Immediate, early (6 weeks) and delayed loading (3 months) of single implants: 4-month post-loading from a multicenter pragmatic randomised controlled trial

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Purpose: To compare the clinical outcome of single, partial and full fixed implant-supported prostheses immediately loaded (within 48 h), early loaded at 6 weeks and conventionally loaded at 3 months (delayed loading).

Materials and methods: Eighty-one patients (27 requiring single implants, 27 requiring partial fixed prostheses and 27 requiring total fixed cross-arch prostheses) were randomised in equal numbers in three private practices to immediate loading (27 patients), early loading (27 patients) and conventional loading (27 patients) according to a parallel group design with three arms. To be immediately or early loaded, implants had to be inserted with a torque superior to 40 Ncm. Implants were initially loaded with provisional prostheses and replaced after 4 months by definitive ones. Outcome measures were prostheses and implant failures and complications.

Results: No patient dropped out up to 4-months post-loading. No implant or prosthesis failed or any complications occurred.

Conclusions: All loading strategies were highly successful and no differences could be observed for implant survival and complications when loading implants immediately, early or conventionally.

Conflict-of-interest statement: This trial was partially funded by MegaGen, the manufacturer of the implants evaluated in this investigation, however data belonged to the authors and by no means did the manufacturer interfere with the conduct of the trial or the publication of its results.

Introduction

Osseointegrated dental implants are placed traditionally following a two-stage protocol. With this approach, implants are left to heal unloaded for 3 to 4 months in mandibles and 6 to 8 months in the maxillae. Successful osseointegrated dental implants are anchored directly to bone. However, in the presence of movements, a soft tissue scar tissue may encapsulate the implant, causing its failure. It has been recommended to keep the implants load-free during the bone healing process to minimise the risk of soft tissue encapsulation. This traditional approach requires longer treatment periods and according to the procedures used, a second surgical intervention may be needed to uncover submerged implants to allow abutment connection. Early attempts to load implants earlier than the traditional protocols were associated with increased failure rates. Removable prostheses are often used during the implant healing period, but many patients find these temporary prostheses uncomfortable. It would therefore be beneficial for the patients if the healing period could be shortened without jeopardising implant success. In
1990, the first longitudinal study was published suggesting that implants could be loaded immediately or early in mandibles of selected patients\(^3\). Nowadays, implants are commonly loaded immediately and early, particularly in fully edentulous mandibles with good bone quality. A Cochrane systematic review suggested that there was no convincing evidence of a clinically important difference in prosthesis failure, implant failure or bone loss associated with different loading times of implants\(^4\). However, the review also stressed that the quality of the evidence was scored as ‘very low’ and there is some evidence of reporting bias, therefore clinicians should treat these findings with caution\(^4\). Occasionally immediately loaded\(^5,6\) and early\(^7\) loaded implants have been associated with clinically relevant increased failure rates, therefore it is important to evaluate whether predictable results can also be obtained when loading dental implants immediately or early in different clinical situations, for example in the case of a missing single tooth, partial and full edentulism.

The aim of this randomised controlled trial (RCT) of parallel group design with three arms was to compare the effectiveness of immediate loading within 48 h (test group 1) versus early loading (test group 2) at 6 weeks versus delayed (or conventional) loading at 4 months (control group). Groups were also balanced for type of edentulism, in fact three subgroups consisting of an identical number of patients requiring the replacement of a single tooth, partial edentulism and full edentulism, were included. The null hypothesis was that there would be no difference in clinical outcomes between the three procedures, against the alternative hypothesis of a difference.

Immediate loading was defined as seating a provisional prosthesis within 48 h of implant placement. Early loading was defined as seating a provisional prosthesis 6 weeks after implant placement, and delayed loading as seating a provisional prosthesis 3 months after implant placement.

This report presents preliminary data at 4-months post-loading. At protocol stage, it was planned to follow-up these patients to the third year of function. The present article is reported according to the CONSORT (Consolidated Standards of Reporting Trials) statement for improving the quality of reports of parallel group randomised trials (http://www.consort-statement.org/).

### Materials and methods

This was a multicenter RCT of parallel group design with three arms, balanced randomisation and blind assessment. After implant placement, an equal number of patients with single, partial or full edentulism, were randomised in equal numbers into three groups according to a parallel group design: immediate loading (within 48 h), early loading at 6 weeks and conventional loading at 3 months (delayed loading).

Patients were recruited and treated in three private dental clinics located in Larissa, Greece, Vilnius, Lithuania and Roma, Italy, all having extensive experience in rehabilitation with immediate loading procedures. Originally five centres agreed to participate in the study but two centres withdrew before initiating the study, without treating any patient. One experienced surgeon at each centre performed all the operations and patients were randomised into equal numbers in three groups according to a parallel group design: immediate loading (within 48 h), early loading at 3 weeks and conventional loading at 3 months.

Any partially or fully edentulous patient requiring at least one implant-supported prosthesis, who was 18 years of age or older, and able to understand and sign an informed consent form was eligible for inclusion in this trial. Only patients allowing placement of one or more implants with minimal dimensions of 7.0 x 3.5 mm were included. In total six implants were to be placed in an edentulous jaw. All patients received thorough explanations and signed a written informed consent form prior to being enrolled in the trial to document that they understood the scope of the study (including procedures, follow-up evaluations and any potential risks involved). Patients were given the opportunity to ask questions pertaining to this investigation, and were apprised of treatment alternatives. The study was open to qualifying patients without regard to sex or race. For patients requiring more than one prosthesis, operators were free to choose the one to be included in the study at the screening visit. Only one prosthesis per patient was entered in the study. Preoperative radiographs (periapical, panoramic, cone-beam computerised tomography scans or other radiographic examinations at the discretion of the operators) together with clinical inspections were used to determine bone
Patients were not accepted into the study if any of the following exclusion criteria was present:

- general contraindications to implant surgery;
- irradiated in the head and/or neck with more than 70 Gy;
- immunosuppressed or immunocompromised;
- treated or under treatment with intravenous aminobisphosphonates;
- uncontrolled diabetes;
- pregnant or nursing;
- substance abusers;
- psychiatric problems and/or unrealistic expectations;
- poor oral hygiene and motivation;
- untreated periodontitis;
- acute infection/inflammation in the area intended for implant placement;
- need of bone augmentation at implant insertion with the exception of filling bone-to-implant gaps at immediate post-extractive implants;
- lack of opposite occluding dentition/prosthesis in the area intended for implant placement;
- severe bruxism or clenching;
- participation in other investigations, if the present protocol could not be properly adhered to;
- unable to commit to a 3-year follow-up;
- referred only for implant placement if the patient could not be followed at the treatment centre.

Patients were 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). Patients were also categorised into two groups: i) whether the opposite jaw had natural dentition/fixed prostheses or ii) removable prosthesis/dentures.

All patients received prophylactic antibiotic therapy at the dental practice: two grams of amoxicillin given 1 h before implant placement. Patients allergic to penicillin were given 600 mg of clindamycin 1 h before implant placement. Patients rinsed with 0.2% chlorhexidine mouthwash for 1 min prior to any intervention. Local anaesthesia was obtained using articaine with adrenaline 1:100,000. Intravenous sedation could also be used. In the presence of a tooth to be extracted, intrasulcular incisions were performed and extended mesially and distally without any vertical incision. Para-crestal or mid-crestal incisions were performed and full-thickness crestal flaps were elevated with a minimal extension to minimise patient discomfort. Teeth extractions were performed asatraumatically as possible to preserve the buccal alveolar bone, using periotomes and small levers. Extraction sockets were carefully cleaned of any granulation tissue.

AnyRidge Xpeed (MegaGen Implant, Gyeongbuk, South Korea) threaded titanium implants with an internal connection were used. Operators were free to choose implant lengths (7.0, 8.5, 10.0, 11.5, 13.0 and 15.0 mm) and diameters (3.5, 4.0, 4.5, 5.0, 6.0 and 7.0 mm) according to clinical indications and their preferences.

After initial drilling of the implant site, a 2 mm-diameter pilot drill was used to prepare the implant site and to subjectively discriminate bone quality into hard, medium or soft. Implant sites were prepared according to bone quality: in hard bone quality the sequence of drills suggested by the manufacturer were used. In medium bone quality, sites were under-prepared using a final drill, one diameter smaller than the one suggested; and in the case of soft bone, sites were underprepared using a final drill, two diameters smaller than suggested.

Implants were inserted in the osteotomy site with the motor set at a torque of 40 N/cm and, once the motor stopped, manually with a dedicated ratchet until seated at the level with the alveolar bone crest. In cases where an implant was inserted with a torque inferior to 40 Ncm, operators were free to decide whether to prepare an alternative implant site, to replace it with a larger diameter or longer implant, in order to attempt to obtain the required insertion torque, or loading it conventionally after 3 months of healing.

Post-extractive implants were placed 1 to 2 mm below the most coronal bone of the surrounding crest and slightly palatally. In the case of a bone-to-implant gap, each center had different strategies: the Greek center did not use any biomaterial or membrane, the Italian centre used granules of anorganic bovine bone (Bio-Oss; 0.25 to 1.00 mm, Geistlich Pharma, Wolhusen, Switzerland) to fill the bone-to-implant gaps and, if needed, the exposed grafted areas were covered with resorbable collagen membranes (Bio-Gide, Geistlich Pharma). The Lithuanian
centre used granules of organic corticocancellous porcine bone (Gen-Os 2 to 4 mm, Tecnoss, Coazze, Italy) with resorbable collagen membranes (Evolu-
tion, Tecnoss) from porcine pericardium.

After having completed the implant placement procedure, the sequentially numbered envelope corresponding to the patient was opened in order to inform when to load the implant; immediately (Figs 1a to 1h), early (after 6 weeks; Figs 2a to 2s), or conventionally (after 3 months; Figs 3a to 3h). According to the random allocation, impression copings or cover screws were placed. Implants were submerged and interrupted sutures were placed. A baseline periapical radiograph of the study implant was taken with the paralleling technique, and if the peri-implant marginal bone levels were not clearly discernible or the implant image was too distorted, a second periapical radiograph was taken. Impressions at implant level with the pick-up impression copings were made for those implants to be immediately loaded.

The following post-surgical instructions were given:
• A cold and soft diet was recommended for 1 week.
• No removable prosthesis compressing the surgical wound should be used for 1 week.
• Ibuprofen 400 mg (or 1 g paracetamol for patients allergic to non steroidal anti-inflamma-
tory drugs) to be taken 2 to 4 times a day during meals, only if needed.
• Patients were prescribed 0.2% chlorhexidine mouthwash for 1 min twice a day for 2 weeks.

 Provisional screw-retained acrylic resin prostheses (which could also be reinforced according to the clinical situation) were fabricated and delivered within 2 days from implant placement for the immediately loaded group. If necessary, abutments were cut and modified on implant analogues. Implants of the early loaded group were exposed at 6 weeks. Implants of the conventionally loaded group were exposed at 3 months and were subjected to identical prosthetic procedures.

During loading with provisional prostheses, periapical radiographs of the early and conventionally loaded implants were taken with the paralleling technique. Patients were seen after 3 days to check the occlusion, and after 10 days for a second checkup of the occlusion, oral hygiene instructions and suture removal.

 Provisional prostheses were replaced after 4 months by definitive screw-retained or cemented metal-ceramic prostheses. All implants were manually tested for mobility by tightening the abutment screws with the removed crowns, with the dedicated manual ratchet at 35 Ncm.

 Patients were to be recalled at least every 6 months for oral hygiene maintenance and prosthetic controls.

 Primary outcome measures were:
• Prosthesis failure: whether or not it was possible to place the prosthesis due to implant failures or secondary to implant losses, or replacement of the definitive prosthesis for any reasons.
• Implant failure: implant failure was defined as implant mobility and/or any infection dictating implant removal or any mechanical failure rendering the implant unusable, such as implant fracture or deformation of the implant-abutment connection. The stability of each implant was measured manually by tightening the abutment screw at definitive prosthesis delivery using a manual wrench with a 35 Ncm force. Rotating implants were considered as failures.
• Any complication and adverse event was to be recorded and reported.

Peri-implant marginal bone level changes will be reported in future reports of this trial. Implant stability was assessed by local blinded outcome assessors, whereas complications were assessed by the treating clinicians who were not blinded.

The sample size was calculated on the primary outcome measure as a proportion of patients experiencing an implant failure. A two-group continuity corrected chi-square test with a 0.050 two-sided significance level has 90% power to detect the difference between a group 1 proportion of 0.100 and a group 2 proportion of 0.200 (odds ratio of 2.250), when the sample size in each group is 286. However, our recruitment capacity could not match the required sample size and therefore it was decided to include 45 patients per group. Originally, five centres agreed to participate in the study, each agreeing to recruit 27 patients (nine patients...
Treatment sequence of one of the patients of Dr Siompas requiring a single tooth replacement and randomly allocated to immediate loading: a) preoperative orthopantomograph showing the edentulous space in area 36; b) implant placement; c) baseline periapical radiograph; d) provisional crown; e) provisional crown in position; f) definitive crown delivered 4 months after immediate loading; g) occlusal view; h) periapical radiograph at delivery of the definitive crown.

In each group) for a total of 45 patients per group. Unfortunately, because two centres withdrew from the study, only 27 patients per group were actually recruited.

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

All data analysis was to be carried out according to a pre-established analysis plan. The patient was the statistical unit of the analyses. A clinician with expertise in dental biostatistics would analyse the data, without knowing the group allocation. Intention to treat analyses were to be performed. The chi-square test was to be used to compare dichotomous variables (failures and complications) between the three groups and between the three centres. All statistical comparisons were to be conducted at the 0.05 level of significance.

Results

One hundred and thirteen patients were originally screened for eligibility but 20 patients from the Lithuanian centre and 12 patients from the Italian centre were not enrolled in the trial. Two patients from the Lithuanian centre were unable to attend follow-ups and the remaining 30 patients did not want to have their implants loaded at a randomly decided time. Eighty-one patients were consecutively enrolled in the trial and randomised: 27 to the immediate, 27 to the early and 27 to the conventional loading groups. As per protocol, each centre recruited nine patients in need of a single implant-
supported crown, nine patients in need of a partial fixed prosthesis and nine patients requiring a cross-arch prosthesis, and randomly allocated them into equal numbers for the three different loading protocols. All patients were treated according to the allocated interventions. No dropout occurred up to
One operator did not achieve a torque of 40 Ncm in four implants in 2 fully edentulous patients: three implants were to be loaded immediately and one early. The operator therefore loaded the implants that achieved at least 40 Ncm torque according to the randomly allocated time and loaded the other implants after 4 months, at delivery of the definitive prostheses. The data of all patients was evaluated in the statistical analyses. Deviations from the operative protocol were the following:

- Dr Siormpas: All patients of the conventionally loaded group were directly rehabilitated with the delivery of the definitive prostheses (4 months after initial loading).

Fig 3a-h Treatment sequence of one of the partially edentulous patients of Dr Siormpas randomly allocated to the conventional loading group: a) preoperative orthopantomograph; b) clinical view at placement of implants in positions 45 and 47; c and d) baseline periapical radiograph at implant placement; e and f) periapical radiographs at initial loading, 3 months after implant placement, with the definitive prosthesis (this is one of the protocol deviations which occurred since the patient should have been initially rehabilitated with a provisional prosthesis instead); g) definitive prosthesis; h) periapical radiograph, 4 months after initial loading.
definitive prostheses without using any interim provisional restorations, and one partially edentulous patient from the early loading group had implants which were not submerged.

- Dr Bechara: Periapical radiographs were not taken as demanded by the research protocol but orthopantomographs were taken in some cases. A partially edentulous patient was included instead of a fully edentulous one (immediate loading group), which was also subjected to horizontal bone augmentation with Gen-Os and Evolution membranes at implant placement. Three fully edentulous patients of the early loaded group were rehabilitated with three (1 patient) and two (2 patients) partial fixed prostheses instead of a single cross-arch prosthesis as per protocol. One partially edentulous patient of the conventional loading group, was rehabilitated with two adjacent single crowns instead of a prosthesis joining both implants. One partially edentulous patient of the immediate loading group, one fully edentulous patient of the immediate loading group and two fully edentulous patients of the early loaded group were horizontally augmented with Gen-Os, in two cases, also using Evolution membranes.

- Dr Pistilli: Three patients with fully edentulous maxillae, 2 allocated to the conventionally loaded group and 1 to the immediately loaded group received eight, seven and seven implants respectively, instead of the six implants as agreed at protocol level. Another patient with a fully edentulous mandible received just two implants instead of the four planned implants due to the fact that the patient had a hypotensive episode during surgery with oxygen saturation dropping to 86 (severe hypoxic condition), which led to the anaesthetist advising stoppage of the procedure. The patient, then randomly allocated to the conventional loading procedure, was rehabilitated with an overdenture supported by two implants. In the conventional loading group 3 patients were subjected to augmentation procedures: one crestal sinus lift at a single implant using anorganic bovine bone (Bio-Oss); one horizontal augmentation with Bio-Oss and collagen resorbable membranes (Bio-Gide) in a partially edentulous patient; and one split-crest procedure using Bio-Oss. Finally, three fully edentulous patients who had post-extractive sites filled with Bio-Oss, also had the buccal bone horizontally augmented with Bio-Oss; two patients, allocated to the immediate loading group, had the graft covered with Bio-Gide membranes; and one patient, allocated to the early loading group, had the graft covered with A-PRF (platelet-rich fibrin) membranes.

Patients were recruited and treated from September 2012 to July 2015. The follow-up focused on the time between implant placement and 4 months after loading. The main baseline patient characteristics are presented in Table 1. Baseline patient characteristics were similar, with the following exceptions: in the conventional loading group there were more mandibular implants, more implants in molar sites, more implants in bone of soft quality, more implants placed with a torque inferior to 40 Ncm and less post-extractive sites than in the other groups.

No prosthesis or implant failures and complications were reported for any of the patients up to 4 months after loading.

Discussion

The present trial was designed to evaluate whether immediate and early loading of dental implants could provide similar clinical outcomes as conventional (delayed) loading, since shorter treatment periods are highly appreciated and requested by many patients. No implant failure or complication was reported; therefore, all three procedures seem to work very well, and it would be up to clinicians and patients to choose which option they prefer.

There are many RCTs comparing immediate, early and conventional loading of dental implants\(^4,6-32\). Our results are in agreement with most of the published RCTs, with the exception of two trials\(^6,7\) that reported higher failure rates of immediately loaded and early loaded implants, respectively.

The most relevant factor which may explain the excellent results obtained in this trial is the high insertion torque at implant placement. To qualify for immediate and early loading, implants had to be inserted with a torque superior to 40 Ncm. To achieve this in medium and soft bone quality, implant sites were underprepared with drills having
a diameter one or two sizes smaller than the final implant diameter. This explanation is supported by the findings of two trials\(^5,33\). In a non-randomised controlled trial of split-mouth design, single implants were either immediately non-occlusally loaded or conventionally loaded. The authors found a strong correlation between low implant insertion torque and implant failures for immediately loaded implants. In fact, out of ten single implants placed with an insertion torque of 20 Ncm, nine failed, whereas only one implant failed out of 10 implants inserted with a torque of at least 32 Ncm\(^5\). The other split-mouth RCT included 50 patients who received two single immediately loaded implants, one randomly inserted with a torque between 25 and 35 Ncm and the other with a torque superior to 80 Ncm. Seven implants inserted with a torque between 25 and 35 Ncm failed versus none of those implants placed with an insertion torque superior to 80 Ncm\(^33\). This difference was statistically significant which suggests that immediate and early loading of dental implants can be successful, if some clinical precautions are taken. Such precautions may include underpreparation of the implant sites particularly in the presence of soft bone, use of implant designs favouring achievement of high insertion torques (35 Ncm or more)\(^33\), and accurate control of loading. Some authors also advocate the use of specific implant surface modifications to reduce the healing time\(^34\), but no evidence supports this hypothesis yet\(^35\). Therefore, if a clinician is able to place implants with good insertion torques (more than 40 Ncm), they could be loaded immediately or early. However, when choosing between immediate and early loading, it might be wiser to load implants immediately, since there are no additional advantages or benefits to early loading\(^4\), and patients are more likely to prefer immediate loading.

The present trial included three centres in Greece, Lithuania and Italy. The advantages of multicenter trials are twofold: more patients can be included,

### Table 1 Patient and intervention characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Immediate (n = 27)</th>
<th>Early (n = 27)</th>
<th>Delayed (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>20 (74.1%)</td>
<td>16 (59.3%)</td>
<td>19 (70.4%)</td>
</tr>
<tr>
<td>Mean age at implant insertion (range)</td>
<td>51.3 ± 16.3</td>
<td>54.3 ± 14.2</td>
<td>55.1 ± 12.6</td>
</tr>
<tr>
<td>Smoking up to 10 cigarettes/day</td>
<td>8 (29.6%)</td>
<td>7 (25.9%)</td>
<td>6 (22.2%)</td>
</tr>
<tr>
<td>Smoking more than 10 cigarettes/day</td>
<td>5 (18.5%)</td>
<td>6 (22.2%)</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>Natural dentition/fixed prosthesis in opposite jaw</td>
<td>26 (96.3%)</td>
<td>26 (96.3%)</td>
<td>25 (92.6%)</td>
</tr>
<tr>
<td>Removable prosthesis/denture in opposite jaw</td>
<td>1 (3.7%)</td>
<td>1 (3.7%)</td>
<td>2 (7.4%)</td>
</tr>
<tr>
<td>Number of implants placed</td>
<td>84</td>
<td>83</td>
<td>82</td>
</tr>
<tr>
<td>Implants in mandibles</td>
<td>31 (36.9%)</td>
<td>23 (27.7%)</td>
<td>47 (57.3%)</td>
</tr>
<tr>
<td>Implants in maxillae</td>
<td>53 (63.1%)</td>
<td>60 (72.3%)</td>
<td>35 (42.7%)</td>
</tr>
<tr>
<td>Implants in incisor sites</td>
<td>27 (32.1%)</td>
<td>20 (24.1%)</td>
<td>18 (22.0%)</td>
</tr>
<tr>
<td>Implants in canine sites</td>
<td>7 (8.3%)</td>
<td>4 (4.8%)</td>
<td>4 (4.9%)</td>
</tr>
<tr>
<td>Implants in premolar sites</td>
<td>33 (39.3%)</td>
<td>35 (42.2%)</td>
<td>28 (34.1%)</td>
</tr>
<tr>
<td>Implants in molar sites</td>
<td>17 (20.2%)</td>
<td>24 (28.9%)</td>
<td>32 (39.0%)</td>
</tr>
<tr>
<td>Implants in immediate extraction sockets</td>
<td>33 (39.3%)</td>
<td>23 (27.7%)</td>
<td>16 (19.5%)</td>
</tr>
<tr>
<td>Implants inserted in sites after less than 3 months of healing</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Implants inserted in sites after more than 3 months of healing</td>
<td>51 (60.7%)</td>
<td>60 (72.3%)</td>
<td>66 (80.5%)</td>
</tr>
<tr>
<td>Implants in sites augmented at implant placement</td>
<td>35 (41.7%)</td>
<td>15 (18.1%)</td>
<td>2 (2.4%)</td>
</tr>
<tr>
<td>Mean implant length</td>
<td>11.0 ± 1.4</td>
<td>10.7 ± 1.1</td>
<td>10.7 ± 1.5</td>
</tr>
<tr>
<td>Mean implant diameter</td>
<td>4.3 ± 0.5</td>
<td>4.3 ± 0.6</td>
<td>4.4 ± 0.5</td>
</tr>
<tr>
<td>Implants in hard bone quality</td>
<td>21 (25.0%)</td>
<td>23 (27.7%)</td>
<td>22 (26.8%)</td>
</tr>
<tr>
<td>Implants in medium bone quality</td>
<td>55 (65.5%)</td>
<td>50 (60.2%)</td>
<td>36 (43.9%)</td>
</tr>
<tr>
<td>Implants in soft bone quality</td>
<td>8 (9.5%)</td>
<td>10 (12.1%)</td>
<td>24 (29.2%)</td>
</tr>
<tr>
<td>Implants inserted with less than 40 Ncm torque</td>
<td>4 (4.8%)</td>
<td>6 (7.2%)</td>
<td>12 (14.6%)</td>
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increasing the precision of the results, and the results are more generalisable when more centres achieve similar results. On the other hand, the logistical organisation of multicenter trials is more complex, and there is always the risk that some centres may inadvertently operate in a different way. The main limitation of this trial is the limited sample size. The number of included patients was too low to detect any significant difference, if any. Unfortunately, two additional centres, that originally agreed to participate in this trial, did not provide any patients. Hopefully this limitation could be overcome by putting together patients from different RCTs, thus increasing the sample size in future systematic reviews. Another limitation consisted of the substantial number of protocol deviations reported; it is impossible to say to what extent they could have affected the results, although the complexity of the interventions increased.

With respect to the generalisability (external validity) of these findings, it should be recognised that these procedures were tested in real clinical conditions and that patient inclusion criteria were broad, therefore the results can be generalised to a wider population, keeping in mind that the operators were highly experienced with immediate loading procedures.

### Conclusions

All loading strategies were successful with no significant difference between them, although immediate and early loading achieved similar results in a shorter period of time. If treatment duration is an issue for the patient, then immediate loading could be a preferable choice, if implants are placed with a sufficient insertion torque.

### References

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