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CLINICAL ORAL IMPLANTS RESEARCH

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A clinical prospective study on alveolar bone augmentation and dental implant success in patients with type 2 diabetes

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Key words: clinical study, dental implants, diabetes mellitus, guided bone regeneration

Abstract

Objectives: The objective of this prospective, controlled clinical study was to determine the outcomes of dental implant therapy with staged guided bone regeneration procedures in patients with type 2 diabetes.

Patients and methods: Twenty-four patients were included in the study. Half of the patients were diagnosed with type 2 diabetes mellitus (group 1) while the other half (group 2) of the patients consisted of patients without diabetes. The edentulous maxillary anterior/premolar regions with sufficient vertical height but inadequate horizontal width were treated with staged guided bone regeneration technique and with one or two implant-supported fixed restorations. The patients were followed up at least for 12 months. The parameters that were evaluated were radiographic evaluations on CBCT images and periapical radiographs, histomorphometric analysis, resonance frequency analysis (RFA) and wound-healing parameters. The data were analyzed statistically.

Results: A total of 43 implants were placed in 24 patients (22 implants in group 1 and 21 implants in group 2). The survival rates of implants were 100% for both groups. The success rate of implants was 95% for group 1 and 100% for group 2. None of the parameters including CBCT findings, RFA values, success rates and wound-healing scores showed a significant difference between the two groups.

Conclusion: Staged guided bone regeneration is a feasible augmentation procedure for the treatment of horizontal bone deficiencies of the maxillary anterior/premolar regions in well-controlled type 2 diabetic patients.

Diabetes mellitus (DM) is a chronic disease characterized with hyperglycemia and deranged metabolism, which result in various serious complications including acquired blindness, kidney failure, neuropathy, myocardial infarction and non-traumatic limp amputation. It is a worldwide epidemic disease with a prevalence of as high as 15–22% in Turkey (Satman et al. 2013). The major subtypes of the disease are type 1 and type 2 DM. While type 1 DM develops most commonly with autoimmune pancreatic β-cell destruction and accounts for 5–10% of the diabetic population, type 2 DM is associated with insulin resistance and relative insulin deficiency with various metabolic disturbances and accounts for 90–95% of the diabetic subjects (Scully & Cawson 2005). Because of the microvascular complications seen in DM, it is considered as a relative contraindication for dental implant therapy by some authors (Dowell et al. 2007). Therefore, success of dental implants in patients with diabetes has been the topic of many preclinical and clinical studies (Farzad et al. 2002; Mealey 2006; Erdogan et al. 2010).

It is known that DM is associated with increased rate of periodontal disease and bone resorption (Mealey 2006). Safety of implant therapy with or without bone augmentation procedures in patients with diabetes is still controversial. The literature contains some data about the success rate of dental implants in non-augmented bone. The success rate of dental implants in patients with DM varies between 68% and 100% (Tawil et al. 2008; Erdogan et al. 2010). The data regarding the success rate of alveolar bone augmentation in DM are less conclusive. Clinical studies, which evaluated the outcomes of bone augmentation techniques, most commonly excluded patients with DM. Limited number

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of studies is present that evaluated the success of some alveolar bone augmentation techniques in patients with diabetes. The augmentation techniques applied in these studies included sinus floor augmentation, guided bone regeneration and onlay autogenous bone augmentation. The survival rate of implants placed in grafted bone varied between 25% and 100% (Farzad et al. 2002; Stricker et al. 2003; Schwartz-Arad et al. 2005; Huynh-Ba et al. 2008; Tawil et al. 2008).

Guided bone regeneration (GBR) technique is a bone augmentation procedure in which osteogenesis occurs within the alveolar defect site that is mechanically prevented from undesirable tissues participating in the healing process (Buser 2009). It can be conducted as a separate procedure to augment the alveolar bone prior to implant placement (staged GBR) or in a single procedure simultaneously with implant placement (Hämmerle et al. 2008; Urban et al. 2011; Block et al. 2012). A number of clinical studies demonstrated that implants placed in regenerated bone by staged GBR procedure have acceptable long-term outcomes (Chiapasco et al. 1999; Buser et al. 2002; Donos et al. 2008). The aim of this prospective, clinical controlled study was to determine the outcomes of dental implant therapy with staged GBR procedures in type 2 patients with diabetes. The primary and secondary parameters appointed for this study were gain in alveolar bone width after the bone augmentation procedure and the amount of marginal bone loss after 1 year loading, respectively, as these parameters widely serve as major parameters in the previous studies (Christensen et al. 2003; Hämmerle et al. 2008; Donos et al. 2008; Misch et al. 2008; Urban et al. 2011; Clementini et al. 2013).

Patients and methods

Study design

The study was designed as a clinical, prospective, cohort, longitudinal and controlled study. The patients were recruited from the Department of Oral Diagnosis and Radiology of the Faculty of Dentistry and from the Department of Endocrinology of the Faculty of Medicine (Çukurova University, Adana, Turkey). Thirty patients, who accepted to participate, were recruited. Half of the patients were in diabetic group (group 1) and the other half consisting of patients without DM were in the control group (group 2).

Dental indication

Localized edentulous maxillary anterior or premolar region with at least 10 mm vertical height and <5 mm bucco-palatal (horizontal) width was selected as the treatment site. The edentulous sites were augmented with GBR technique in a separate procedure, and then the patients were treated with one or two implant-supported fixed restorations. For patients, who had multiple implant placements, only one edentulous region was considered for the study. Edentulous sites other than the maxillary anterior and premolar regions or with severe alveolar bone loss, which require more advanced augmentation procedures, were excluded.

Diabetic inclusion/exclusion criteria

The patients in group 1 were patients with type 2 diabetes, whose diagnosis had been made at least 5 years ago. All patients were on active medical treatment and receiving oral medications, insulin or combination therapies. Their previous diabetes history was confirmed with the physician's report. The diabetic status of the patients was moderately or well controlled (Sacks et al. 2011). Namely, preoperative HbA1c levels were between 6% and 7.5%. Patients with type 1 DM, diagnosed <5 years ago or with HbA1c level above 7.5% or <6%, were excluded. The HbA1c levels of the patients were measured 1 week before the bone augmentation surgery at the same laboratory.

Systemic exclusion criteria

Patients, who had any of the following conditions, were excluded from the study: Current smoking, metastatic cancer, previous radiation therapy in maxillofacial region, severe heart failure, thyrotoxicosis, osteoporosis requiring active medical treatment, active alcoholism or drug abuse, significant hematological disorders, end-stage renal or liver disease, immunocompromised status including HIV, chronic use of steroids or NSAIDs, and physical or mental handicaps, which hinder compliance to the study.

Bone augmentation protocol

The edentulous maxillary anterior/premolar regions with sufficient vertical height but inadequate horizontal width were included. All patients had cone beam computed tomography (CBCT) scanning preoperatively. The bone augmentation technique of choice was staged GBR with 50–50% mixture of autogenous bone and synthetic bone substitute (Straumann Bone Ceramic, Straumann, Switzerland) plus collagen membrane (Bio-Gide, Geistlich, Switzerland). Autogenous bone was harvested from the mandibular ramus area with bone scrapers. The implants were placed 5 months after the bone augmentation. The prostheses were delivered 4 months after the implant placement.

Treatments

Initial dental diagnostic visit

Patients, who accepted to participate, filled a detailed informed consent form. They were informed about the purpose and the protocol of the study, the potential complications and the benefits from the treatment. The study was approved by the Cukurova University Ethical Review Committee (Report no: 2010–4) and carried out in accordance with the ethical rules of the Declaration of Helsinki. Panoramic radiographs, CBCT scans, and impressions for diagnostic casts were obtained from all patients at the initial visit. Vertical and horizontal bone volumes were evaluated in the CBCT images. The patients with horizontal bone width <5 mm were appointed for bone augmentation surgery.

Bone augmentation surgery

Staged GBR technique was used in this study. All surgeries were performed at the Department of Oral and Maxillofacial Surgery clinics under local anesthesia and with IV sedation if needed. All patients received either 2 g. amoxicillin or 600 mg. clindamycin (patients allergic to penicillin) orally or their intravenous equivalents for prophylactic antibiotic coverage, 1 h before the surgical procedure. For providing local anesthesia and hemostasis, articaine with adequate amount of epinephrine was used. The vital signs of the patients were monitored during the surgery. Initially, the recipient site was exposed using a full thickness, rectangular mucoperiosteal flap. Depending on the size of the recipient site, the amount of bone graft material was determined. Through a linear incision at the mandibular molar/retromolar region, the alveolar bone was exposed. Autogenous bone was collected with scraping technique from the alveolar cortical bone by using bone scrapers. (Ebner 502-Grafter, Maxilon Labs., Hollis, NH, USA) The autogenous bone collected from the donor site was mixed with the same amount of synthetic biphasic calcium phosphate (Straumann Bone Ceramic, Basel, Switzerland). After drilling small perforations at the recipient site for better vascular supply, the graft material was applied. A collagen membrane (Bio-Gide, Geistlich, Swizerland)

was placed over the graft material. Horizontal cuts were made under the periosteum of the flap to extend the flap to cover the augmented region without tension. Flaps were sutured with 4.0 Vycril sutures. Patients were prescribed antibiotic, antiseptic mouthwash and analgesics to use in the postoperative period.

Implant surgery

The patients were recalled 5 months after the bone augmentation surgery for implant placement. The surgeries were performed under local anesthesia and IV sedation if needed. The same premedication and postoperative medication protocol used in the first surgery were applied. A mucoperiosteal flap was raised and implant site osteotomies were prepared according to dental implant manufacturer's recommendation except using a trephine drill instead of pilot drill to collect bone biopsy for histological evaluation. After the trephine drill, standard Straumann dental implant system (Institute Straumann, Basel, Switzerland) protocol was followed for implant placement. Depending on the amount of vertical height, 10 mm or 12 mm long, and 4.1 mm wide, bone level implants with chemically modified hydrophilic surface (Slactive®, Straumann, Basel, Switzerland) were placed. If the implant replaced the 2nd incisor tooth, a 3.3-mm-wide implant was installed. After the installation of implants, the flaps were closed primarily.

Prosthetic treatment

The patients were recalled 4 months after the implant placement for prosthetic treatments. After the exposure of the implants and placement of healing abutments in the first visit, standard prosthetic treatment protocol was followed. Two crowns were splinted if two adjacent implants were restored. All regions were rehabilitated with fixed restorations. The patients used interim removable partial dentures during the healing and prosthetic treatment periods.

Interpretation of data

After the delivery of the prosthesis, the patients were recalled every 3 months until the 12th month for clinical and radiographic evaluations. Dental periapical radiographs were obtained in each visit. The observer of the radiographic parameters was blinded to the patient's identity. The observers of the clinical parameters were aware of patient's identity. The parameters that were evaluated in the study were as follows.

Outcomes of augmentation procedure based on the CBCT evaluations

Cone beam computed tomography scans were obtained from all patients with Iluma Cone Beam CT Scanner (Imtec Imaging, LLC, Ardmore, OK, USA) two times; before the augmentation procedure and before the implant placement surgery. The exposure parameters were set as 120 kVp, 3.8 mA, and 20 s. The alveolar ridge width was measured at the axial plane. A vertical line, which is on the bisecting angle between the palatal and buccal cortical bones, was drawn from the tip of the alveolar crest to the base of the alveolar bone. The buccal–palatal width at the 4 mm coronal aspect of the osseous crest on this line was considered as the crestal width. The region of interest was standardized for each patient by making the measurement at the same distance from the neighboring tooth. The difference in net bone width gain was compared between the diabetic group and the control group. The measurement method is shown in Fig. 1.

Periimplant marginal bone level changes

They were calculated from the implant neck to the crestal bone level using standardized periapical radiographs by means of parallel technique. To have a consistent method of data collection, all radiographs were taken by the same investigator. The X-ray unit was operated at 60 kVp, 10 mA, and 0.3 s. The measurements were performed using

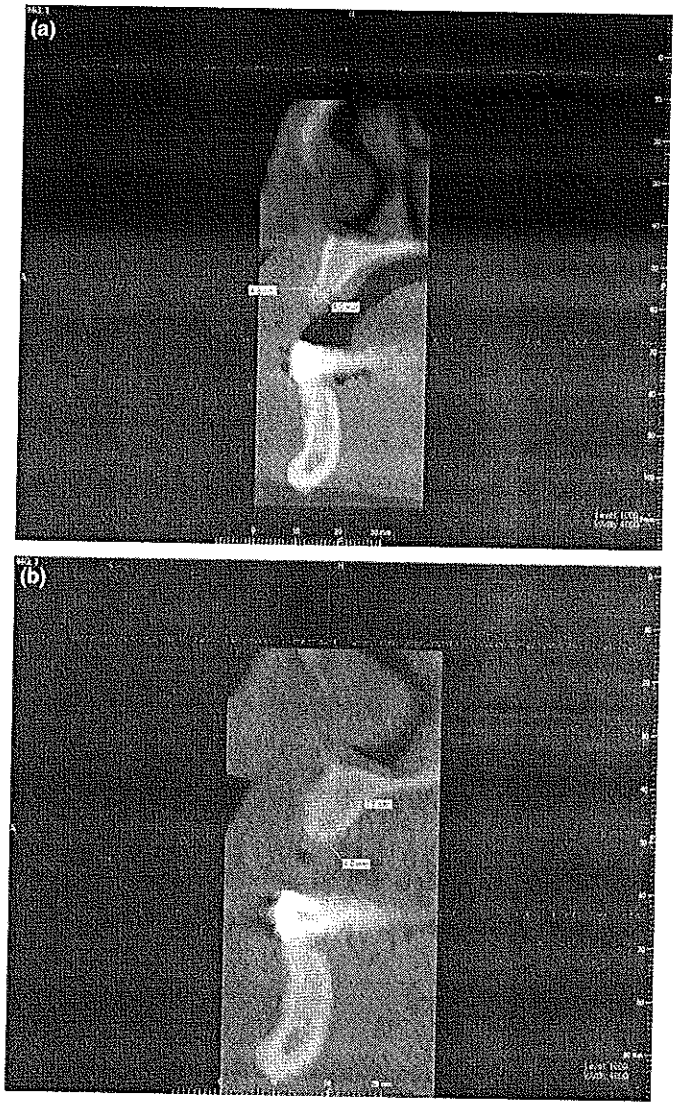

Fig. 1. Measurement method of the alveolar crest width; A vertical line, which is on the bisecting angle between the palatal and buccal cortical bones, is drawn from the tip of the alveolar crest to the base of the alveolar bone. The buccal–palatal width at 4 mm apical to osseous crest is measured. (a) preoperative measurement (b) same patient 5 months after the augmentation procedure.

image-analyzing software (Image J, version 1.33u; Wayne Rasband, National Institutes of Health, Bethesda, MD, USA). All radiographs were individually calibrated according to implant length. Periimplant bone level was determined by measuring the distance between the implant shoulder and the first crestal bone-to-implant contact on mesial and distal aspects of implants. Mesial and distal values were averaged to obtain a single bone level value per implant. Bone level at the time of implant placement was compared with that at the time of last follow-up visit.

Histologic evaluation

Bone biopsies that were collected during the implant placements underwent histologic evaluations after preparing undecalcified histological sections. The sections were prepared using an electric diamond saw and grinding system (Exakt; Exakt Vertriebs, Norderstedt, Germany). The 50-μm-thick sagittal sections were prepared and stained with toluidine blue. The samples were examined under light microscope (Olympus BX50, Olympus Corp, Tokyo, Japan). The sections were evaluated with regards to newly formed bone, residual bone substitute particles, marrow space and the condition of the pristine bone. Neither a qualitative nor a quantitative histological comparison between the groups was made because of the limited number of samples.

The course of postsurgical healing

It was determined with a standardized clinical evaluation grading system. The wound healing both at the recipient and donor sites were graded at 7th and 14th postoperative days by the same surgeon, who performed the surgeries. The following scheme was used for scorings: 1 = no exposure, no drainage (pus or exudates), no inflammation, and no pain; 2 = no exposure, no drainage (pus or exudates), mild inflammation, and mild pain; 3 = no exposure, active drainage (pus or exudates), severe inflammation, and mild–severe pain; 4 = exposure of bone or graft, active drainage (pus or exudates), severe inflammation, and persistent pain.

Implant stability measurement

Resonance frequency analysis (RFA) measurements were performed in two perpendicular directions (mesio-distal and oro-facial), and a mean value was calculated for each implant. RFA was performed at implant insertion and at implant loading (4 months postoperatively). For this study, the wireless device was used (Ostell Mentor®, Integration diagnostics AB, Sävedalen, Sweden).

The clinical success rate at the 1st year

It was evaluated 12 months after the delivery of the prostheses. The particular implant was accepted as successful if the corresponding implant has (1) no pain or tenderness upon function (2) no mobility (3) no exudates history and (4) <2 mm radiographic bone loss from initial surgery (Misch et al. 2008).

Statistical analysis

The data were analyzed with SPSS 1.1.5 software for Windows (SPSS, Chicago, IL, USA) statistically, and the level of significance was set at $P = 0.05$. The sample size of the study was determined based on the power analysis considering important mean difference in alveolar width gain as 1 mm, standard deviation 0.5 mm for both groups, significance level 0.05, and power 0.80 (A priori: compute N, given alpha, power, ES: GPower 3.1, University of Dusseldorf, Germany) The estimate of the bone width gain was obtained from the study by Hämmerle et al. (2008). Data distribution was assessed using Kolmogorov–Smirnov test. There was normal distribution for all continuous variables. Due to the small sample size, a nonparametric test – Mann–Whitney U-test – was used for the comparisons of implant site parameters (wound-healing scores and CBCT measurements), implant stability measurements, and marginal bone level changes. As the patient is the independent variable of the study, the RFA scores and marginal bone loss values were averaged to a single value for patients, who received more than one implant installments. Chi-square test was used for comparison of the success rates.

Results

A total of 30 patients were recruited for the study. The study was conducted between December 2010 and December 2013. Three patients from each group were excluded. One female patient in group 1 stated that she experienced several occasions of hypoglycemic states during the first postoperative week after the augmentation surgery. She refused to continue the treatment. Two other patients were excluded because of the absence of bone formation at recipient site that were detected during the implant placement surgeries. Implants could not be placed in these patients and they were excluded as well. These patients were treated with tooth-supported restorations. Therefore, this group consisted of 12 patients. In group 2, there were early flap opening and loss of bone graft in one patient. Another two patients could not undergo implant placement procedure because of the absence of bone formation at the augmentation site. These patients underwent onlay block graft augmentation procedures in the 2nd surgery. These 3 patients were also excluded from the study. Therefore, this group consisted of 12 patients as well.

The mean ages of the patients in group 1 and group 2 were 52.6 ± 7.3 and 49.5 ± 9.3, respectively. There were 7 females and 5 males in the group 1 and 5 females and 7 males in group 2. There were no significant differences between the groups with regard to age and gender ($P > 0.05$). The duration of diabetes, initial fasting glucose levels, and initial HbA1c levels of patients in the group 1 were shown in Table 1.

Restorative treatment

A total of 43 implants were placed in 24 patients (22 implants in group 1 and 21 implants in group 2). All implants were restored with cement-retained single crowns, splinted two adjacent crowns or bridges. All implants were restored successfully and they survived up to last follow-up visit at the 12th month. In group 1, 7 implants replaced the incisor teeth (1st and 2nd incisors), 3 implants replaced the canine teeth, and 12 implants replaced the premolar teeth. In group 2, 9 implants replaced the incisor teeth, 4 implants replaced the canine teeth, and 8 implants replaced the premolar teeth. None of the implants had the clinical symptoms including pain, tenderness upon function, and mobility of the implant and exudates history (Fig. 2).

Alveolar bone width gain

The mean gain in alveolar bone width was 2.96 ± 0.59 mm in group 1 and 2.86 ± 0.64 mm in group 2. This difference between the two groups with regard to gain in alveolar bone width was not significant between the two groups ($P > 0.05$; Table 2).

Table 1. **Mean and median values of diabetes mellitus-related parameters of patients in group 1**

	N	Range	Median	Mean	SD
Duration of diabetes (Years)	12	5–18	7.5	8.2	3.5
Initial HbA1c (%)	12	6.1–7.5	6.8	6.7	0.3
Initial fasting glucose level (mg/Dl)	12	95–164	126	126.6	22.8

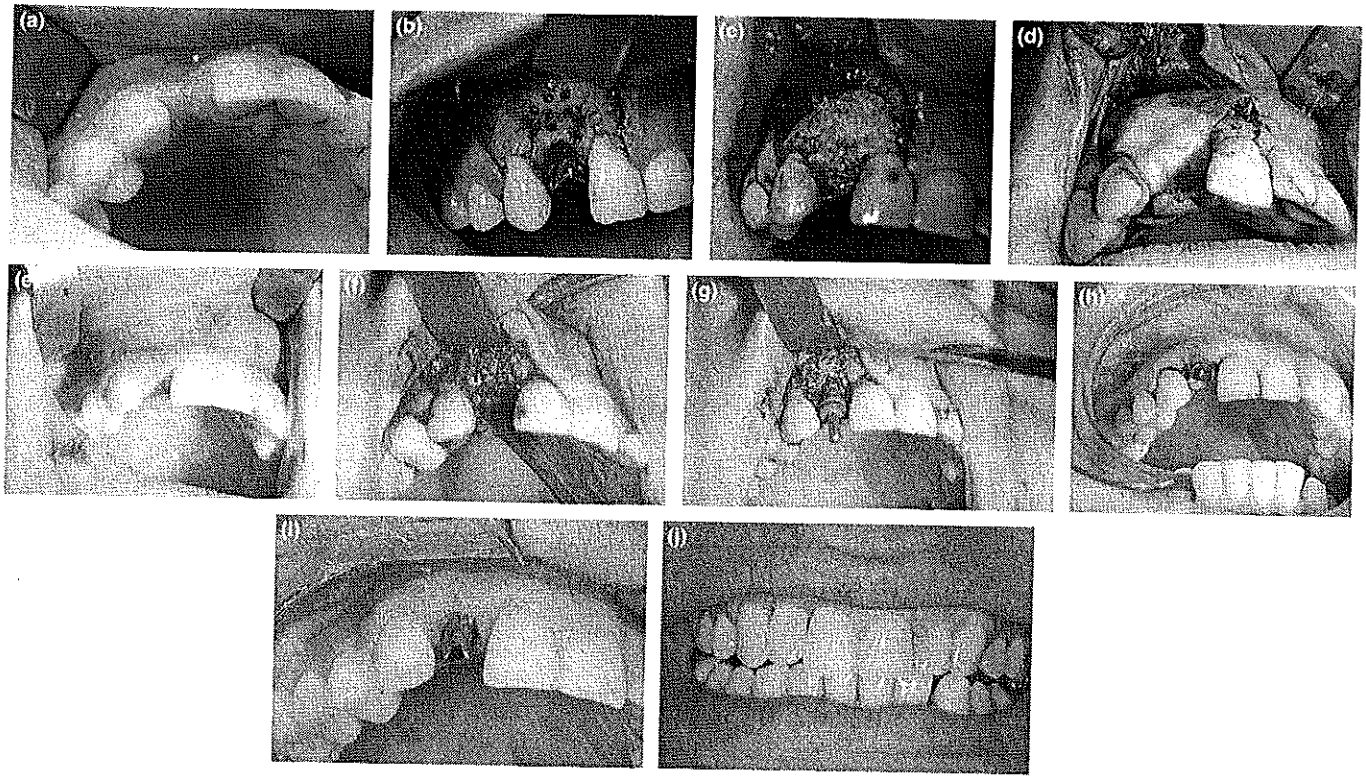

Fig. 2. Photographs showing clinical phases of a patient in group 2 (a) preoperative intraoral photograph (b) intraoperative photograph showing perforations at the buccal aspect of the recipient site (c) intraoperative photograph showing recipient site after graft material placement (d) intraoperative photograph showing recipient site after collagen membrane placement (e) intraoral photograph showing clinical situation after 5 months after augmentation surgery (f) intraoperative photograph showing healing of grafted site before implant placement. Note the presence of the residual graft particles (g) intraoperative photograph showing implant osteotomy site with a paralleling pin (h) intraoral photograph showing clinical situation after placement of healing abutment (4th month after implant placement) (i) intraoral photograph showing clinical situation after placement of abutment (j) intraoral photograph showing the definite crown after cementation.

Table 2. Comparisons of the alveolar bone width measurements between the two groups

	Group	N	Median	Mean	SD	*P* Value
Preoperative mean horizontal width (mm)	1	12	3.5	3.75	0.69	0.23
	2	12	3.9	3.98	0.53	
Postoperative mean horizontal width (mm)	1	12	6.4	6.81	0.90	0.66
	2	12	6.9	6.88	0.81	
Gain in horizontal width (mm)	1	12	2.9	2.96	0.59	0.77
	2	12	3.0	2.86	0.64	

Wound-healing scores

Mean values of the healing scores for recipient and donor sites at the 7th and the 14th postoperative days were shown in Table 3. There were no significant differences between the groups for both sites and both follow-up examinations.

Implant stability scores

The mean value of RFA measurements at implantation was 55.4 ± 6.5 ISQ for group 1 and 59.6 ± 4.1 ISQ for group 2. The mean value of RFA scores at the prosthesis delivery phase was 73.7 + 3.5 ISQ for group 1 and 75.7 ± 3.2 ISQ for group 2. There were no significant differences between the groups for both RFA measurements ($P > 0.05$; Table 4).

Table 3. Comparisons of the healing scores for recipient and donor sites at 7th (1st follow-up) and 14th (2nd follow-up) postoperative days (FU, follow-up)

	Group	*N*	Median	Mean	SD	*P* value
Healing score for recipient bed 1st FU	1	12	2	2.25	0.75	0.58
	2	12	2	2.17	0.38	
Healing score for recipient bed 2nd FU	1	12	1	1.50	0.52	0.41
	2	12	1	1.42	0.79	
Healing score for donor site 1st FU	1	12	2	2.17	0.83	0.17
	2	12	2	1.75	0.45	
Healing score for donor site 2nd FU	1	12	1	1.25	0.45	0.28
	2	12	1	1.08	0.28	

Marginal bone loss values

The mean value of the marginal bone loss from the delivery of the prostheses to the 12th month based on digital periapical radiographs was 1.13 ± 0.34 mm for group 1 and 0.93 ± 0.31 mm for group 2 (Fig. 3; Table 5). This difference was not statistically significant between the groups ($P > 0.05$). The mean marginal bone loss was less than 2 mm for all implants except for one implant from group 1. A saucer-shaped defect >4 mm was detected in this implant at the 6th month after the delivery of the prosthesis, which was placed in the right 1st premolar region. For this implant, a proposed periimplantitis management protocol was initiated (Lang et al. 2000). The progressive bone loss was eliminated, and a stable marginal bone level was achieved 16 months after the delivery of the crown. According to the success criteria appointed in this study, this implant was considered in *compromised survival* category; thus, it was not considered as successful.

Table 4. Comparisons of the resonance frequency analysis (RFA) measurements between the two groups

	Group	N	Median	Mean	SD	P value
RFA score at implantation (ISQ Unit)	1	12	56	55.4	6.5	0.087
	2	12	59	59.6	4.1	
RFA score before delivery (ISQ Unit)	1	12	73	73.7	3.5	0.148
	2	12	75	75.7	3.2	

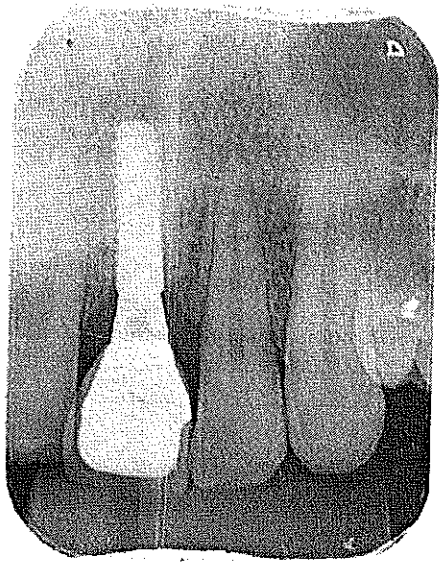

Fig. 3. Periapical radiographs obtained 12 months after the delivery of the prostheses from a patient from group 2.

Implant survival rates

The survival rates of implants were 100% for both groups. The success rate of the implants was 95% for group 1 and 100% for group 2 ($P > 0.05$).

Histologic evaluation

In many cases, bone biopsy could not be collected because of the risk of damaging the implant osteotomy site. Some samples were destroyed while retrieving the specimen from the trephine drill. They could not undergo histologic evaluation as well. Six specimens from group 1 and 5 specimens from group 2 were suitable for histologic evaluations. Histologic sections of all specimens showed evidence of new bone, presence of residual bone substitute particles, and marrow space (Fig. 4). In all samples, there was a distinctive layer of woven bone around the most external layer of bone substitutes. Little connective tissue was present in all samples. There was no notable difference between the samples from group 1 and group 2.

Discussion

Diabetes mellitus is a complex systemic disease, which comprises metabolic and vascular components. Although the etiology is different, similar clinical conditions are encountered in both subtypes of DM. The reduced prognosis of dental implant therapy and related surgical procedures in patients with diabetes is generally associated with the effects of DM on wound-healing process. Various animal studies showed that the bone-healing process was impaired in diabetic subjects compared with non-diabetic ones (Kotsovilis et al. 2006). There are several known physiological factors contributing to wound-healing deficiencies in patients with diabetes, which include decreased angiogenic response, growth factor production, collagen accumulation, macrophage function, and epidermal barrier function (Scully & Cawson 2005). Although most authors do not propose DM as a contraindication or a significant risk factor for dental implant therapy, current literature suggests some decrease in the success rate in surgical procedures associated with dental implant therapy. The success rate of dental implants in patients with DM varies between 68% and 100% (Balshi & Wolfinger 1999; Fiorellini et al. 2000; Farzad et al. 2002; Peled et al. 2003; Moy et al. 2005; Dowell et al. 2007; Khandelwal et al. 2013).

The rate of complications might be affected by some factors in patients with diabetes including the type of DM, current glycemic status, and the duration of diabetes. It is assumed that type 1 DM may have greater effect on the success of implant treatment (Salvi et al. 2008). However, the impact of different types of DM on dental implant success rate has not been studied so far. This assumption might be due to longer effective period of the disease, as type 1 DM develops in the earlier years of the lifespan. Olson et al. (2000) have investigated effects of the duration of diabetes on implant success, and they concluded that implant success is significantly associated with the duration of the diabetic history. On the contrary, the study by Tawil et al. (2008) showed no affects of the duration of diabetes on the survival of implants or occurrence of complications such as periimplantitis.

General assessment of metabolic control in DM is generally determined based on hemoglobin A1c (HbA1c) levels. The extent of glycosylation of hemoglobin A is used for long-term determination of general assessment of patients with diabetes (Scully & Cawson 2005). It increases in the presence of hyperglycemia and reflects glucose levels in the blood over 6–12 weeks preceding administration of the test. According to ADA criteria, the HbA1c level should be below 7% for well-controlled diabetes mellitus (Sacks et al. 2011). The level might reach as high as 20% in uncontrolled cases. Usually, the studies evaluating the dental implant success rate in DM exclude the patients with uncontrolled diabetic status. However, some studies evaluated the patients at different glycemic states. Dowell et al. evaluated the success rate and complications in patients with type 2 diabetes. They grouped the patients with diabetes according to their HbA1C levels as well controlled (HbA1c level 6–8%), moderately controlled (8.1–10%) and poorly controlled (>10%) (Dowell et al. 2007). There were no differences between the three groups with regard to implant success and occurrence of complications. Similarly, a recent study by Khandelwal et al. (2013) demonstrated clinically successful implant placement even in poorly controlled patients with diabetes (HbA1C> 7.5–11.4%). A prospective study by Tawil et al. (2008) showed that significant statistical correlation exists between the HbA1c level and periimplantitis. They showed that there was increased number of implant loss in patients with HbA1c levels above 7%. However, the number of subjects was not enough to perform a statistical analysis. The authors concluded that HbA1c is the most important factor affecting implant complication rate. The aim of the present study was to compare the outcomes of bone augmentation between the patients with diabetes and healthy patients. The HbA1c levels of the patients with diabetes in the present study were between 6% and

Table 5. Comparison of the marginal bone loss values based on digital periapical radiographs 12 months after delivery of prostheses

	Group	N	Median	Mean	SD	P Value
Marginal Bone Loss (mm)	1	12	1.1	1.13	0.34	0.225
	2	12	0.9	0.93	0.31	

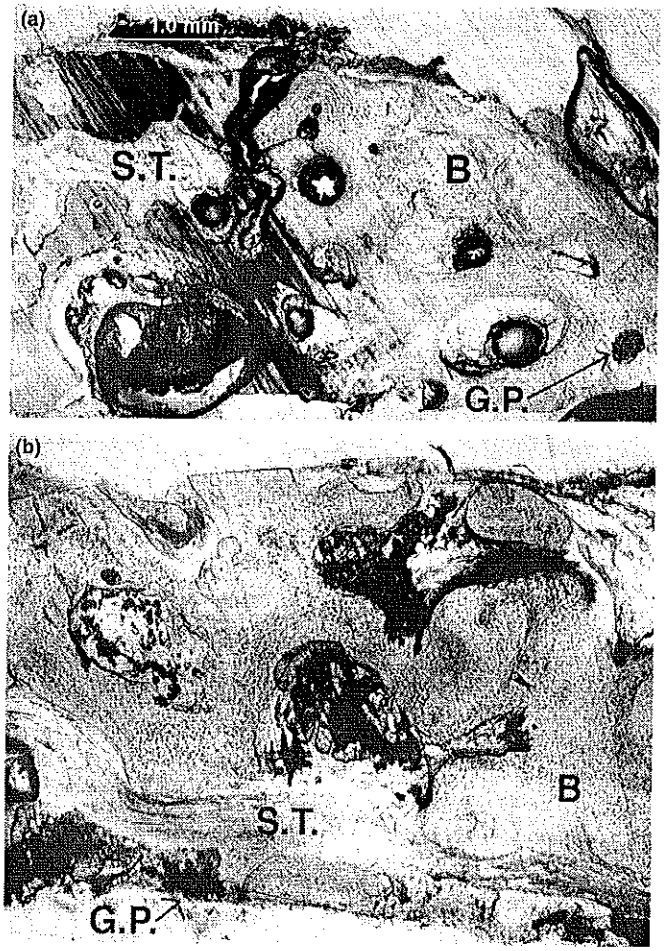

Fig. 4. Histologic features of bone specimen obtained after 5 months of a healing period. (Magnification10×) (a) specimen from group 1 (b) specimen from group 2 (B, bone tissue; S.T, soft tissue; G.P, residual graft particles).

7.5%. We observed that complication rates and wound healing did not significantly changed between the patients with diabetes and healthy patients.

There are few clinical studies that evaluated the success rate of alveolar bone augmentation in patients with DM. Clinical studies on bone augmentation techniques mostly excluded patients with DM. To our knowledge except one study conducted by Tawil et al. (2008) there is no other prospective clinical study in the literature dealing with the outcomes of alveolar bone augmentation procedures in patients with diabetes. In a retrospective study by Farzad et al., three patients with DM underwent an alveolar bone augmentation procedure. The type of the augmentation technique was not mentioned in the publication (Farzad et al. 2002). None of the patients had any complication, and the grafts have survived in all patients. Schwartz-Arad et al. (2005) applied onlay autogenous bone augmentation to four patients with diabetes and three of the grafts have failed. The prospective study by Tawil et al. (2008) evaluated implant and alveolar bone augmentation success rates in patients with type 2 DM. The GBR technique was used in 20 patients, while sinus lift procedure was used in 34 patients. The success rate was 85% for GBR procedures and 91.1% for sinus lift procedures. In a retrospective study by Huyn-Ba et al., the success rates of dental implants placed in augmented sinus of 7 patients with well-controlled DM were evaluated. The authors concluded that well-controlled DM is not one of the predictors of implant failure for implants placed in augmented sinus (Huynh-Ba et al. 2008). In the present study, the success rate for implants in diabetic group was 95%. This success rate can be considered acceptable in the context of current dental implantology literature. Of all patients recruited for the study, two patients from group 1 and three patients from group 2 could not undergo implant placement because of surgical complications and lack bone formation (fibrous tissue formation) after the augmentation procedure. These patients had to be excluded from the study as the study parameters could not be applied. There are several possible reasons for these complications such as poor compliance to postoperative instructions and medications, mobilization of graft material during healing phase or idiopathic patient-surgery-related factors. If the success of the augmentation procedure was taken into consideration, it would be 86% for group 1 and 80% for group 2. A study by Hämmerle et al. (2008) used a similar GBR augmentation method used in our study. There was lack of bone formation in 1 of 12 patients corresponding to 91% success rate. According to our knowledge, there are no universally accepted criteria for evaluation of the success rate of implants placed with staged alveolar bone augmentation techniques. Therefore, we evaluated the success rate of the treatment according to the condition of implants that were successfully placed in augmented ridges as the other previous studies (Buser et al. 2002; Hämmerle et al. 2008; Tawil et al. 2008; Urban et al. 2011; Block et al. 2012).

Guided bone regeneration is one of the most commonly applied augmentation procedures in dental implantology. It is generally conducted simultaneously with implant placement. However, in cases with more advanced bone loss, staged GBR is required. It is difficult to determine a clear indication for simultaneous or staged approach. The quality and quantity of the available alveolar bone for providing adequate primary stability of the implant is the essential condition to choose the type of the GBR procedure. A systematic review by Donos et al. (2008) demonstrated that the success rates of implants placed with a staged approach ranged from 75% to 98.3%. Some variations in the healing times, materials, and surgical principles exist among the previous studies. The time between the augmentation and re-entry surgery depend on the material used for GBR and may be between 4 and 12 months (Buser et al. 2002; Christensen et al. 2003; Donos et al. 2008; Hämmerle et al. 2008; Clementini et al. 2013). In the present study, a relatively shorter healing time (5 months) was chosen because of the utilization of the autogenous bone in combination with the bone substitute and to shorten the overall duration of the treatment. However, the shortened healing period resulted in decreased mineralization level of the bone regenerate at the augmentation site. The primary stability of the implants was relatively low according to surgeon's tactile feeling and

it was confirmed by the RFA analyses. An equal mixture of autogenous bone chips and a synthetic bone substitute consisting of 60% hydroxyappetite and 40% b-tricalcium phosphate was used. Longer healing period might be required for the technique and graft material used in the current study. We observed that the bone regenerate was mostly ossified at the time of the implants exposures for placement of healing abutments (4 months after implant placement) and a satisfactory implant stability was confirmed by RFA analyses. Determination of the implant stability, which is related to histological osseointegration of the implant, with RFA measurement is considered a reliable method (Khandelwal et al. 2013). In the present study, mean RFA values at the time of installment of the implants and at the time of delivery of the prostheses (4 months after the placement) did not differ significantly between the groups.

Determination of the course of early wound healing in human studies by objective parameters is problematic because of ethical reasons. In the present study, the course of wound healing was determined using a scoring system developed by our group for this study. Although the data obtained from this scoring may be considered subjective, it can still be considered useful for determining the course of the wound healing as the evaluations are simply based on the absence or the presence of specific signs and symptoms including exposure of graft material, drainage (pus or exudates), inflammation, and pain. The course of healing both for recipient and donor sites at the 7th and 14th postoperative days was evaluated, and there were no differences between the groups in any of sites or evaluation time.

One of the major parameters of the success of dental implants is the marginal bone loss around the implant neck. Different success criteria exist about the amount of acceptable marginal bone loss. Although a universally accepted implant and ridge augmentation success criteria lacking, usually up to 2 mm of marginal bone loss in the first post loading year is still acceptable for success (Christensen et al. 2003; Donos et al. 2008; Misch et al. 2008; Clementini et al. 2013). In the present study, only one implant had more than 2 mm marginal bone loss. We determined the implant success according to criteria by Misch et al. (2008). According to this classification system, this implant presented in the compromised survival category; thus, it was not considered as successful. According to the mean value of the marginal bone loss based on digital periapical radiographs obtained by parallel technique, there was no significant difference between the patients with diabetes and healthy patients. Despite the popularity of parallel technique, some errors may occur, as strict parallelism between implant axes and film plane is difficult to obtain (Sewerin 1990). Hence, customized X-ray positioning stents might provide better reproducible images for long-term clinical examination of marginal bone. Another drawback of the present study was the lack of examination of the periimplant tissues by means of probing around the implants. Assessment of probing depth provides significant information about the bone level around the implant as well as health of soft tissue attachment. Therefore, this assessment method would make significant contribution to the assessment of marginal bone loss.

Histological evaluation of the specimens obtained from the augmented ridges provides valuable information about the outcomes of the regeneration process. Furthermore, histomorphometric analysis allows researchers to obtain quantitative data regarding the bone formation and the condition of graft material at the particular region. However, in human studies, it is sometimes difficult to collect appropriate material because of the risk of damaging the implant osteotomy site. In the present study, collecting a sample from the region was not possible in some cases because the dimensions of the region of interest were very limited or the sample was ruined during the handling of the specimen. These types of problems were also reported in other previous studies (Urban et al. 2001; Choi et al. 2013). In the present study, 6 specimens from group 1 and 5 specimens from group 2 were suitable for histologic evaluations. All samples from both groups had a similar appearance showing various amounts of vital bone, connective tissue, marrow space, and residual bone substitute particles.

In the present study, there was a mean horizontal bone gain of 2.92 ± 0.59 mm in group 1 and 2.86 ± 0.64 mm in group 2 according to CBCT examinations. Previous studies using a similar technique showed higher amount of horizontal bone gain. A study by Urban et al. (2011) reported an average of 5.52 mm increase in alveolar width in 25 augmented alveolar ridges. Hämmerle et al. (2008) obtained an average of 3.6 mm width gain in 12 ridges upon re-entry at 9–10 months after the augmentation. A study by Block et al. evaluated the gain in the alveolar width in a more detailed manner by using CBCT examinations. They measured the gain at the midway from apical to coronal aspect as 3.2 mm 6 months after the augmentation procedure (Block et al. 2012). Because the measurement methods differ among the studies, these values cannot be considered for comparisons. Except CBCT measurements, another measurement method of the alveolar width is the direct measurement with calipers intraoperatively. Our previous experience showed that intraoperative measurement of the alveolar crest width by means of calipers does not provide accurate data for evaluation of bone volume changes after augmentation procedures. Several factors such as the locations of the tips of the caliper and the bucco-palatal angulation or orientation of the caliper affect accuracy of the measurement. Even though, the surgeon intends to make measurement exactly at the same point with the previous surgery, sometimes it is very difficult to conduct it in wide augmentation zones. Thus, we decided to evaluate gain in alveolar width by means of CBCT measurements, in which standard and accurate measurement can be performed easily. In all cases of the present study, the amount of width gain was sufficient enough for placement of the implants. There was no difference between group 1 and group 2 with regard to amount of bone width gain.

Conclusions

The results of the present study suggest that type 2 diabetic patients with HbA1c levels below 7.5% may undergo staged GBR procedures securely. The sample size of the present study consisted of limited number of subjects, and the data presented here are only first year's findings. Thus a long-scale, longer term, cohort study is needed to verify our findings. Staged guided bone regeneration is a feasible augmentation procedure for the treatment of horizontal bone deficiencies of the maxillary anterior/premolar regions in well-controlled type 2 diabetic patients.

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