Long-Term Retrospective Evaluation of Dental Implants Placed in Resorbed Jaws Reconstructed With Appositional Fresh-Frozen Bone Allografts

Carlo Maiorana, MD, MSc,* Pier Paolo Poli, DDS,† Andrea Enrico Borgonovo, MD, MSc,‡ Davide Rancitelli, DDS,§ Anna Chiara Frigo, MSc,¶ Stefano Pieroni, DDS,|| and Franco Santoro, MD, MSc#

Introduction: *The aim of this study was to evaluate the outcome of fresh-frozen bone allografts in preprosthetic surgery for implant placement purposes.*

Materials and Methods: *The cohort comprised 45 patients treated with fresh-frozen bone block grafts and dental implants. Clinical and radiological evaluations were performed to evaluate the survival rate. The data were statistically analyzed with the Kaplan-Meier estimator to assess the influence of possible predictors of implant failure on survival.*

Results: *Overall, 262 implants were retrospectively analyzed. The survival rate was 90.84% over a mean follow-up of 50 months. Comparing the donor site and the position of the implants, no statistically significant differences could be detected (P = 0.7194 and P = 0.2901, respectively), whereas sex resulted in a marginally statistically significant difference (P = 0.0581). When considering age categorized on the median value (≤55/>55 years), age resulted in a statistically significant difference (P = 0.0340), with higher failures found in older people.*

Conclusion: *Implant loss was strictly related to the lack of primary osseointegration. Female sex and old age were found to be risk factors, which could negatively influence implant survival. (Implant Dent 2016;25:1–9)*

Key Words: block grafts, bone augmentation, homologous bone, survival rate

Bone loss in edentulous jaws negatively influences the functions of the stomatognathic system. It is associated with changes of the maxillo-mandibular relationship and reduces the support for prosthesis. Furthermore, alterations of some muscle attachments may occur, leading to circumoral hypotonia and collapse of the tissues, thus resulting in compromised facial form and aesthetics. Reconstructive preprosthetic surgery was advocated to provide suitable prerequisites for prosthesis that will restore function, be stable and retentive, and preserve the noble structures, which at the same time satisfies aesthetic demands.[1] The treatment of edentulous atrophic jaws with dental implants seems to be a predictable therapy; however, it represents a major challenge because implant-supported rehabilitation requires adequate quantity and quality of the alveolar bone to be successful. For this reason, bone regeneration procedures become mandatory to create the conditions for prosthetic-driven implant placement. Several therapeutic bone reconstruction approaches were proposed depending on the severity of the bone atrophy, including the use of growth and differentiation factors, particulate and block grafting materials, distraction osteogenesis, ridge split techniques, and guided bone regeneration.[2] The use of autogenous bone grafted from intra- or extra-oral donor sites has been considered to be the gold standard material in case of reconstructive surgery, because of its intrinsic biological properties associated with

*Professor and Chairman, Department of Dental Implants, Maxillofacial Surgery and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
†Resident, Department of Dental Implants, Maxillofacial and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
‡Assistant Professor, Department of Dental Implants, Maxillofacial Surgery and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
§PhD Fellow, Department of Dental Implants, Maxillofacial Surgery and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
¶Assistant Professor, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy.
||Resident, Department of Dental Implants, Maxillofacial Surgery and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
#Full Professor, Dental Clinic Director, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.

Reprint requests and correspondence to: Pier Paolo Poli, DDS, Department of Dental Implants, Maxillofacial and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Via Commenda 10, 20122 Milan, Italy, Phone: 00390255032621, Fax: 00390255032513, E-mail: poliodontoiatria@gmail.com

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the lack of possibility of disease transmission or host rejection.[3] Nevertheless, some drawbacks were reported, including donor site morbidity, limited availability, increased operating time, and possible complications related to the harvesting procedure such as neurosensory disturbances, prolonged healing, and opportunistic infections.[4]

To overcome these limitations, bone-harvesting research activities were directed toward the application of biomaterials and bone substitutes. An alternative to the use of autogenous bone is allogeneic grafts. Allografts have proven to be clinically useful, particularly in case of limited availability of autologous bone, because tissue banks could provide grafts of any size and shape needed.[5,6] Additional advantages include decreased trauma for the patient, reduced operative time, and absence of donor site morbidity.[7] Homologous bone is obtained from human donors and is successively treated and stored in different ways, including fresh-frozen bone allograft (FBBA), freeze-dried bone allograft (FDBA), decalcified FDBA, demineralized freeze-dried bone allograft, and cryopreserved processing modalities.[8] Initially, allografts were believed to have disadvantages such as risk of host reactions due to genetic differences, disease transmission, and ethical and religious issues. Despite these problems, the use of allografts, particularly fresh-frozen bone (FFB), has actually increased over the last years. This is probably due to the absence of negative reports concerning its antigenicity and the demonstration of reduced immunological reaction in experimental models when homologous bone is treated by freezing at low temperatures, which suggests that FFB could represent an adequate alternative to autografts.[9] Another concern with the use of banked allograft was the transmission of infection, most notably hepatitis and acquired immunodeficiency syndrome. Nowadays, guidelines on donor selection, tissue procurement, tissue preservation, tissue storage, and adequate record-keeping procedures have been designed by bone banks to ensure the supply of safe allogeneic bone.[10] This concept was emphasized by Virolainen et al,[11] who have not observed any significant allergic reactions, rejection, or any unexpected antibodies after allograft transplantation over a long-term time span. Moreover, Aho et al,[12] analyzing fresh-frozen allograft specimens after transplantation in the treatment of large bone defects, found no histological signs of immunologic reaction and no clinical rejection episodes during a long-term follow-up. FFB is harvested aseptically from different anatomical areas of live or deceased donors and then immediately frozen and stored at −80°C; in the absence of contraindications emerging from the results of the screening procedures, it can be used for implantation.[13] Regarding the use of FFB in oral and maxillofacial surgery, the effectiveness and the reliability of this material for alveolar ridge reconstruction in preprosthetic surgery has been recently demonstrated[14–16]; however, long-term studies are still lacking.

The intent of this article was to assess the clinical effectiveness and predictability of appositional FFB allografts in preprosthetic surgery. To this end, the survival of implants placed in reconstructed jaws by means of FFB was retrospectively evaluated in relation to possible predictors of implant failure.

MATERIALS AND METHODS

The group under examination consisted of a consecutive sample of 45 patients (29 women and 16 men), with a mean age of 53.9 years (median = 55, range = 32–66 years). All of the procedures were performed in the same hospital (Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy) in the period between December 2007 and December 2012. Reconstructive and implant placement surgeries were performed by 3 surgeons, whereas prosthetic rehabilitations were performed by the same prosthodontic team. Both the surgical and the prosthetic team belonged to the same department (Implant Center for Edentulism and Jawbone Atrophies, Maxillofacial Surgery and Odontostomatology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, University of Milan, Italy).

Inclusion and Exclusion Criteria

Inclusion criteria were total or partial edentulism associated with different degrees of vertical and horizontal bone loss (according to class II to VI Cawood and Howell[17] atrophy classification) requiring bone augmenting procedures to perform an ideal prosthetic-driven implant placement. Patients who underwent reconstructive surgery with appositional FFB block grafts were included. Only dental implants placed in augmented sites have been retrospectively evaluated.

Exclusion criteria were poor oral hygiene, active periodontal infections, uncontrolled systemic pathologies, current head or neck irradiation, psychological disorders, bisphosphonates administration, presence of smoking habit (>10 cigarettes/d), alcoholism, and drug use. Also, pregnant or lactating female patients were excluded.

Treatment Procedures

During the dental visit, each patient was thoroughly informed about the proposed elective FFB-grafting procedure. The preoperative routine included blood tests, an interview with the anesthesiologist for general anesthesia, the signature in the informed consent form for the surgery, the test to determine the patient's blood group, and the signature in a specific informed consent form for the use of the bone graft from the regional Musculoskeletal Tissue Bank (MTB) (Gaetano Pini Orthopaedic Institute, Milan, Italy). The reference MTB supplied the informed consent forms for the FFB grafting procedure, together with the application forms for the bone specimen (including information on its origin, shape, and size). The tissue specimen was then booked at the reference MTB, which made available a wide range of specimens in different shapes and sizes. Once the specimens have been harvested, they were then sent to the MTB for preparation and examination, together with blood samples to be subjected to serologic tests, which included tests for detecting antibodies and antigens, and blood cultures. The processing of fresh allogeneic bone did not involve decalcification or

Table 1. Implant Locations and Implants per Patient Data

Implants Data					
Implants Location*					
Maxilla			Mandible		
Site†	No. of Implants (%)	No. of Failures (%)	Site†	No. of Implants (%)	No. of Failures (%)
2	5 (2.56)	0 (0)	18	1 (1.49)	0 (0)
3	15 (7.69)	4 (28.57)	19	4 (5.97)	0 (0)
4	9 (4.61)	1 (7.14)	20	3 (4.47)	0 (0)
5	21 (10.76)	2 (14.28)	21	5 (7.46)	0 (0)
6	23 (11.79)	0 (0)	22	7 (10.44)	1 (10)
7	27 (13.84)	2 (14.28)	23	9 (13.43)	1 (10)
8	5 (2.56)	0 (0)	24	5 (7.46)	1 (10)
9	7 (3.58)	1 (7.14)	25	0 (0)	0 (0)
10	15 (7.69)	1 (7.14)	26	3 (4.47)	0 (0)
11	11 (5.64)	1 (7.14)	27	2 (2.98)	0 (0)
12	14 (7.17)	1 (7.14)	28	6 (8.95)	1 (10)
13	17 (8.71)	0 (0)	29	7 (10.44)	1 (10)
14	22 (11.28)	1 (7.14)	30	9 (13.43)	3 (30)
15	4 (2.05)	0 (0)	31	6 (8.95)	2 (20)
Total	195 (100)	14 (100)	Total	67 (100)	10 (100)

Implants Data		
Implants per Patient‡		
No. of Implants	No. of Patients (%)	No. of Failures (%)
1	1 (2.22)	0 (0)
2	5 (11.11)	1 (4.16)
3	4 (8.88)	3 (12.55)
4	5 (11.11)	2 (8.33)
5	4 (8.88)	0 (0)
6	9 (20)	3 (12.55)
7	2 (4.44)	4 (16.66)
8	10 (22.22)	4 (16.66)
9	2 (4.44)	7 (29.16)
10	1 (2.22)	0 (0)
11	1 (2.22)	0 (0)
12	1 (2.22)	0 (0)
Total	45 (100)	24 (100)

*For both maxilla and mandible, the number of implants (%) and the number of failures (%) are reported according to the position.
†Position of the implant according to the Universal Numbering System (American Dental Association "*Current Dental Terminology Third Edition [CDT-3]*" 1999). Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
‡The number of patients (%) and the number of failures (%) are reported according to the number of implants placed in each patient.

irradiation but consisted of an initial disinfection with a polychemotherapeutic solution (for 72 hours at –4°C), saline lavage, and cutting into blocks, which were then packed in double sterile bags and stored in tanks at a constant temperature of – 80°C.

Preoperative reconstructive procedure. Before surgery, each patient received proper oral hygiene instructions and a professional oral hygiene treatment. At the end of initial therapy, before starting the surgical procedures, the patients demonstrated proper plaque control. As none of the patients referred penicillin allergy, the antibiotic therapy consisted of 2 g of amoxicillin clavulanate (Augmentin, GlaxoSmithKline S. p.A., Verona, Italy) before the surgery and 1 g twice daily for 7 days starting 1 hour after the surgery. Patients were also asked to make rinses with chlorhexidine 0.2% (Dentosan; Recordati S. p.A., Milan, Italy) 3 times a day starting from 1 week before the surgery up to the sutures removal. Each patient underwent preoperative radiological examinations, including orthopantomographs and computed tomography.

Surgical reconstructive procedures (T0). The surgical procedures were performed under general anesthesia. On the day of surgery, a sealed container with the graft preserved under controlled temperature was delivered. Once freed from its outer packaging, the specimen was still wrapped in a sealed double sterile bag. It was then transferred to the operating room, where the double bag was opened in a sterile environment and the tissue specimen was defrosted in an abundant solution of saline and rifampicin at a temperature of 37° for 1 hour, in compliance with the instructions provided by the reference MTB. Once the specimen has been defrosted, it was debrided if necessary to remove nonbony tissues, cut into blocks, and contoured or morcellized, based on the treatment plan. Before the incision, 8 mg of dexamethasone phosphate (Soldesam; Laboratorio Farmacologico Milanese s.r.l., Varese, Italy) was intramuscularly injected to reduce postoperative swelling. Local vasoconstriction was induced by infiltration with articaine/epinephrine 1:100.000. A full-thickness flap was elevated to expose the bone defects. Allogeneic fresh-frozen cortico-cancellous block grafts precontoured onto a stereolithographic model were used to replace the missing bone. Before fixing the homologous onlay blocks with osteosynthesis screws, cortical perforations of the recipient bed were performed with a 1.5-mm diameter carbide bur. The bone grafts were then covered with the same morcellized FFB, which was maintained *in situ* by means of resorbable collagen membranes (Bio-Gide; Geistlich Pharma AG, Wolhusen, Switzerland). The surgical wound was then sealed with horizontal mattress sutures and interrupted sutures, after releasing the flap by means of periosteal incisions.

Postoperative procedures. The forms supplied by the MTB, used to notify that the tissue specimen has been used

Table 2. Implant Failures

Implant Number	Patient Number	Age	Sex	Type of Graft	Diameter (mm)	Length (mm)	Arch	Position*	T0–T1† (mo)	T2‡ (mo)
68	10	61	F	Iliac crest	4.25	10	Right mandible	30	6	49
69	10	61	F	Iliac crest	4.25	10	Right mandible	31	6	49
92	15	63	F	Iliac crest	3.8	11.5	Left mandible	20	6	49
93	15	63	F	Iliac crest	4.25	11.5	Left mandible	19	6	49
94	15	63	F	Iliac crest	4.25	11.5	Left mandible	18	6	49
96	15	63	F	Iliac crest	3.8	11.5	Right mandible	28	6	49
97	15	63	F	Iliac crest	3.8	11.5	Right mandible	29	6	49
98	15	63	F	Iliac crest	4.25	10	Right mandible	30	6	49
99	15	63	F	Iliac crest	4.25	10	Right mandible	31	6	49
106	18	60	F	Iliac crest	3.8	11	Right maxilla	5	7	28
143	24	64	F	Iliac crest	4.3	10	Right maxilla	3	6	26
150	24	64	F	Iliac crest	4.3	10	Left maxilla	14	6	26
155	26	72	F	Femoral epiphysis	3.5	10	Right maxilla	7	4	86
167	29	61	F	Femoral epiphysis	4	12	Right maxilla	6	6	48
168	29	61	F	Femoral epiphysis	4	12	Right maxilla	7	6	48
169	29	61	F	Femoral epiphysis	4	12	Left maxilla	9	6	48
178	31	52	M	Iliac crest	4	12	Right maxilla	5	8	74
179	31	52	M	Iliac crest	4	12	Right maxilla	7	8	74
193	34	60	F	Iliac crest	4	10	Right mandible	30	7	69
228	40	51	F	Iliac crest	3.75	8	Right maxilla	3	4	70
229	40	51	F	Iliac crest	3.75	8	Left maxilla	10	4	70
230	40	51	F	Iliac crest	3.75	8	Left maxilla	11	4	70
231	40	51	F	Iliac crest	3.75	8	Left maxilla	12	4	70
256	45	64	F	Iliac crest	3.3	11	Right maxilla	7	7	29

*Position of the implant according to the Universal Numbering System (American Dental Association "*Current Dental Terminology Third Edition [CDT-3]*" 1999). Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
†Time interval between the reconstructive surgery (T0) and the implant placement (T1).
‡Longest follow-up achieved by each implant (T2).

and to describe possible adverse reactions, were filled in and sent back to the MTB within a few days after surgery. To control the patients' postoperative pain, oral administration of 500 mg of paracetamol and 30 mg of Ketorolac (Lixidol; Hoffman-La Roche, Basilea, Svizzera) was followed. Patients were instructed to use a chlorhexidine 0.2% (Dentosan; Recordati S.p.A., Milan, Italy) rinse twice daily until suture removal. Sutures were removed after 14 days. Patients were placed on a soft diet during the first 3 months after surgery to limit occlusal loading and reduce micromovements, which might interfere with osseointegration. Health conditions were checked monthly, until the second surgical step.

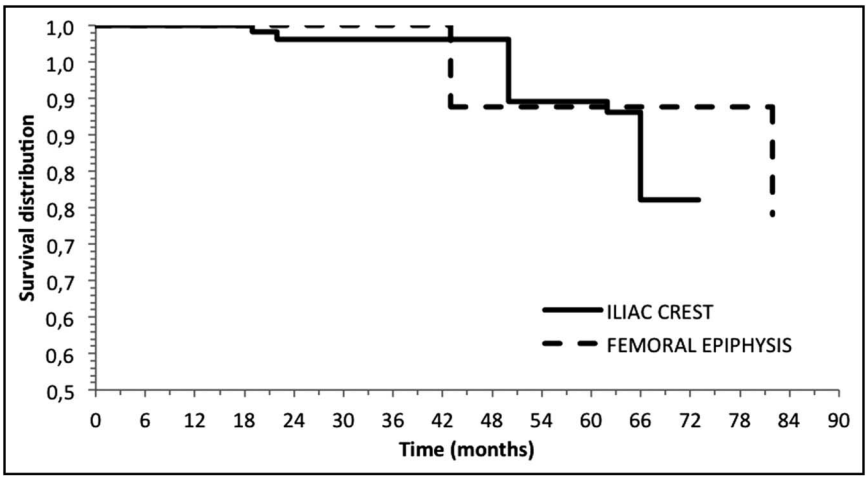

Fig. 1. Kaplan-Meier curve related to the donor site (iliac crest vs femoral epiphysis). Comparing the source of the graft, no statistically significant difference related to the implant survival could be found ($P = 0.7194$).

Implant placement (T1). Six to 8 months after preprosthetic surgery, cone beam computed tomography (CBCT) was conducted to assess the graft's integration and therefore to plan the placement of rough-surface implants (blueSKY dental implants, Bredent GmbH & Co.KG, Senden, Germany, Camlog Screw-line dental implants; Camlog Biotechnologies, Basel, Switzerland, Premium Kohno dental implants; Sweden and Martina SPA, Due Carrare, Padova, Italy). After elevation of a mucoperiosteal flap, the fixation screws were carefully removed and implants were positioned according to the manufacturer

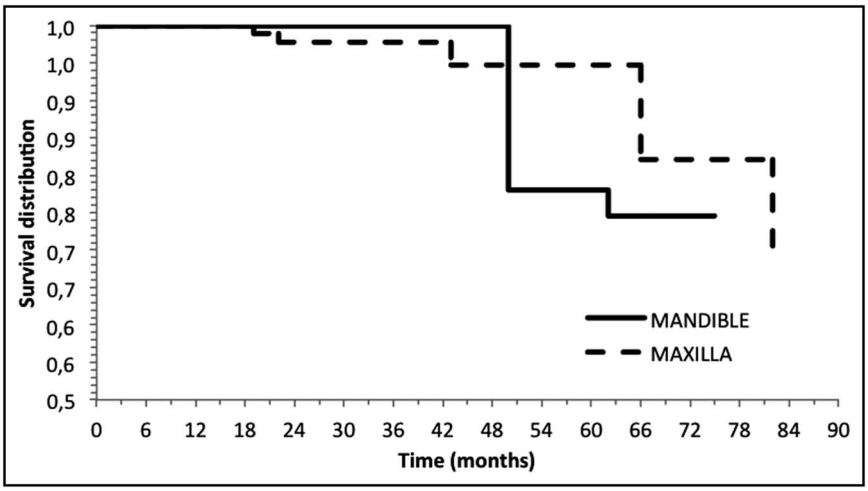

Fig. 2. Kaplan-Meier curve related to the recipient site location (maxilla vs mandible). No statistically significant effect with respect to the different positions of the implants could be observed ($P = 0.2901$).

instructions in a prosthetically driven position. A first intention wound closure was obtained. Implants were left unloaded for at least 3 months; prosthetic rehabilitation was subsequently performed. All patients were included in a strict professional hygiene recall protocol and underwent clinical evaluation every 6 months. A radiological follow-up evaluation with periapical X-rays and orthopantomographs was conducted once a year.

Data Sources

A recall program was conducted for all 45 patients between September 2014 and December 2014 (T2). Clinical and radiological assessments by means of orthopantomographs were performed to evaluate the survival rate, namely whether the implant was still physically in the mouth or has been lost.[18] Furthermore, the analysis was interrelated with possible predictors of implant failures concerning this type of surgery, including the following: (1) source of the FFB specimens (iliac crest or femoral epiphysis donor sites), (2) implant recipient anatomical site position (maxilla or mandible), (3) sex, and (4) age of the patients.

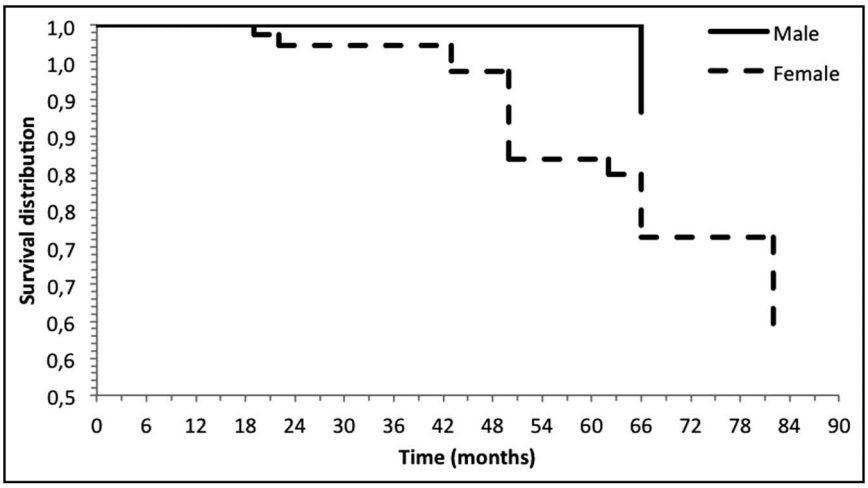

Fig. 3. Kaplan-Meier curve related to the sex of the patients (male vs female). Sex influence on implant survival was marginally statistically significant ($P = 0.0581$).

Statistical Analysis

The analyses of data were performed using dedicated software (IBM SPSS Statistics for Windows, version 21.0; IBM Corp., Armonk, NY). Results are presented as count and percentages in each category for categorical variables and as mean and SD, median, minimum, and maximum for quantitative variables. For the analysis of survival from failure, time zero was defined as the date of the insertion of the implant. The survival time was calculated as the difference between the date of implant placement and the date of the failure or the date of the last follow-up, and in this case the patient was censored.

Survival was estimated with the Kaplan-Meier method. The impact of the potential predictors of failure (source of the FFB grafts, implant recipient site position, sex, and age, categorized according to the median value) was analyzed with univariate Cox regression with sandwich covariance estimation to take into account the multiple implants in each patient. Results are presented as P value, hazard ratio (HR), and 95% confidence interval (CI). P values < 0.05 were considered statistically significant.

RESULTS

Of the 45 patients included in the analysis, 29 (64.4%) were females and 16 (35.6%) were males; 21 (46.7%) patients had more than 55 years of age and the mean age was 53.9 years (SD = 7.2, min = 32, max = 66).

A total of 262 implants (mean = 5.8, SD = 2.6, minimum = 1 and maximum = 12 per patient) were included in this study and were therefore retrospectively evaluated. Implants' data including the position of the implants and the number of implants per patient are reported in Table 1. A total of 24 (9.16%) implants failed to osseointegrate and were consequently removed (Table 2). According to the Kaplan-Meier estimator, the survival rate of implants placed after bone augmentation procedures by means of FFB was 90.84%, with a minimum follow-up of 18 months and a maximum of 82 months. All

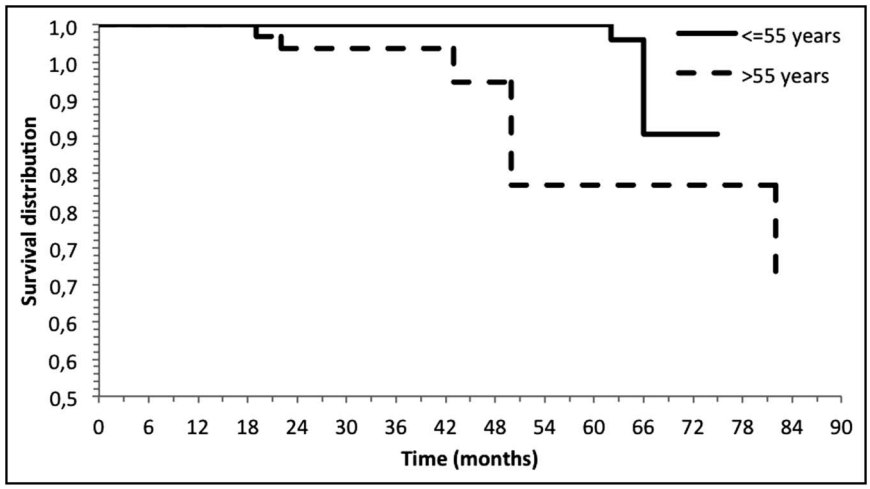

Fig. 4. Kaplan-Meier curve related to the age of the patients according to the median value (≤55 vs >55 years). A statistically significant difference in terms of implant survival was found ($P = 0.0340$).

except 6 implants were inserted after a mean of 6.4 months after the preprosthetic surgery. The 6 implants placed simultaneously with the graft procedure reached a survival rate of 100% over a maximum follow-up of 46 months and were nevertheless included in the retrospective study.

1. A total of 227 (85.6%) implants were positioned in jaws reconstructed with FFB grafts harvested from the iliac crest, whereas 35 (14.4%) implants were placed in jaws augmented with FFB blocks retrieved from the femoral epiphysis. Failed implants were 20 (7.6%) when iliac crest donor site was considered; conversely, 4 (11.4%) implants failed in the femoral epiphysis group. Comparing the type of graft, no log-rank statistically significant difference was found in implant survival ($P = 0.7194$, iliac crest vs femoral epiphysis HR = 1.52, 95% CI = 0.16–14.78) (Fig. 1). Clinically, at the second-stage surgery after 6 months of healing time, both type of grafts appeared integrated to the recipient bed; however, a slight trend toward a higher bone resorption and bleeding was observed when femoral head allografts were used. Furthermore, a clear distinction between the resident bone and the homologous blocks was more difficult in case of femur FFB compared with iliac crest allografts.
2. The implants placed in the maxilla were 195 (74.4%), whereas 67 (25.6%) implants were inserted in the mandible. The failures were 14 (7.2%) in the upper and 10 (14.9%) in the lower jaw. No statistically significant effect dealing with different sites could be found ($P = 0.2901$, mandible vs maxilla HR = 2.07, 95% CI = 0.54–8.00) (Fig. 2).
3. Overall, 160 (61.1%) implants were placed in the female patients, whereas 102 (38.9%) implants were positioned in the male sample. The failures were 22 (13.7%) in women and 2 (2.0%) in men. The sex effect on survival resulted in a marginally statistically significant difference ($P = 0.0581$, females vs males HR = 7.18, 95% CI = 0.94–55.12) (Fig. 3).
4. When considering age categorized on the median value (≤55/>55 years), 125 (47.7%) implants were positioned in patients aged 55 years or below. The failures were 6 (4.8%) and 18 (13.1%), respectively. The age effect resulted in a statistically significant difference ($P = 0.0340$, ≤55 vs >55 years HR = 4.10, 95% CI = 1.11–15.10) (Fig. 4).

DISCUSSION

The use of FFB allografts in oral implantology is increasing; however, only few studies have analyzed possible variables that might compromise the outcome of the rehabilitation.[14,19] Accordingly, this study was designed to assess the influence of various risk indicators on the failure rate of implants placed in sites augmented with FFB appositional block grafts. To identify possible predictors, a retrospective analysis over 262 dental implants placed in augmented ridges was conducted. According to the Kaplan-Meier estimator, the implant survival rate was 90.84% with a maximum follow-up of 6.8 years. This result corroborates with those reported in recent literature studies. Franco et al[19] retrospectively evaluated 114 double-etched implants inserted into FFB grafts positioned in both jaws, reporting a survival rate of 96.5% over a mean follow-up of 23 months. Carinci et al[16] analyzed the clinical outcome of 287 implants placed in resorbed maxillae augmented with FFB grafts and found a survival rate of 98.3% over a mean follow-up of 26 months. The same research group obtained a survival rate of 96.8% over a mean follow-up of 20 months on a series of 63 implants inserted in mandibles reconstructed with FFB onlay grafts.[20] When the survival rate was interrelated with possible predictors of implant failures, interesting results emerged from the Kaplan-Meier analysis.

Considering the donor site, no statistically significant differences were found between the iliac crest and the femoral epiphysis ($P = 0.7194$). Clinically, allografts harvested from both the hip and the femur seemed to be a predictable alternative to autogenous bone grafts when used for alveolar ridge reconstruction before implant placement. The reliability of the femoral head to repair osseous defects was pointed out in a case series by D'Aloja et al,[21] who found good osseointegration of the grafts with no signs of tissue necrosis or immunological reactions. Subsequently, the same group treated 14

patients with FFB grafts, reporting an overall success rate of 100% when implants were placed from 4 to 8 months after the reconstructive procedure. No complications during the implants placement occurred, and good osseointegration was observed in all cases.[22] So far, as supposed by Spin-Neto et al, the real histological behavior of clinical-size implants toward the osseointegration process in femoral head FFB grafts still remains unknown. This concept could probably be extended to iliac crest allografts, which have nevertheless shown comparable outcomes. Viscioni et al retrospectively evaluated 133 standard-diameter implants inserted into 41 patients who underwent reconstructive procedures with FFB harvested from the hip. The authors reported a survival rate of 99.2% over a mean follow-up of 23 months stressing the reliability of the iliac crest donor site.[23] With respect to a direct comparison between femoral epiphysis and iliac crest, only a limited number of studies have been identified, and from a clinical perspective, the level of evidence is weak. Neovascularization represents an important issue associated with new bone formation. A significantly higher percentage of newly formed vessels in the FFB allograft from the femoral head than in the iliac crest could be found, which suggests that the greater bone resorption and bleeding observed at the second-stage surgery when femur FFB blocks were used may be explained by the different grade of the angiogenetic process.[13] Therefore, although the implant survival rate was comparable, it seemed that a different histological behavior could be found between the 2 sources in relation with their different microstructures. In the study mentioned above, significant differences were evident for the percentage of total bone and nonmineralized tissue, which resulted higher in the iliac crest and in the femoral head, respectively.[13] This could demonstrate the greater bone resorption pattern and bleeding of the femur FFB when compared with the hip allografts that was observed in this study. Thus, although the healing time was the same for the 2 donor sites, it is reasonable to expect that faster incorporation of the graft might be found when femoral head allografts are used. This might be explained by the different characteristics of the 2 grafts. The femur's head consists of cancellous bone coated with a thin layer of compact bone that is not maintained during the bone segment shaping; the iliac crest has both cortical and cancellous parts. This different cortical-to-cancellous bone ratio, together with different remodeling of cortical bone compared with cancellous bone, could influence graft integration.[24] For such reasons, it is our opinion that a differentiated healing time between the 2 donor sites should be taken into account. Particularly in case of hip allografts, a higher failure rate in graft incorporation and/or implants osseointegration may occur when a reduced healing time before implant placement is observed. However, according to Rodella et al, because evidence is lacking, further studies are needed to assess how, where, and whether there should be specific guidelines regarding the right choice of harvesting the bone from a specific donor site over another.[25]

When the implant recipient site was compared, a statistically significant difference could not be found ($P = 0.2901$); however, a higher failure rate was found in the mandible when compared with the maxilla (14.9% vs 7.2%). To the best of our knowledge, most of the studies currently available in the literature have focused on a single jaw, making a direct comparison difficult to perform, because the maxillary bone has greater vascularization and the FFB has a greater chance to integrate at the recipient site.[26] D'Aloja et al[22] performed 14 bone reconstruction procedures, 12 (86%) on the maxilla and 2 (14%) on the mandible, using both blocks and morcellized FFB allografts, reporting an overall success rate of 100%; however in our opinion, the results were not comparable because of the limited sample size. The results reported in this study are in accordance with those obtained in a retrospective study by Franco et al,[14] in which the site of the graft did not statistically affect the clinical outcome. The same group evaluated 114 double-etched implants inserted in 28 patients: 32 (28.1%) were placed in the mandible and 82 (71.9%) in the maxilla. Two implants failed in the posterior maxilla, as well as in the posterior mandible. In agreement to the findings of this study, no statistically significant differences in terms of recipient sites were found.[19] A higher number of patients were enrolled in a subsequent retrospective study by Viscioni et al, in which 23 (17.3%) implants were placed in the mandible and 110 (82.7%) were inserted in the maxilla. No statistically significant differences between the 2 jaws or among tooth sites could be detected, supporting the results reported in this study.[23]

Unexpectedly, relevant differences were found when interrelating survival with the variables sex and age. Failures were higher in the female sample with respect to the male group (13.7% vs 2%, respectively), with a marginally statistically significant difference ($P = 0.0581$). In addition, when considering the age categorized on the median value ($\leq 55/>55$ years), older patients exhibited a higher proportion of failures (4.8% vs 13.1%, respectively). In this comparison, the age effect was statistically significant ($P = 0.0340$). Although a multivariate analysis interrelation between age and sex could not be performed because of the limited number of events occurred in the male group ($n = 2$), it might be deduced that postmenopause hormonal imbalances affecting female patients associated with physical, endocrine, and metabolic changes in older adults may negatively affect bone healing. Accordingly, August et al[27] reported a 41% less failure rate of maxillary implants in the estrogen-supplemented postmenopausal women compared nonsupplemented women. However, rather than aging itself, the specific nature of the disease process, such as osteoporosis, and local bone quality and quantity at the implant site, mostly related to aging, may be considered more important for successful dental implant treatment.[28] When the results reported in this study were contrasted with similar retrospective studies, it seemed that the survival rate was not influenced by sex[19,20]; furthermore a better outcome for female

patients was also reported.[16] In our opinion, because of a higher risk of implant failure associated with osteoporosis and aging, these patients might best be served preoperatively by appropriate referral and endocrinological examinations.

The timing of implant failures deserves some words to be spent. Indeed, all of the implants that have been lost in this study failed to osseointegrate within the first 6 months after their placement. In accordance, other studies have reported a similar trend,[16,20] underling that infection or lack of osseointegration was the main reasons of failures while an increased marginal bone resorption was generally insufficient to provoke implant loss. Analyzing the timing of failures, which was strictly on the first 6 months after implantation, we speculated that the problem could also be related to the quality of the regenerated bone, which may have presented an inadequate quantity of vital cells, necessary to promote the integration of the graft. Differently, once the graft appeared to be clinically well integrated, no more failures occurred, highlighting how the integration of the block graft plays an essential role for future osseointegration of the implants. As a confirmation of this, Pereira et al[29] found a positive strong correlation between healing time and vital bone percentage. Therefore, a healing time of at least 6 months between graft and implant placement should be respected. This was recently supported by Dias et al,[26] who observed good vascularization and bleeding of the blocks 6 months after grafting.

CONCLUSION

The use of FBBAs in preprosthetic surgery constitutes a predictable alternative to autogenous bone grafts, reducing patient morbidity. No statistically significant differences could be found when using femoral epiphysis or iliac crest allografts irrespective of the anatomical position of the implants. Care has to be taken especially in case of female and/or elderly patients, because these variables coupled together constituted a risk factor that could negatively influence the survival rate of the implants.

DISCLOSURE

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the article.

APPROVAL

Because of the retrospective nature of this study, our Institutional Review Board and the local Ethics Review Committee did not require any authorization request to proceed with the study. In any case, signed informed consent was obtained from each patient included in this study.

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