Immediate, early (3 weeks) and conventional loading (4 months) of single implants: Preliminary data at 1 year after loading from a pragmatic multicenter randomised controlled trial

Key words  conventional loading, early loading, immediate loading, peri-implant marginal bone levels, single dental implant

Purpose: To compare the clinical outcome of single implants which underwent immediate non-occlusal loading with implants subjected to early non-occlusal loading at 3 weeks, and implants conventionally loaded at 4 months.

Materials and methods: One hundred and five patients in five private practices requiring a single implant-supported crown were randomised to immediate loading (35 patients), early loading (35 patients) and conventional loading (35 patients) groups. To be immediately or early loaded, implants had to be inserted with a torque superior to 45 Ncm. Immediately and early loaded implants received non-occluding temporary crowns, whereas conventionally loaded implants were directly restored with definitive crowns. Temporary crowns were replaced by definitive ones after 4 months. Outcome measures were crown and implant failures, complications and peri-implant marginal bone level changes recorded by a blinded assessor.

Results: Two patients dropped out from the immediate loading group up to 1-year post-loading. Two implants failed, one in the immediately loaded and one in the early loaded group (P = 0.601). One immediately loaded implant and two early loaded implants were affected by one complication each (P = 0.162). Mean peri-implant marginal bone loss after 1 year was -0.120 ± 0.230 mm (95% CI -0.35, 0.10) for immediate, -0.390 ± 0.840 mm (95% CI -1.23, 0.45) for early and -0.201 ± 0.306 mm (95% CI -0.51; 0.11) for conventionally loaded implants. There were no statistically significant differences for any of the outcome measures between the three loading strategies up to 1-year post-loading.

Conclusions: No major clinical differences were observed with regard to implant survival, complications and marginal bone level changes when loading single implants immediately, early or conventionally.

Conflict-of-interest statement: This trial was partially funded by JDentalCare, 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 the results. Dr Tommaso Grandi, Paolo Guazzi, Rawad Samarani and Marco Esposito are consultants for JDentalCare.
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 maxillae. Successful osseointegrated dental implants are anchored directly to bone. However, in the presence of movement, a soft-tissue interface may encapsulate the implant, causing its failure. To minimise the risk of soft tissue encapsulation, some clinicians have recommended keeping implants unloaded. This traditional approach requires longer treatment periods, and according to the procedures used, a second surgical intervention is needed to connect the abutments to the implant. Early attempts to load implants earlier 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 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. 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. However, the review also stressed that the quality of the evidence was scored as being very low and that there is some evidence of reporting bias, therefore clinicians should treat these findings with caution. Occasionally immediately and early loaded implants have been associated with clinically relevant increased failure rates, it is therefore important to evaluate whether predictable results can also be obtained when loading dental implants immediately or early in more critical situations, such as in the replacement of single teeth.

The aim of this randomised controlled trial (RCT) was to compare the effectiveness of immediate non-occlusal loading (test group 1) versus early non-occlusal loading (test group 2) at 3 weeks versus conventional loading at 4 months (control group) of single implants. The null hypothesis was that there would be no difference in success rates, complications and peri-implant marginal bone level changes between the three procedures, against the alternative hypothesis of a difference.

Immediate non-occlusal loading was defined as placing a non-occluding provisional crown on the same day of implant placement. Early loading was defined as seating a non-occluding provisional crown 3 weeks after implant placement, and conventional loading as seating a definitive crown 4 months after implant placement.

This report presents preliminary data at 1-year post-loading. At protocol stage, the aim was to follow up these patients up to the tenth 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

Patients were recruited and treated in five private dental clinics located in Beirut, Lebanon (three centres) and Modena, Italy (two centres), all having extensive experience in the rehabilitation associated with immediate loading procedures. Originally 10 centres agreed to participate in the study but five centres withdrew during the course of the study without contributing any patients. One experienced surgeon at each centre performed all the operations and patients were randomised in equal numbers into three groups according to a parallel group design: immediate loading (same day), early loading at 3 weeks and conventional loading at 4 months.

Any patient requiring a single implant, at least 8 mm long and 3.7 mm in diameter, to support a single crown, who was 18 years old or older, and able to understand and sign an informed consent form was eligible for inclusion in this trial. 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). The patients were allowed an opportunity to ask questions pertaining to this study, and were informed of...
Immediate, early and conventional loading

treatment alternatives. The study was open to qualifying patients with no consideration given to sex or race. For patients with more than one eligible implant site, the operator was free to choose the site to be included in the study at the screening visit. Only one implant/crown per patient was entered in the study. Pre-operative radiographs (intra-oral, panoramic, cone beam computed tomography (CBCT) scans or other radiographic examinations at the discretion of the operators) together with clinical inspections were used to determine bone volumes and anatomic landmarks. 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 amino-bisphosphonates.
- 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 for immediate post-extractive implants.
- Lack of opposite occluding dentition/prosthesis in the area intended for implant placement.
- Participation to other investigations, if the present protocol could not be properly adhered to.
- Unable to commit to a 10-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: non-smokers, moderate smokers (up to 10 cigarettes per day) and heavy smokers (more than 10 cigarettes per day). Patients were also categorised into two groups: whether the opposite jaw had natural dentition/fixed prostheses or removable prostheses/dentures.

All patients received prophylactic antibiotic therapy: 1 g of amoxicillin and clavulanic acid every 12 h from the day before surgery to the sixth post-surgical day. Patients allergic to penicillin were given 250 mg clarithromycin every 12 h from the day before surgery to the sixth post-surgical day. Patients rinsed with 0.2% chlorhexidine mouthwash for 1 min prior to any intervention. Local anaesthesia was obtained using articain with adrenaline 1:100.000. In the presence of a tooth to be extracted, intrasulcular incisions were performed and extended mesially and distally without any vertical incision. In the presence of an interdental edentulous ridge a para-crestal or a mid-crestal incision was performed from the distal surface of the more mesial tooth to the mesial surface of the distal tooth. Vertical releasing incisions were sometimes performed only at the mesial line angle of the tooth mesial to the surgical area. Full-thickness crestal flaps were elevated with a minimal extension to minimise patient discomfort. Implants could also be placed flapless. Teeth extractions were performed as atraumatically as possible to preserve the buccal alveolar bone, using periotomes and small levers. Extraction sockets were carefully cleaned of any granulation tissue.

JD Evolution (J DentalCare, Modena, Italy) tapered thread titanium implants with internal connection and double acid-etched treated surface were used. Operators were free to choose implant lengths (8.0, 10.0, 11.5, 13.0 and 15.0 mm) and diameters (3.7, 4.3, 5.0 and 6.0 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 as suggested by the manufacturer. For sites with hard bone quality all the suggested sequence of drills were used. For sites with medium bone quality, the site was underprepared using a drill, one diameter smaller than what should have been used; and in the case of soft bone, a drill, two diameters smaller than what should have been used, was used instead.

Implants were inserted in the osteotomy site with the motor set with a torque of 45 Ncm and, once the motor stopped, implants were placed manually with a ratchet (JDTorque, JDentalCare) until they were level with the alveolar bone crest. The wrench used was able to perform torque measurements within a range of 15 to 80 Ncm, with 5% precision. The
actual insertion torque was recorded using the manual ratchet. In the case that an implant was inserted with a torque inferior to 45 Ncm, the surgeon was free to decide whether to replace it with a larger diameter implant in order to attempt to obtain the required insertion torque, or loading it conventionally after 4 months of healing.

Post-extractive implants were placed 1 mm below the vestibular bone crest and slightly palatal. In the case of a bone-to-implant gap, granules of anorganic bovine bone (Bio-Oss 0.25 to 1.00 mm, Geistlich Pharma, Wolhusen, Switzerland) were used to fill the gap and, if needed, the exposed grafted areas were covered with a collagen fleece (Medicipio C Collagen Fleece, Novdento Dental Products, Bad Saulgau, Germany).

After having completed the implant placement procedure, the sequentially numbered envelope corresponding to the patient was opened to know when to load the implant, either immediately (Figs 1a to 1j), early (after 3 weeks; Figs 2a to 2f), or conventionally (after 4 months; Figs 3a to 3g). According to the random allocation, an impression coping or a healing abutment was placed. Implants were not submerged. When needed, interrupted sutures were placed using a monofilament thread. A baseline intraoral radiograph of the study implant was taken with the paralleling technique, and if the marginal bone levels were not clearly discernible or the resultant implant image was too distorted a second periapical radiograph was taken.

An impression with the pick-up impression copings were made for those implants to be immediately loaded and provisional non-occluding screw-retained resin crowns were fabricated and delivered on the same day of implant placement. It was also
possible to use a titanium abutment on which the practitioner cemented a resin crown. If necessary, the abutment was cut and modified on an implant analogue. The prefabricated provisional restoration was relined with acrylic resin, refined, polished and cemented. Occlusion was checked to avoid any static or dynamic contact with the opposite dentition.

The following post-surgical instructions were given:

- Ibuprofen 400 mg (or paracetamol 1 g for patients allergic to NSAIDs) to be taken 2 to 4 times a day during meals, only if needed.
- 1 g of amoxicillin and clavulanic acid every 12 h until the sixth post-surgical day. Patients allergic to penicillin were given 250 mg clarithromycin instead.
- Patients were prescribed 0.2% chlorhexidine mouthwash for 1 min twice a day for 2 weeks.
- A soft diet was recommended for 1 week.
No prosthesis which compressed the implant was to be used during the entire implant healing period.

Patients were seen after 3 days to check the occlusion, and after 10 days for a second occlusion check-up, for oral hygiene instructions and for suture removal, when needed.

Impressions of early loaded implants were also taken at the time of surgery and provisional non-occluding screw-retained resin crowns were delivered 3 weeks after implant placement. Impressions of implants of the conventionally-loaded group were taken 1 to 3 weeks before delivery of the definitive crowns. All the prosthetic procedures were identical between the three groups, with the exception that conventionally loaded implants received occluding definitive metal-ceramic crowns. Provisional crowns were replaced after 4 months by definitive screw-retained or cemented metal-ceramic single crowns. At the 4-month post-implant placement endpoint, all implants were manually tested for mobility by tightening the abutment screws with the removed crowns using the JDTorque manual ratchet at 35 Ncm.

Patients were recalled at least every 6 months for oral hygiene maintenance and prosthetic controls. At the 1-year post-loading follow-up, the stability of the crown was assessed using the metallic handles of two instruments and peri-apical radiographs were taken.

Primary outcome measures were:
- Crown failure: whether it was not possible to place the crown due to implant failures or secondary to implant losses, or replacement of the definitive crown for any reason.
- 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 crown delivery and using the handles of two dental mirrors without removing the crowns at 1-year post-loading.
- Any complication and adverse event was recorded and reported.

Secondary outcome measure was:
- Peri-implant marginal bone level changes assessed on periapical radiographs taken with the paralleling technique at implant placement and 1 year after loading. In the case of unreadable radiographs, new radiographs were made. Non digital radiographs were scanned in TIFF format with a 600 dpi resolution. Peri-implant marginal bone levels were measured using the Scion Image (Scion Corporation, Maryland, USA) software. The software was calibrated for...
every single image using the known distance of two consecutive threads. Measurements of the mesial and distal bone crest level adjacent to each implant was made to the nearest 0.01 mm. Reference points for the linear measurements were: the coronal margin of the implant collar and the most coronal point of bone-to-implant contact or the highest level of the bone if it was above the implant abutment junction. Implants with bone up to the coronal margin of the implant collar were given a value of zero. Mesial and distal measurements of each implant were averaged and a mean was calculated at group level.

Implant stability was assessed by local blinded outcome assessors, whereas marginal bone level changes were assessed by a single centralised blinded assessor (Dr Luca Sbricoli). Complications were assessed by the treating clinicians who were therefore 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 was 286. However our recruitment capacity could not match the required sample size and therefore it was decided to include 70 patients per group. Originally, 10 centres agreed to participate in the study, each agreeing to recruit 21 patients (seven patients in each group) for a total of 70 patients per group. Unfortunately, due to the withdrawal of five centres from the study only 35 patients per group were actually recruited.

Ten computer-generated restricted randomisation lists were created with three groups consisting of an equal number of patients. Only one of the investigators, 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 implant placement, therefore treatment allocation was concealed to the investigator in charge of enrolling and treating the patients included in the trial.

All data analysis was carried out according to a pre-established analysis plan. The patient was the statistical unit of the analyses. A medical doctor (Dr Giovanni Grandi) with expertise in dental biostatistics analysed the data, without knowing the group allocation. Intention-to-treat analyses were performed, however it was requested by a referee to also perform per protocol analyses. The chi-square test was used to compare dichotomous variables (failures and complications) and the ANOVA test was used for continuous outcome (bone level changes) between the three groups. When necessary, prevalence was compared using contingency tables and the chi-squared test. Comparisons between each time points and the baseline measurements were made with paired t-tests, to detect any changes in marginal peri-implant bone levels for each study group. All statistical comparisons were conducted at the 0.05 level of significance.

Results

All patients eligible for this trial agreed to participate, however two patients at Dr Samarani’s centre were not included in the study since an insertion implant torque superior to 45 Ncm could not be achieved (this is a protocol deviation since it was agreed that patients whose implants could not be inserted with more than 45 Ncm torque were to be moved to the conventional loading group following an intention-to-treat analysis). One hundred and five patients were consecutively enrolled in the trial and randomised: 35 to the immediate, 35 to the early and 35 to the conventional loading groups. All patients were treated according to the allocated interventions. Two patients did not return for the delivery of the definitive crown at the 1-year follow-up and were considered as drop-outs. Both patients belonged to the immediately loaded group and are currently working overseas.

Initially seven implants could not be placed with a torque superior to 45 Ncm which was the minimal implant stability required. These implants were equally distributed between groups (Table 1) and centres (Table 3). Two implants were in the immmedi-
ately loaded group: one implant, inserted at 40 Ncm, was immediately loaded anyhow, whereas the other implant, inserted at 35 Ncm, was conventionally loaded at 4 months instead. Three implants were in the early loaded group: one implant, inserted at 40 Ncm, was early loaded, whereas the other two implants, both inserted at 35 Ncm, were conventionally loaded at 4 months instead. Finally, two implants, allocated to the conventionally loaded group, were inserted with 20 and 40 Ncm torques. The data of all patients was evaluated in the statistical analyses. Deviations from the operative protocol were the following:

- Dr Samarani: for five patients allocated to the immediately loaded group, the provisional crowns were delivered the following day because crowns fabricated at the laboratory were preferred.
- Dr Tohme: two patients allocated to the immediately loaded group had their single implants permanently splinted to other implants. Two patients allocated to the early loading group did not return after 3 weeks to have the provisional crowns, but came after 4 months and received definitive crowns, instead. Two patients allocated to the conventional loading group did not return after 4 months to have the definitive crowns, but came after 14 and 20 months, respectively.

Patients were recruited and treated from January to September 2014. The follow-up focused on the time between implant placement and 1 year after loading. The main baseline patient characteristics are presented in Table 1. Baseline patient characteristics were similar in terms of sex, age, smoke, opposite dentition and bone quality. Indeed there were some differences in terms of position of implants and implant size; there were more conventionally loaded implants inserted in mandibles and in molar sites which were in general shorter in comparison to the other groups. Of the implants which were immediately loaded; more were placed flapless and inserted in augmented extraction sockets, and fewer were inserted in non-augmented extraction sockets.

- Crown and implant failures: Two implants failed both for infection, one immediately loaded and one early loaded. The immediately loaded implant displayed postoperative pain, oedema and signs of infection with pus. It was mobile 3 weeks after

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients’ and interventions’ characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediate (n = 35)</td>
</tr>
<tr>
<td>Females</td>
<td>18 (51.4%)</td>
</tr>
<tr>
<td>Mean age at implant insertion (range)</td>
<td>51.43 ± 12.43 (22-73)</td>
</tr>
<tr>
<td>Smoking up to 10 cigarettes/day</td>
<td>4 (11.4%)</td>
</tr>
<tr>
<td>Smoking more than 10 cigarettes/day</td>
<td>2 (5.7%)</td>
</tr>
<tr>
<td>Natural dentition/ fixed prosthesis in opposite jaw</td>
<td>35 (100%)</td>
</tr>
<tr>
<td>Removable prosthesis/denture in opposite jaw</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Implants placed flapless</td>
<td>23 (66.0%)</td>
</tr>
<tr>
<td>Implants inserted in mandibles</td>
<td>7 (20.0%)</td>
</tr>
<tr>
<td>Implants inserted at incisor sites</td>
<td>8 (22.9%)</td>
</tr>
<tr>
<td>Implants inserted at canine sites</td>
<td>2 (5.7%)</td>
</tr>
<tr>
<td>Implants inserted at premolar sites</td>
<td>22 (62.9%)</td>
</tr>
<tr>
<td>Implants inserted at molar sites</td>
<td>3 (8.6%)</td>
</tr>
<tr>
<td>Implants inserted in non-augmented extraction sockets</td>
<td>4 (11.4%)</td>
</tr>
<tr>
<td>Implants inserted in augmented extraction sockets</td>
<td>21 (60.0%)</td>
</tr>
<tr>
<td>Mean implant length</td>
<td>13.06 ± 1.68</td>
</tr>
<tr>
<td>Mean implant diameter</td>
<td>4.20 ± 0.42</td>
</tr>
<tr>
<td>Hard bone quality at implant site</td>
<td>7 (20.0%)</td>
</tr>
<tr>
<td>Medium bone quality at implant site</td>
<td>27 (77.1%)</td>
</tr>
<tr>
<td>Soft bone quality at implant site</td>
<td>1 (2.9%)</td>
</tr>
<tr>
<td>Implants initially inserted with &lt; 45 Ncm torque</td>
<td>2 (5.7%)</td>
</tr>
</tbody>
</table>
Immediate, early and conventional loading

placement in a non-smoker male. It was inserted as an immediate post-extractive implant in position 14 in conjunction with anorganic bovine bone augmentation in a site characterised by medium bone quality. It was successfully replaced after 4 months. The early loaded implant was inserted in a male patient who was a heavy smoker; this was placed in position 46, characterised by hard bone quality. Postoperatively the implant displayed pain and pus and was removed 3 weeks after its placement. The patient refused to have the implant replaced. There were no statistically significant differences in prosthesis and implant failures between the three procedures (*P* = 0.601).

- Marginal bone level changes (Table 2): at implant placement there was no statistically significant difference between the three groups: bone levels were 0.03 ± 0.08 mm (95% CI -0.05; 0.01) for immediate, 0.01 ± 0.05 mm (95% CI -0.04; 0.06) for early and 0.01 ± 0.05 mm (95% CI -0.35; 0.06) for conventionally loaded implants. One year after loading, there was no statistically significant difference between the three groups for peri-implant bone levels (0.15 ± 0.27 mm (95% CI -0.12; 0.42) for immediate, 0.40 ± 0.84 mm (95% CI -0.43; 1.24) for early and 0.21 ± 0.31 mm (95% CI -0.10; 0.52) for conventionally loaded implants (*P* = 0.141) and bone loss -0.12 ± 0.23 mm (95% CI -0.35; 0.10) for immediate, -0.39 ± 0.84 mm (95% CI -1.23; 0.45) for early and -0.20 ± 0.31 mm (95% CI -0.51; 0.11) for conventionally loaded implants (*P* = 0.113). All three groups gradually lost statistically significant marginal peri-implant bone at 1-year post-loading: *P* = 0.0042 for immediate, *P* = 0.0102 for early and *P* = 0.0004 for conventionally loaded implants.

- Complications: four complications occurred in four patients, one at an immediately loaded implant (postoperative pain, oedema and infection with pus; the implant was then removed 3 weeks after its placement), and three complications at early loaded implants (postoperative pain and pus which determined implant removal 3 weeks after its placement; screw loosening of the provisional crown 3 weeks after loading; peri-implant mucositis at 4 months during the final prosthetic stage. It was solved by a curettage, antibiotics and 0.2% chlorhexidine mouthwash). There were no statistically significant differences in complications between the three procedures (*P* = 0.162).

- Post-hoc per protocol analyses were requested by a referee to compare implant failures, complications...
and bone level changes between the three groups. There were no statistically significant differences for implant failures ($P = 0.532$), complications ($P = 0.099$) and bone level changes ($P = 0.344$) (Table 4).

### Discussion

The present investigation was designed to evaluate whether immediate and early non-occlusal loading of single implants could provide similar clinical outcomes as conventional loading, since shorter treatment periods are highly appreciated and requested by many patients. Only two implants were lost, one immediately and one early loaded over a 1-year post-loading period. While this is a good outcome and the only two failed implants most likely failed due to infection, it is worth noting that none of the conventionally loaded implants failed, suggesting that conventional loading remains the gold standard, especially for single implants.

There are many RCTs comparing immediate with conventional loading of single implants$^{6,13-21}$, and only one trial comparing immediate versus early loading of single implants$^{22}$. Our results are in agreement with the published RCTs, with the exception of one trial$^6$ that presented a 25% failure rate of immediately loaded single implants. However in the latter case, implants were placed flapless and this might explain the different outcome.

How is it possible to explain the positive outcome for immediate and early loaded implants? To decrease the risk of early failures of immediately and early loaded implants, various clinical ‘tips’ have been suggested such as the under-preparation of the implant site to achieve high primary stability$^8$ and the use of a non-occluding temporary prosthesis during the first 2 months of healing$^9$. Two RCTs were published comparing immediately loaded single implant-supported crowns in occlusion or not in occlusion$^{10,11}$. The results, also summarised in a meta-analysis of a Cochrane systematic review$^4$, did not show any trend in favour of crowns not placed in occlusion during the implant healing phase. The lack of difference could be explained by the fact that even if the crowns were not put in direct occlusion, patients used them functionally when chewing. The most relevant factor which may explain the positive results obtained in this trial is the high insertion torque at implant placement. To qualify for immediate loading, implants had to be inserted with torque superior to 45 Ncm. To achieve this in medium and soft bone, under-preparation was performed using shaping drills, which were one to two sizes smaller than the final implant diameter. This explanation is in agreement with the findings of two trials$^{5,12}$. In a controlled clinical trial of split-mouth design where single implants undergoing either immediate non-occlusal loading or conventional loading, the authors found a strong correlation between insertion torque and implant failures for immediately loaded implants. In fact, out of 10 single implants placed with an insertion torque of 20 Ncm, nine failed, whereas only one implant failed out of 10 implants inserted with a 32 Ncm torque$^5$. The other split-mouth RCT showed a statistically significant difference with more failures (seven failures) of immediate non-occlusally loaded single implants when inserted with a torque between 25 and 35 Ncm than implants (no failure) placed with an insertion torque superior to 80 Ncm$^{12}$. It can be concluded that immediate and early loading of single dental implants can be successful if some

### Table 4

<table>
<thead>
<tr>
<th>Implant placement</th>
<th>1 year after loading</th>
<th>Difference placement – 1 year</th>
<th>P-value intragroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>N Mean ± SD (95% CI)</td>
<td>N Mean ± SD (95% CI)</td>
<td>N Mean ± SD (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Immediate loading</td>
<td>31 0.03 ± 0.08 (-0.05;0.01)</td>
<td>31 0.15 ± 0.27 (-0.12;0.42)</td>
<td>31 0.12 ± 0.23 (-0.35;0.10)</td>
</tr>
<tr>
<td>Early loading</td>
<td>28 0.01 ± 0.06 (-0.05;0.07)</td>
<td>28 0.31 ± 0.60 (-0.29;0.91)</td>
<td>28 0.30 ± 0.61 (-0.31;0.91)</td>
</tr>
<tr>
<td>Conventional loading</td>
<td>40 0.01 ± 0.04 (-0.03;0.05)</td>
<td>40 0.30 ± 0.66 (-0.36;0.96)</td>
<td>40 0.29 ± 0.66 (-0.37;0.95)</td>
</tr>
<tr>
<td>P-value intergroup</td>
<td>0.452</td>
<td>0.419</td>
<td>0.344</td>
</tr>
</tbody>
</table>

*Statistically significant difference.

In one patient of the immediate loaded group and in two patients of the early loaded group, an insertion torque inferior to the required 45 Ncm was obtained, therefore implants were conventionally loaded instead, according to the original research protocol.
clinical precautions are taken. Such precautions may include: under-preparation 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)\textsuperscript{12} and an accurate control of loading. Some authors also advocate the use of specific implant surface modifications to reduce the healing time\textsuperscript{23}, but no evidence supports this hypothesis\textsuperscript{24}. Therefore if clinicians are able to achieve a good insertion torque at implant placement (more than 35 Ncm), they should consider loading the implant immediately or early, however if they have to choose between immediate and early loading, it might be better to opt for an immediate loading procedure, since there are no advantages or benefits with early loading\textsuperscript{4} and patients, most likely, would prefer immediate loading.

The present trial included five centres in Lebanon and Italy. The advantages of multicenter trials are two-fold: more patients can be included, therefore increasing the precision of the results, and the results are more generalisable when more centres achieve similar results. On the other hand, the logistic 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, despite being the largest RCT ever published on the timing of implant loading is the limited sample size. The number of patients included may be too low to detect any significant difference, if any, though in future systematic reviews this limitation could hopefully be overtaken by increasing the sample size by putting together patients from different RCTs.

With respect to the generalisability (external validity) of these findings, it is important to note 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.

\section*{Conclusions}

All loading strategies were successful with no significant difference between them, though immediate and early non-occlusal loading achieved similar outcomes in a shorter period of time. If the duration of the treatment is an issue for the patient, then an immediate loading procedure could be a preferable choice if a sufficient insertion torque is obtained at implant placement.

\section*{References}