A 10-year report from a multicentre randomised controlled trial: Immediate non-occlusal versus early loading of dental implants in partially edentulous patients

Purpose: To compare peri-implant bone and soft-tissue levels of immediate non-occlusally loaded versus non-submerged early loaded implants in partially edentulous patients 10 years after loading.

Materials and methods: Fifty-two patients were randomised in five Italian private practices: 25 in the immediately loaded group and 27 in the early loaded group. To be immediately loaded, single implants had to be inserted with a torque of at least 30 Ncm, and splinted implants with a torque of at least 20 Ncm. Immediately loaded implants were provided with non-occluding temporary restorations within 48 h. After 2 months, the provisional restorations were put in full occlusion. Implants were early loaded after 2 months. Definitive restorations were provided 8 months after implant placement. Outcome measures were prosthesis failures, implant failures and complications, recorded by non-blinded assessors, and peri-implant bone and soft-tissue levels evaluated by blinded assessors.

Results: Fifty-two implants were loaded immediately and 52 early. Three patients with 8 implants dropped out from the immediate group versus two patients with 3 implants from the early loaded group; all remaining patients were followed for at least 10 years after loading. One single immediately loaded implant failed 2 months after placement. Three patients with immediately loaded implants and two with early loaded implants were affected by complications. There were no statistically significant differences for implant/prosthesis failures (Fisher’s exact test: $P = 0.294$; difference = 4%, 95% CI: -16% to 24%) and complications between groups (Fisher’s exact test: $P = 0.574$; difference = 4.5%, 95% CI: -12% to 21%). Both groups gradually lost peri-implant bone in a highly statistically significant way at 2, 8 and 14 months, and at 4, 5 and 10 years. After 10 years, immediately loaded patients lost an average of 1.34 mm and early loaded patients lost 1.42 mm of peri-implant marginal bone. At 10 years, there was a statistically significant recession ($P < 0.001$) of the vestibular soft tissues from baseline (delivery of the final restorations 8 months after implant placement) at both immediate (0.38 mm) and early (0.25 mm) loaded implants. There were no statistically significant differences in terms of peri-implant bone (difference = 0.08 mm, 95% CI: -0.49 to 0.65; $P = 0.49$) and soft-tissue level changes (difference = 0.07 mm, 95% CI: -0.48 to 0.62; $P = 0.469$) between the two groups at 10 years after loading.

Conclusions: In well-maintained patients, complications are uncommon and healthy and stable peri-implant tissues can be maintained for 10 years around both immediate and early loaded implants.

Conflict-of-interest statement: This trial was independently designed and initiated by the investigators. BIOMET 3i, the manufacturer of the implants used in this investigation, provided partial economic support at a later stage, and finally ZIMMER-BIOMET partially supported the present publication, however data belonged to the authors and by no means did the sponsor interfere with the conduct of the trial or the publication of its results.
Introduction

The delivery of immediate prostheses after placement of dental implants is highly appreciated by patients. This would enable patients to have their treatment periods drastically reduced while they could live a normal life with minimal discomfort1,2. In carefully selected cases, immediate and early loading procedures can be successful3, though not all authors have shown predictably high success rates4-8. While several randomised controlled trials (RCTs) compared peri-implant marginal bone level changes of implants undergoing immediate, early and delayed loading1,2,4-9,19, less information is available on the stability of peri-implant soft tissues when comparing different loading strategies3. It may be interesting to note that meta-analyses of these RCTs showed statistically significant less bone loss (0.1 mm) in favour of immediate loading when compared to conventional loading, however, such a difference is unlikely to have any clinical significance3. There is also fairly little reliable information on the long-term effectiveness of implants loaded at different times, especially on the long-term maintenance of hard and soft peri-implant tissues. Such information is essential to properly understand the actual prognosis of implant-supported prostheses.

The primary aim of this RCT was to compare immediate non-occlusal loading versus early loading in partially edentulous patients. The secondary aim was to provide long-term data on the stability of peri-implant tissues. Immediate non-occlusal loading was defined as the seating within 48 h after implant placement of a provisional prosthesis not in occlusal contact for about 2 months. Early loading was defined as placing a provisional prosthesis after 2 months of the unloaded period.

This report presents the clinical data at 10 years after implant loading. Previous publications reported on 14-20, 21, 48- and 60-month22 data. 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

Any partially dentate patient requiring at least one dental implant, 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 participants were informed of the nature of the study and signed a written informed consent form prior to enrolment in the study. For patients with multiple edentulous areas to be restored, the operator was free, at the screening visit, to select one area to be included in the trial. Smokers were included and patients were grouped according to what they declared: i) non smokers; ii) moderate smokers (if smoking up to 10 cigarettes per day); iii) heavy smokers (if smoking more than 10 cigarettes per day). Patients were not accepted into the study if any of the following exclusion criteria was present:

- general contraindications to implant surgery;
- irradiation in the head and neck area;
- poor oral hygiene and motivation;
- untreated periodontal disease;
- uncontrolled diabetes;
- pregnancy or lactation;
- substance abuse;
- psychiatric problems or unrealistic expectations;
- lack of opposing occluding dentition in the area intended for implant placement;
- severe bruxism or clenching;
- infection or severe inflammation in the area intended for implant placement;
- need for bone augmentation procedures including sinus lifting.

Patients were recruited and treated in five private dental clinics located in northern Italy: Como (2 centres), Milan (2 centres) and Monza (1 centre), all having extensive experience in the treatment of patients with immediate loading procedures. The investigators have worked, and are still working together, in the same team for at least 5 years prior to the initiation of this study at the IRCCS Galeazzi, University of Milan, therefore they developed similar clinical operative procedures. One experienced surgeon at each centre performed all the operations. Patients were randomised to have implants non-occlusally loaded immediately (test group) or early (control group) in a parallel group study design. Only
one prosthesis in the area selected at screening was considered for each patient.

Patients were instructed to use 0.2% chlorhexidine mouthwash for 1 min, twice a day, starting 3 days prior to the intervention and thereafter for 2 weeks. All patients received prophylactic antibiotic therapy: Amoxicillin 2 g 1 h prior to the intervention and 2 g 6 h postoperatively. Patients allergic to penicillin were given clarithromycin 500 mg 1 h prior to the intervention. Ibuprofen 600 mg was given 1 h prior to intervention and then twice a day for 3 days.

Full-thickness crestal flaps were elevated after crestal incision with a minimal extension to minimise patient discomfort. Teeth extractions were performed asatraumatically as possible to preserve the buccal alveolar bone. The choice of the implant diameter and length was left up to the surgeon. At 4 centres, Full OSSEOTITE Tapered Implants with the external hexagon connections system (FOSS; Zimmer Biomet 3i, Florida, USA) were used exclusively and inserted according to the manufacturer’s instructions. At the Como 1 centre, 16 of the 35 implants placed consisted of the FOSS configuration, while 19 out of the 35 were prototypes of tapered implants from the same manufacturer with identical surface characteristics. Implant diameters used were 4.0, 5.0 and 6.0 mm; lengths used were 8.5, 10.0, 11.5, 13.0 and 15.0 mm.

Bone density at drilling was subjectively evaluated and the bone at the implant site was classified as either ‘hard’, ‘medium’ or ‘soft’. Resistance to implant insertion was objectively recorded with the Osseocare equipment (Nobel Biocare, Kloten, Switzerland). In the protocol-formulation phase, it was decided that single implants with a torque resistance of less than 30 Ncm or splinted implants with a torque resistance of less than 20 Ncm that were randomised to the immediately loaded group could be treated as belonging to the early loaded group according to an intention-to-treat analysis, however all implants achieved the minimal insertion torque required.

In soft bone, underpreparation was performed using a shaping drill one size smaller than the drill suggested by the manufacturer. In general, implants were placed at crestal level in healed edentulous ridges and slightly subcrestally in immediate post-extraction sockets. In cases where a residual gap more than 1.5 mm was present between the implant surface and the bone wall, the gap was filled with granular anorganic bovine bone (Bio-Oss, Geistlich Pharma, Wolhusen, Switzerland). A non-submerged technique was employed. Before placing the abutments, the envelope containing the randomisation code was opened, allowing the surgeon to know whether the implant was to be loaded immediately or early. Impression copings or healing screws were placed accordingly, and interrupted sutures were placed using a monofilament thread. An impression with the pick-up impression copings was made for the implants to be immediately loaded, and healing abutments were placed. Ice packs were provided, and a soft diet was recommended. Smokers were told to avoid smoking for 48 h postoperatively.

Acrylic resin provisional restorations were provided to patients of the immediately loaded group the following day. The occlusal surface of the provisional restoration was ground to avoid any static or dynamic occlusal contact with the opposite dentition. All provisional prostheses of the immediately loaded group were placed within 48 h. Sutures were removed 2 weeks after implant placement.

Two months after implant placement, resin was added to the immediate non-occlusally loaded restorations putting them in full occlusion. Patients of the early loaded group received provisional restorations identical to those of the immediately loaded groups with full occlusal contacts 2 months after implant placement. Final metal-ceramic restorations were cemented 8 months after implant placement.

Patients were recalled for oral hygiene maintenance and prosthetic controls every 3 months up to the first year and thereafter every 6 months.

Primary outcome measures, assessed by the treating clinicians, who were therefore not blinded, were:

- Prosthesis failure: the planned prosthesis could not be placed or was lost because of implant failure, or was replaced for any reason.
- Implant failure: the presence of any mobility of the individual implant (assessed manually by rotating the implant) at insertion of the provisional and definitive prostheses, and/or any infection dictating implant removal as well as implant fracture
Zuffetti et al Immediate versus early loading: 10-year follow-up

222


or any mechanical complication rendering the implant unusable to support a prosthesis. After insertion of the definitive restorations, prostheses were not removed to assess clinical mobility of individual implants.

- Any biological or prosthetic complications. Examples of possible biological complications were: numbness of the lower lip and chin, peri-implant mucositis (heavily inflamed soft tissue without bone loss), peri-implantitis (bone loss with suppuration or heavily inflamed tissues), fistulas, etc. Examples of possible prosthetic complications were fracture of the implant, abutment screw, framework, occlusal material, etc.

Secondary outcome measures were:

- Peri-implant marginal bone-level changes on periapical radiographs made with the paralleling technique. Periapical radiographs were taken at implant placement, 2, 8, 14, 48, 60 months and 10 years after implant placement. Radiographs were scanned (HP Scanjet 3c/t, Hewlett Packard, Cernusco sul Naviglio, Milan, Italy), digitised in JPG, converted to TIFF format with a 600 dpi resolution, and stored in a personal computer. 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 (0.9 mm for FOSS implants and 0.6 mm for the prototype implants). Measurements of the mesial and distal bone crest level adjacent to each implant were 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 the bone-to-implant contact.

- Vestibular soft tissue recessions (height of the clinical crown) measured with a digital calliper (Calliper IP54, Sham, Guilin, China) on hard plaster models. Impressions were taken at 8 months (after delivery and adjustment of the final restorations), 14 months, 60 months and 10 years using a high-dimensional stability alginate (Zhermack, Hidrogum 5, Badia Polesine, Italy). Plaster models were immediately prepared using extra-hard plaster (type 4). For incisors, the reference point was the middle of the incisal margin; for canines and premolars it was the tip of the cuspid; and for molars the deepest occlusal vestibular margin between the two cusps. Measurements were done vestibularly from the occlusal reference point perpendicular to the marginal gingiva.

Up to 1 year, all radiographic and soft tissue measurements were made in duplicate, after at least a 15-day interval, and the two values were averaged. However, after the first year, since the difference between the two assessments was negligible, only one assessment was taken. These measurements were made by two independent, masked, calibrated outcome assessors. One measured all radiographs and the other the clinical crown heights on plaster models up to 1 year after loading. For the 48- and 60-month assessment, the assessors were switched, i.e. the one who performed the bone level assessment up to 1 year performed the soft tissue assessment and vice-versa. For the 10-year assessment, two new trained assessors blindly evaluated the peri-implant bone levels and the soft tissue levels. All radiographs were coded so that the outcome assessor was blind to which group the implants belonged to. Also the assessors were not informed of the aims of the study. Since the assessor did not know which crown(s) to measure on the plaster models, the implant-supported crown(s) were marked with a black spot. The outcome assessors did not know the dates that the radiographs or the plaster models were created.

The sample size was chosen based on calculations of the number of patients likely to have at least one restoration failure (primary outcome measure). In a study on partially edentulous patients, the proportion of failures in the immediately loaded group was 0.39 compared to 0.04 in the conventionally loaded group. 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 0.39 and a proportion of 0.04 (odds ratio of 0.065), when the sample size in each group is 26 patients. It was planned to include 30 patients in each group to compensate for possible dropouts.

A manually generated restricted randomisation list was used to create two groups with an equal
number of patients. Only one of the investigators (Dr Marco Esposito), not involved in the selection and treatment of the patients, was aware of the randomisation sequence and had access to the randomisation list stored in a password-protected portable computer. The randomised codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened sequentially only after the implants to be included in the trial were inserted, thereby concealing treatment allocation from the investigators in charge of enrolling and treating the patients.

All data analysis was carried out according to a pre-established analysis plan. The patient was the statistical unit of the analyses. Two biostatisticians and one clinician (Dr Giovanni Grandi) analysed the data over time, without knowing the group allocation. Differences in the proportion of failures and other complications between the groups were compared using Fisher’s exact probability test. The average mesial and distal implant surface radiographic values and the buccal crown length values were averaged for each patient. Comparisons between each time point and the baseline measurement were made by paired tests, to detect any changes in bone or soft-tissue levels. An analysis of covariance was used to compare the mean radiographic and soft-tissue values at 10 years (outcome variable), with the baseline value as a covariate. Differences among centres for dichotomous outcomes were calculated using the chi-squared test. Between-centre differences in mean radiographic and soft tissue values at 10 years were calculated using an analysis of covariance with the baseline value as a covariate. All statistical comparisons were conducted at the 0.05 level of significance.

Results

All patients eligible for this trial agreed to participate. Fifty-two patients were consecutively enrolled in the trial and randomised: 25 to the immediately loaded group and 27 to the early loaded group. The planned number of 30 patients per group was not achieved since the centres decided to stop patient recruitment at the end of May 2005. All patients were treated according to the allocated interventions. All implants achieved the required minimal insertion torque.

Five patients dropped out during the entire follow-up periods (Table 1). This included two with three implants from the early loaded group and three patients with eight implants from the immediately loaded group and more precisely:

- one early loaded patient with two implants moved to another town after the 14-month evaluation;
- one early loaded patient with one implant moved to another town after the 6-year follow-up;
- one immediately loaded patient with three implants moved to another town after the 5-year follow-up;
- one immediately loaded patient with three implants died after the 5-year follow-up;
- one immediately loaded patient with two implants died after the 5-year follow-up.

The data of all remaining patients were evaluated in the statistical analyses.

Patients were recruited and treated from October 2004 to May 2005 and they were followed for at least 10 years after initial loading (Figs 1a to 1b and 2a to 2b). Initially six centres agreed to participate by treating ten patients each, however two centres withdrew before starting the trial and a new centre was added as a partial replacement. The remaining

### Table 1

Patient and in parenthesis dropout distribution across centres. Originally six centres were supposed to treat 10 patients each.

<table>
<thead>
<tr>
<th>Centre</th>
<th>Immediate (n = 25)</th>
<th>Early (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Como 1 (Dr Testori)</td>
<td>9 (3 patients with 8 implants)</td>
<td>6 (1 patient with 2 implants)</td>
</tr>
<tr>
<td>Como 2 (Dr Ritzmann)</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Milan 1 (Dr Zuffetti)</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Milan 2 (Dr Capelli)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Monza (Dr Galli)</td>
<td>4</td>
<td>6 (1 patient with 1 implant)</td>
</tr>
</tbody>
</table>
envelopes containing the randomisation codes were redistributed among the centres with higher recruitment capacities. The patient distribution across the various centres is shown in Table 1. The main baseline patient characteristics are presented in Table 2. Patients were generally healthy. Three patients suffered from hypertension and one from hepatitis C. By chance, these four patients were all randomised to the early loaded group.

Fifty-two implants were placed in the immediately loaded group and 52 in the early loaded group. The lengths and diameters of the inserted implants are presented in Table 3, whereas the bone density, which was subjectively evaluated, and the maximum insertion torque (primary implant stability) appear in Table 4. There were no apparent significant baseline imbalances between the two groups with the exception of more smokers receiving immediately loaded implants. Deviations from the operative protocol were the following:

1. One centre (Como 1) also used some prototypes of tapered implants with identical surface characteristics by the same manufacturer (19 out of 35 inserted implants).

2. The centres asked to use only autogenous bone chips to fill bone-to-implant gaps at immediate post-extractive implants but actually used a bone substitute instead.

3. One patient from the immediately loaded group was provided with the final restoration after 2 months instead of the planned 8 months.

4. One patient from the early loaded group received the definitive prosthesis 14 months after implant placement, because of a cardiac disease. However this patient's implants were assessed for stability at the planned 8-month interval.

Implant/prosthesis failures: A single implant and its provisional crown, inserted with a primary stability of 50 Ncm in medium bone density in position 25 (second left upper premolar) of a non-smoking patient, failed 2 months after placement in the immediately loaded group. The failed implant was successfully replaced with another implant after 6 months of healing. There were no statistically significant differences in prosthesis and implant failures amongst
the two interventions (Fisher’s exact test: $P = 0.294$; difference = 4%, 95% CI: -16% to 24%).

Complications: Five complications were reported affecting five different patients, three immediately loaded and two early loaded patients. There were no statistically significant differences in complications amongst the two interventions (Fisher’s exact test: $P = 0.574$; difference = 4.5%, 95% CI: -12% to 21%).

The following complications occurred at immediately loaded implants:
- One patient had mucositis around implants in positions 45, 46 and 47, 9 years after loading. It was successfully treated with intrasulcular 0.2% chlorhexidine irrigation.
- One patient had recessions of the soft tissues around implants in positions 45 and 46, 9 years after loading, exposing the titanium abutments (Figs 2a to 2b). No treatment was attempted.
- One patient had recessions of the soft tissues around the implant in position 16, 9.5 years after loading, exposing the titanium abutment. No treatment was attempted.

The following complications occurred at early loaded implants:
- One patient was affected by peri-implantitis around two implants in position 36 and 37, detected 33 months after implantation. The patient did not show up for regular recalls between months 14 and 33. On the control periapical radiograph, bone loss up to the fourth threads was observed, however clinically, the peri-implant tissues appeared healthy with no
An evident sign of pathology. A flap was immediately elevated, which revealed the presence of cement around the exposed margins of the prosthesis. The excessive cement was removed, the defect was carefully debrided and the implant surface thoroughly cleaned with a jet of bicarbonates. The defect was filled with granular anorganic bovine bone (Bio-Oss, Geistlich Pharma, Wolhusen, Switzerland) and covered with a resorbable collagen membrane (Bio-Gide, Geistlich Pharma). The postoperative healing was uneventful and health was maintained over time. • One patient chipped his mandibular partial prosthesis 8 years after loading. The tooth was polished resolving the problem.

Peri-implant marginal bone level changes: Both groups gradually lost marginal peri-implant bone in a highly statistically significant way \((P < 0.001)\) at 2, 8, 14, 48 and 60 months, and 10 years (Table 5). After 2 months, patients in the immediately loaded group lost an average of 0.5 mm peri-implant bone versus 0.6 mm for the patients in the early loaded group (Table 6). After 8 months, patients in the immediately loaded group lost an average of 0.9 mm of peri-implant bone versus 1.0 mm for the patients in the early loaded group (Table 6). After 14, 48 and 60 months, patients of both groups lost an average of 1.1, 1.2 and 1.2 mm of peri-implant bone, respectively (Table 6). Finally after 10 years, immediately loaded patients lost an average of 1.34 mm of peri-implant marginal bone and early loaded patients lost 1.42 mm of peri-implant marginal bone (Table 6). Ten years after loading there was no statistically significant difference between the two loading strategies for peri-implant bone-level changes, when an analysis of covariance was applied \((P = 0.49)\).

Vestibular soft tissue recessions: After 10 years, there was a statistically significant recession of the vestibular soft tissues from baseline (delivery of the final restorations 8 months after implant placement) at both immediately \((0.38 \text{ mm}; P < 0.0001)\) and early loaded implants \((0.25 \text{ mm}; P < 0.0001)\). There were no statistically significant differences between the two loading strategies for soft tissue changes \((P = 0.469; \text{Table 7})\).

Finally the comparisons between centres did not show any statistically significant difference (Tables 8 and 9) with the exception of the Milan 2 centre that reported statistically more buccal soft tissue recessions than Como 2 \((P = 0.001)\), Como 1, Milan 1 and Monza \((P < 0.001)\).

**Discussion**

The primary aim of this trial was to compare the clinical outcome of immediate and early loading in partially edentulous patients, however the long-term tissue stability of peri-implant tissues was also evalu-
ated. The data presented cover a follow-up period of 10 years after implant placement. Both loading strategies achieved good clinical results, which could be maintained over a 10-year period. The mean peri-implant marginal bone loss was in the range of 1.4 mm whereas buccal soft tissues receded by only 0.3 mm. These results are strengthened by the fact that the methodology of this report was robust: patients were randomised, group allocation was concealed to clinicians, and all treated patients were accounted for with no exclusions. Only five (9.6%) dropouts occurred over a follow-up period of at least 10 years after loading, which is a remarkable result considering the duration of the trial. Assessment of the peri-implant tissue stability was done by calibrated, independent, blinded outcome assessors, using objective, validated and reproducible outcome measures.

Also the number of complications was low, without any significant negative clinical consequence and which were equally distributed between groups. Remarkably only one episode of peri-implantitis occurred during the entire follow-up period. We considered this complication to be of ‘iatrogenic’ origin because the excess of cement accidentally displaced submucosally at the time of definitive prosthesis cementation, and formed a thick collar, which favoured plaque accumulation and retention. This induced a chronic inflammatory reaction that destroyed the peri-implant tissues, forming crater-like bone defects around the two affected implants. It is interesting to observe that this complication developed between months 14 and 33, the period in which the patient stopped coming in for regular maintenance visits. It was only detected after probing and was finally confirmed by a periapical radiograph. Surprisingly, at the time of diagnosis, the superficial peri-implant soft tissue looked firm, pink and healthy. The lesion was successfully treated with a regenerative procedure using granules of poorly resorbable anorganic bovine bone and a resorbable membrane. Peri-implant tissue health could be obtained and maintained up to the 10-year recall interval. In order to minimise the risk of iatrogenic peri-implantitis, the authors suggested avoiding the use of large amounts of cement, ensuring careful peri-implant cleaning after cementation and the use of a radio-opaque cement so that any excessive

### Table 7
Comparison of soft-tissue recessions between groups and time periods.

<table>
<thead>
<tr>
<th></th>
<th>8-14 months Mean Diff (SD)</th>
<th>8-60 months Mean Diff (SD)</th>
<th>8 months-10 years Mean Diff (SD)</th>
<th>P-value comparing 8 months with 10 years</th>
<th>P-value comparing immediate vs early loading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate loading</td>
<td>24 0.13 (0.40)</td>
<td>24 0.20 (0.40)</td>
<td>21 0.38 (0.75)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Early loading</td>
<td>27 0.01 (0.37)</td>
<td>26 0.05 (0.37)</td>
<td>25 0.25 (0.45)</td>
<td>&lt; 0.0001</td>
<td>0.469</td>
</tr>
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</table>

*Change statistically different from baseline (8 months after implant placement).

### Table 8
Comparisons between study centres for the various outcome measures expressed at patient level (N = number of patients) at 10-years post-loading.

<table>
<thead>
<tr>
<th></th>
<th>Como² (N = 15)</th>
<th>Como² (N = 7)</th>
<th>Milan¹ (N = 12)</th>
<th>Milan¹ (N = 8)</th>
<th>Monza (N = 10)</th>
<th>Total (N = 52)</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dropouts</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>0.10</td>
</tr>
<tr>
<td>Patients with prosthesis failures</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0.37</td>
</tr>
<tr>
<td>Patients with implant failures</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0.37</td>
</tr>
<tr>
<td>Patients with complications</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>5</td>
<td>0.07</td>
</tr>
</tbody>
</table>

aChi-square test

### Table 9
Mean radiographic and soft tissue peri-implant marginal change estimates with baseline assessments as a covariate per centre at 10 years (N = number of patients).

<table>
<thead>
<tr>
<th></th>
<th>Bone level changes</th>
<th>Soft tissue level changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
</tr>
<tr>
<td>Como¹ (N = 11)</td>
<td>1.65 (1.27; 2.03)</td>
<td>0.21 (-0.18; 0.60)</td>
</tr>
<tr>
<td>Como² (N = 7)</td>
<td>1.27 (0.64; 1.90)</td>
<td>0.13 (0.02; 0.24)</td>
</tr>
<tr>
<td>Milan¹ (N = 12)</td>
<td>1.42 (0.57; 2.27)</td>
<td>0.12 (-0.28; 0.52)</td>
</tr>
<tr>
<td>Milan² (N = 8)</td>
<td>1.23 (0.83; 1.63)</td>
<td>1.01 (0.08; 1.94)*</td>
</tr>
<tr>
<td>Monza (N = 8)</td>
<td>1.31 (0.78; 1.84)</td>
<td>0.08 (-0.38; 0.54)</td>
</tr>
</tbody>
</table>

* Vs Como²: P = 0.001, Vs Como¹, Milan¹, Monza: P < 0.001.
cement could be visible on periapical radiographs and then promptly removed. The use of screw-retained prostheses should also be considered.

It is also interesting to observe that the implants used in the present investigation did not have a machined collar but were roughened until the neck (Full-Osseotite implant surface), nevertheless they performed very well over a long time period, with only one episode of cement-induced peri-implantitis. Such a positive outcome can also be attributed to the thorough maintenance programme, which the patients agreed to participate in. To better appreciate such an achievement, it should be noted that a retrospective study with a follow-up of 9 to 14 years, on implants with a machined surface, reported a 7% prevalence of peri-implantitis at implant level and 16% at patient level.

In the present trial, the pattern of peri-implant bone loss was virtually identical for both groups. About 0.5 mm of bone was lost during the first 2 months. Eight months after baseline, the average bone loss was about 1 mm. An additional 0.1 mm of bone was lost over the next 6 months, an average of 1.2 mm of bone was lost by both groups after 5 years and an additional 0.2 mm was lost between years 5 and 10 (Table 6). The authors were unable to compare the long-term results with other investigations that used the same study implant because these could not be identified. While the original plan was to follow these patients for 5 years, the authors prolonged the follow-up to 10 years. It would be even more interesting to follow this cohort of patients for longer periods.

When answering the question of whether there are any differences in marginal bone-level changes between immediate and early loaded implants, our findings suggest that no difference should be expected. This is in agreement with a meta-analysis, that included this trial plus two other similar RCTs, showing, at 1 year after loading, no statistically significant differences between the two loading strategies (P = 0.19; mean difference: -0.06 mm, 95% CI from -0.16 to 0.03), favouring immediate loading.

When clinically interpreting the findings of a statistically significant recession of vestibular soft-tissue levels after delivery of the definitive restorations, we need to consider that 0.38 mm (immediately loaded group) and 0.25 mm (early loaded group) are virtually not clinically detectable. It is possible though that some soft tissue recessions may have occurred during the first 8 months when the provisional restorations were in use. Nevertheless, vestibular soft tissue levels remained stable over a 10-year period with only three implants in two immediately loaded patients showing some visible titanium about 9 years after loading.

The main limitations of this trial are the small sample size and the use of some implant prototypes by one of the centres instead of the implants decided upon at the protocol stage. The prototypes were similar to the commercially available implants used in this trial and were randomly placed into groups, because group allocation was concealed, without the knowledge of the clinician. In fact, they were randomly distributed between the two groups in approximately equal numbers (Table 2), therefore, it is unlikely that this protocol violation significantly impacted the outcome of the present study.

The decision to avoid static and dynamic occlusal contacts on immediately loaded prostheses with the opposite dentition for the first 2 months was dictated by the desire to minimise the risk of early implant failures. This decision was purely based on clinical reasoning, even though, most likely, these restorations were actually loaded during chewing. Surprisingly, two RCTs that have investigated this hypothesis did not find any statistically significant difference or even a clinical trend when comparing immediate occlusal versus non-occlusal loading. However, a more recent RCT, although not showing any statistically significant difference between immediately loaded prostheses in occlusion or not, showed at least a clinical trend favouring non-occlusal loading. Therefore, from a clinical point of view, it is tempting to suggest not placing provisional restorations in direct contact with the opposite dentition, when possible, particularly in those situations where the clinician fears that problems might arise (i.e. posterior regions, low implant insertion torques, signs of parafunctions, etc).

With respect to the generalisability (external validity) of these findings, on the one hand, patient inclusion criteria were broad, and both techniques were tested in real clinical conditions, therefore the results can be easily generalised to a wider population. On the other hand, the clinicians who delivered the interventions were highly trained and the maintenance protocols were rather strict, therefore caution should be exercised by less experienced clinicians.
clinicians when applying immediate or early loading procedures, especially if patients do not comply with adequate maintenance protocols.

### Conclusions

The long-term prognosis of well-maintained dental implants can be optimal. The timing of loading (immediate or early) does not appear to have any significant clinical impact on marginal peri-implant bone or soft-tissue levels. While an average of 1.4 mm of peri-implant bone was lost over 10 years, almost no (0.25 to 0.38 mm) buccal soft-tissue recessions occurred from delivery of definitive restorations up to 10-years post-loading.

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### References


