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Immediately loaded zygomatic implants vs conventional dental implants in augmented atrophic maxillae: 1-year post-loading results from a multicentre randomised controlled trial

Key words *atrophic maxilla, bone augmentation, bone substitute, immediate loading, zygomatic implants*

Purpose: To compare the clinical outcome of immediately loaded cross-arch maxillary prostheses supported by zygomatic implants vs conventional implants placed in augmented bone.

Materials and methods: In total, 71 edentulous patients with severely atrophic maxillas without sufficient bone volumes for placing dental implants, or when it was possible to place only two implants in the anterior area (minimal diameter 3.5 mm and length of 8 mm) and less than 4 mm of bone height subantrally, were randomised according to a parallel group design to receive zygomatic implants (35 patients) to be loaded immediately vs grafting with a xenograft, followed after 6 months of graft consolidation by placement of six to eight conventional dental implants submerged for 4 months (36 patients). For immediate loading, zygomatic implants had to be inserted with an insertion torque superior to 40 Ncm. Screw-retained metal reinforced acrylic provisional prostheses were provided, to be replaced by definitive Procera Implant Bridge Titanium prostheses (Nobel Biocare, Göteborg, Sweden), with ceramic or acrylic veneer materials 4 months after initial loading. Outcome measures were: prosthesis, implant and augmentation failures, any complications, quality of life (OHIP-14), patients' number of days with total or partial impaired activity, time to function and number of dental visits, assessed by independent assessors. Patients were followed up to 1 year after loading.

Results: No augmentation procedure failed. Five patients dropped out from the augmentation group. Six prostheses could not be delivered or failed in the augmentation group vs one prosthesis in the zygomatic group, the difference being statistically significant (difference in proportions = -16.5%; $P = 0.045$; 95% CI: -0.34 to -0.01). Eight patients lost 35 implants in the augmentation group vs two patients who lost four zygomatic implants, the difference being statistically significant (difference in proportions = -20.1%; $P = 0.037$; 95% CI: -0.38 to -0.02). A total of 14 augmented patients were affected by 22 complications, vs 28 zygomatic patients (40 complications), the difference being statistically significant (difference in proportions = 34.8%; $P = 0.005$; 95% CI: 0.12 to 0.54). The 1-year OHIP-14 score was 3.93 ± 5.86 for augmented patients and 3.97 ± 4.32 for zygomatic patients with no statistically significant differences between groups (mean difference = 0.04; 95% CI: -2.56 to 2.65; $P = 0.747$). Both groups had significantly improved OHIP-14 scores from before rehabilitation ($P < 0.001$ for both augmented and zygomatic patients). On average, the number of days of total infirmity was 7.42 ± 3.17 for the augmented group and 7.17 ± 1.96 for the zygomatic group, the difference not being statistically significant (mean difference = -0.25; 95% CI: -1.52 to 1.02; $P = 0.692$). The number of days of partial infirmity were on average 14.24 ± 4.64 for the augmented

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group and 12.17 ± 3.82 for the zygomatic group, the difference being statistically significant (mean difference = -2.07; 95% CI: -4.12 to -0.02; $P = 0.048$). The mean number of days that needed to have a functional prosthesis was 444.32 ± 207.86 for augmented patients and 1.34 ± 2.27 for zygomatic patients, the difference being statistically significant (mean difference = -442.98; 95% CI: -513.10 to -372.86; $P < 0.001$). The average number of dental visits was 19.72 ± 12.22 for augmented patients and 15.12 ± 5.76 for zygomatic patients, the difference not being statistically significant (mean difference = -4.61; 95% CI: -9.31 to 0.92; $P = 0.055$).

Conclusions: Preliminary 1-year post-loading data suggest that immediately loaded zygomatic implants were associated with statistically significantly fewer prosthetic failures (one vs six patients), implant failures (two vs eight patients) and time needed to functional loading (1.3 days vs 444.3 days) when compared to augmentation procedures and conventionally loaded dental implants. Even if more complications were reported for zygomatic implants, they proved to be a better rehabilitation modality for severely atrophic maxillae. Long-term data are absolutely needed to confirm or dispute these preliminary results.

Conflict-of-interest statement: *This study was originally supported by Nobel Biocare (Göteborg, Sweden), the manufacturer of the implants, and of the provisional and definitive prosthetic components used in this study, which were provided free to the patients; however, before any results were known, Nobel Biocare withdrew the financial support and recruitment had to be stopped. Tecnoss (Giaveno, Italy) kindly donated the bone substitutes and the membranes, whereas Global D (Brignais, France) donated the osteosynthesis screws. Data property belonged to the authors and the manufacturers in no means interfered with the publication of the results.*

■ Introduction

Dental implants are used to replace missing teeth[1]. The placement of dental implants can be limited by the presence of insufficient bone volume to allow their anchorage. In order to solve this problem, several bone augmentation procedures have been developed. In principle, the missing bone is taken from a donor site (e.g. the iliac crest), transplanted where needed and implants are then placed. Sometimes, major bone grafting operations have to be undertaken under general anaesthesia, requiring patients to be hospitalised for a few days. Some degree of morbidity related to the donor site must be expected, although more recently bone substitutes are being used to minimise morbidity[2-4], and two to three surgical interventions may be needed before the implants can be functionally used. Sometimes patients have to wait more than 1 year before a prostheses can be fixed to the implants and the total cost of the treatment is high. At the start of the 1990s, a long screw-shaped implant – the zygomatic implant[5] – was developed by Professor P-I Brånemark as an alternative to bone augmentation procedures. Zygomatic implants are generally inserted through the alveolar crest to engage the body of the zygomatic bone[6], passing through the maxillary sinus or not, depending on the individual local anatomic conditions[7]. One to three zygomatic implants can be inserted through the alveolar crest to engage the body of each zygomatic bone, however more commonly two zygomatic implants are placed in each zygoma, which can be loaded immediately if inserted with a sufficient torque[8]. This is a major potential advantage over conventional bone augmentation procedures since patients could be functionally rehabilitated in a single day instead of undergoing two to three surgical procedures over several months[3,9]. Therefore, zygomatic implants are an alternative to conventional bone augmentation and implant rehabilitation for severely atrophic maxillae[6]. Despite zygomatic implants having been in use for almost 20 years[5,6,10-12], reliable comparative trials evaluating the effectiveness and potential risks compared with conventional augmentation procedures are still lacking[13]. The only randomised controlled trial (RCT) published on zygomatic implants was a split-mouth study comparing drilling vs piezosurgery for zygomatic implant site preparation[14].

The aim of this RCT of parallel group design was to compare the clinical outcome of immediately loaded cross-arch maxillary prostheses supported by zygomatic implants vs conventional implants placed in augmented bone for the rehabilitation of patients with atrophic or severely atrophic maxillas. It was planned to report data up to 15 years after loading and this is the second of the planned publications. Data at 4 months post-loading were previously reported[15]. This article is reported according the CONSORT statement for improving the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

Materials and methods

Trial design

This was a three-centre RCT of parallel group design with two arms, balanced randomisation and blind outcome assessment, when possible. Patients with totally edentulous atrophic maxillae were randomly allocated to bone augmentation with a bone substitute and six to eight conventionally loaded dental implants (augmentation group) or four zygomatic implants or two zygomatic and two conventional implants, to be immediately loaded (zygomatic group). Originally, another two centres agreed to participate in this trial and should have each treated 20 patients, but they never provided any data.

Eligibility criteria for participants

Any patient with a severely atrophic edentulous maxilla without sufficient bone volume for placing dental implants at all, or when it was possible to place only two implants in the anterior area (minimal diameter 3.5 mm and length of 8 mm) as evaluated on TC scans and having a residual bone height under the maxillary sinus less than 4 mm as measured on cone-beam computer tomography (CBCT) or conventional computer tomography (CT) scans requesting a fixed prosthesis, who was 18 or older and able to understand and sign an informed consent form, was eligible for the trial. Coronal slices were added to conventional CBCT/CT scans to evaluate the osteomeatal complex and the sinus epithelium conditions. Only patients with healthy sinuses were asked to join the trial. Patients were not admitted in the study if any of the following exclusion criteria was present:

- General contraindications to implant surgery;
- Irradiated in the head and neck region with more than 70 Gray;
- Immunosuppressed or immunocompromised;
- Treated or under treatment with intravenous amino-bisphosphonates;
- Untreated periodontal disease;
- Poor oral hygiene and motivation;
- Uncontrolled diabetes;
- Pregnant or lactating;
- Addiction to alcohol or drugs;
- Psychiatric problems;
- Lack of opposite occluding dentition/prosthesis;
- Restricted mouth opening (less than 3.5 cm interarch anteriorly);
- Acute or chronic infection/inflammation in the area intended for implant placement;
- Unable to commit to a 15-year follow-up;
- Participating in other studies, if the present protocol could not be properly adhered to;
- Referred only for implant placement.

Patients were categorised according to the degree of the maxillary atrophy into: i) atrophic, if there was sufficient bone to place at least two 8 mm long × 3.5 mm wide implants in the frontal portion of the maxilla, and ii) severely atrophic if there was not sufficient bone to place at least two 8 mm long × 3.5 mm wide implants in the anterior portion of the maxilla. Patients were also categorised into three groups according to what they declared: i) non-smokers, ii) moderate smokers (up to 10 cigarettes per day), and iii) heavy smokers (more than 10 cigarettes per day).

After signing the informed consent form, patients were randomly allocated to zygomatic implants (depending on the degree of jaw atrophy) – either four zygomatic implants (Fig 1), or two zygomatic and two conventional implants (Fig 2), to be immediately loaded, or bone augmentation with a bone substitute (depending on the degree of jaw atrophy), either bilateral sinus lift and horizontal augmentation (Fig 3) or bilateral sinus lift only followed by delayed placement of six to eight conventional implants to be

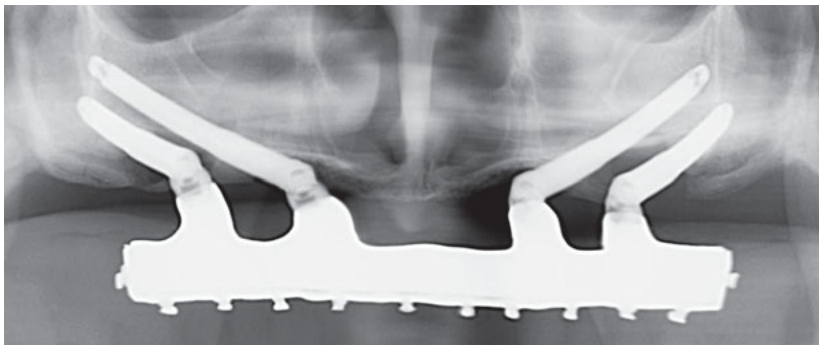

Fig 1 Panoramic radiograph at 1-year after loading of one of the patients with a severely atrophic maxilla randomly allocated to receive four immediately loaded zygomatic implants (Dr Roberto Pistilli, Rome).

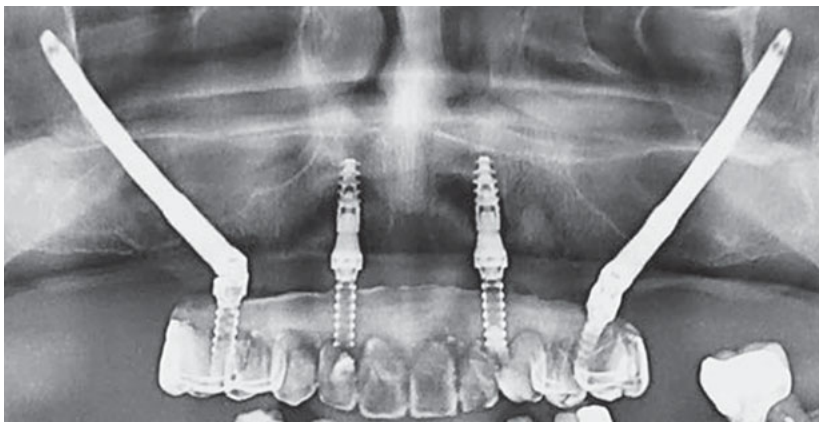

Fig 2 Panoramic radiograph at 1 year after loading of one of the patients with an atrophic maxilla randomly allocated to receive two immediately loaded zygomatic and two conventional implants (Dr Pietro Felice, Bologna). The patient is wearing a definitive prosthesis with a structure in carbon fibres lined with composite material (Dr Saverio Mascellani; protocol deviation).

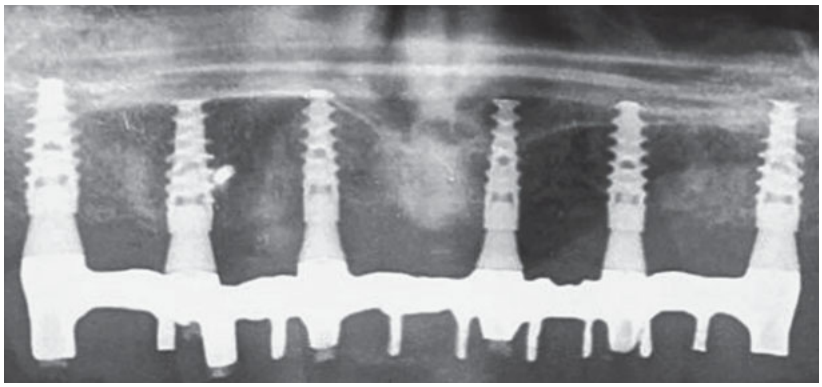

Fig 3 Panoramic radiograph at 1-year after loading of one of the patients with an severely atrophic maxilla randomly allocated to receive and six to eight conventionally loaded implants after augmentation with bone substitutes (Dr Pistilli, Rome). The patient is still wearing the provisional prosthesis (protocol deviation).

loaded after 4 months of unloaded healing, according to the indications contained in the sequentially numbered envelope corresponding to the patient's recruitment number.

Setting and locations

Patients were treated at three different centres: i) the Hospital Clinic in Barcelona, Spain (27 out of 40 planned patients); ii) Sant'Orsola Malpighi Polyclinic in Bologna (10 out of 20 planned patients) and San Filippo Neri Hospital in Rome, Italy (34 out of 30 planned patients).

The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were adhered to. The ethical committees of the Hospital Clinic in Barcelona (HCP/2011/063) approved the study on 2 May 2011, by the Sant'Orsola Malpighi hospital in Bologna (Prot. n 1633/2011) on 19 July 2011, and by the San Filippo Neri Hospital (prot. n. v.f. 03/2013 and prot n. 50/C.E.F.S.N.) on 27 May 2013. All patients received thorough explanations, understood and signed a written informed consent form prior to being enrolled.

Surgical procedures

Stereolithographic models of the maxillae were created from CBCT/CT scans to better plan the implant insertion angles. Anatomical landmarks to be avoided, such as the infraorbital foramens and the correct implant insertion axes, were marked with a pencil. Diagnostic wax-up and surgical guides were prepared to help clinicians select the most appropriate position and angle of each implant. Efforts were made to plan implant exits at crestal level rather than palatally.

Patients rinsed with a 0.2% chlorhexidine mouthwash for 1 min prior to surgical procedures. Surgeons were free to decide with the patients their preferred type of anaesthesia (general anaesthesia with local anaesthesia, local anaesthesia with sedation or local anaesthesia alone) to deliver treatment. Articaine with adrenaline 1:100.000 was injected locally to reduce bleeding and increasing visibility. Before augmentation and implantation procedures, systemic antibiotics (1750/250 mg of amoxicillin-clavulanic acid or 600 mg of clindamycin for patients allergic to penicillin) were administered orally, or in the case of intravenous sedation/general anaesthesia (875/125 mg of amoxicillin-clavulanic acid or 300 mg of clindamycin) intravenously prior to bone augmentation and implant installation. Patients were randomised to two groups: zygomatic implants or bone augmentation. However, according to the degree of bone atrophy of the maxilla there were two different treatment alternatives in each group:

- For zygomatic implants:

1. Four zygomatic implants in severely atrophic maxillae (Fig 1)

Quadruple zygomatic implants, two per side, were placed and immediately loaded (within 1 week) when they were placed with an insertion torque superior to 40 Ncm, otherwise the implants were submerged for 4 months. After crestal and release incisions, a mucoperiosteal flap was elevated exposing the maxilla to allow the identification of the infraorbital foramen and the incisura between the zygomatic arch and the lateral and medial surface of the frontal process of the zygomatic bone. Where necessary a 10 × 5 mm window, or wider windows extending from the sinus floor to the base of the zygomatic bone, was opened on the lateral wall of the maxillary sinus close to the infrazygomatic crest, and the sinus lining was lifted carefully. As an alternative and preferably, when anatomical conditions allowed it, zygomatic implants were not inserted through the sinus cavity, but into or onto the bone external to the sinus. Surgical templates were used to position the implant exit into the oral cavity at crestal level and not on the palate. A retractor was placed on the incisura between the zygomatic arch and the lateral and medial surface of the anterior process of the zygomatic bone to facilitate the correct three-dimensional orientation of the implant. First, a round bur was used. While drilling, adequate saline irrigation was provided. Next, a 2.9 mm diameter twist drill was used to penetrate the outer cortical layer of the zygomatic bone at the incisura. The length of the zygomatic implant was determined with a straight depth indicator. A 3.5 mm diameter pilot drill was then used, followed by the 3.5 mm twist drill. Brånemark System Zygoma Ti-Unite Implants RP (Nobel Biocare, Gothenburg, Sweden) of the following lengths: 30 mm, 35 mm, 40 mm, 42.5 mm, 45 mm, 47.5 mm, 50 mm and 52.5 mm and a diameter of 4 mm, were inserted to try to achieve an insertion torque of at least 40 Ncm to allow for immediate loading. Bicortical engagement was always obtained, meaning that the tip of the implant protruded for 1 mm to 2 mm on the other side of the zygoma. After the first implant was placed, the same procedures were repeated to place the second implant. It was attempted to place the implant apexes about 1 cm apart. Centres were allowed, at their discretion, to cover exposed implant threads using a paste made of 600 to 1000 micron prehydrated collagenated cortico-cancellous granules of porcine origin, mixed with OsteoBiol Gel 0 in a sterile syringe (OsteoBiol mp3, 1 cc, Tecnoss) and resorbable collagen barriers (OsteoBiol Evolution, Tecnoss). As an alternative, in 14 patients from the Italian centres the Bichat's fat pads were exposed and gently shifted medially to cover the exposed implant portions. Flaps were then sutured with simple, interrupted 4-0 resorbable sutures (Vicryl, Ethicon FS-2, Johnson & Johnson, New Brunswick, NJ, USA) around the impression copings.

2. Two zygomatic and two conventional implants in atrophic maxillae (Fig 2)

One zygomatic and one conventional implant were placed on each side and were immediately loaded (within 1 week), if an insertion torque of at least 40 Ncm was obtained, otherwise they were submerged for 4 months.

The same procedure, as previously described, was used to place the zygomatic implants. In addition, one conventional Nobel Active implant (Nobel Biocare) with internal connection was placed on each side in the anterior zone (canine to canine) following the manufacturer's instructions in a bid to achieve an insertion torque superior to 40 Ncm to allow immediate loading. Operators were free to choose implant lengths (8.5 mm, 10 mm, 11.5 mm, 13 mm and 15 mm) and diameters (3.5 mm, 4.3 mm and 5.0 mm) according to the clinical indications and their preferences. The following post-surgical instructions were given:

- 875/125 mg of amoxicillin-clavulanic acid or 300 mg of clindamycin for patients allergic to penicillin three times a day for 1 week;
- 600 mg Ibuprofen prescribed 4 times a day during meals for 1 week; but patients were instructed not to take them in the absence of pain;
- Xylometazoline hydrochloride (nasal decongestant) 1 mg, 5 drops three times a day for 2 weeks;
- A soft diet was recommended for 2 weeks;
- 0.2% chlorhexidine rinses twice a day for 2 weeks;
- Patients were recalled and checked on day 3; day 10 (suture removal) and month 1.

For augmentation procedure and conventional implants

3. Augmentation procedure and conventional implants in severely atrophic maxillae (Fig 3)

In the posterior maxilla, bilateral two-stage sinus lift procedures were performed. After crestal and release incisions and mucoperiosteal flap elevation, a window was designed above the maxillary sinus floor using rotating burs or piezo-surgery. After internal displacement of the bony window, the maxillary epithelium lining was carefully elevated and the sinus was packed with the mp3 bone substitute. In case of rupture of the sinus lining, resorbable barriers (OsteoBiol Evolution) were used to contain the graft. In the anterior maxilla, collagenated blocks (OsteoBiol, Sp-Block) of equine cancellous bone were used as onlays/veneers. The blocks were hydrated before use for 5 min to 10 min with a sterile, lukewarm physiological solution or with antibiotics. Afterwards, they were modelled to be adapted to the receiving site, which was accurately decorticated to guarantee maximum contact and high blood perfusion. Blocks were fixed with osteosynthesis self-drilling Ti6Al4V microscrews (Graftek, Global D), with 1.5 mm or 2 mm diameters and of various lengths from 4 mm to 19 mm. To fill the gaps between the recipient bone and the bone blocks, mp3 bone substitute granules were used. As an alternative, small defects could be grafted only with bone substitute granules according to clinical indications and the surgeon's preference. Nasal sinus lift procedures using mp3 bone substitute granules could also be implemented. All the grafted areas and the maxillary windows were covered with OsteoBiol Evolution resorbable barriers from equine pericardium. After 6 months of healing, six to eight conventional Nobel Active implants were placed and left to heal submerged for 4 months. Just prior to implant placement, a second CBCT scan was made to properly evaluate bone anatomy and to plan implant placement.

4. Augmentation procedure and conventional implants in atrophic maxillae

Operators were free to choose one- or two-stage lateral window sinus lift procedures, as previously described, depending as to whether the implants could be stabilised or not. In the case of a one-stage sinus lift procedure, implants were left to heal submerged for 6 months. In the case of a two-stage sinus lift procedure, six to eight conventional Nobel Active implants were placed after 6 months healing, and left to heal submerged for 4 months.

The same postoperative instructions as before were given, and the following was added:

- Avoid blowing the nose and using drinking straws.
- Keep the mouth open in the case of sneezing in order to decrease intra-sinus pressure.
- Patients with severely atrophic maxillae (subjected to horizontal augmentation procedures)

were not allowed to wear any removable denture up to 1 month postoperatively.

Prosthetic procedures

Prosthetic procedures at implants to be immediately loaded were initiated immediately after flap suturing. Panoramic radiographs were taken to verify proper seating of all the impression copings. A self-curing acrylic resin (DuraLay, Reliance Dental Manufacturing, Worth, IL, USA) was positioned on a brass wire, to further stabilise the impression copings in position. A pick-up impression was taken using a polyether material (Impregum, 3M ESPE, Milan, Italy) and, when possible, the patient's denture, with holes in the resin palate, as a customised tray. Healing caps were positioned before a screw-retained metal reinforced acrylic cross-arch provisional prosthesis was delivered within 1 week.

Three months after initial loading, the provisional prostheses were removed, implant stability was checked by tightening the abutment screws with a 15 Ncm torque using a manual torque wrench, and a definitive impression at abutment level was taken using a rigid impression material and impression copings with an open tray, as previously described. Within 1 month, definitive screw-retained cross-arch fixed Procera Implant Bridge Titanium (Nobel Biocare) with ceramic or acrylic veneer materials were to be delivered. However, due to a financial misunderstanding, 35 patients at the Italian centres did not receive the definitive prosthesis 4 months after loading and the remaining patients did not receive Procera Implant Bridge Titanium prostheses.

Patients were enrolled on an oral hygiene programme, with recall visits every 6 months. Operators were free to increase maintenance frequency (every 2 to 4 months) based on individual needs. Dental occlusion was evaluated at each maintenance visit. Follow ups were conducted by local, independent, blinded outcome assessors.

Outcome measures

Outcome measures were:

- Prosthesis failure defined as a prosthesis that could not be delivered because of implant failures, or prosthesis replacement because of any reasons.
- Implant failure defined as an implant displaying rotational mobility, any infection dictating implant removal, and/or any mechanical complication rendering the implant unusable (e.g. implant fracture or deformation of the connecting platform). Implant stability assessments were done, with the removed prostheses, at abutment connection (augmented group only) and at delivery of the definitive prostheses or 4 months after loading and at 1 year after loading, by tightening the abutment screws with a 15 Ncm torque. Rotating implants were considered failures and were removed. It was possible that a few zygomatic implants displayed a slight horizontal mobility due to their lengths and possible lack of alveolar bone at their exits. This was recorded, but if the implants were not rotating, they were considered successful and left in place.
- Any biological or prosthetic complications.
- Failure of the augmentation procedure: The augmentation procedure was to be considered a failure if, after it had been performed it was not possible to place the planned implants in the augmented site.
- Peri-implant marginal bone levels on periapical radiograph were to be reported at the end of the 1 year post-loading follow-up, however the Spanish centre took only panoramic radiographs and the Italian centres did not take periapical radiographs as planned since Dr Felice and Dr Pistilli only took periapical radiographs of eight patients each.
- Oral Health Impact Profile (OHIP-14) that measures people's perceptions of the social impact of oral disorders on their wellbeing[16]. There are 14 questions that can be answered in the following way: never = 0, hardly ever = 1, occasionally = 2, very often = 3, fairly often = 4. The maximum score that can be obtained is 56 and corresponds to the most negative outcome. It was recorded at patient enrolment prior to delivery of any interventions and 1 to 2 weeks after definitive prostheses delivery or about 4-and-a-half months after initial loading and at 1 year after loading. Patients with a complete treatment failure who were rehabilitated with alternative treatments other than the randomly allocated intervention they were supposed to have were not accounted for.

- The number of days patients had total or partial impaired activity: Days of total impaired activity are those days that, according to the patient, he/she could not perform his/her ordinary life activities, including work. Days of partial impaired activity are those days that, in the patient's opinion, he/she could only partially perform his/her ordinary life activities, including work. This should have been assessed at the delivery of the definitive prostheses but was actually assessed 3 months after loading.
- Time to function: Number of days from the first surgical intervention to delivery of the implant-supported provisional prosthesis.
- Number of sessions with the clinician: The total number of appointments, including those for maintenance and treatment of complications, required by the patient over the entire follow-up period (up to 1 year post-loading).

Sample size, random sequence, allocation concealment and blinding

The sample size was calculated for the primary outcome measure (patient experiencing at least one implant failure): a two-group continuity corrected chi-square test with a 0.050 two-sided significance level has 80% power to detect the difference between a proportion of 0.100 and a proportion of 0.300 for patients experiencing at least one implant failure (odds ratio of 3.857) when the sample size in each group is 72. It was planned to recruit 65 patients per group over a 3-year recruitment interval period since this was the maximum number that clinicians committed to treat, but only 35 and 36 patients per group could actually be recruited.

Five computer-generated restricted randomisation lists were created with an equal number of patients in both groups. Only one of the investigators (Dr Esposito), who was not involved in the selection and treatment of the patients, was aware of the randomisation sequence and had access to the randomisation list stored on his password-protected portable computer. The randomised codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened in order after patients were enrolled on the trial, therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

Dental practitioners, who were not involved in the treatment of the patients, measured the following parameters at each centre: implant failures, quality of life (OHIP-14), the number of days a patient had either total or partial impaired activity, time to function, and the number of dental visits, assessed without knowing group allocation, when possible. Complications were registered and treated by the treating dental practitioners in a non-blinded mode.

Statistical methods

All data analysis was carried out according to a pre-established analysis plan. A dental practitioner (Dr Ippolito), with expertise in statistics analysed the data, without knowing the group codes. The patient was the statistical unit of the analyses. Differences in the proportion of prosthetic failures, implant failures, augmentation procedure failures and complications were compared between groups using the Fisher's exact probability test. Differences between the groups in the number of days with total or partial impaired activity, time to function, and number of sessions with the clinicians were compared by independent-samples *t* tests. A Mann-Whitney U-test was used to compare the OHIP-14 scores between groups. Comparisons between the 4 months and 1-year post-loading endpoints and the pre-operative measurements were made by Wilcoxon tests, to detect changes in OHIP-14 scores for each study group. Comparisons among the three centres were carried out using a one-way ANOVA for continuous variables (difference for number of days with total or partial inactivity, time to function, and number of session with the clinicians), a Pearson's chi-square test for categorical data (difference in proportions for drop-out, prosthetic, implant and augmentation procedure failures, and complications) and a Kruskal-Wallis test for ordinal variables (difference in OHIP-14 scores). Finally, the *post hoc* test used was an independent *t* test with Bonferroni correction of the *P* value ($P = 0.017$). All statistical analyses were conducted using the Statistical Package for Social Sciences Software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). All statistical comparisons were conducted at a 0.05 level of significance.

Results

Ninety-three patients were screened for eligibility, but 22 patients were not enrolled on the trial: 16 patients did not want to participate in the trials for various reasons: three patients had more bone volume than the inclusion criteria, two were under treatment with biphosphonates, and one because breast cancer had just been diagnosed. Seventy-one patients were considered eligible and were consecutively enrolled and treated in the trial. All patients were treated according to the allocated interventions. Five patients dropped out from the augmentation group: two due to death from lung and gastric cancer and one patient one month after the augmentation procedure for depression after her husband's death before the 4-month post-loading follow-up. The other two patients were seen the last time at the 4-month follow-up, but did not return for the 1-year follow-up, one because they moved to another town, but reported to have no problems, and the other because they became unreachable. The data of all remaining patients was evaluated in the statistical analyses with the exception of the peri-implant bone level changes. The following protocol deviations were observed:

- Thirty-five patients from the Italian centres and three from the Spanish centre did not receive the definitive prosthesis during the first 4 months in function.
- The nine patients who were rehabilitated with definitive prostheses in Bologna and Roma did not receive the planned Procera Implant Bridge Titanium prosthesis, but conventional screw-retained cast metal-acrylic, metal-ceramic cross-arch or carbon fibres-composite prostheses.
- Patients received different numbers than those attributed by the random list (Spanish centre only).
- The Spanish centre recruited and treated 27 instead of the 40 planned patients. Dr Felice recruited 24 instead of the 20 initially planned patients, but due to organisational reasons, only the first 10 patients were treated in Bologna while the remaining 14 patients recruited in Bologna centre were treated by Dr Felice at the centre in Rome. The Rome centre recruited 20 patients, but 34 – 14 from the Bologna centre – were treated in Rome.
- One patient, who should have received only two zygomatic implants (one per side) actually received one additional zygomatic implant since the distance between the conventional implant in position 11 and the zygomatic one was considered too long by the surgeon (Dr Pistilli).
- In one patient, absorbable haemostatic gelatine sponges (Spongostan Special, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA) were used to protect the sinus epithelium after its displacement.
- The Spanish centre took only panoramic radiographs and the Italian centres did not take periapical radiographs as planned for all patients since Dr Felice and Dr Pistilli each only took periapical radiographs of eight patients.
- One augmented patient postponed the abutment connection of 28 months for personal reasons (Spanish centre).

Patients were initially treated from February 2012 to September 2015. The follow-up of all patients was up to 1 year after prosthetic loading.

The main baseline patient characteristics are presented in Table 1. There were no apparent systematic baseline imbalances between the two groups.

An overall comparison of all outcome measures at 1 year post-loading is presented in Table 2.

- Prosthetic failures (Tables 3a and 3b): Six prostheses could not be delivered or failed in the augmentation group vs one prosthesis in the zygomatic group; the difference being statistically significant (difference in proportions = -16.5%; $P = 0.045$; 95% CI: -0.34 to -0.01).
- Implant failures (Tables 3a and 3b): Eight patients lost 35 implants in the augmentation group vs 4 implants in two patients from the zygomatic group; the difference being statistically significant (difference in proportions = -20.1%; $P = 0.037$; 95% CI: -0.38 to -0.02).
- Complications (Tables 3a and 3b): 28 zygomatic patients were affected by 40 complications vs 14 augmented patients (22 complications); the difference being statistically significant (difference in proportions = 34.8%; $P = 0.005$; 95% CI: 0.12 to 0.54).
- Quality of life (OHIP-14): The initial OHIP-14 score was 27.58 ± 8.97 in augmented patients

Table 1 Main patients and interventions characteristics (71 patients).

	Zygomatic implants (35 patients)	Conventional implants (36 patients)
Females (%)	18 (51.4%)	21 (58.3%)
Age (range)	58.31 (43-74)	57.58 (36-71)
Non-smoker	22 (62.9%)	23 (63.9%)
Smoking up to 10 cigarettes/day	3 (8.6%)	8 (22.2%)
Smoking more than 10 cigarettes/day	10 (28.6%)	5 (13.9%)
Severely atrophic maxilla (no possibility to place conventional implants)	29 (82.9%)	23 (63.9%)
Atrophic maxilla (possibility to place two frontal implants)	6 (17.1%)	13 (36.1%)
General + local anaesthesia	35 (100.0%)	33 (91.7%)
Sedation + local anaesthesia	0 (0.0%)	3 (8.3%)
Both sinus lift and augmentation with blocks/granular bone	NA	19 (52.8%)
Only 1-stage sinus lift	NA	2 (5.5%)
Only 2-stage sinus lift	NA	15 (41.7%)
Total number of inserted implants	141 (37.2%)	238 (62.8%)
Implants inserted with a torque superior to 40 Ncm	136 (96.5%)	158 (66.4%)
Implants inserted with a torque up to 40 Ncm	5 (3.5%)	80 (33.6%)
Zygoma implants with the neck fully embedded in crestal bone	102 (77.9%)	NA
Zygoma implants with exposed threads	81 (61.8%)	NA
Zygoma implants with exposed threads which have been grafted	39 (29.8%)	NA
Number of 8.5 mm long implants	2 (1.4%)	38 (16.0%)
Number of 10 mm long implants	0 (0.0%)	84 (22.2%)
Number of 11.5 mm long implants	4 (2.8%)	42 (17.6%)
Number of 13 mm long implants	4 (2.8%)	46 (19.3%)
Number of 15 mm long implants	0 (0.0%)	28 (11.8%)
Number of 35 mm long implants	7 (5.0%)	NA
Number of 40 mm long implants	25 (17.7%)	NA
Number of 42.5 mm long implants	13 (9.2%)	NA
Number of 45 mm long implants	28 (19.9%)	NA
Number of 47.5 mm long implants	17 (12.1%)	NA
Number of 50 mm long implants	32 (22.7%)	NA
Number of 52.5 mm long implants	9 (6.4%)	NA
Number of 3.4 mm diameter implants	0 (0.0%)	1 (0.4%)
Number of 3.5 mm diameter implants	6 (4.3%)	151 (63.4%)
Number of 3.75 mm diameter implants	2 (1.4%)	0 (0.0%)
Number of 4 mm diameter implants	131 (92.9%)	NA
Number of 4.3 mm diameter implants	1 (0.7%)	86 (36.1%)
Number of 5 mm diameter implants	1 (0.7%)	0 (0.0%)

NA = not applicable

Table 2 Overall comparisons of all outcome measures at 1 year post-loading.

	Zygomatic implants	Augmentation	Difference	95% CI	*P* value
Patients with prosthetic failures	1 out of 35	6 out of 31	-16.5%	-0.34 to -0.01	0.045*
Patients with implant failures	2 out of 35	8 out of 31	-20.1%	-0.38 to -0.02	0.037*
Patients with complications	28 out of 35	14 out of 31	34.8%	0.12 to 0.54	0.005*
OHIP-14	N = 34; 3.97 ± 4.32	N = 27; 3.93 ± 5.86	0.04	-2.56 to 2.65	0.747
Days of total infirmity	N = 35; 7.17 ± 1.96	N = 33; 7.42 ± 3.17	-0.25	-1.52 to 1.02	0.692
Days of partial infirmity	N = 35; 12.17 ± 3.82	N = 33; 14.24 ± 4.64	-2.07	-4.12 to -0.02	0.048*
Days to functional loading	N = 35; 1.34 ± 2.27	N = 33; 444.32 ± 207.86	-442.98	-513.10 to -372.86	< 0.001*
Number of dental visits	N = 35; 15.12 ± 5.76	N = 31; 19.72 ± 12.22	-4.61	-9.31 to 0.92	0.055

*Statistically significant differences

Table 3a Description of prosthetic failures, implant failures and complications at the zygomatic group in chronological order.

Patient/Centre	Timing	Description	Outcome
PROSTHESIS FAILURES			
Pat 15/Dr Felice	3w pl	Lost three zygomatic implants out of four with the provisional prosthesis	Back to old denture
IMPLANT FAILURES			
Pat 15/Dr Felice	2-5w pip	Day 12 post-loading the posterior left zygomatic implant was mobile (removed) Prosthesis delivered on the three remaining implants Week 3 post-loading prosthesis mobile: both anterior zygomatic implants were mobile (removed) Posterior right zygomatic implant had 2 mm anteroposterior mobility (kept in place)	Not replaced
Pat 2/Dr Pistilli	10 m pl	Lost one posterior left zygomatic implant (painful & mobile)	Not replaced
COMPLICATIONS			
Pat 11/Dr Felice	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 13/Dr Felice	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 2/Dr Pistilli	Implantation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 3/Dr Pistilli	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 4/Dr Pistilli	Post-implantation	Mayor swelling involving also the lower lip	Healed spontaneously in 2 weeks
Pat 15/Dr Felice	2-5w pip	Day 12 post-loading the posterior left zygomatic implant was painful and mobile Week 3 post-loading both anterior zygomatic implants were painful and mobile	Three implants removed + antibiotic therapy
Pat 10/Dr Felice	3w pip	Major swelling under the right eye	Amoxicillin + clavulanic acid 875/125 mg every 8 h for 10 days + painkillers – recurrence After 2 weeks exploratory surgery necrotic Bichat's fat pad into the sinus - removed + amoxicillin + clavulanic acid 875/125 mg every 8 h for 10 days + painkillers – solved
Pat 16/Spain	1 m pip	Sinusitis	Improved with amoxicillin-clavulanic acid 875/125 mg every 8 h for 1 month and nasal rinses with isotonic seawater (Rhinomer); persistent cacosmia right nasal fossa that slowly disappeared on its own
Pat 1/Spain	1 m pip 4 m pip	Zygoma and peri-orbital infection evolving in (see below) Chronic fistula	Cutaneous debridement + levofloxacin 500 mg/day for 10 days Resection + implant apex resection – solved
Pat 20/Spain	1 m pip	Headache	Solved spontaneously
Pat 25/Spain	1 m pip 4 m pip 4 m pip	Right maxillary sinusitis Right maxillary tumefaction Peri-implant mucosa recessions at front implants	Amoxicillin-clavulanic acid 875/125 mg every 8 h for 7 days Amoxicillin-clavulanic acid 875/125 mg every 8 h for 7 days – solved Not treated
Pat 3/Spain	2 m pip	Right maxillary sinusitis	Amoxicillin-clavulanic acid 875/125 mg every 8 h for 1 week – solved
Pat 4/Dr Felice	3 m pip	Peri-implant mucositis + fistula at anterior left zygoma implant	Prosthesis removal and debridement – healed after 1 week + maintenance every 2 months
Pat4/Spain	5 m pl	Right maxillary sinusitis with fistula next to implant 13	Right functional endoscopic sinus surgery and endoscopic septoplasty 8 months after implant placement. Good evolution until 6 months later, when symptoms reappeared

Table 3a *(cont.)* Description of prosthetic failures, implant failures and complications at the zygomatic group in chronological order.

Patient/Centre	Timing	Description	Outcome
Pat 20/Spain	9 m pl	Vestibular exposure of implant threads in 23, with pus and headache	Implant threads removal and connective tissue graft from palate – solved
Pat 2/Dr Pistilli	10 m pl	Posterior left zygomatic implant painful and mobile	Removed
Pat 5/Dr Felice	11 m pl	Fracture of the resin prosthetic lining	Repaired in the dental chair
Pat 3/Dr Felice	12 m pl	Fracture of the MUA abutment screw of the left anterior standard implant	Removed using ultrasounds and replaced
Pat 17/Spain	12 m pl	Awkwardness in the anterior wall of the maxilla, swelling and fistual at implant 16. Pain at pressure with finger at 26	Amoxicilin-clavulanic 875/125 mg every 8 h for 1 week + Chlorhexidin gel – solved

w = weeks; m = months; pl = post-loading; pip = post-implant placement. All patients treated at the Italian centres (21 patients), experienced a transient (from 1 week to 3 months) paraesthesia of the infraorbitary nerves.

Table 3b Description of prosthetic failure, implant failures and complications at augmented group in chronological order.

Patient/Surgeon	Timing	Description	Outcome
PROSTHESIS FAILURES			
Pat 19/Spain	2 to 34 m pip	Three out of eight implants lost 11 migrated to nasal space 2 months after placement 22 mobile 30 months after placement 24 mobile 34 months after placement	Delayed prosthesis placement
Pat 1/Dr Felice	ab	Six out of 6 implants mobile at abutment connection	Back to old denture
Pat 7/Dr Felice	ab	Seven out of eight implants mobile at abutment connection	Back to old denture
Pat 18/Spain	ab	Three out of eight implants mobile at abutment connection Three implants replaced after 6 months	Delayed prosthesis placement
Pat 7/Spain	13 m pip	Six out of eight implants lost for infection	Placement of four zygomatic implants successfully loaded
Pat 11/Spain	14 to 45 m pip	Six out of eight implant removed	Placement of four zygomatic implants
IMPLANT FAILURES			
Pat 19/Spain	2 to 34 m pip	Three out of eight implants lost 11 migrated to nasal space 2 months after placement 22 mobile 30 months after placement 24 mobile 34 months after placement	Spontaneously came out from the nose New left nasal floor elevation + implant placement 23, 35 months after first implant placement
Pat 1/Dr Felice	ab	Six out of six implants mobile at abutment connection Patient wore denture from day 20 post-implantation	Back to old denture
Pat 7/Dr Felice	ab	Seven out of eight implants mobile at abutment connection Patient wore denture from week 2 post-implantation	Back to old denture
Pat 18/Spain	ab	Three out of eight implants mobile at abutment connection One replaced implant mobile at new abutment connection	Three implants replaced after 6 months

Pat 5/Spain	ab	Three out of eight implants mobile: Implant 23 mobile at abutment connection Implant 11 mobile 3 months after abutment connection Implant 16 mobile 4 months after abutment connection	All three implants replaced 16 months after placement of first implants
Pat 6/Spain	7 m pip	Lost implant 16 out of 8 implants	
Pat 7/Spain	13 m pip	Six out of eight implants lost for infection	Surgical removal of the infected graft and placement of four zygoma implants
Pat 11/Spain	14 m pip	Six out of eight implants removed Implants 11, 23, 24 and 25 lost 14 months after placement Implant 14 lost 39 months after implant placement Implant 13 removed 45 month after implant placement	11 and 26 replaced 22 months after initial placement Placed two zygoma implants in position 22 and 25, 38 months after first implant placement Replaced by two zygoma implants in position 12 and 15, 45 months after loading
COMPLICATIONS			
Pat 5/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 8/Spain	Augmentation 9 m pip	Sinus epithelium perforation of right side Exposed vestibular surface of implant 23 at second phase surgery	Placed Evolution membranes Connective tissue graft
Pat 11/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 12/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 15/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 18/Spain	Augmentation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 22/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 24/Spain	Augmentation 32 m pip	Sinus epithelium perforation of right side At abutment connection peri-implant bone loss at 15 and 27	Placed Evolution membrane Curettage and chlorhexidine
Pat 26/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 6/Dr Felice	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 9/Dr Pistilli	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 18/Dr Pistilli	Augmentation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 7/Spain	Augmentation 13 m pip	Onlay block fragmentation when placing implant 24 Left maxilla infected The infection progressed to the right side until she lost six implants 13 months after their placement	 Amoxicillin-clavulanic acid 875/125 Bilateral bone graft removal and right maxillary sinus curettage + placement of four zygoma implants
Pat 19/Spain	2 m pip	Implant 11 migrated into the nasal space Since the patient lost another two implants a new nasal floor elevation was done, but the nasal mucosa was perforated on the right side Peri-implantitis at 23 and at right maxillary implants	Spontaneously came out from the nose Right implants could not be placed Improved after curettage and better hygiene

w = weeks; m = months; pl = post-loading; pip = post-implant placement; ab = abutment connection

and 29.29 ± 9.40 for zygomatic patients (Table 4a). The initial OHIP-14 did not significantly differ between groups ($P > 0.05$). The OHIP score at 1 year post-loading was 3.93 ± 5.86 for augmented patients and 3.97 ± 4.32 for zygomatic patients, with no statistically significant differences between groups (mean difference = 0.04; 95% CI: -2.56 to 2.65; $P = 0.747$; Table 4b). When looking at the individual items, the only statistically significant difference between groups was observed when asking whether the patient had found it

Table 4a OHIP-14 at baseline, before the implant-supported prosthesis rehabilitation began.

How often in the last year have you had problems with your upper prosthesis?		
Question	**Zygoma implants (n = 35)**	**Augmented group (n = 36)**
OH1 Have you had trouble pronouncing any words?	2.26 ± 1.48	2.67 ± 1.10
OH2 Have you felt that your sense of taste has worsened?	2.20 ± 1.18	2.53 ± 1.11
OH3 Have you had painful aching in your mouth?	2.06 ± 1.03	1.64 ± 1.02
OH4 Have you found it uncomfortable to eat any foods?	3.37 ± 1.06	3.17 ± 1.06
OH5 Have you felt self-conscious?	2.80 ± 1.08	2.50 ± 1.11
OH6 Have you felt tense?	2.14 ± 1.00	2.00 ± 1.04
OH7 Has your diet been unsatisfactory?	2.46 ± 1.15	2.69 ± 1.24
OH8 Have you had to interrupt meals?	2.23 ± 1.06	2.17 ± 0.97
OH9 Have you found it difficult to relax?	2.06 ± 1.24	1.64 ± 1.10
OH10 Have you been a bit embarrassed?	2.26 ± 1.20	2.28 ± 1.19
OH11 Have you been a bit irritable with other people?	0.94 ± 0.97	0.83 ± 0.74
OH12 Have you had difficulty doing your usual jobs?	1.57 ± 1.36	1.06 ± 1.17
OH13 Have you felt that life in general was less satisfying?	2.06 ± 1.11	1.61 ± 1.15
OH14 Have you been totally unable to function?	0.89 ± 0.76	0.81 ± 0.75
Total score	29.29 ± 9.40	27.58 ± 8.97

Data are presented as mean ± standard deviation. Possible answers: 0 (never), 1 (hardly ever), 2 (occasionally), 3 (very often) to 4 (fairly often).

Table 4b OHIP-14 assessed 1 year after initial loading.

How often in the last four months have you had problems with your upper prosthesis?			
Question	**Zygoma implants (n = 34)**	**Augmented group (n = 27)**	***P* value**
OH1 Have you had trouble pronouncing any words?	0.56 ± 0.66	0.59 ± 0.69	0.864
OH2 Have you felt that your sense of taste has worsened?	0.09 ± 0.38	0.11 ± 0.42	0.813
OH3 Have you had painful aching in your mouth?	0.56 ± 0.93	0.30 ± 0.61	0.306
OH4 Have you found it uncomfortable to eat any foods?	0.50 ± 0.83	0.33 ± 0.62	0.364
OH5 Have you felt self conscious?	0.38 ± 0.65	0.48 ± 0.89§	0.775
OH6 Have you felt tense?	0.50 ± 0.62	0.30 ± 0.67	0.087
OH7 Has your diet been unsatisfactory?	0.21 ± 0.48	0.15 ± 0.53	0.298
OH8 Have you had to interrupt meals?	0.38 ± 0.55	0.59 ± 0.69	0.238
OH9 Have you found it difficult to relax?	0.29 ± 0.52	0.59 ± 0.64	0.043*
OH10 Have you been a bit embarrassed?	0.12 ± 0.48	0.11 ± 0.42	0.839
OH11 Have you been a bit irritable with other people?	0.21 ± 0.64	0.07 ± 0.38	0.265
OH12 Have you had difficulty doing your usual jobs?	0.06 ± 0.34	0.07 ± 0.27	0.450
OH13 Have you felt that life in general was less satisfying?	0.12 ± 0.48	0.15 ± 0.53	0.813
OH14 Have you been totally unable to function?	0.00 ± 0.00	0.07 ± 0.27	0.110
Total score	3.97 ± 4.32§	3.93 ± 5.86	0.747

Data are presented as mean ± standard deviation. Possible answers: 0 (never), 1 (hardly ever), 2 (occasionally), 3 (very often), to 4 (fairly often).
*Statistically significant differences. All changes from baseline were statistically significantly different in both groups ($P < 0.05$). § Statistically significant differences between 4 months and 1 year values.

difficult to relax (OH9): patients with zygomatic implants were more satisfied than augmented patients (0.29 ± 0.52 vs 0.59 ± 0.64; $P = 0.043$). Both groups had significantly improved OHIP-14 scores from before rehabilitation ($P < 0.05$ both for augmented and zygomatic patients).

- Patients' number of days with total or partial impaired activity: Days of total infirmity were on

Table 5 Comparison of the clinical outcomes of the three treating surgeons at 1 year post-loading.

	Spain	Dr Felice	Dr Pistilli	*P* value
Number of treated patients	27	24	20	NA
Dropout	2	2	1	0.908
Patients with failed prosthesis	4	3	0	0.210
Patients with failed implants	6 (22 implants)	3 (16 implants)	1 (1 implant)	0.236
Patients with failed augmentation procedure	0 out of 13	0 out of 13	0 out of 10	NA
Patients with complications	18 (29 complications)	12 (20 complications)	12 (16 complications)	0.480
OHIP 14	5.59 ± 7.88	2.68 ± 1.49	3.35 ± 1.90	0.593
Mean of total infirmity days	8.44 ± 3.18	7.04 ± 2.27	6.16 ± 1.42	0.010*
Mean of partial infirmity days	14.32 ± 5.40	12.61 ± 4.34	12.40 ± 2.21	0.252
Mean of days to functional loading	270.09 ± 375.90	157.14 ± 166.76	162.30 ± 165.56	0.281
Average number of patient dental visits	23.09 ± 13.55	14.80 ± 3.24	12.95 ± 2.16	< 0.001*§

Data are presented as mean ± standard deviation. NA: not applicable; significant comparisons: * Spain vs Dr Pistilli; § Spain vs Dr Felice.

average 7.42 ± 3.17 for the augmented group and 7.17 ± 1.96 for the zygomatic group; the difference being not statistically significant (mean difference = -0.25; 95% CI: -1.52 to 1.02; $P = 0.692$). Days of partial infirmity were on average 14.24 ± 4.64 for the augmented group and 12.17 ± 3.82 for the zygomatic group; the difference being statistically significant (mean difference = -2.07; 95% CI: -4.12 to -0.02; $P = 0.048$).

- Time to function: The mean number of days wearing a functional prosthesis were 444.32 ± 207.86 for augmented patients and 1.34 ± 2.27 for zygomatic patients; the difference being statistically significant (mean difference = -442.98; 95% CI: -513.10 to -372.86; $P < 0.001$).
- Number of dental visits: The average number of dental visits was 19.72 ± 12.22 for augmented patients and 15.12 ± 5.76 for zygomatic patients; the difference being not statistically significant (mean difference = -4.61; 95% CI: -9.31 to 0.92; $P = 0.055$).

The comparison of the clinical outcomes between the three treating surgeons is presented in Table 5. There were differences among surgeons for days of total impaired activity ($P = 0.010$; with significantly more days of impaired activity in the Spanish group than Dr Pistilli's group) and number of dental visits ($P = 0.001$; with a higher number of visits in the Spanish group than in both Italian groups).

Discussion

This trial was designed to understand whether it would be better to rehabilitate edentulous patients with atrophic maxillae by either performing bone augmentation procedures with bone substitutes and delayed placement of conventionally loaded standard dental implants or using immediately loaded zygomatic implants. Despite having more complications with zygomatic implants, the interpretation of the overall data suggests a more favourable outcome for zygomatic implants, since fewer implant and prosthesis failures occurred and patients could be rehabilitated within a couple of days when using zygomatic implants vs an average of 15 months if augmented. Obviously, these results apply only for the short-term period (1 year after loading). It would be sensible to wait for longer follow-ups (up to 10 years) before drawing definitive conclusions.

The main reasons why significantly more complications were reported for zygomatic implants is linked to the presence of post-operative paraesthesiae of both infraorbital nerves, affecting all patients treated at both Italian centres, but none at the Spanish centre. All paraesthesiae were transient, ranging from 1 week to 3 months, and were solved spontaneously. A plausible explanation for this difference is the possibly different surgical approaches of the surgeons, with the Italian operators opening wider flaps to better visualise the zygomatic bone. The Italian centres were less experienced with zygomatic implants when compared to the Spanish centre.

Patient quality of life, measured with the OHIP-14 score, significantly improved under both rehabilitation procedures, with no major difference between the two options. Only when it came to patients having difficulty relaxing was a statistically significant difference favouring zygomatic patients observed. It is difficult to provide a convincing explanation for this difference.

Days of total infirmity were similar for both groups, most likely depending on the major surgical interventions performed under general anaesthesia, whereas an average of two fewer days of partial infirmity were reported by patients rehabilitated with zygomatic implants; the difference being statistically significant. The number of visits required to rehabilitate the patients were also less when using zygomatic implants. In fact, patients with zygomatic implants required five fewer visits than the augmented patients. Even though the difference was not statistically significant, the *P* value was very close to significance ($P = 0.055$), suggesting that, also under the aspect of fewer numbers of visits, the rehabilitation with zygomatic implants proved advantageous.

The reason why at the 4-month post-loading follow-up 35 patients at the Italian centres were not rehabilitated with a definitive prosthesis as planned at protocol stage was due to a misunderstanding among the Italian centres and NobelBiocare, since the Italian centres did not ask for the definitive abutments and the definitive titanium Procera frameworks as agreed at protocol level, believing patients had to pay for definitive prostheses entirely by themselves. As a consequence, 35 patients were not able or willing to pay for the definitive prosthesis. As soon as the misunderstanding emerged, patients were called back and offered the definitive prostheses, and were only charged the dental technician's costs for lining the titanium frameworks with composite-resin or ceramic.

It is not possible to compare the present results with those of similar RCTs, as none are available. The only other published RCT on zygomatic implants compared the use of rotational drills vs piezo-surgery using specifically designed inserts in a split-mouth to prepare the sites for zygomatic oncology implants[17].

The main limitations of the present investigation were the small number of included patients, however sufficient to provide some useful indications, able to generate hypotheses for future investigations and the poor adherence to the research protocol regarding periapical radiographs to evaluate peri-implant marginal bone level changes.

Both procedures were tested in real clinical conditions and patient inclusion criteria were broad, therefore the results of the present trial can be generalised to larger populations with similar characteristics, keeping in mind that placement of zygomatic implants is a complex procedure requiring skilled and experienced operators, since potentially severe complications may occur.

Despite the good clinical performance of zygomatic implants, some unpleasant complications did occur, suggesting that their use should be limited to patients with severely atrophic maxillae. In the presence of less atrophic maxillae allowing the placement of short implants (4 mm to 6 mm long), it could be wiser to use short implants in view of the good results so far reported[9,18-24], even though this hypothesis has not yet been properly tested.

Conclusions

Preliminary 1-year post-loading data suggest immediately loaded zygomatic implants were associated with statistically significantly fewer prosthetic failures (one vs six patients), implant failures (two vs eight patients), and time needed to functional loading (1.3 days vs 444.3 days) when compared with augmentation procedures and conventionally loaded dental implants. Even if more complications were reported for zygomatic implants, they proved to be a better rehabilitation modality for severely atrophic maxillae. Long-term data are absolutely needed to confirm or dispute these preliminary results.

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