A retrospective 10-year mean follow-up of implants placed in ridges grafted using autogenous mandibular blocks covered with bovine bone mineral and collagen membrane

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Abstract

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Objectives: to report the clinical and radiographic outcomes of patients presenting with edentulous and atrophic ridges and treated with autogenous mandibular bone blocks and rehabilitated with implant-supported prostheses.

Materials and methods: from 1997 to 2015, 75 patients presenting with bone defects of the jaws were grafted with autogenous mandibular bone blocks. One-hundred-eighty-two implants were placed 4 to 12 months later and loaded 3 to 10 months later: the mean follow-up was 10 years (range: 3-16 years). The following outcomes were recorded: a) complication rate of the reconstructive procedure; b) bone graft resorption before implant placement; c); peri-implant bone resorption; d) implant-related complications; e) implant survival and success rates.

Results: Post-operative recovery was uneventful in the majority of patients. An early dehiscence occurred in three patients, but with no significant bone loss, while 3 experienced temporary paresthesia. The mean vertical and horizontal bone resorption before implant placement was 0.18 mm (standard deviation (SD)=0.43) and 0.15 mm (SD=0.42), respectively.

The mean peri-implant bone loss ± standard deviation was 1.06±1.19 (range 0.00 to 5.05) at patient level, and 1.11±1.26 (range 0.00 to 5.20) at implant level.

Two implants in 2 patients lost integration and were removed; 10 implants in 7 patients developed peri-implantitis, but healed after surgical treatment.

The cumulative implant survival and success rates were 98.11% and 85.16%, respectively.

Conclusion: implants placed in areas reconstructed with mandibular bone blocks presented survival rates consistent with those obtained for implants placed in native bone.

1 – INTRODUCTION

Bone defects of the jaws derived from the resorptive changes that follow tooth extraction, long standing edentulism, periodontal disease, infections, or trauma sequelae, are a common finding in partially or totally edentulous patients seeking for an implant-supported rehabilitation (Bergman, & Carlsson, 1985; Schropp, et al., 2003, Araujo, & Lindhe, 2005; Pietrokovski, et al., 2007; Chiapasco, et al., 2009; Hammerle, & Tarnow, 2018).

When the lack of residual bone volume is such that it does not make it possible to place even short and/or narrow diameter implants, or vertical and/or horizontal relationships are so unfavourable to compromise the final prosthetic outcome, regeneration/reconstruction procedures of the residual bone may be indicated (Chiapasco, et al., 2009; Benic, & Hammerle, 2014).

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Different techniques have been proposed over the years, including guided bone regeneration (distraction osteogenesis (Chin, & Toth 1996; Chiapasco, et al., 2004), grafting autogenous unaltered tooth material (Pohl, et al. 2017; Ramanauskaite, et al. 2019), and onlay grafting with autogenous bone blocks (Von Arx, & Buser, 2006; Chiapasco, et al., 2009; Esposito, et al., 2009; Nkenke, & Neukam, 2014; Schwartz-Arad, et al., 2016).

These procedures appear to be safe and predictable, with survival rates of implants placed in the reconstructed bone consistent with those obtained with implants placed in pristine bone (Donos, et al., 2008).

Among these, the use of autogenous bone blocks taken from the mandibular ramus is one of the most frequently used procedures. Furthermore, the combination of autogenous blocks with particulated xenografts such us bovine bone mineral (BBM) and resorbable collagen membranes have shown to provide better outcomes in terms of maintenance of initial bone gain over time as compared to the use of bone blocks only (Proussaefs, & Lozada, 2003; Von Arx, & Buser, 2005; Jensen, & Terheyden, 2009; Cordaro, et al., 2011; Wiltfang, et al., 2012; Milinkovic, & Cordaro, 2014; Sanz-Sánchez, et al., 2018; Chiapasco, et al., 2018, Elnayef, et al., 2018).

Favourable results have been reported in terms of bone volume stability and implant survival rates over time, ranging from 60% to 100% for machined surface implants (mean: 81.6%) and from 90% to 100% for rough surface implants (mean: 94.2%) (Clementini, et al., 2011; Chiapasco, et al., 2014).

However, some limitations were observed, including: a) acceptance by patients, b) morbidity related to the procedure, and c) potential complications both in the donor and the recipient sites, such as wound dehiscence and exposure of the graft (Cordaro, et al., 2002; Chiapasco, et al., 2006, 2009; Cordaro, et al., 2011).

The aim of this retrospective longitudinal cohort study, is to present the medium- to long- term clinical and radiographic results of implant-supported prostheses in patients reconstructed with autogenous bone blocks taken from the mandibular ramus, covered with bovine bone mineral particles and a collagen membrane. The following outcomes were recorded: a) complication rate of the reconstructive procedure; b) bone resorption before implant placement; c); peri-implant bone resorption; d) implant-related complications; e) implant survival and success rates.

2 - MATERIAL AND METHODS

2.1 - Study design

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This study was a retrospective longitudinal cohort study evaluating short and medium-to-long term outcomes of patients affected by atrophic edentulous jaws, treated with mandibular ramus block grafts covered by bovine bone mineral and a collagen membrane, and rehabilitated with dental implants.

An initial informed consent was obtained from all patients prior to treatment, providing a detailed description of the procedure, including potential side effects and complications.

In 2017 the authors presented a request to the Ethic Committee of the University of Milan, in order to obtain permission to use all data collected over the years as regards these patients, including charts, radiographs, et cetera. Once obtained, the authors contacted all the previously treated patients (with the exclusion of the unreachable ones) to obtain permission to publish their data in a scientific publication.

A new informed consent, including the purpose of the recall program, the necessity of clinical and radiographic controls, and the patients' authorization to use their data for statistical analysis was signed by all of them.

The study was performed in accordance with the principles stated in the Declaration of Helsinki and the Good Clinical Practice Guidelines, and was approved by the Ethics Committee of the University of Milan, Italy (Registration No. 2016/ST/244; Protocol of Final Approval No. 7347/2017).

2.2 - Study Population

From 1997 to 2015, 75 patients (21 males, 54 females) aged between 18 and 78 years (mean: 49 years, STD 14.7), requesting to rehabilitate an edentulous area in the upper and/or lower jaw with an implant-supported dental prosthesis, and presenting with relevant horizontal and/or vertical bone defects in the edentulous area, were recruited for this study. In 7 patients, reconstructive procedures were performed in two sites (for a total of 82 sites).

Patients were enrolled if presented a bone atrophy at the edentulous site whose severity was incompatible with: a) implant placement with simultaneous bone augmentation; b) placement of short (≤6 mm) or narrow (<3 mm) implants; c) sinus floor elevation with no reconstruction of the alveolar bone crest.

Adequacy of the residual bone volume was defined based on the possibility to place dental implants in a prosthetically driven position.

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Initial patient screening included: a) evaluation of the residual dentition and periodontal status; b) intra-oral photographs; c) panoramic and peri-apical radiographs; d) preoperative impressions, study models, and manufacturing of a diagnostic wax- up to optimize the final prosthetic restoration. A computed tomography was performed to three-dimensionally assess the residual bone volume in the edentulous spaces.

Exclusion criteria for the surgical procedure were the following: a) severe kidney and/or liver disease; b) congenital or acquired immunodeficiency; c) ongoing antiblastic chemotherapy at the time of first examination; d) sequelae of radiotherapy in the head and neck area; e) oral mucosa diseases, such as lichen planus; f) full mouth plaque score (FMPS) and full mouth bleeding score (FMBS) < 20%; g) non-compliant patients; h) tobacco abuse (>10 cigarettes per day) or alcohol abuse; i) non compensated diabetes; j) active periodontal disease at the time of first examination (in these cases, patients underwent etiologic therapy and motivation in personal oral hygiene and were re-evaluated for surgical treatment).

Ongoing bisphosphonate therapy with oral or parenteral administration was inserted as an exclusion criterion since 2007.

Exclusion criteria for enrolment in this study were the following: a) patients' inability to attend an updated follow-up visit with clinical and radiographic evaluations; b) patients' inability to compile a questionnaire on patient-reported outcome measures; c) loss of clinical data concerning the surgical and prosthetic treatments. Reasons for exclusion were recorded during data collection.

2.3 - Clinical Protocol

All patients were treated by the same surgeon (MC) and the same prosthetic team. Bone grafting and subsequent implant placement were performed in sterile conditions under local anaesthesia or under general anaesthesia with naso-tracheal intubation, according to both patient's preference and defect extent**.** In all patients, re-opening of submerged implants was performed under local anaesthesia. The following steps were adopted during treatment.

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2.3.1 - Pre-operative Patients Preparation

All patients were prepared to both the reconstructive procedure and the second stage implant surgery according to the following protocol: (a) professional oral hygiene 2 weeks prior to surgery; (b) local antisepsis with 0.2% chlorhexidine mouthwashes starting 3 days before surgery; and (c) antibiotic prophylaxis consisting of oral administration of amoxicillin and clavulanate (2 g) 1 hour before surgery. In case of general anaesthesia, antibiotics were infused intra-venously at the time of induction.

2.3.2 - Reconstructive Procedure

The following protocol was adopted:

1. Access to the mandibular ramus for bone harvesting was obtained through an incision following the "linea obliqua externa" of the ascending ramus and the elevation of a full thickness flap. A cortico-cancellous bone block was harvested using piezo-electric instruments or fine fissure burs, combined with fine chisels. Moreover, autogenous bone chips were locally collected with a manual bone scraper. Care was taken to avoid any damage to the inferior alveolar nerve, whose tri-dimensional position had been evaluated preoperatively through computed tomography scans. The harvested bone was kept into sterile saline and the access was closed with simple interrupted sutures (silk or PGA 4/0).
2. The defect site was exposed through a full-thickness crestal incision with mesial and distal releasing cuts. After careful defect debridement and perforations of the buccal cortical walls of the defect with a small round bur, to promote the access of bone marrow cells to the defect, the bone blocks were modelled and adapted to the local anatomy, to correct the horizontal and/or vertical bone deficiency. All sharp edges of the blocks which could increase the risk of dehiscence were accurately smoothed with diamond burs. A sterilised prosthetic stent was utilised in the majority of cases to optimize the reconstruction and allow the subsequent placement of implants in a prosthetically driven way. The blocks were fixed with titanium micro-screws (1.5 mm in diameter) and all remaining gaps between the bone blocks and the recipient sites were filled with autogenous bone particles obtained with scrapers. A mild over-correction of the defect was always performed both during vertical and horizontal augmentations.
3. A layer of slowly resorbable xenograft (Bio-Oss®, Geistlich Pharma, Wolhusen, Switzerland) mixed with autogenous bone chips was placed over the grafts and stabilized with collagen membranes (Bio-Gide®, Geistlich Pharma, Wolhusen, Switzerland) to eliminate sharp edges,

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to harmonize the shape of the reconstructed area, and to reduce the risk of bone resorption (Proussaefs, & Lozada, 2003; Von Arx, & Buser 2005; Cordaro, et al., 2011; Wiltfang, et al., 2012; Sanz-Sánchez, et al., 2018; Chiapasco, et al., 2018, Elnayef, et al., 2018).

4. Periosteal releasing incisions of the flaps were performed to obtain a tension-free and water-tight closure with horizontal internal mattress and simple interrupted sutures using 4/0 or 5/0 silk or PGA.

Based on case variability within the study population, patients could receive, during the same surgical session, adjunctive surgical procedures, as follows:

1. Patients presenting with bone atrophy of the posterior maxilla requiring sinus grafting in addition to a tri-dimensional bone augmentation, received a sinus floor elevation with a lateral approach. Sinuses were grafted with a mixture of particulated autogenous bone and bovine bone mineral (Bio-Oss®, Geistlich Biomaterials,) with a one-to-one ratio, approximately. The bone blocks were then adapted over the lateral access to the sinus, according to local anatomy.

2. Patients presenting with bone atrophy in the posterior edentulous mandible received a single surgical access through an extended trapezoidal flap, which allowed both the harvesting and grafting procedures.

3. Patients presenting with impacted mandibular third molars at the site of harvest, with clinical and/or radiographic signs indicating the need for an extraction (signs of pericoronitis, history of recurrent infections, unfavourable contact with the second molar), underwent tooth removal during the harvesting procedure.

The following postsurgical instructions were prescribed: (a) application of ice packs over the reconstructed surgical site for 6–8 hours after surgery; (b) oral antibiotics (amoxicillin and clavulanate - 3 g per day for 6 days); (c) nonsteroidal anti-inflammatory (NSAIDs) therapy for 3–5 days after surgery (most commonly ketoprofen 80mg or ibuprofen 600mg twice a day); paracetamol 1000 mg was prescribed to patients unable to assume NSAIDs; (d) cold and liquid diet for the first 2 days after surgery and a soft diet until suture removal; (e) 0.2% chlorhexidine mouth rinses, twice per day for 21 days, combined with normal oral hygiene manoeuvres on the remaining dentition (if present); (f) when a concomitant sinus elevation was performed, patients were instructed to avoid any pressure peak in the upper respiratory tract which could have damaged the elevated Schneiderian membrane. This included sneezing with their mouth open,

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avoiding to blow their nose for the first 15 postoperative days, or to fly, to make underwater sports, and recreative activities for 3–4 postoperative weeks.

Sutures were removed 14–21 days after surgery. For 6 postoperative weeks, patients were not allowed to wear any type of removable prosthesis that could traumatize the reconstructed area. Vacuform retainers including resin teeth, Maryland bridges, or conventional bridges on available natural teeth (when available abutments on the adjacent dentition were already present in the patients mouth), were fabricated to provide a purely cosmetic restoration, taking care to avoid any form of occlusal trauma and any compression on the operated area.

2.3.3 - Implant Placement

Four to 12 months (mean = 6 months) after the reconstructive procedure, implants were placed in the reconstructed areas. A surgical template was used to optimize implant positioning according to the prosthetic treatment plan. Titanium screws placed at the time of bone grafting were removed only if their position interfered with implant placement. All implants were placed according to a submerged healing protocol. Postoperative instructions and therapy were equivalent to the ones of the reconstructive procedure.

According to case variability within the study population, patients could receive the following co-exposures:

1. Patients presenting with a lack of keratinised tissue buccal to the implant abutments and/or a reduced vestibule depth in the reconstructed area, received a vestibuloplasty in association with a free gingiva graft harvested from the palate, to improve local anatomy and to create an adequate width of the keratinized mucosa around the implants.

2. Patients presenting with an adequate amount of keratinised mucosa in the reconstructed sites, but a lack of soft tissue volume buccal to the implant abutments, received a bilaminar soft tissue augmentation procedure without vestibuloplasty. An autogenous connective tissue graft obtained through the extra-oral de-epithelisation of a free gingival graft, was placed under the buccal flap elevated for implant re-opening, and was stabilised with resorbable 6/0 PGA sutures.

2.3.4 - Prosthetic Phases

Patients started the prosthetic phases 3 to 10 months after implant placement (mean=4.5 months, SD=1.5). Provisionals were maintained for 3–9 months, to achieve optimal soft tissue

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adaptation and conditioning. Finally, fixed definitive prostheses (cemented or screw-retained) were delivered.

2.4 - Follow-up

During the time following the bone grafting procedure, patients were re-evaluated at suture removal, 1 month after surgery, 3 months after surgery and 2 weeks before implant placement. After implant placement, clinical controls were carried out at suture removal, 1 month after surgery and 2 weeks prior to implant re-opening. After implant uncovering, patients were controlled at the time of suture removal, abutment connection, and at the time of prosthetic loading.

After the start of prosthetic loading, patients were followed for 3 to 16 years, to assess peri-implant hard and soft tissue conditions, the stability of the reconstructed bone, and the onset of implant-related and/or prosthesis-related complications. The recall frequency for patients' maintenance and clinical evaluation was established through a continuous multilevel assessment of the patients risk profile for periodontal and peri-implant disease (Lang, & Tonetti, 2003). The frequency of recall ranged from 3 to 12 months.

Frequency of patients recall prior to the publication of the article by Lang & Tonetti (2003) (13 patients) was arbitrarily set every 3 to 6 months, based on patients previous history of caries and periodontal disease, patients compliance to oral hygiene instructions, and the overall complexity of the treated case.

Peri-apical radiographs were taken immediately after implant placement, at provisional prosthetic load, at prosthetic finalization, and annually thereafter. Radiographic examinations through periapical or panoramic radiographs were performed annually after implant placement.

2.5 – Analysis

2.5.1 - Complication rate of the reconstructive procedure

During the time following bone grafting and prior to implant placement, short-term complications regarding the donor and/or grafting site were recorded in the patients' chart.

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2.5.2 - Bone resorption before implant placement

The volumetric resorption of the grafted sites were estimated intra-operatively at the time of implant placement, adopting the titanium micro-screws used in the reconstructive procedure as the reference. Using a UNC15 periodontal probe, the distance between the screw head and the bone profile was measured after flap elevation at the mesial and distal aspect of each screw, to asses which length of the screw was located at a supra-bony level after graft resorption. Measurements were rounded at the nearest half millimeter, and the arithmetic mean of the mesial and distal values was recorded for each screw.

2.5.3 - Peri-implant bone resorption

Marginal peri-implant bone loss was evaluated on routine annual periapical radiographs using a dedicated image processing software (ImageJ® 1.38v U. S. National Institutes of Health, Bethesda, MD, USA). The analysis was performed on digital radiographs or digitalized conventional films, by measuring the distance between the implant shoulder and first bone-to-implant contact, at the mesial and distal aspect of each implant. Dimensional distortion was corrected by setting the known length and diameter of each implant in the software. Radiographs taken immediately after implant placement were considered as baseline. All measurements were rounded to the nearest half millimetre. A mean bone resorption value was then calculated for each implant and for each patient. All measurements were evaluated by one examiner (GT). Calibration was performed on repeated measurements collected on the first 10 patients (27 implants) and a Kappa intra-class correlation coefficient was calculated to estimate the presence of intra-examiner the consistency among different measurement sessions.

2.5.4. Implant-related complications

Cases of peri-implant mucositis and peri-implantitis in which disease resolution was achieved by non-surgical and/or surgical means were considered as implant-related complications.

2.5.5 - Implant survival/success rates

Criteria used to determine implant survival were the following: (a) absence of persistent pain or dysesthesia; (b) absence of mobility; (c) absence of continuous peri-implant bone loss; (d) absence of peri-implant infection. Failed implants were considered those presenting: (a) continuous peri-implant bone loss; (b) mobility or (c) fractures; (d) symptoms of persistent

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paresthesia/dysesthesia or (e) chronic pain; (f) presence of peri-implant infection not responding to medical/surgical treatment.

Successful implants were considered those presenting: a) absence of persistent pain or dysesthesia; b) absence of mobility; c) absence of continuous bone loss; d) absence of peri-implant infection; peri-implant bone resorption < 2 mm at the end of the observation period.

2.6 - Statistical Analysis

Statistical evaluation was performed with the IBM SPSS Statistics software (Version 24, SPSS Inc., Chicago, IL, USA).

Implant survival data were expressed in percentages and analysed by means of Kaplan–Meier curves to determine the cumulative survival rates. Implants were considered the statistical unit of analysis. Pearson's chi-square or Fisher's exact test, as appropriate, were used to evaluate: (a) the effect of patients' gender, smoking, area of edentulism on the occurrence of adverse events related to implants, considering either the patient, the implant, or the prosthesis as the unit of analysis; (b) the effect of the defect morphology (horizontal, vertical, combined) on implant survival and implant related complications, considering the implant or the prosthesis as the unit of analysis; (c) the effect of co-interventions (sinus lift, vestibuloplasty with free gingiva grafts, buccal soft tissue augmentation with a bilaminar technique) on implant survival and implant related complications, considering the implant or the prosthesis as the unit of analysis; (d) the effect of cemented or screw-retained final prosthetic restorations, on implant survival and implant related complications, considering the implant or the prosthesis as the unit of analysis. Where possible, odds ratio and 95% confidence intervals (CI) were estimated.

A generalized estimating equation (GEE) with the patient as the analysis unit was performed to take into account the clustering of implants into patients, and to evaluate the simultaneous effect of various co-factors and co-interventions on the occurrence of adverse events like implant failure and biological complications (peri-implantitis). Implant failure and biological complications were set as dependent variables in different GEEs. The model was based on the following predictors: (a) smoking habits (smoking less than 10 cigarettes a day and non-smoking patients); (b) gender; (c) area of implant placement (maxilla or mandible); (e) follow-up duration; (f) sinus augmentation; (g) vestibuloplasty with free gingival grafts. The number of implants per patient was considered as the offset variable. The follow-up duration was the weight scale variable. The main factors considered for the final analysis were the following co-interventions: sinus floor elevation and grafting, vestibuloplasty, smoking habits, maxillary or mandibular arch and patients' gender. Significance threshold was set at $p = 0.05$.

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Peri-implant bone resorption data were expressed as means (± *SD*). Descriptive statistical methods were adopted for this outcome. Mean data were calculated utilizing patients as the statistical unit of analysis, because of the vast heterogeneity of clinical scenarios and number of implants placed among the different cases.

3 – RESULTS

Out of 75 patients (82 sites) treated and 182 rough surface implants placed in the reconstructed areas, 8 patients and 23 implants were lost to follow-up at different times of the observation period (see Table 1). Follow-up from the start of prosthetic loading ranged from 3 to 16 years (mean= 10 years, SD= 3.5).

Distribution of type of initial defects, reconstructive procedures, surgical co-interventions, and number of implants placed in the reconstructed areas are reported in tables 2-3-4-5.

A clinical case is reported from figure 1 to figure 4.

3.1 - Complication rate of the reconstructive procedures

The majority of patients recovered from the reconstructive procedure uneventfully (69 out of 75 patients. None developed severe surgical complications.

Six out of 75 patients underwent early complications. Out of these, 3 patients reported a transient paresthesia of the inferior alveolar nerve at the mandibular side that received the harvesting procedure (Table 2). All signs and symptoms of nerve disfunction regressed spontaneously within 2 to 8 weeks.

Two patients underwent a dehiscence of the flap at the grafting site, with consequent graft exposure, between 2 and 4 weeks after suture removal. Treatment consisted of local curettage with manual curettes and perforations of the graft surface with 0.2mm round burs mounted on a low-speed straight handpiece under constant irrigation with sterile saline until spontaneous bleeding was detectable through the perforations, to promote secondary healing thanks to the formation of granulation tissue followed by re-epithelization over the previously exposed bone. A spontaneous closure of the dehiscence occurred 5 to 8 weeks later. In these patients, a minor bone loss occurred during wound healing, which was still compatible with the placement of implants according to the original, prosthetically driven project. One patient presented with suppuration but without any clinically detectable dehiscence in the area of the grafted site three

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weeks after surgery which was solved with systemic antibiotic therapy for 10 days. At the time of implant placement, no significant bone loss was however observed.

3.2 - Bone resorption before implant placement

At time of implant placement, bone resorption around the fixation screws ranged from 0 to 2 mm (mean=0.15 mm; SD=0.42mm) and from 0 mm to 2 mm (mean=0.18 mm; SD: 0.43mm) in the horizontal and vertical dimension, respectively (see table 2 for further details) .

3.3 - Peri-implant bone resorption

The mean vertical peri-implant bone loss ± standard deviation was 1.06±1.19 (range 0.00 to 5.05) at patient level, and 1.11±1.26 (range 0.00 to 5.20) at implant level. The Kappa intra-class correlation coefficient calculated on repeated measurements collected from the first 10 patients (27 implants) was 0.88 Frequency distribution and interquartile ranges of resorption are also reported in Table 6.

3.4 - Implant related complications

None of the implants placed in the reconstructed bone was lost before prosthetic loading or presented biological complications.

After prosthetic loading, there were 12 implants in 9 patients affected by biological complications. Two implants (one per patient) were removed due to loss of integration, 11 months and 12 years after prosthetic loading, respectively.

Ten implants in 7 patients developed peri-implantitis with no implant mobility, 36 to 84 months after prosthetic loading (Table 3). In all cases, a combined non-surgical and surgical treatment protocol was delivered aiming to stop disease progression and maintain the implants.
First, non-surgical therapy with dedicated peek ultrasonic devices (PI ultrasonic insert, EMS electro medical systems SA, Nyon, Switzerland) and topical application of chlorhexidine gel was delivered at the affected site. One month later, surgical treatment was performed. Six implants in 4 patients, presenting with supra-bony defects, developed approximately 3 to 7 years after the start of loading, were treated with open flap debridement and implantplasty performed with diamond polishing burs, decontamination with 1% chlorhexidine gel, rinsing with sterile saline, and closure with an apically repositioned flap. Radiographic controls, performed yearly during the observation period (last controls ranging from 2 to seven years after treatment of peri-implantitis), showed no further progression of bone resorption. On the other hand, 4 implants in 3 patients, presenting with contentive infra-bony

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defects developed approximately 3 to 9 years after the start of loading, were treated with a reconstructive approach consisting of decontamination of the implant surface through an open flap debridement with dedicated titanium brushes (Ti-Brush, Straumann Institute AG, Basel, Switzerland). Then, a 1% chlorhexidine gel for 1 minute followed by EDTA 24% (Straumann® PrefGel®) for 2 minutes were applied. Subsequent reconstruction of the peri-implant hard tissues was performed using a collagen-linked bovine bone mineral (Bio-Oss Collagen®, Geistlich Biomaterials, Switzerland) within the infra-bony component of the defect, as suggested by some Authors (Roccuzzo, et al., 2011). Finally, the flap was closed around the implant neck/abutment with a 6/0 resorbable PGA suture. Radiographic and clinical controls performed 2,3, and 4 years after treatment of peri-implantitis, respectively, demonstrated an almost complete regeneration with disappearance of the infrabony defects.

Overall, the cumulative complication rate at patient level was 16.78% and at implant level it was 8.29%.

Implant complications were not associated with pre-implant bone resorption, as all implant failures and peri-implantitis cases occurred in patients that did not show bone resorption prior to implant placement. Only one patient who showed 0.5mm bone resorption in both horizontal and vertical dimension before implant placement, developed peri-implantitis.
No major prosthetic complications requiring the manufacturing of a new prosthetic restoration were reported during the observation period, thus leading to a 100% survival rate of the restorations.
A synthesis of the distribution of patients, prostheses, and implants according to the main individual factors (e.g., smoking habits, gender, area of edentulism), with details on the number of adverse events (implant loss and peri-implantitis) occurred during follow-up, is presented in Table 3.
The occurrence of pre-implant complications, using ramus graft in combination or not with sinus augmentation procedure is presented in table 4. The incidence of implant complications using or not vestibuloplasty and free gingival grafts is shown in Table 5.

The main results of the generalized estimating equations are reported in Table 7. None of the co-interventions taken into account showed a significant effect on the occurrence of implant failures or peri-implantitis. No other factors showed a significant impact on outcomes.

3.5 - Implant survival/success rates

The overall survival and success rates of implants at the end of the observation period were 98.11% and 85.16%, respectively.

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Fig. 5 shows the Kaplan–Meier curve as regards success rate, considering the implant as analysis unit.

4 – DISCUSSION

Medium- to long-term results of this cohort retrospective study seem to confirm the efficacy of reconstruction of atrophic ridges using autogenous bone blocks taken from the mandibular ramus, as already reported by previous publications (Chiapasco, et al., 1999; Cordaro, et al., 2002; Von Arx, & Buser 2006; Donos, et al., 2008; Cordaro, et al., 2011; Chiapasco, et al., 2014; Moraschini, et al., 2015; Aloy-Prosper, et al., 2015).

Positive results include limited morbidity, low complication rates after the reconstructive procedure, stability of the augmented bone over time, and good implant survival rates (Chiapasco, et al., 1999 – 2006; Donos, et al., 2008; Chiapasco, et al., 2009; Clementini, et al., 2011; Moraschini, et al., 2015)

With respect to patients' morbidity, patients' reported outcome measures from this study do not support any specific association of grafting with autogenous bone blocks with severe patient discomfort and morbidity.

Results from this study corroborate a clinical trial which concluded that mandibular bone harvesting is associated to low objective and subjective morbidity (Raghoebar, et al., 2007).

As reported in a systematic review by Chiapasco et al 2009, the incidence of neural disturbances related to bone harvesting of mandibular ramus ranged from 0 to 5%. In this case series, paresthesia involved only 3 patients (4%), but all of them recovered within 1 to 2 months after the surgical procedure.

As regards the complication rate of the reconstructive procedure, this study demonstrated that an uneventful healing occurred in the majority of patients (72 of 75 patients). Only 3 patients reported early infection and/or dehiscence which healed after local treatment within 8 weeks, with no significant damage to the grafted bone.

In this study, the incidence of dehiscences was lower as compared to data reported by other studies (Chaushu, et al., 2010) or systematic reviews (Milinkovic & Cordaro, 2014; Chiapasco et al., 2006-2009) and no significant bone loss was reported, also in case of dehiscence,. These positive results might be related to the relevant periosteal releasing incisions, to the accuracy in suturing, the systematic use of antibiotics, and chlorhexidine mouth washes.

Furthermore, the coverage of the bone graft with a resorbable collagen membrane might reduce the risk of "direct" bone graft exposure in case of an early dehiscence, as the membrane acts as

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a protective shield as regards the graft (Proussaefs, & Lozada, 2003; Von Arx, & Buser, 2005; Jensen, & Terheyden 2009; Cordaro, et al., 2011).

The second factor which may explain the "rescue" of exposed grafts is the very limited extent of these dehiscences and the prompt treatment by local curettage and perforations of the graft with small round burs to obtain bleeding form the basal bone and, consequently, formation of granulation tissue over the exposed area. This eventually evolved in secondary re-epithelization over the graft with preservation of the initial volume.

The only limit of mandibular ramus harvesting may be represented by the quantity of available bone. In case of extreme atrophy involving extensive areas of the jaws, it is often necessary to use extra-oral donor sites such as the iliac crest (Vermeeren, et al., 1996; Verhoeven, et al., 1997; Becktor, et al., 2004; Chiapasco, et al., 1999, 2009; Van der Meij, et al., 2005) or the calvarium (Donovan, et al., 1994; Iizuka, et al., 2004; Gleizal, et al., 2007, Chiapasco et al., 2013; Smolka, 2014; Chiapasco et al., 2018).

As far as bone volume augmentation stability over time is concerned, this study showed a very limited horizontal and vertical resorption both before implant placement (0 - 2 mm; mean=0.15 mm; SD=0.42mm, and 0 - 2 mm; mean=0.18 mm; SD: 0.43mm, respectively). After implant placement vertical peri-implant bone resorption was therefore consistent with that reported for implants placed in native, non-reconstructed bone (Pjetursson, et al., 2012; Jung, et al., 2012; Van Velzen, et al., 2015; De Medeiros, et al., 2016; Niu et al., 2017). As regards horizontal bone resorption after implant placement, the authors are well aware that without CBCTs it is impossible to obtain annual controls. However, the irradiation dose would be unjustified and non -ethical. For this reason, only clinical controls verifying the absence of implant threads exposure in the buccal or lingual aspects, as well as the absence of soft tissues contour changes have been done every year after the completion of prosthetic rehabilitation. Clinical evaluation demonstrated (within the limits of this type of evaluation) stability of the graft width over the years. The authors are aware that such evaluation is not the most precise, but is the least harmful for patients' health.

In this study, mandibular bone grafts were covered with a protective layer of deproteinized bovine bone mineral (DBBM) stabilized by a collagen resorbable membrane, as advocated by Prossaefs & Lozada (2003). This procedure seems to confirm that a layer of slowly resorbable xenograft in association with a collagen membrane may prevent the risk of autogenous bone resorption thanks to the osteoconductive and space making properties of DBBM. These results are comparable with data from the test group of a randomized controlled clinical trial, comparing

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grafting with autogenous mandibular bone blocks with (test) or without (control) covering the blocks with a xenograft and a collagen membrane (Von Arx, & Buser, 2006; Cordaro, et al., 2011).

According to data reported in tables 6 and Figure 5, it appears that the use of vestibuloplasty in association with free gingival grafts taken from the palate reduced the incidence of implant failures and peri-implantitis, although the difference is not statistically significant.

The GEE (Figure 5) demonstrated also that other co-interventions such as smoking habits, gender and site of reconstruction (maxilla vs mandible) did not significantly influenced the final outcomes.

5 – CONCLUSION

Despite the descriptive nature of this retrospective longitudinal cohort study and the variability of the selected patients (including different patients anamnesis, defects locations, defect morphologies, and prosthetic rehabilitations), medium- to long-term results confirm the efficacy of reconstruction of atrophic ridges using autogenous bone blocks taken from the mandibular ramus covered by a protective layer of bovine bone mineral and stabilized by a collagen membrane. Overall implant survival rate placed in the reconstructed area and marginal peri-implant bone stability were extremely satisfactory and similar to results obtained for implants placed in native bone.

AUTHORS CONTRIBUTIONS

Matteo Chiapasco performed all surgical procedures, took care of the study concept, and performed a critical revision of the article. David Palombo took care of the study design and submission to the ethic committee, performed the literature review, drafted the article, and contributed to data analysis/interpretation. Grazia Tommasato performed the recall of all patients with data collection, contributed to data analysis/interpretation and to a critical revision of the article. Massimo del Fabbro performed the statistical analysis.

CONFLICT OF INTEREST

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LEGENDS TO ILLUSTRATIONS

Fig. 1a-b: Initial clinical and radiographic situation showing vertical and horizontal resorption of the mandible distal to tooth 3.5

Fig. 2a-2b-2c: Reconstruction of the defect with horizontal and vertical autogenous onlay bone grafts taken from the mandibular ramus fixated with titanium micro-screws, water-tight suture, and panoramic radiograph at the end of surgery

Fig. 3a-3b: Second surgery at the time of implant placement: it is clearly visible that the heads of the micro-screws are in close contact with the surface of grafts, meaning that no resorption occurred.

Fig. 4a-4b: radiographic controls after the final, implant-supported prosthetic restoration, at 1 and 10 years, respectively, showing stability of the augmented bone with no peri-implant bone resorption.

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Table 1. Life table analysis of implants (standard actuarial method)

Interval, years	No. of implants	No. of patients	No. of failures	implants lost to follow-up	interval survival rate	cumulative survival rate
0-1	182	75	1	0	99.45%	99.45%
1-2	181	75	0	0	100.0%	99.45%
2-3	181	75	0	0	100.0%	99.45%
3-4	181	75	0	0	100.0%	99.45%
4-5	181	71	0	14	100.0%	99.45%
5-6	167	63	0	18	100.0%	99.45%
6-7	149	61	0	2	100.0%	99.45%
7-8	147	58	0	8	100.0%	99.45%
8-9	139	50	0	15	100.0%	99.45%
9-10	124	45	0	12	100.0%	99.45%
10-11	112	38	0	18	100.0%	99.45%
11-12	94	31	0	19	100.0%	99.45%
12-13	75	22	1	26	98.67%	98.12%
13-14	48	15	0	17	100.0%	98.12%
14-15	31	8	0	15	100.0%	98.12%

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>15	16	5	0	16	100.0%	98.12%

Table 2. incidence of complications occurring before and after implant placement according to type of reconstruction (horizontal, vertical, combined). The site reconstruction was the unit of analysis (n=82)

Interventions	**N. grafting procedures (patients/implants)**	**Pre-implant complications**			**Post-implant complications**	
		paresthesia	Vertical bone graft resorption (0.5 to 2mm)	Horizontal bone graft resorption (0.5 to 2mm)	Implant failure (patients)	Peri-implantitis (patients)
Combined vertical+horizontal defects	48 (44/107)	2	6	6	2 (2)	7 (6)
Only horizontal defects	20 (19/46)	1	Not measured	3	0	3 (1)
Only vertical defects	14 (14/29)	0	4	Not measured	0	0
p-value*		0.25	0.04	0.45	0.34	0.04

*Fisher exact test;

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Table 3. Data distribution per patient, prostheses, and implants, and significance of individual factors for implant failures and peri-implantitis occurred during the follow-up.

	Patients (imp failure/ peri-implantitis)	**P-value**	**Prostheses (imp failure/ peri-implantitis)**	**P-value**	**Implants (imp failure/ peri-implantitis)**	**P-value**
No total	75 (2/7)		89 (2/7)		182 (2/10)	
Smokers	10 (1/2)	0.23/	11 (1/2)	0.24/0.19	25 (1/2)	0.24/0.27
Non smokers	65 (1/5)	0.19	70 (1/5)		157 (1/8)	
Male	21(1/2)	0.41/	26 (1/2)	0.42/0.33	50 (1/2)	0.59/0.40
Female	54 (1/5)	0.33	63 (1/5)		132 (1/8)	
Maxilla	33 (1/1)	0.50/	48(1/1)	0.50/0.04*	75 (1/1)	0.49/0.03*
Mandible	44 (1/6)	0.10	44 (1/6)		107 (1/9)	

* statistically significant

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Table 4. **Occurrence of pre-implant complications, using ramus graft in combination or not with sinus augmentation procedure. The patient was the unit of analysis (n=75).**

Interventions	**N. patients**	**Pre-implant complications**		
		paresthesia	Vertical bone graft resorption (0.5 to 2mm)	Horizontal bone graft resorption (0.5 to 2mm)
Ramus graft alone	60	2	9	8
Ramus graft+sinus augmentation	15	1	1	1
O.R. (95% CI), p-value*		2.07 (0.18, 24.51), p=0.49	2.47 (0.29, 21.19), p=0.27	2.15 (0.25, 18.69), p=0.31

*Fisher exact test; O.R.=odds ratio, CI= confidence intervals

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Table 5. Incidence of implant complications using or not vestibuloplasty and free gingival graft procedure. The patient was the unit of analysis (n=75).

Interventions	**N. patients (implants)**	**Complications after implant placement**		
		Failed/unsuccessful implants*	Implant survival/success	Peri-implantitis
No vestibuloplasty+FGG	70 (168)	2/27	97.85%/84.12%	6
Vestibuloplasty+FGG	5 (12)	0/0	100%/100%	1
O.R. (95% CI), p-value**		p=0.87/p=0.13	--	2.67 (0.26, 27.86), p=0.40

*Implants with marginal bone resorption >2mm were considered unsuccessful; **Fisher exact test; FGG= free gingival graft; O.R.=odds ratio, CI= confidence intervals

Table 6 - Peri-implant bone resorption at the end of the observation period. Values are in mm.

	Per patient (n=75)	**Per implant (n=180)**

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mean value	1.06	1.11
Standard deviation	1.19	1.26
min value	0.00	0.00
1st quartile (25%)	0.00	0.00
2nd quartile (50%)	0.625	0.95
3rd quartile (75%)	1.45	1.51
max value	5.05	5.20

Frequency distribution of peri-implant bone resorption	**Number of patients (%)**	**Number of implants (%)**
< 1 mm	43 (57.3)	90 (49.5)
1 – 1.99 mm	21 (28.0)	59 (32.4)
2 – 2.99 mm	4 (5.3)	10 (5.5)
3 – 3.99 mm	3 (4.0)	7 (3.8)
≥ 4 mm	4 (5.3)	14 (7.7)
Implants removed	2 (2.7)	2 (1.1)

Table 7. Main results of the Generalized Estimating Equations using the Generalized Linear Model for estimating the effect of main co-interventions and individual factors on implant failure and peri-implantitis. The patient is the unit of analysis.

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Dependent variable	Co-intervention	OR (95%CI)	Standard error	p-value
Implant failure	Sinus lift	1.63 (0.92, 2.89)	0.29	0.09
	Vestibuloplasty	0.38 (0.14, 1.05)	0.52	0.06
	Smoking habits	1.18 (0.52, 2.69)	0.42	0.69
	Jaw (mandible)	0.62 (0.34, 1.12)	0.30	0.11
	Gender (female)	0.98 (0.63, 1.53)	0.23	0.93
Peri-implantitis	Sinus lift	1.44 (0.82, 2.52)	0.29	0.20
	Vestibuloplasty	0.38 (0.14, 1.05)	0.52	0.06
	Smoking habits	1.03 (0.48, 2.22)	0.39	0.94
	Jaw (mandible)	0.65 (0.35, 1.20)	0.32	0.17

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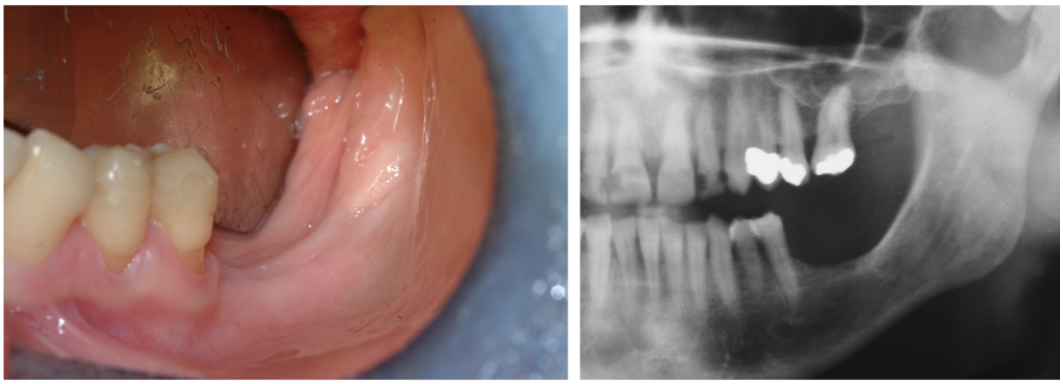

Fig. 1A

Fig. 1B

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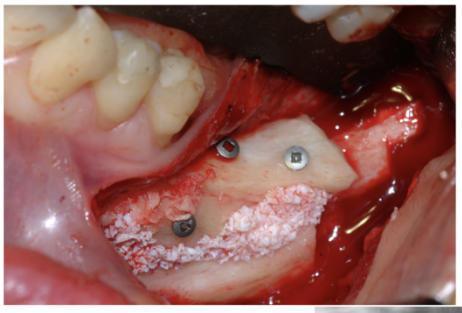

Fig. 2A

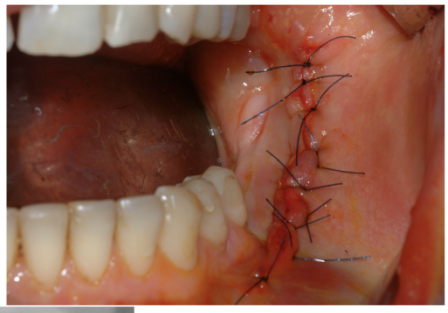

Fig. 2B

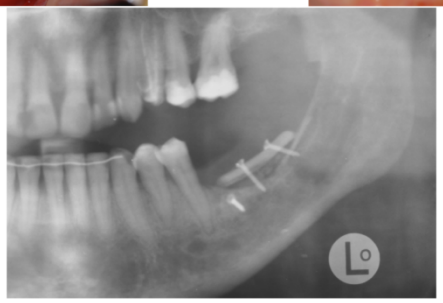

Fig. 2C

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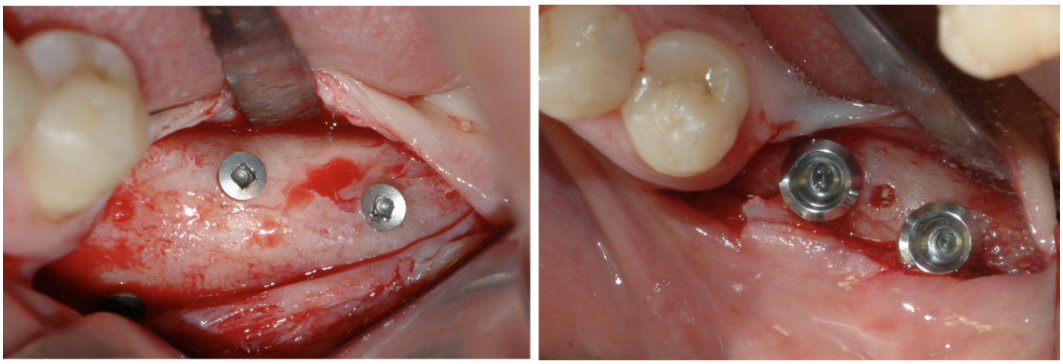

Fig. 3A

Fig. 3B

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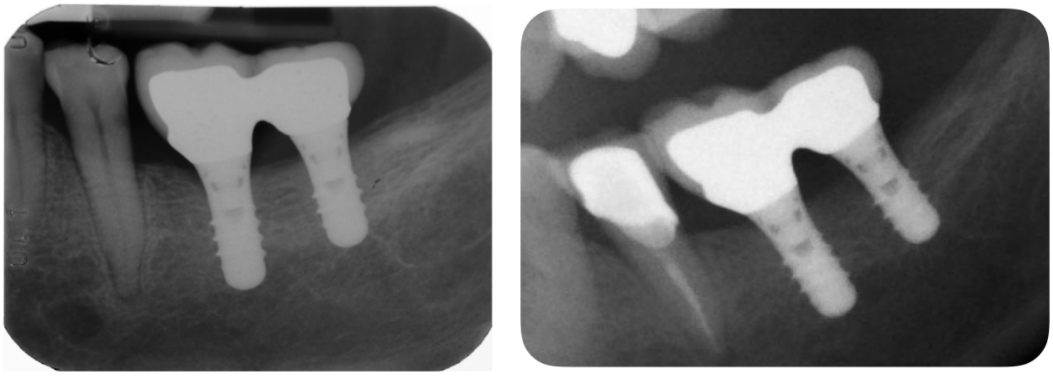

Fig. 4A

Fig. 4B

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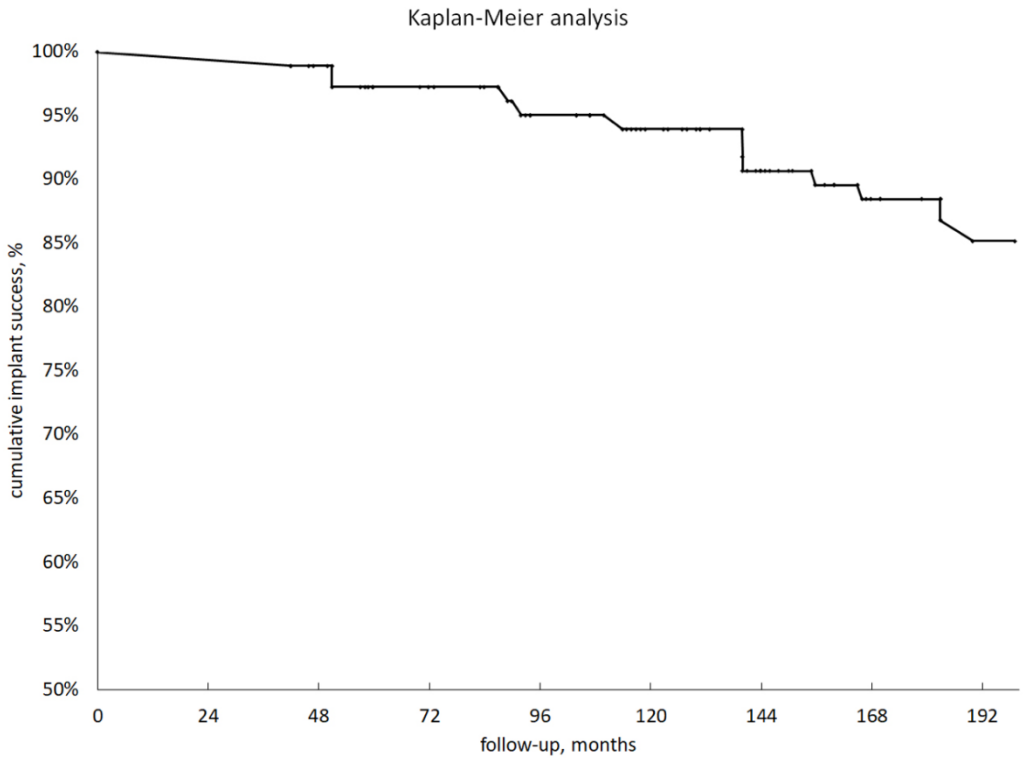

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