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Zygomatic versus conventional dental implants in augmented maxillae: a pragmatic multicenter randomised clinical trial

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Study coordinator: Marco Esposito

Co-Investigators: Roberto Pistilli, Wachtel Hannes

1. Study objectives

To compare the long-term clinical outcome of cross-arch maxillary bridges supported by zygomatic implants versus conventional implants placed in augmented bone.

2. Background

Dental implants are used for replacing missing teeth.(1) Placing dental implants is limited by the presence of adequate bone volume permitting 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 (for example the iliac crest), transplanted where needed and then implants are 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, though more recently bone substitutes are used to minimize morbidity,(2, 3) and 2 to 3 surgical interventions may be needed before the implants can be functionally used. Sometimes patients have to wait more than 1 year before a prosthesis can be fixed to the implants and the total cost of the treatment is high. At the beginning of the 1990s a long screw-shaped implant was developed by Professor P-I Brånemark as an alternative to bone augmentation procedures: the zygomatic implant.(4) Zygomatic implants are generally inserted through the alveolar crest to engage the body of the zygomatic bone.(5) One to 3 zygomatic implants can be inserted through the posterior alveolar crest to engage the body of each zygomatic bone. The potential main advantages of zygomatic implants could be that bone grafting may not be needed and a fixed prosthesis could be fitted the same day of their placement. Despite that zygomatic implants have been used for more than 20 years, their effectiveness has never been compared with conventional dental implants in augmented maxillae.(6)

3. Study design

Pragmatic multicenter randomised clinical trial of parallel group design.

1 Randomisation: using computer generated random numbers**,** centralized with sequentially

sealed opaque envelopes provided by the study coordinator.

2 Allocation concealment: Only patients willing to be randomized to either intervention will be recruited. The number of patients not willing to participate or not eligible will be reported and it must be explained why theses patients were not included. At least a week of time will be given to the patient to decide whether (s)he wishes to join the study. The sealed envelopes containing the randomized code will be opened ONLY AFTER the patient has been recruited in the study and has signed the informed consent.

3 Blinding: each centre will have an independent outcome assessor since blinding of the outcome assessor is not possible. One independent assessor (Dr Gerardo Pellegrino) will evaluate peri-implant marginal bone levels on intraoral radiographs for all centres.

At each centre there will be up to 2 surgical teams: one in charge of placing zygomatic implants and the other in charge of augmenting and placing conventional implants. There could be also a single team performing both procedures. In each team there will be a single surgeon and a single prosthodontist in charge of performing of surgical and prosthetic procedures (they could be the same person). All the procedures and the follow-ups have to be conducted at the treatment centres. Operators, procedures and materials will be similar at each centre.

4. Clinical centres

This study will be performed at 9 different international centres. Each centre will recruit 20 patients, 10 to be treated with zygomatic implants and 10 with augmentation procedures and conventional dental implants.

1) Main investigator: Dr Rubén Davó (Barcelona, Spain)
In charge of surgical procedures (zygomatic implants): Dr. Rubén Davó
In charge of surgical procedures (conventional implants): Dr. Carles Marti-Pages (Maxillofacial Surgery, Clinic Hospital)
In charge of prosthetic procedures (zygomatic implants): Dr. José Luis Marín
In charge of prosthetic procedures (conventional implants): Dr. José Luis Marín Galindo
Independent outcome assessor: Dr. Eloy García (Maxillofacial Surgery, Clinic Hospital)
In charge of data collection: Dr. Rubén Davó; Dr. Carles Martí Pagés; Dr. J.L. Marín

2) Dr Chantal Malevez (Bruxelles, Belgium)
In charge of surgical procedures (zygomatic implants): Dr Chantal Malevez & Dr P. Daelemans
In charge of surgical procedures (conventional implants): Dr Chantal Malevez & Dr P. Daelemans
In charge of prosthetic procedures (zygomatic implants): Dr F. Durdu
In charge of prosthetic procedures (conventional implants): Dr F. Durdu
Independent outcome assessor: Dr M. Khamaktchian
In charge of data collection: Chantal Malevez

3) Dr Guna Seelan (Chennai, India)
In charge of surgical procedures (zygomatic implants): Dr Gunaseelan Rajan
In charge of surgical procedures (conventional implants): Dr Gunaseelan Rajan
In charge of prosthetic procedures (zygomatic implants): Dr Saravana Kumar
In charge of prosthetic procedures (conventional implants): Dr Saravana Kumar
Independent outcome assessor: Dr B. Praveen
In charge of data collection: B. Praveen

4) Dr James Chow (Hong Kong, China)
In charge of surgical procedures (zygomatic implants): Dr James Chow
In charge of surgical procedures (conventional implants): Dr William Li
In charge of prosthetic procedures (zygomatic implants): Dr Adam Siu

In charge of prosthetic procedures (conventional implants): Dr Adam Siu
Independent outcome assessor: Dr Raymond Chow
In charge of data collection: Dr James Chow

5) Dr Giuseppe Luongo (Neaples/Rom, Italy)
In charge of surgical procedures (zygomatic implants): Prof Luigi Califano & Prof Giorgio Iannetti
In charge of surgical procedures (conventional implants): Dr Giuseppe Luongo & Dr Giampaolo Cassone
In charge of prosthetic procedures (zygomatic implants): Dr Pasquale Piombino
In charge of prosthetic procedures (conventional implants): Dr Roberto Ferrigno
Independent outcome assessor: Dr Sandro Ferrara
In charge of data collection: Dr Sandro Ferrara

6) Dr Pietro Felice and Roberto Pistilli (Bologna/Rom, Italy)
In charge of surgical procedures (zygomatic implants): Dr Pietro Felice
In charge of surgical procedures (conventional implants): Dr Pietro Felice
In charge of prosthetic procedures (zygomatic implants): Dr Roberto Pistilli
In charge of prosthetic procedures (conventional implants): Dr Roberto Pistilli
Independent outcome assessor: Dr Chersoni Stefano
In charge of data collection: Dr Elisa Soardi Antonini

7) Dr Dennis Rohner (Aarau, Swizterland)
In charge of surgical procedures (zygomatic implants): Dr Dennis Rohner
In charge of surgical procedures (conventional implants): Dr Dennis Rohner
In charge of prosthetic procedures (zygomatic implants): Dr Tobias Otto
In charge of prosthetic procedures (conventional implants): Dr Rainar Oberholzer
Independent outcome assessor: Dr Christoph Zizelmann
In charge of data collection: Dr Dennis Rohner

8) Dr Dr Wolfang Bolz and Prof Hennes Wachtel (Munich, Germany)
In charge of surgical procedures (zygomatic implants): Dr Wolfgang Bolz
In charge of surgical procedures (conventional implants): Prof Hannes Wachtel
In charge of prosthetic procedures (zygomatic implants): Dr Wolfgang Bolz
In charge of prosthetic procedures (conventional implants): Dr Marc Hinze
Independent outcome assessor: Robert Niedermayer
In charge of data collection: Robert Niedermayer

9) Prof Ashraf Ayoub (Glasgow, UK)
In charge of surgical procedures (zygomatic implants): Prof Ashraf Ayoub
In charge of surgical procedures (conventional implants): Prof Ashraf Ayoub
In charge of prosthetic procedures (zygomatic implants): Mr Raj Patel
In charge of prosthetic procedures (conventional implants): Mr Lee Sevario
Independent outcome assessor: Dr Vince Bissel
In charge of data collection: Mr Kurt Naudi

5. Sample size

The sample size was calculated for the primary outcome measures (implant failure): a two group continuity corrected chi-square test with a 0.050 two-sided significance level will have 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. The additional 36 patients will be recruited to compensate for drop-outs over a 15-year period.

6. Eligibility criteria

6.1 Inclusion criteria

Patients with fully edentulous and atrophic maxilla not having sufficient bone volumes for placing dental implants at all or when it is possible to place only 2 implants in the front area (minimal diameter 3.5 mm and length of 8 mm) as evaluated on TC scans. No more than 4 mm of bone height should be available subantrally.

6.2 Exclusion criteria

- General contraindications to implant surgery.
- Patient irradiated in the head and neck region with > 70 Gray.
- Immunosuppressed or immunocompromised patients.
- Patients who took or are taking amino-bisphosphonates intravenously.
- Patients with poor oral hygiene and motivation.
- Patients with untreated periodontitis.
- Uncontrolled diabetes.
- Pregnancy or lactation.
- Addiction to alcohol or drugs.
- Psychiatric problems.
- Lack of opposite occluding dentition/prosthesis.
- Restricted mouth opening (less than 3.5 cm inter-arch anteriorly).
- Patients with an acute or chronic infection/inflammation in the area intended for implant placement.
- Patient unable to commit to 15 year follow-up
- Patients participating in other investigations, if the present protocol cannot be properly adhered to.
- Patients referred only for implant placement.

7. Device description and specifications

7.1 Zygomatic implants

Branemark System Zygoma Ti-Unite Implants RP (Nobel Biocare, Gothenburg, Sweden) having the following lengths: 30, 35, 40, 42.5, 45, 47.5, 50 and 52.5 mm.

7.1 Conventional dental implants

Nobel Active implants (Nobel Biocare) with internal connection. Operators are free to choose implant lengths (8.5, 10, 11.5, 13 and 15 mm) and diameters (3.5, 4.3 and 5.0 mm) according to the clinical indications and their preferences.

7.3 Augmentation materials

- Bone substitutes:

Blocks: collagenated blocks (OsteoBiol, Sp-Block, Tecnoss, Coazze, Italy) of equine cancellous bone. OsteoBiol Sp-Block must be hydrated before use for 5/10 minutes with sterile lukewarm physiological solution or with antibiotics. Afterwards, it can be adapted to the receiving site which must be accurately decorticated in order to guarantee maximum contact; the block must always be fixed with osteosynthesis microscrews and should be protected with a resorbable barrier (OsteoBiol, Evolution membrane).

Granules: a paste made of 600-1000 micron pre-hydrated collagenated cortico-cancellous granules of porcine origin, properly mixed with OsteoBiol Gel 0 in sterile syringe (OsteoBiol mp3, 1 cc) will

be used to augment the maxillary sinus. The use of autogenous bone or other bone substitutes is not allowed.

- Screws for connecting the blocks:
Self drilling Ti6Al4V screws (Graftek, Tekka, Brignais, France) diameters 1.5 or 2 mm (various lengths from 4 to 19 mm).

- Barriers:
The grafted areas will be covered with a resorbable collagen membrane derived from equine pericardium (OsteoBiol, Evolution). The use of other types of membranes is forbidden.

7.4 Prosthetic materials
Provisional acrylic reinforced screw-retained cross-arch fixed bridges.
Definitive screw-retained cross-arch fixed Procera Implant Bridge Titanium (Nobel Biocare) with ceramic or acrylic veneer materials.

8. Outcome measures

The outcome measures will be:

8.1 Prosthesis success
When prosthesis placement will not be possible due to implant failure or the prosthesis is lost due to implant failures

8.2 Implant success
Implant mobility assessed manually with the removed prosthesis and/or any infection dictating implant removal. Assessments will be done at abutment connection, delivery of the provisional and definitive prostheses, 1, 3, 5, 7, 10, 15 years of loading by tightening the abutment screws with the removed prostheses using a manual wrench with a 15 Ncm force. Rotating implants will be considered failures and should be removed. It may be possible that a few zygomatic implants may display a slight horizontal mobility due to their lengths and possible lack of alveolar bone at their exits, this will be noted into the CRF forms but the implants, if not rotating, will be considered as successful.

8.3 Complications
Any biological and prosthetic complication at the implant sites (number and type) occurring during the entire follow-up time will be recorded and reported per study group.

8.4 Failure of the augmentation procedure
The augmentation procedure will be considered a failure if, after it has been performed, it will not be possible to place the planned implants in the augmented site.

8.5 Marginal bone levels on intra-oral radiographs
To be evaluated on intraoral radiographs taken with the paralleling technique at implant placement, at delivery of the provisional prostheses, 1, 3, 5, 7, 10 and 15 years after loading. Only the zigomatic implants with the neck embedded into crestal bone will be radiographically evaluated. Those placed adjacent to the crestal bone will not be subjected to bone level assessments since they have no bone around them. Ideally digital radiographs should be taken. Conventional radiographs will be scanned digitized in JPG, converted to TIFF format with a 600 dpi resolution, and stored in a personal computer. Peri-implant marginal bone levels will be measured using the UTHSCSA Image Tool 3.0 (The University of Texas Health Science Center, San Antonio, USA) software. The software will be calibrated for every single image using the known distance between 2 threads.

Measurements of the mesial and distal bone crest level adjacent to each implant will be made to the nearest 0.01 mm and averaged at patient level and then at group level. The measurements will be taken parallel to the implant axis. Reference points for the linear measurements are: the most coronal margin of the implant collar and the most coronal point of bone-to-implant contact.

8.6 Oral Health Impact Profile OHIP-14 (quality of life)
To be filled in at patient enrolment prior of delivering any interventions, 1-2 weeks after delivery of the definitive prostheses, 1, 3, 5, 7, 10 and 15 years after loading.

8.7 Patients' number of days with total or partial impaired activity assessed at delivery of the provisional prosthesis
Days of total impaired activity are those days that, according to the patient opinion, (s)he could not perform his/her ordinary life activity including work.
Days of partial impaired activity are those days that, according to the patient opinion, (s)he could only partially perform his/her ordinary life activity including work.

8.8 Time to function
Number of days from the fist surgical intervention to the delivery of the implant-supported provisional prosthesis

8.9 Number of sessions with the dentist
Total number of appointments, including those for maintenance and treatment of complications, required by the patient over the entire follow-up period.

9. Study Procedures and Assessments

9.1. Pre-treatment procedures
Screening visit, radiographic assessment and group allocation (APPENDIX 1)
Patients will be assessed to establish their eligibility for the study evaluating their CT scans or Cone Beam 3D imaging. Coronal slices should be added to the conventional CT scans in order to evaluate the osteomeatal complex and sinus mucosa state. Only patients with healthy sinuses will be asked to join the trial. Please complete APPENDIX 1 (Patient eligibility CRF) and record the number and reason of non-included patients. Patients will be informed on the nature of the study, they have to show that they understood the nature of the research and they will be given at least a week for reflecting before signing the detailed informed consent. The OHIP short questionnaire will be filled by the patient and the patient will be allocated to one of the 2 groups following the indications contained in the sequentially numbered envelope corresponding to the recruitment number of the patient. After randomisation patients will be asked for which procedure they would have preferred to choose.

Diagnostic was-up may be necessary. Surgical guides will be prepared to help clinicians to select the most appropriate position and angulation of each implant. For zigomatic implants, efforts will be made to plan implant exits at crestal level rather than palatally.

9.2. Surgical procedures
Prior to each surgical intervention, patients will rinse for 1 minute with chlorhexidine 2% to decrease the intra-oral bacteria load.

Surgeons are free to decide with the patients the preferred type of anaesthesia (local anaesthesia alone, local anaesthesia with sedation or general anaesthesia with local anaesthesia) to deliver. This information will be recorded.

Antibiotic prophylaxis will consist of 2 g of Augmentin (or 600 mg of clindamycin for patients allergic to penicillin) to be administered orally, or in case of intravenous sedation/general anaesthesia Augmentin 1 g (or clindamycin 300 mg) intravenously prior to bone augmentation and implant installation.

According to the outcome of the randomisation and to the degree of bone atrophy of the maxilla and there are 4 different surgical options:

Zygomatic implants

Very atrophic maxillas:

Quadruple zygomatic implants, 2 per side possibly immediately loaded (within 1 week). Implants need to achieve an insertion torque of at least 40 Ncm in order to be loaded immediately otherwise a 4-month submerged healing will be required.

After crestal incision and flap elevation exposing the maxilla to allow the identification of the infraorbital foramen and of the incisura between the zygomatic arch and the lateral and medial surface of the frontal process of the zygomatic bone, a 10 x 5 mm window or wider windows extending from the sinus floor to the base of the zygomatic bone, may be opened on the lateral wall of the maxillary sinus close to the infrazygomatic crest, and the sinus lining carefully lifted. In alternative, ideally and if anatomical conditions allow, the implant will not be inserted through the sinus cavity but into the bone laterally to it. The implant exit should be at crestal level and not on the palate. A retractor is placed to the incisura between the zygomatic arch and the lateral and medial surface of the frontal process of the zygomatic bone to facilitate the correct 3-dimensional orientation of the implant. A round bur is used first. While drilling it is important that adequate irrigation is provided. Then the twist drill of 2.9 mm diameter is used until it penetrates the outer cortical layer of the zygomatic bone at the incisura. The length of the implant to be used is determined with the straight depth indicator. The 3.5 diameter pilot drill is then used followed by the 3.5 mm twist drill. The zigomatic implant is finally inserted, hopefully with of insertion torque at least 40 Ncm to allow for immediate loading. After the first implant is placed, the same procedures will be repeated to place the second implants. Implant apexes have to be placed about 1 cm apart. **Centres are allowed, at their discretion, to cover exposed threads with the MP3 granules and Osteobiol Evolution resorbable barrier (this information will be recorded).**

The following post-surgical instructions will be given:

- Augmentin 1 g (or Clindamycin 300 mg) 3 times a day for 1 week.
- Ibuprofen 600 mg will be prescribed to be taken 4 times a day during meals for 1 week, but patients will be instructed not to take them in absence of pain.
- Otrivin (nasal decogestionant) 5 drops 3 times a day for 2 weeks.
- A soft diet is recommended for 2 weeks.
- 0.2% chlorhexidine rinses twice a day for 2 weeks.
- Patients will be recalled and checked at day 3; day 10 (suture removal) and month 1.

Atrophic maxillas:

1 zygomatic and 1 conventional implant per side, possibly immediately loaded (within 1 week). Implants need to achieve an insertion torque of at least 40 Ncm to be loaded immediately otherwise a 4-month submerged healing will be required.

The same procedure previously described will be used to place one zygomatic implant per side. In addition, one conventional implant (Nobel Active) per side will be placed in the anterior zone (canine to canine) according to the manufacturer' instructions. It is important that an insertion torque of at least 40 Ncm is also obtained for the conventional implant.

The following post-surgical instructions will be given:

- Augmentin 1 g (or Clindamycin 300 mg) 3 times a day for 1 week.

- Ibuprofen 600 mg will be prescribed to be taken 4 times a day during meals for 1 week, but patients will be instructed not to take them in absence of pain.
- A soft diet is recommended for 2 weeks.
- Otrivin (nasal decogestionant) 5 drops 3 times a day for 2 weeks.
- 0.2% chlorhexidine rinses twice a day for 2 weeks.
- Patients will not be allowed to wear any removable denture up to one month postoperatively.
- Patients will be recalled and checked at day 3; day 10 (suture removal) and month 1.

Augmentation procedure and conventional implants

Very atrophic maxillas:

- Posteriorly: 2-stage sinus lift with lateral window approach using a granular bone substitute and a resorbable barrier. After internal displacement of the bony window, the maxillary membrane will be carefully elevated and the sinus will be packed with the MP3 granules. In case of rupture of the sinus lining a resorbable barrier (Osteobiol Evolution) will be used to contain the graft or the operation will be postponed.
- Anteriorly: Bone substitute blocks (Osteobiol SP-Block) will be used as onlays/veneers, where needed, fixed with titanium screws and covered with a resorbable barrier (Osteobiol Evolution). The recipient site will be perforated with a drill to increase bleeding. The bone substitute granules will be used to fill the gaps between the recipient bone and the bone block. In alternative small defects can be treated with the granules and barriers alone according to clinical indications and preference of the surgeon. All bone blocks and the maxillary windows will be covered with OsteoBiol Evolution resorbable barriers fixed with pins.

The following post-surgical instructions will be given:
- Augmentin 1 g (or Clindamycin 300 mg) 3 times a day for 1 week.
- Ibuprofen 600 mg will be prescribed to be taken 4 times a day during meals for 1 week, but patients will be instructed not to take them in absence of pain.
- Otrivin (nasal decogestionant) 5 drops 3 times a day for 2 weeks.
- A soft diet is recommended for 2 weeks.
- To avoid blowing the nose and using drinking straws.
- In case of sneezing to try to keep the mouth open in order to decrease intra-sinus pressure
- 0.2% chlorhexidine rinses twice a day for 2 weeks.
- Patients will not be allowed to wear any removable denture up to one month postoperatively.
- Patients will be recalled and checked at day 3; day 10 (suture removal) and month 1.

Just prior to implant placement a second CT scan will be made to properly evaluate bone anatomy and to plan implant placement. After 6 months healing, 6 to 8 conventional Nobel Active implants will be placed and left to heal submerged for 4 months.

Atrophic maxillas:

1- or 2-stage (depending whether the implants can be stabilised or not) sinus lift with lateral window approach using OsteoBiol mp3 bone substitute granules and OsteoBiol Evolution resorbable barriers. In case of rupture of the sinus lining a resorbable barrier (OsteoBiol Evolution) will be used to contain the graft or the operation will be postponed.

The following post-surgical instructions will be given:
- Augmentin 1 g (or Clindamycin 300 mg) 3 times a day for 1 week.
- Ibuprofen 600 mg will be prescribed to be taken 4 times a day during meals for 1 week, but patients will be instructed not to take them in absence of pain.
- Otrivin (nasal decogestionant) 5 drops 3 times a day for 2 weeks.
- A soft diet is recommended for 2 weeks.
- To avoid blowing the nose and using drinking straws.

- In case of sneezing to try to keep the mouth open in order to decrease intra-sinus pressure
- 0.2% chlorhexidine rinses twice a day for 2 weeks.
- Patients will be recalled and checked at day 3; day 10 (suture removal) and month 1.

In case of 1-stage sinus lift procedure, implants will be left to hear submerged for 6 months. In case of a 2-stage sinus lift procedure, after 6 months healing, 6 to 8 conventional Nobel Active implants will be placed and left to heal submerged for 4 months.

9.3. Prosthetic Procedures

Quadruple zygomatic implants in very atrophic maxillas and 2 zygomatic and 2 conventional implants (immediate loading)

Immediately after insertion of the implants, Zygoma Abutment Multi-unit or Zygoma 17 degree Abutment Multi-unit and Multi-unit NobelActive Internal abutments (straight, 17 and 30 degrees; Nobel Biocare) will be placed. Periapical radiographs will be taken to verify proper seating of all abutments, a rubber dam will be used to cover the surgical incisions and the sutures, and an impression will be taken with a rigid impression material and impression copings with an open tray. A screw-retained reinforced full acrylic cross-arch provisional bridge will be delivered within 1 week.

Conventional implants in atrophic maxillas (conventional loading)

After implants exposure, Multi-unit NobelActive Internal abutments (straight, 17 and 30 degrees), (Nobel Biocare) will be placed, periapical radiographs will be taken to verify proper seating of all abutments, Multi-unit straight abutments will be tightened with a torque of 35 Ncm, whereas angulated Multi-unit abutments with 15 Ncm using the Manual Torque Wrench Prosthetic and Screwdriver Machine Multi-unit. An impression will be taken with a rigid impression material and impression copings using an open tray. A screw-retained reinforced full acrylic cross-arch provisional bridge will be delivered within 1 week.

Common procedures

1-2 weeks after delivery of the provisional bridges, patients will be recalled for a check-up.

3 months after delivery of the provisional bridges, prostheses will be removed, implant stability will be checked by tightening the abutment screws with a 15 Ncm torque using the Manual Torque Wrench Prosthetic and Screwdriver Machine Multi-unit, and the definitive impression at abutment level will be taken with a rigid impression material and impression copings with an open tray.

Within one month definitive screw-retained metal-ceramic or metal acrylic definitive cross-arch Procera Implant Bridges (Nobel Biocare) will be delivered.

1-2 weeks after delivery of the provisional bridges, patients will be recalled for a check-up and will be asked to fill in the OHIP-14.

9.4. Maintenance and follow up visits

Professional maintenance will be delivered every 6 months after loading to all patients. Individual operators can decide to increase maintenance frequency (every 3-4 months) based on individual needs. Dental occlusion will be evaluated at each maintenance visit.

In case of suspected implant failures, sinusitis, peri-implantitis, suppuration, erythema, prosthetic complications, etc., observed during any of the scheduled visit or during an unplanned visit, periapical radiographs and clinical pictures have to be taken and the “Complication, protocol deviation and drop-out CRF” (APPENDIX 4) should be filled in.

The following parameters will be recorded by the independent assessors just after delivery of the definitive prostheses and at 1, 3, 5, 7, 10, 15 years:

1) OHIP-14
2) The occlusion will be checked
3) Periapical radiographs with the paralleling technique
4) Bridges will be removed and the stability of the individual implants tested by tightening the abutments with a torque of 15 Ncm
5) The number of visits since the previous follow-up time-point.

10. Statistical analysis

All data analysis will be carried out according to a pre-established analysis plan by a biostatistician with expertise in dentistry blinded to group allocation. A comparison of the baseline characteristics between groups will be presented. Differences in the proportion of prosthetic failures, implant failures, augmentation procedure failures and complications will be compared between the groups using the Fisher's exact probability test. Differences between the groups in mean marginal bone level changes, quality of life number of days with total or partial impaired activity, time to function, and number of sessions with the dentists will be compared by t-tests. Comparisons between the various follow-up endpoints and the baseline measurements will be made by paired tests, to detect any changes in mean marginal bone level changes for each study group. An analysis of covariance will be used to compare the mean radiographic values at baseline and 1 year, with the baseline value as a covariate. All statistical comparisons will be conducted at the 0.05 level of significance.

11. Publication plan

1) 4 months after loading (Esposito et al to EJOI)
2) 1 year after loading (Malevez et al to JOMI)
3) 3 years after loading (Davó et al to COIR)
4) 5 years after loading (Luongo et al to EJOI)
5) 7 years after loading (Seelan or et al to JOMI)
6) 10 years after loading (Felice et al to EJOI)
7) 15 years after loading (Chow et al to EJOI)

All study participants delivering the agreed data will be in the authors' list in each publication.

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