.

Treatment procedures

All surgical procedures were performed by one experienced periodontist (P. N. Ø.). Mucoperiosteal flaps were elevated for defect access including granulation tissue removal and root surface debridement following routine anaesthesia and sulcular incisions. Considerable care was taken to preserve the inter-dental gingival tissues for optimal defect coverage at wound closure. Autogenous bone was harvested from the chin area using a 5-mm-diameter trephine burr. The harvested bone was morselized and implanted to fill the intra-bony defect. For the autogenous bone graft+GTR sites, a chair-side-prepared bioresorbable polylactic acid barrier (Atrisorb®, Atrix Laboratories Inc., Fort Collins, CO, USA) extending 3 mm over the defect margins was placed to cover the bone graft. The control sites received the autogenous bone graft solo. The mucoperiosteal flaps were repositioned to cover the implanted materials and sutured (Gore Tex® Suture CV-5, W.L. Gore & Associates Inc., Flagstaff, AZ, USA).

The post-surgery protocol included administration of amoxicillin (500 mg; b.i.d.) and ibuprofen (400 mg; q.i.d.) for 10 days. Periodontal dressing (Coe Pack, Coe Laboratories Inc., Chicago, IL, USA) was used during the first week post-surgery. Mechanical plaque control was not performed in the surgical and adjacent areas for 3 weeks. Thus, plaque control was maintained by rinsing with a chlorhexidine solution thrice daily (Peridex® 0.12%, Procter & Gamble, Cincinnati, OH, USA) until suture removal at 3 weeks post-surgery. The subjects were then given repeat oral hygiene instructions as warranted and had their teeth scaled, root planed and polished at 3, 6 and 9 months post-surgery. These procedures aimed at controlling the supra and subgingival biofilms and special care was taken to avoid disturbing wound healing and tissue maturation.

Complete gingival wound closure for primary intention healing was observed post-surgery for all defect sites. Nevertheless, the bioresorbable PLA device became exposed within 1 week in five patients, within 2 weeks in 16 patients and within 3 weeks in 17 patients (Nygaard-Østby et al. 2008). No adverse reactions or relevant clinical findings other than gingival recession were observed.

Following completion of the original 9-month study, the patients remained in the practice's routine maintenance programme. They were assigned to supportive periodontal therapy based on individual needs and were thus reviewed and treated at 3-, 4- or 6-month intervals as appropriate. At these appointments, the patients' oral hygiene standards and gingival health were reviewed and oral hygiene procedures were reinforced as necessary. Moreover, the patients' teeth were scaled, root planed as needed and polished by the practice's hygienists. Fluoride application was administered and patients were advised to use a fluoride toothpaste and daily rinse using a 0.05% sodium fluoride solution.

Recordings

Two experienced examiners (V. B., O. N.) with good intra- and inter-examiner reproducibility (overall κ of 0.92 and 0.76, respectively) performed all recordings including oral hygiene standards (Silness & Løe 1964); gingival health

(Løe & Silness 1963); probing depths; bleeding on probing; clinical attachment levels; probing bone levels (recorded following local anaesthesia, the probe was forced through the soft tissue towards the bone until definite tissue resistance was met) (Renvert et al. 1981); gingival recession; and tooth mobility (Miller 1938). Recordings were made to the nearest mm at the mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual and mesio-lingual aspects of the defect-associated teeth using a periodontal probe (CP 15 UNC, Hu Friedy, Chicago, IL, USA). Attachment levels, probing bone levels and gingival recession were recorded from the cemento-enamel junction. The examiners were masked to the original treatment protocol.

Intra-surgery recordings, made after defect debridement, included total defect depth, depth of the three-wall intra-bony component of the defect, defect width and defect sector (Choi et al. 1996, Nygaard-Østby et al. 1996). Briefly, total defect depth was determined measuring the distance from the alveolar crest to the fundus of the defect from its buccal and lingual inter-proximal aspects. Depth of the three-wall component was determined as the distance from the most apical inter-proximal bone crest to the fundus of the defect. Defect width was determined as the buccal–lingual extension of the defect at the alveolar crest and defect sector as the crestal circumference of the defect estimated relative to the circumference of the defect-associated tooth and expressed in degrees thereof. Only measurements made on the experimental teeth are reported.

Statistical analysis

A per-protocol statistical analysis was used in the present study. Comparison of patient demographics between groups was performed using a *t*-test and a χ^2 test. Linear regression models were used to generate group means and standard errors based on the deepest defect site for all clinical parameters. When longitudinal comparisons were performed within experimental groups, the analysis took into account the longitudinal nature of the data. Wald tests were used for between- and within-group comparisons and the level of significance was set at 5%. The final *p*-value was adjusted for multiple comparisons. The distribution of the data was assessed, and no substantial departure from normality was observed. No subgroup analyses were performed. The analysis was performed using the statistical package Stata for Mac (Stata 11, Stata Corporation, College Station, TX, USA).

Table 2. Baseline clinical characteristics for patients completing the 10-year follow-up (means ± SE)

	Autogenous bone graft	Autogenous bone graft+GTR	*p*-value
Plaque index	0.5 ± 0.1	0.5 ± 0.1	0.99
Gingival index	0.9 ± 0.1	0.9 ± 0.2	0.84
Bleeding on probing (%)	96.2 ± 3.8	92.3 ± 5.1	0.55
Probing depth (mm)	7.3 ± 0.2	7.6 ± 0.4	0.48
Clinical attachment level (mm)	9.2 ± 0.6	9.0 ± 0.5	0.85
Probing bone level (mm)	9.6 ± 0.6	10.2 ± 0.7	0.55
Gingival recession (mm)	1.9 ± 0.5	1.4 ± 0.3	0.43

GTR, guided tissue regeneration.

Table 3. Baseline defect characteristics for patients completing the 10-year follow-up (means ± SE)

	Autogenous bone graft	Autogenous bone graft+GTR	*p*-value
Total defect depth	5.2 ± 0.3	5.4 ± 0.5	0.78
Three-wall component	4.1 ± 0.3	3.9 ± 0.2	0.67
Defect width	7.7 ± 0.4	6.7 ± 0.4	0.09
Defect sector (°)	110.0 ± 9.3	91.9 ± 1.6	0.08

GTR, guided tissue regeneration.

Results

Twenty-six (65%) out of the 40 patients originally included in the study were available at the 10-year follow-up (Fig. 1). Overall, seven patients were lost in each experimental group for various reasons. Four patients of the autogenous bone graft group and six patients of the autogenous bone graft+GTR group had left the practice and were inaccessible to follow-up. One patient in each experimental group had their experimental teeth extracted by the referring dentists for unknown reasons. One patient who received an autogenous bone graft lost the experimental tooth due to exfoliation, and another patient who also received an autogenous bone graft was re-operated.

There were no relevant differences between the autogenous bone graft and the autogenous bone graft+GTR groups at baseline relative to gender and age distribution among the 26 patients available for the 10-year follow-up (Table 1). Defect sites were similarly distributed among maxillary and mandibular teeth. There were also no statistically significant differences in defect-related parameters between the groups (Table 2). Baseline oral hygiene standards were high, as shown by low plaque and gingival indices. Bleeding on probing was observed in a majority of the defect sites. Moreover, there were no remarkable differences in probing depths, clinical attachment and probing bone levels among the treatment groups, or differences in gingival recession. Table 3 shows the intra-surgery defect characteristics for the patients completing the 10-year follow-up. There were no statistically significant differences in the total defect depth, the three-wall component of the intra-bony defect, defect width and defect sector between the groups.

The plaque and gingival indices at the experimental sites remained low over the 10-year observation interval, without remarkable differences between treatment groups (Table 4). Nevertheless, a statistically significant reduction of the gingival index from baseline to 9 months and 10 years was observed for the autogenous bone graft group. There were no significant differences in bleeding on probing at the experimental sites between treatment groups at baseline and 9 months; bleeding on probing ranged between 85% and 96% (Table 4). However, following the 10-year maintenance programme, a significant decrease in bleeding on probing was observed approximating 42% for the autogenous bone graft group and 35% for the autogenous bone graft+GTR group.

Probing depths changed significantly from baseline to 9 months in both groups and remained unchanged at the 10-year observation (Table 5). The mean probing depths for the autogenous bone graft group significantly decreased from 7.3 mm at baseline to 4.4 mm at 9 months and remained essentially the same (4.6 mm) at the 10-year observation. For the autogenous bone graft+GTR group, the mean probing depths were 7.6, 4.5 and 3.4 mm at baseline, 9 months and 10 years, respectively ($p<0.05$). The mean probing depth reductions were significantly greater for the autogenous bone graft+GTR group compared with the autogenous bone graft group at 10 years (4.2 *versus* 2.7 mm, $p=0.023$). Residual probing depths ≥ 6 mm were observed in 31% of the defect sites for the autogenous bone graft group, whereas no defect sites exhibited deep residual probing depths in the autogenous bone graft+ GTR group at 10 years (Fig. 2). Nevertheless, no significant differences were observed in the frequency of deep pockets between treatments ($p=0.15$).

The mean clinical attachment level improved significantly from baseline to 9 months (2.5 mm; $p<0.05$) in the autogenous bone graft group and remained unchanged at the 10-year observation (2.2 mm) (Table 5). In the autogenous bone graft+GTR group, the change was also significant between baseline and 9 months (2.5 mm; $p<0.05$). The mean clinical attachment gain from baseline to 10 years was 3.8 mm ($p<0.05$). There was no statistically significant difference in the mean clinical attachment gain between the groups at 9 months; at 10 years, a borderline significant difference was observed (2.2 *versus* 3.8 mm, $p=0.067$).

In the autogenous bone graft group, the mean probing bone levels showed a statistically non-significant improvement (1.9 mm; $p>0.05$) at 9 months (Table 5). The mean bone-level gain remained virtually unchanged (1.3 mm) at 10 years. In the autogenous bone graft+GTR group, a significant improvement was observed from baseline to 9 months (2.5 mm; $p<0.05$) and to 10 years (3.9 mm; $p<0.05$). The autogenous bone graft+GTR group showed a significantly greater mean probing bone-level gain than the autogenous bone graft group at 10 years (3.9 *versus* 1.3 mm, $p=0.034$). Defects receiving an autogenous bone graft+GTR were four times more likely to show a bone-level gain ≥ 4 mm than defects that received an autogenous bone graft only (Fig. 2); however, this was not a statistically significant difference ($p=0.11$).

There were minor non-significant increases in the mean gingival recession from baseline to 9 months and 10 years for the autogenous bone graft group (0.4 and 0.6 mm, respectively; $p>0.05$) and the autogenous bone graft+GTR group (0.6 and 0.7 mm, respectively; $p>0.05$). There were no statistically significant differences in gingival recession between groups (Table 5).

Table 4. Oral hygiene standards and gingival/periodontal health at baseline, 9 months and 10 years for patients completing the 10-year follow-up (means ± SE)

	Baseline	9 months	10 years
Autogenous bone graft			
Plaque index	0.5 ± 0.1 Aa	0.7 ± 0.2 Aa	0.4 ± 0.1 Aa
Gingival index	0.9 ± 0.1 Aa	0.5 ± 0.2 Ba	0.5 ± 0.1 Bb
Bleeding on Probing (%)	96.2 ± 3.8 Aa	84.6 ± 6.5 Aa	42.3 ± 12.2 Ba
Autogenous bone graft+GTR			
Plaque index	0.5 ± 0.1 Aa	0.5 ± 0.1 Aa	0.5 ± 0.1 Aa
Gingival index	0.9 ± 0.2 Aa	0.7 ± 0.2 Aa	0.9 ± 0.1 Aa
Bleeding on probing (%)	92.3 ± 5.1 Aa	92.3 ± 5.1 Aa	34.6 ± 12.9 Ba

Upper case letters refer to comparisons within experimental groups between experimental periods (baseline *versus* 9 months *versus* 10 years); lower case letters refer to comparisons between experimental groups (autogenous bone graft *versus* GTR+autogenous bone *graft*) within each experimental period.
Different letters indicate significant differences between time points and groups ($p<0.05$).
GTR, guided tissue regeneration.

Discussion

The objective of this 10-year randomized-controlled trial follow-up was to evaluate the stability of treatment outcomes following implantation of an

Table 5. Probing depth, clinical attachment level, probing bone level and gingival recession at each observation period and changes from baseline for patients completing the 10-year follow-up (means ± SE in mm)

	Observation period			Change overtime		
	baseline	9 months	10 years	baseline to 9 months	baseline to 10 years	9 months to 10 years
Autogenous bone graft						
Probing depth	7.3 ± 0.2A	4.4 ± 0.3B	4.6 ± 0.5B	2.9 ± 0.4a	2.7 ± 0.5a	0.2 ± 0.5a
Clinical attachment level	9.2 ± 0.6A	6.6 ± 0.6B	7.0 ± 0.8B	2.5 ± 0.6a	2.2 ± 0.7a	0.4 ± 0.9a
Probing bone level	9.6 ± 0.6A	7.8 ± 0.7A	8.3 ± 0.9A	1.9 ± 0.7a	1.3 ± 0.9a	0.5 ± 1.1a
Gingival recession	1.9 ± 0.5A	2.2 ± 0.5A	2.5 ± 0.6A	0.4 ± 0.4a	0.6 ± 0.5a	0.2 ± 0.6a
Autogenous bone graft+GTR						
Probing depth	7.6 ± 0.4A	4.5 ± 0.5B	3.4 ± 0.3B	3.2 ± 0.4a	4.2 ± 0.5b	1.1 ± 0.5a
Clinical attachment level	9.0 ± 0.5A	6.5 ± 0.6B	5.2 ± 0.8B	2.5 ± 0.4a	3.8 ± 0.5a	1.2 ± 0.6a
Probing bone level	10.2 ± 0.7A	7.6 ± 0.7B	6.2 ± 0.9B	2.5 ± 0.4a	3.9 ± 0.8b	1.4 ± 0.9a
Gingival recession	1.4 ± 0.3A	2.0 ± 0.3B	2.1 ± 0.5B	0.6 ± 0.3a	0.7 ± 0.3a	0.1 ± 0.5a

Upper case letters refer to comparisons within experimental groups between experimental periods (baseline *versus* 9 months *versus* 10 years); lower case letters refer to comparisons between experimental groups (autogenous bone *graft versus* autogenous bone *graft*+GTR) for clinical parameter changes from baseline.
Different letters indicate significant differences between time points and groups ($p<0.05$).
GTR, guided tissue regeneration.

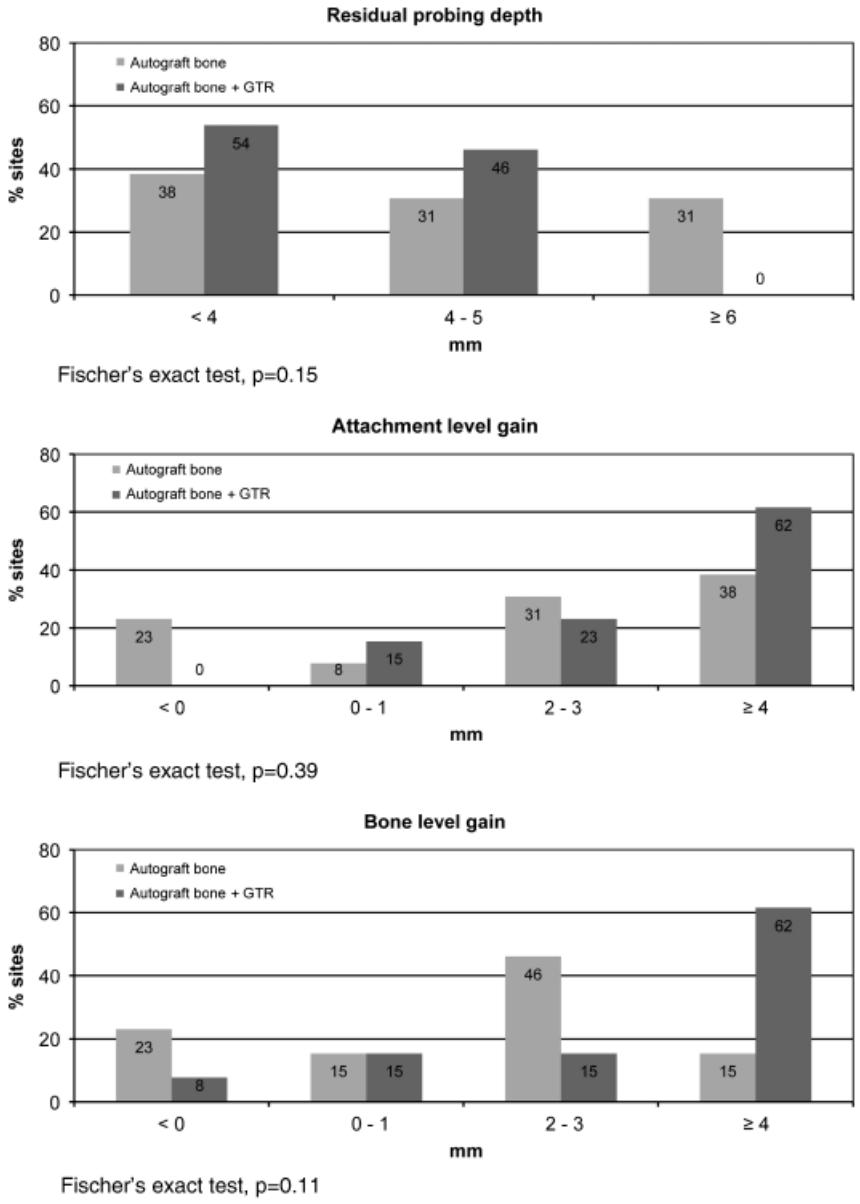

Fig. 2. Distribution of defect sites according to residual probing depths, attachment and bone-level gain (change from baseline). The statistical evaluation did not indicate any significant differences between groups. Fischer's exact test, $p = 0.15$, 0.39, 0.11.

autogenous bone graft with or without GTR in the treatment of deep intra-bony periodontal defects. Oral hygiene standards and gingival health, gingival, periodontal and alveolar bone changes initially monitored over a 9-month period were evaluated following 10 years in a private practice maintenance programme. There were no relevant differences between the autogenous bone graft and the autogenous bone graft+GTR groups at baseline relative to demographics and defect characteristics among the 26 patients available to follow-up. High oral hygiene standards at baseline and throughout the initial 9 months were confirmed at the 10-year observation. Bleeding on probing observed in a majority of the defect sites at baseline and 9 months were significantly reduced at 10 years. There were no remarkable differences in probing depths, clinical attachment and probing bone levels among the treatment groups, or significant differences in gingival recession at 9 months and 10 years. In other words, in the presence of apparent high oral hygiene standards, favourable results observed at 9 months were maintained for both treatment concepts, autogenous bone graft and autogenous bone graft+GTR, over 10 years.

The results of conservative and resective periodontal therapy have been shown to be stable in the long term in the presence of high oral hygiene standards (Lindhe & Nyman 1984, Axelsson et al. 2004). In the present study, significant improvements in periodontal conditions at 9 months were maintained over the 10-year observation period. Pocket depth reduction, attachment and bone-level gain and gingival recession were all generally stable. These observations compare well with the long-term (3 years or more) results of clinical studies reported previously on periodontal regenerative therapy including guided tissue regeneration, application of matrix factors or implantation of bone derivatives (Becker & Becker 1993, Cortellini et al. 1996, Cortellini & Tonetti 2004, Sculean et al. 2004, 2006, 2007, 2008, Stavropoulos & Karring 2004, 2005, Heden & Wennström 2006, Eickholz et al. 2007, Sakallioglu et al. 2007, Slotte et al. 2007, Orsini et al. 2008, Pretzl et al. 2008, 2009), as well as with the short- and long-term results summarized in systematic and authoritative reviews (Cortellini & Tonetti 2000, Rosen et al. 2000, Trombelli et al. 2002, Murphy & Gunsolley 2003, Needleman et al. 2006). As it appears, long-term stability should also be expected for regenerative periodontal therapies. This is an interesting observation taking into account the considerably diverse biological rationales among regenerative therapies.

In the present study, a significant reduction in bleeding on probing was observed at 10 years post-treatment compared with that observed at baseline and at 9 months. There was no difference between the treatment groups. This may possibly suggest that tissue maturation following the autogenous bone graft protocols in the presence of high oral hygiene standards proceeds over several months and may not be complete at 9 months. This may in turn imply that 9-month healing intervals following periodontal reconstructive protocols at least including an autogenous bone graft but possibly also bone biomaterials and biologicals may be too short for conclusive clinical evaluations. However, more likely, this may be a reflection of the relatively insensitive dichotomous nature of the bleeding on probing recordings used in this study. Whereas site pretreatment commonly exhibited profuse bleed-

ing on probing, the examiner's impression was that later time point positive registrations exhibited comparatively contained bleeding on probing.

Long-term studies have shown the critical importance of high oral hygiene standards for tooth retention and maintained gingival and periodontal health following a conservative periodontal therapy (Axelsson et al. 2004). Similarly, treatment outcomes following resective surgical protocols have been maintained successfully over the long term in the presence of high oral hygiene standards (Lindhe & Nyman 1984). Also, the outcomes of regenerative treatment protocols including guided tissue regeneration, application of an enamel matrix derivative or bone biomaterials as stand-alone therapies or in combinations apparently benefit from successful plaque control protocols (Becker & Becker 1993, Cortellini et al. 1996, Cortellini & Tonetti 2004, Sculean et al. 2004, 2006, 2007, 2008, Stavropoulos & Karring 2004, 2005, Heden & Wennström 2006, Eickholz et al. 2007, Sakallioglu et al. 2007, Slotte et al. 2007, Orsini et al. 2008, Pretzl et al. 2008, 2009). The present study was conducted in concert with this fundamental concept of periodontal therapy. In the absence of high oral hygiene standards, conservative and surgical cause-related periodontal therapies generally appear to be ineffective in both short- and long-term perspectives (Nyman et al. 1977, Becker et al. 1984). This should probably be expected for the outcomes of regenerative periodontal protocols as well.

Similar to that in other long-term studies, an attrition rate of 35% (14 of 40 subjects) was observed in the present study after 10 years (Sculean et al. 2004, 2006, 2007, Stavropoulos & Karring 2005, Heden & Wennström 2006, Pretzl et al. 2008, 2009). Loss of participants in clinical trials may decrease the power to detect significant differences between treatments. This may explain, at least in part, some of the borderline significant differences observed in the present results, as a sample size of 17 subjects in each group was estimated to be necessary to detect a difference of 1.0 ± 1.0 mm between treatments with a significance level of 5% and power of 80% in the initial evaluation. Moreover, attrition may introduce a bias in the estimates because only ''survivors'' may be available for analysis. In order to estimate the impact of attrition rate on the results, we conducted a comparison between patients who participated for 9 months and 10 years. No significant differences were observed between 10-year participants and dropouts with regard to age and baseline clinical characteristics. However, individuals who participated in the 10-year follow-up showed statistically greater clinical attachment-level gain and bone-level gain at 9 months than dropouts. No differences were observed in probing depths, gingival recession and bleeding on probing between participants and dropouts. Collectively, these findings may indicate that some degree of bias is present in the final estimates. In perspective, patient-related reasons for dropping out of treatment programmes may be several: death, moving to other areas, low understanding of the importance of follow-up, etc. It can also be discussed whether dropouts should be considered losers or that the reason for their dropout may not only be due to lack of compliance but also rather other significant unrelated social factors.

The results in this study do not clearly indicate that GTR may provide an additional benefit to periodontal reconstructive surgery including an autogenous bone graft. Borderline significant differences between treatments at the 10-year follow-up complicate the judgement of whether GTR should or should not be advocated as an adjunct to an autogenous bone graft for deep intra-bony periodontal defects, at least using the chair-side-prepared bioresorbable polylactic acid barrier. If the statistical differences between treatments can be accepted as clinically relevant and cost-effective, then GTR could be used. On the other hand, if the results are not deemed clinically relevant and cost-effective, then GTR should not be used in spite of statistical differences between treatments. There is also a possibility that some bias has been introduced into the study due to the attrition rate along the 10-year follow-up. Thus, differences between treatments may be somewhat smaller or larger than actually observed. Last, but not the least, it is difficult to provide a biological rationale explaining why the changes observed between 9 months and 10 years in the group that received GTR occurred as a result of the surgical procedure considering tissue maturation in all likelihood being complete at the 9-month observation. In the face of this and from the perspective of the short-term findings of the present randomized-controlled trial, it appears prudent to interpret with caution the treatment differences observed and assume that further more clear-cut evidence is necessary to indicate GTR as an adjunct treatment for an autogenous bone graft.

Conclusions

The results of this randomized study suggest that statistically significant differences were found with the adjunct use of GTR to an autogenous bone graft at 10 years. Nevertheless, these results should be interpreted with caution in the light of its clinical relevance and biological rationale. Importantly, the resolution of deep intra-bony periodontal defects can be maintained in the presence of a structured maintenance programme emphasizing high oral hygiene standards.

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Clinical Relevance

Scientific rationale for the study: Histologic cases and clinical studies have suggested that autogenous bone grafts have the potential to stimulate regeneration of periodontal structures. Few, if any, reports have focused on the effect of autogenous bone graft combined with guided tissue regeneration. The objective of this randomized-controlled trial was to evaluate the adjunctive effect of GTR to autogenous bone graft in the treatment of deep intrabony periodontal defects. The objective of this long-term follow-up was to evaluate the stability of this treatment.

Principal findings: The results suggest that autogenous bone graft supports significantly improved long-term clinical conditions. GTR yielded significant probing depth reduction and probing bone gain at 10 years; however, the clinical relevance of this finding is unclear.

Practical implications: More importantly, reduced probing depths, attachment levels and gingival recession appear to be stable over 10 years in the presence of a structured maintenance programme promoting high oral hygiene standards.