The use of computer-guided flapless dental implant surgery (Nobel guide®) and immediate function to support a fixed full-arch prosthesis in fresh frozen homologous bone grafted patients: a retrospective cohort study with 5 to 8-year follow-up

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The introduction of computer-assisted and guided surgery has radically improved the possibility of using all available bone for implant support, reducing the need for extensive grafting procedures and allowing for better implant placement and restoration. Moreover, fresh frozen homologous bone (FFB) grafts have shown good osteoconductive properties and biocompatibility with results comparable to autologous bone patients. The purpose of this retrospective cohort study was to evaluate the survival and the success rate of implants and related fixed full arch prosthesis at the 5 to 8 years follow-up when performed with immediate function using a flapless surgical procedure and computer-aided technology (NobelGuide®, Nobel Biocare® AB, Goteborg, Sweden) in patients previously treated with FFB grafts; treated at the University of Verona with the NobelGuide® system from January 2007 to December
2012 with at least 5 years follow-up were reviewed. Survival implants and survival prosthesis' percentage reached 95% in a 5 to 8-year period. This study indicates that patients previously augmented with FFB graft for maxillary or mandibular bone atrophy can be safely treated with implant supported prosthesis based on the NobelGuide® protocol, with the aid of computer-generated guide.

The introduction of computer-assisted and guided surgery has radically improved the possibility of using all available bone for implant support, reducing the need of extensive grafting procedures and allowing for better implant placement and restoration, both in grafted and nongrafted sites (1). Indeed, now it is possible to make use of all the available osseous volume during the planning and the surgical phase. This approach allows an accurate placement of implants using a flapless technique under the guidance of a surgical template, generated from the preoperative virtual planning of the implant. In this way, precise implant installation is possible through a thick layer of soft tissues, having the drills and the implants guided by a computer-generated surgical guide.
The planning is also useful to avoid obstacles or structures in the reconstructed bone such as screws, osteotomy sites and discontinuity of bone segments (2). This technique has shown to be as successful as traditional implant surgery with flap access (3-5).
Moreover, the beneficial effect of flapless surgery without exposure of the periosteum may minimize bone resorption (6-19).
However, a major prerequisite for a restoration driven implant surgery remains the availability of bone of adequate length and width, suitable for the proper placement of implants of sufficient length. Physiological resorption of the alveolar processes of the maxillary bones can lead to insufficient bone volume, especially in patients who have been edentulous for a long period of time, making it virtually impossible to place implants (20). Several solutions have been proposed to obviate bone volume deficiency (2, 21-26). The endpoint of most of these techniques is the augmentation of available bone volume with onlay and inlay grafts (27-28).
Recently the use of fresh frozen homologous bone (FFB) grafts have shown good osteoconductive properties and biocompatibility with results comparable to those of autologous bone but with a reduced morbidity, lower surgical risk and shorter operative time (29) without modification of the traditional techniques (30-31). Histological studies have confirmed these results, showing the presence of new bone and osteoclast activity 4 months after grafting, with 80% mature bone observed after 12 months (32). FFB grafts resulted in volumes of bone similar to those obtained with autologous bone grafts, however the amount of residual bone particles seems to be greater, which may indicate a slower remodeling process (33).
FFB is a widely used substitute for autologous bone especially in large reconstructions when block grafts are indicated (34). The behavior of FFB when used in combination with computer guided implant surgery is still not well understood, as studies are absent in the literature. Due to the extended regenerations of the jaws FFB was the first choice and it was used even in the sites where it was not necessary to reduce the differences between the grafted sites. The purpose of this retrospective cohort study was to evaluate the survival and the success rate of implants and related fixed full arch prosthesis at the 5 to 8 year follow-up when performed with immediate function using a flapless surgical procedure and computer-aided technology (NobelGuide®, Nobel Biocare® AB, Goteborg, Sweden) in patients previously treated with FFB grafts.

MATERIALS AND METHODS

Inclusion criteria: clinical charts of patients with edentulous arches treated at the University of Verona with the NobelGuide® system from January 2007 to December 2012 with at least 5 years follow-up were reviewed. Patients› medical history and clinical data were collected, together with panoramic radiographs and CT scans. The inclusion criteria used were the following: medical history negative for pathologies generally contraindicating implant surgery (35-38), initial edentulism and previous pre-prosthetic surgery with application of fresh frozen bone grafts to restore a sufficient bone volume for implant rehabilitation of the jaws (Fig. 1-3). In particular, pre-prosthetic surgical treatment should have been carried out by the following techniques: ridge preservation with filling of the extraction sockets with FFB bone chips (A) (39) posterior bilateral maxillary sinus augmentation with lateral window with bone chips (B) (40-42) together with anterior maxillary bone block veneer surrounded by bone chips (C) (43-44) Le Fort I osteotomy with inlay technique of Keller (D) (29). In addition, all implant/prosthetic treatment and follow-up should have been carried out according to the NobelGuide® protocol (1). All the surgeries were performed by the same operator.

Grafting material: the material used in the pre-prosthetic surgical treatment was FFB. The FFB, obtained from the Veneto Tissue Bank in Treviso (Italy), is a mineralized, non-irradiated and only disinfected, frozen homologous bone. The bone harvesting was obtained from the anterior and posterior iliac crest, in the first 12 hours after donor death. The bone was then disinfected, for at least 72 hours at -4°C, in a polychemotherapeutic solution. The sample was then subdivided into cortico-medullary blocks or morcellized, packed in double sterile casing, and frozen at -80°C (45). Surgical procedure: six months after FFB grafts, if plates or osteosynthesis screw were used, these were removed and a temporary total or partial removable acrylic resin prosthesis was made.

NobelGuide® procedure has been described previously for dentate and edentulous patients (46-50). Based on computer planning a fixed metal-acrylic resin complete denture was constructed prior to the implant surgery and was immediately adapted and inserted after surgery. The technician inserted several gutta-percha markers (Hygienic, Coltène/Whaledent Inc. Mahwah, NJ, USA) in small holes with the diameter of 1.5 mm made in the prosthesis, as indicated by the NobelGuide® protocol. The markers are necessary to the software (Procera® or NobelClinician®, Nobel Biocare® AB, Goteborg, Sweden) for coupling two CT scans: one of the patients and one of the prosthesis. Once the modifications on the denture were complete, it was possible to send the patient to a radiological centre where a double CT scan was carried out: one of the patients wearing the prosthesis/radiological guide, correctly inserted, and one of the prosthesis alone. After 3D reconstruction of the CT images in the software, the Procera® or NobelClinician® software allowed us
to plan the implant virtually according to the desired prosthetic result (Fig. 4-5). The surgical operations were performed under localregional anesthesia. The implants used were Brånemark System MKIII® (MKIII), Brånemark System Groovy® (Groovy) e NobelSpeedy Groovy® (NobelSpeedy) (Nobel Biocare® AB, Goteborg, Sweden) with an oxidized surface (TiUnite®, Nobel Biocare® AB,
Goteborg, Sweden). Once the template was stabilized using a surgical index and three anchor pins, the flapless implants were inserted, according to the drill sequence specific for the type of implant planned. The template was then removed and the correct position of the implants was checked and temporary abutments were screwed in place.

The prosthodontist relined a prefabricated provisional fixed metal-acrylic complete denture, including the temporary abutments in the prosthesis with resin and made it functional by adjusting occlusal contacts. One gram of amoxicillin/clavulanate (GlaxoSmithKline plc., Brentford, Middlesex, United Kingdom) every twelve hours for 6 days was prescribed. The patients were then dismissed. Sutures were removed after 15 days and the patients were given oral hygiene instructions. The main follow-up appointments were delivery of the final fixed prosthesis (6-12 months), professional oral hygiene every 6 months, and regular control once a year to maintain good oral health and monitor the absence of complications and compliance with oral hygiene instructions. A radiographic evaluation (orthopantomogram or periapical radiograph of the implants) was performed each year. Clinical assessment. Implant survival was considered if these conditions were satisfied (from Malò 2007 modified) (51):

1. Presence of the implant as planned in the NobelGuide® treatment plan after surgery and during follow-up.
2. Clinical stability of the implant in the surrounding peri-implant bone at follow-up (bridge removed and implants individually checked).
3. Satisfactory function without any discomfort to the patient at follow-up.
4. No suppuration or infection present at follow-up.
5. No radiolucent areas around the implants at follow-up.

Implant success defined in the scientific literature as the absence of infectious complications affecting peri-implant soft and hard tissues and the absence of more than 2 mm of peri-implant bone loss (PBL) (52-58) was considered. It was also recorded implants Pocket Probing Depth (PPD), soft tissue dehiscence, Mombelli Plaque Index (mPI) and the Mucosal Plaque Score (59-61). Survival of the prosthesis was considered if all these conditions were met immediately after surgery and during the follow-up:

1. Presence in the mouth of the original prosthesis (in-situ criterion) (62).

2. Presence of at least all the anterior teeth (for aesthetics) and two posterior occlusal units (premolar/molar) for function (59) as planned in the NobelGuide® treatment plan. Clinical assessments were performed from two calibrated operators. Statistical analysis: the nominal and ordinal variables were tested with Fisher's Exact Test to evaluate association of implant failures due to diabetes or smoking. Peri implants parameter variables clinically and radiologically recorded were described using an Average and Standard Deviation. Bone loss Level (PBL) analysis was performed using Spearman rank to evaluate correlation between keratinized tissue width (67) and bone loss.
The Kruskal–Wallis Test was used to evaluate if the bone loss amount was correlated to the graft type or implants type. The Wilcoxon Mann-Whitney Test was used to evaluate the different bone loss amount surrounding tilted implants or straight ones. We decided to use non parameters Test because PBL variable resulted asymmetrically distributed; moreover the Shapiro-France tests and Shapiro-Wilk are highly significant ($p < 0.001$), suggesting a marked deviation from normality, and also was found a certain instability of variance between the groups in the study.
A possible correlation between keratinized mucosa width and plaque index, bleeding index and probing depth values was made using the Spearman test. The Wilcoxon-Mann-Whitney test was used to highlight differences between the maxillary torque and mandibular torque and maxillary and mandibular bone loss level. The significance for all tests was set at a p-value less than 0.05 (α=5%).

RESULTS

Characterization of the population: a total of 45 patients met the criteria of inclusion, receiving a total of 239 implants. NobelSpeedy was inserted significantly more in the maxilla compared to MK III and Groovy ($p<0.001$). The patients' follow-up ranged from 5 to 8 years (mean 69 months). (Fig. 6-8) The median age was 64 (interquartile range: 59-69) years (minimum 43, maximum 78 years), 9 patients were male (20%) and received 35 implants, 36 were females (80%) and received 204 implants. The median number of implants per prosthesis was 4 (range 4-6). A total of 54 full arch prosthesis were made, 34 in the maxilla and 20 in the mandible. Three patients (6.7%) were smokers (considered as current exposure to smoking at intake) and received a total of 17 implants.
Implant survival: at 5 years was 94.6%. During the 5 to 8-year follow-up 13 failures (5.4%) were detected. Eight failures happened in the first year after NobelGuide® surgery. Seven patients (15.5%) had at least one failure. One patient had 5 failures. The patient with 5 failures was a heavy smoker of up to 60 cigarettes a day treated with ridge preservation (A) but the failure was immediate due to fracture of the complete maxilla during implant placement which precluded the possibility to proceed with the NobelGuide® protocol: the implants had to be removed and the maxilla stabilized with osteosynthesis. Five of the failures were detected at implant placement, due to the fracture of jawbone during surgery, two were detected at 6 months, four at 60 months, and one at 72 months. The low number of failures precluded a detailed analysis of risk factors.
Failures tended to be more frequent in the maxilla (3.3%) than in the mandible (2.1%), but the difference did not reach statistical significance ($p=0.35$).
However, data showed that failures occurred more frequently in implants placed in smokers than non-smokers ($p = 0.010$, Odds ratio 12.7). Five implants (29.4%) of 17 in smokers (28.5%) failed. Only 8 fixtures out of 222 (3.6%) in non-smokers failed. Implants placed as the distal abutment of the prosthesis were more likely to fail ($p=0.04$, Odds ratio 3.8). Torque level at implant placement was not
related to implant failure ($p=0.08$). Implant success At the 5-8 year follow up was 85%. Two hundred three implants out of 239 reach success. The mean PBL was 1.86 (dev. St. ± 1.24 range 1.55-2.3). Bone resorption was considerably higher ($p<0.001$) in the maxilla. PBL was significantly influenced by different grafting procedures ($p<0.01$), and by different type of fixture ($p<0.01$) (Fig. 9).
Soft tissues The mean PPD was 2.12mm (dev. St.±1.04 range 1-6). The mean mPI was 0.74 (dev. St.±0.74 range 0-3). The mean mBI was 0.43 (dev. St.±0.55 range 0-2). The mean soft tissue dehiscence around fixtures was 0.35mm (dev. St.±0.86 range 0-5). The average
MPS was 1.15 (dev. St.±0.38 range 0-3). The mean width of KT was 1.23mm (dev. St.±1.05 range 0-4) but did not present a significative correlation with mBI, mPI, MPS ($p >0.01$).

Prosthesis survival

One out of 20 (5%) mandibular full arch fixed metal-acrylic prosthesis failed during the follow-up. Otherwise in the 34 maxillary full arch fixed prosthesis there was not failures. As for implant failure, the low number of prosthetic failures precluded a detailed analysis of risk factors.

Miscellaneous complications

One patient experienced a fracture of the surgical stent in the mandible which was repaired during the surgery. The position of 2 implants in another patient was slightly aberrant from the planned position, resulting in a minor vestibular bone dehiscence at implant placement. The complication did not preclude achievement of sufficient torque, implant integration and a favorable emergence profile for the final prosthesis.

One patient had the fracture of maxillary bone during implant surgery. There was the failure of five implants also, which had been removed and after a 6 month rigid fixation, it was possible to go on with the procedure and deliver a fixed prosthesis to the patient. In the other patients, who had the failure of a single implant, it was possible to maintain the fixed restoration removing the failed implant and inserting another one. There was one prosthetic failure in one patient, who did not accept the restoration. In one patient there was the fracture of a resin tooth of the prosthesis. Three implants (1%) had a positive diagnosis for periimplantitis. A total of 13 implants failed (5%). Table I, Table II, Table III, Table IV and Table V.

DISCUSSION

The cumulative survival rate was 95%. Implant success rate was 85%, 20 implants (8%) did not show signs of inflammation or suppuration but had a PBL value higher than those reported in the success criteria also those were not classified successful. Three implants (1%) had a positive diagnosis for periimplantitis. During the 5 to 8-year follow-up 13 failures (5%) were detected. The low number of failures precluded a detailed analysis of risk factors. Failures had a tendency to be more frequent in the maxilla (3.3%) than in the mandible (2.1%), 8 failures in the maxilla happened in the first years after NobelGuide® surgery, while 5 failures in the mandible happened 4 at 5 years and 1 after 6 years (1). During the follow-up, implants placed in smokers were more likely to fail than implants placed in non-smokers (28.5% vs 3.6%). The lower survival rate of implants placed in smokers has been well documented in the literature (62). In our study survival of implants placed in reconstructed bone with FFB was comparable to those obtained with autologous bone grafts (64), FFB grafts (65) and NobelGuide® treatment on native (1), or fibula reconstructed bone (66). In fact, it has been shown that the use of various dentoalveolar bone grafting procedures to reconstruct deficient implant recipient sites are not an independent risk factor for implant failure (68). Peri-implant soft tissues had been investigated, particularly mBI, mPI and MPS

are index to identify different degrees of soft tissue inflammation and condition allowing the clinician to evaluate the need of additional treatments. The values of these index showed an average good condition of soft tissues around implants, which is fundamental for the long-term maintenance of full arch prosthesis implant supported. Peri-implant Bone Loss was evaluated at 1 year and at 5 years after implants load. At 1 year the average PBL values were of 0.66±0.65mm while at follow up of 1.86±1.24mm, these data agree with success criteria (51). Bone resorption resulted higher in the upper jaw (58), this is due to the lower quality and minor density of the of maxillary bone. In literature it is even reported a higher risk of failure of implants positioned in the maxilla (69-73).

In this study, it has also been evaluated the Keratinized Tissue (KT) width around dental implants, as a matter of fact this is a variable of emergent interest in implant therapy. In literature there are discordant results about the possible relations between KT and implant health, in our study there was not a significative relationship between Keratinized tissue width surrounding implants and PBL. Implant position did not condition significantly PBL, particularly tilted implants compared to straight did not showed a meaningful major PBL (74-75).

The type of implant and the different grafting procedure influenced significantly bone resorption. Speedy Groovy manifested a higher resorption but this data must be argued because those implants had been used mainly in the maxilla. MK III Groovy showed a lower bone resorption than Speedy Groovy and MK III. The grafting procedures with a significantly greater PBL were sinus lift and Le Fort I inlay still for the same reason of lower quality of maxillary bone. Initial torque level at implant placement was not related to implant failure. Furthermore, torque level may not be a proper measurement of implant primary stability.

In one patient 5 implants failed because of fracture of the basal bone at implant placement. The reason for this is still unclear but it may have speculated that the presence of a surgical stent in an atrophic maxilla may transfer the stress exerted by the implants on basal bone. This, together with the fact that no fracture of grafted bone surrounding the implant occurred in our patients, may indicate that complex implant/surrounding bone is safely stabilized by the stent, but the resulting stress may be exerted outside the ferrule of the stent. One patient experienced a fracture of the surgical stent in the mandible which was repaired during the surgery. Fracture of the surgical stent has already been described as a possible complication which can be related to insufficient thickness or imperfect fitting of the stent in relation to the amount of stress generated by implant insertion (76). In another patient the position of 2 implants deviated slightly from the planned position. This complication did not preclude achievement of sufficient torque, implant integration and a favorable emergence profile for the final prosthesis.

An individual error can occur at each step of the guided surgery protocol, starting from the radiographic guide to the placement of the implant leading to incorrect implant placement (9,77-78). Particularly stereolithographic surgical guide stents have the potential to be dissimilar from the original scan denture. The ISO threshold setting in the conversion software is a very sensitive component of the production process (79-81). The only prosthetic failure occurred in one patient who did not accept the restoration, also it was removed and substituted with a mobile device. In one patient there was the fracture of a resin tooth of the full arch fixed prosthesis, hence the prosthesis was repaired through the

substitution of the broken tooth. Based on the results of our retrospective study, we can conclude that:
1. Survival of implants was high, reaching 95% in a 5 to 8-year period.
2. Survival of the prosthesis was high reaching 95% in a 5 to 8-year period.
3. Factors significantly related to failure of the implants were smoking.
4. Factors significantly related to PBL were implant position (maxillary or mandibular), type of implant and graft procedure.
5. A higher torque level at implant insertion did not correspond to a lower risk of implant failure.

This study indicates that patients previously augmented with FFB graft for maxillary or mandibular bone atrophy can be safely treated
with implant supported prosthesis based on the NobelGuide® protocol, with the aid of computergenerated guide. This procedure may be a promising treatment option, offering several advantages to both clinicians and patients, while keeping the same degree of predictability in terms of torque levels, survival and success of the implants and the prosthesis compared with conventional treatment.

However, in our study the low number of implants and prosthetic failures precluded a detailed analyses of risk factors associated to these failures. Before drawing any general conclusion, the benefit of the procedure should be further evaluated by prospective clinical trials where the possible endpoints of the treatment should be more thoroughly evaluated and compared with conventional protocols on the same study population.