Immediate non-occlusal vs. early loading of dental implants in partially edentulous patients: a multicentre randomized clinical trial. Peri-implant bone and soft-tissue levels

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Abstract
Objectives: To compare peri-implant bone and soft-tissue levels of immediately non-occlusally loaded vs. non-submerged early loaded implants in partially edentulous patients up to 14 months after placement.

Material and methods: Fifty-two patients were randomized 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 ≥30 N cm, and splinted implants with a torque of ≥20 N cm. Immediately loaded implants were provided with non-occluding temporary restorations within 48 h. After 2 months, the provisional restorations were placed in full occlusion. Implants were early loaded after 2 months. Final restorations were provided 8 months after placement. Blinded assessors evaluated peri-implant bone and soft-tissue levels.

Results: Fifty-two implants were immediately loaded and 52 were early loaded. No dropout occurred. One single immediately loaded implant failed 2 months after placement. Both groups gradually lost peri-implant bone in a highly statistically significant manner at 2, 8, and 14 months. After 14 months, patients of both groups lost an average of 1.1 mm of peri-implant bone. There were no statistically significant differences between the two loading strategies for peri-implant bone and soft-tissue level changes (P > 0.05). After 14 months, the position of the soft tissues did not change significantly from baseline (delivery of the final restorations 8 months after placement).

Conclusions: There were no statistically or clinically significant differences between immediate and early loading of dental implants with regard to peri-implant bone and soft-tissue levels as evaluated in the present study.

Immediate and early loading of dental implants are techniques that are gradually gaining popularity. Such procedures are highly appreciated by the patients who can have their treatment periods drastically reduced and are able to live a normal life with minimal discomfort due to edentulism. A systematic Cochrane review concluded that in carefully selected cases, such procedures can be successful (Esposito et al. 2007), but not all trials have shown predictably high success rates (Tawse-Smith et al. 2002; Ottoni et al. 2005; Oh et al. 2006). This suggests that such procedures are likely to be technique sensitive.

To date, no published trial has reported on the stability of peri-implant tissues when comparing immediate vs. early loaded implants (Esposito et al. 2007), although a few trials have provided reliable information regarding marginal bone-level changes when comparing immediately vs. conventionally loaded implants (Cannizzaro & Leone 2003; Hall et al. 2006), and early
Material and methods

Any partially dentate patient requiring dental implants who was 18 or older and able to sign an informed consent form was eligible for inclusion in this trial. All participants were informed of the nature of 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. Patients were not accepted into the study if any of the following exclusion criteria was present: (1) general contraindications to implant surgery, (2) irradiation in the head and neck area, (3) poor oral hygiene and motivation, (4) uncontrolled diabetes, (5) pregnancy or lactation, (6) substance abuse, (7) psychiatric problems, (8) lack of opposing occluding dentition in the area intended for implant placement, (9) severe bruxism or clenching, (10) active infection or severe inflammation in the area intended for implant placement, (11) a need for bone-augmentation procedures including sinus lifting, and (12) a gap between one of the bone walls and the surface of a post-extraction implant of more than 1.5 mm.

Patients were recruited and treated in five private dental clinics located in northern Italy: Como [two centres], Milan [two centres], and Monza [one centre], all having extensive experience in the treatment of patients with immediate loading procedures. One experienced surgeon at each centre performed all the operations. No ethical or Institutional Review Board approval was sought; however, all patients signed a written informed consent form.

Partially edentulous patients requiring dental implants were randomized to have implants non-occlusally loaded immediately (test group) or early (control group).

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

Full-thickness crestal flaps were elevated with a minimal extension to minimize 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 four centres, Osseotite-tapered FNT implants [Biomet 3i, Palm Beach, FL, USA] were used exclusively and inserted according to the manufacturer’s instructions. At the Como centre, 16 out of the 35 implants placed were the FNT variety, while 19 out of the 35 were prototypes of tapered implants from the same manufacturer with identical surface characteristics. The implant diameters used were 4, 5, and 6 mm, the lengths used were 8.5, 10, 11.5, 13, and 15 mm.

Bone density at drilling was subjectively evaluated and the bone at the implant site was classified as either ‘hard,’ ‘medium,’ or ‘soft’ [Trisi & Rao 1999]. Resistance to implant insertion was recorded objectively with the Osseocare equipment [Nobel Biocare AB, Göteborg, Sweden]. In the protocol-formulation phase, it was decided that single implants with a torque resistance of ≤ 30 N cm or splinted implants with a torque resistance of ≤ 20 N cm that were randomized to the immediately loaded group should instead be treated as belonging to the early loaded group. In soft bone, under-preparation was performed using a shaping drill one size smaller than the final implant diameter. In general, implants were placed at the crestal level in healed edentulous ridges and slightly subcrestally in immediate post-extraction sockets. In cases where a residual gap of ≤ 1.5 mm was present between the implant surface and the bone wall, the gap was filled with autogenous bone chips. No other type of bone-grafting material was used. A non-submerged technique was used. Before placing the abutments, the envelope containing the randomization 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 occlusal contact with the opposite dentition. All provisional restorations 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 immediately non-occlusally loaded restorations to put them in full occlusion. Patients of the early loaded group received provisional restora-
tions identical to those of the immediately loaded groups with full occlusal contacts. Final metal–ceramic restorations were cemented 8 months after implant placement.

Patients were recalled every 3 months for oral hygiene maintenance and prosthetic controls up to the first year after implant placement. Thereafter, patients with excellent oral hygiene will be recalled every 6 months.

Outcome measures evaluated for the present study were:

1) Peri-implant marginal bone-level changes on intraoral radiographs made with the paralleling technique. Periodical X-rays were taken at implant placement, 2, 8, and 14 months after implant placement. Radiographs were scanned (HP Scanjet 3c/t, Hewlett Packard, Cernusco sul Naviglio, Milan, Italy), digitized 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, Frederick, MD, USA) software. The software was calibrated for every single image using the known distance of two consecutive treads (0.9 mm for FNT implants, Fig. 1a, 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 bone-to-implant contact (Fig. 1b and c). For those implants placed intentionally in a supracrestal position, the height of the implant collar was subtracted (1.25 mm for the FNT implants, Fig. 1b, and 0.75 mm for the prototype implants).

2) Soft-tissue stability (height of the clinical crown) measured with a digital calliper (Calliper IP34, Sham, Guillin, China) on plaster models (Fig. 2). Alginate impressions were taken at 8 months (after delivery and adjustment of the final restorations) and 14 months. Hard plaster models were immediately prepared. For incisors, the reference point was the middle of the incisal margin; for canines and bicuspids it was the tip of the cusp (Fig. 3), and for molars the deepest occlusal vestibular margin between the two cusps. Measurements were performed vestibularly from the occlusal reference point perpendicular to the marginal gingiva. All measurements were taken twice, after a 15-day interval, and the two values were averaged.

![Fig. 1. Measurement of marginal bone levels on a digitized radiograph: (a) the software is calibrated using the distance of two consecutive threads (0.9 mm) and (b) the known height of the implant neck (1.25 mm). (c) The measurement is taken from the implant–abutment junction to the most coronal point of bone-to-implant contact.](image-url)
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 recent study [Ottoni et al. 2005] of partially edentulous patients, the proportion of failures in the immediately loaded group was 0.39 compared with 0.04 in the conventionally loaded group. A two-group continuity-corrected \( \chi^2 \) test with a 0.05 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 of 26 patients. It was planned to include 30 patients in each group to compensate for possible drop-outs.

These outcome measures were assessed by two independent, blinded, calibrated outcome assessors. One measured all radiographs and the other measured the clinical crown height on plaster models. All radiographs were coded so that the outcome assessor was blinded to which group the implants belonged to, nor was the assessor informed of the aims of the study. Because 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 either the radiographs or the plaster models were created.

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A manually generated restricted randomization list was used to create two groups with equal numbers of patients. Only one of the investigators, not involved in the selection and treatment of the patients, was aware of the randomization sequence and had access to the randomization list stored in a password-protected portable computer. The randomized 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. A biostatistician with expertise in dentistry analysed the data, without knowing the group allocation. The average radiographic values for the mesial and distal surfaces were calculated and averaged for each patient. Average crown length values were also calculated 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 values at 14 months, 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 randomized: 25 to the immediately loaded group and 27 to the early loaded group. The planned number of 30 patients per group was not achieved because the centres decided to stop patient recruitment at the end of May 2005. All patients were treated according to the allocated interventions. No patient dropped out, all implants achieved the required minimal implant stability, and the data of all patients were evaluated in the statistical analyses.

Patients were recruited and treated from October 2004 to May 2005. The follow-up focused on the time between implant placement and 14 months after implant placement. The patient distribution in 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. These four were all included in 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, subjectively evaluated, and the maximum insertion torque (primary im-

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**Table 1. Patients’ distribution in the various centres**

<table>
<thead>
<tr>
<th>Centre</th>
<th>Immediate (n = 25)</th>
<th>Early (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Como 1</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Como 2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Milan 1</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Milan 2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Monza</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>
plant stability) appear in Table 4. There were no apparent significant baseline im-
balances between the two groups.

No patient dropped out or was excluded from the trial, and all were followed up to
14 months post-implant-placement. A single implant and its provisional crown, in-
serted with a primary stability of 50 N cm in medium-density bone, failed 2 months
after placement in the immediately loaded group. The failed implant was successfully
replaced with another implant after 6 months of healing.

Both groups gradually lost marginal peri-
implant bone in a highly statistically sig-
nificant way [P<0.001] at 2, 8, and 14
months (Table 5). After 2 months, patients
in the immediately loaded group lost an
average of 0.5 mm peri-implant bone vs.
0.6 mm for the patients in the early loaded
group (Table 6). After 8 months, patients in
the immediately loaded group lost an aver-
age of 0.9 mm of peri-implant bone vs.
1 mm for the patients in the early loaded
group (Table 6). After 14 months, patients
of both groups lost an average of 1.1 mm of
peri-implant bone (Table 6). 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 = 0.91).

After 14 months, the position of the soft
tissues did not change significantly from
the baseline (delivery of the final restora-
tions 8 months after placement, Table 7).
Vestibular soft tissues receded 0.1 mm in
the immediately loaded group and re-
ained virtually stable in the early loaded
group (Table 7). There were no statistically
significant differences between the two
loading strategies for soft-tissue changes
(Table 7).

Discussion

The aim of the present report was to
evaluate whether marginal peri-implant
bone and soft tissues behaved in a different
way around immediately non-occlusally
loaded and early loaded implants in par-
tially edentulous patients. The data pre-
sented cover a follow-up of 14 months after
implant placement. Longer follow-ups
(3 and 5 years) will be presented in future
publications. It is possible to conclude
safely that no statistically or clinically
significant differences were present be-
tween the two tested procedures 14
months after placement. These results are
strengthened by the fact that the metho-
dology of this report is rather robust: pa-
tients were randomized and group
allocation was concealed to clinicians.
Clinicians knew about the outcome of
randomization only after having completed
implant placement. All patients who were
asked to join the trial agreed to be enrolled.
All treated patients were accounted for
with no exclusions. The assessment of
the outcome measures was performed by
calibrated, independent, blinded outcome
assessors, using rather objective, validated,
and reproducible outcome measures. Also,
the narrow confidence intervals for the
mean differences between the treatments
suggest that the results are reliable. In
addition, the data originate from a multi-
centre trial including five private practices.
The advantages of multicentre trials are
twofold: more patients can be recruited,
increasing the precision of the results, and
the results are more generalizable if more
centres achieve similar results. On the
other hand, the logistic organization of
multicentre trials is more complex, and
there is always the risk that some centres
may inadvertently deviate from the proto-
col. This trial involved a group of experi-
enced clinicians who had already worked
together in several other trials and used
homogenous and standardized procedures
for treating patients. In addition, a detailed
research protocol was discussed and agreed
upon a priori. Despite these precautions,
some violations of the protocol occurred,
the most notable one being the use by one
of the centres of some implant prototypes
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
without the clinician knowing at place-
ment into which group they were going to
be included because group allocation was
concealed. Therefore, it is unlikely that
this protocol violation significantly im-
peaked the outcome of the present study.
With respect to the generalizability (exter-
nal validity) of these findings, patient-
 inclusion criteria were broad, and both
techniques were tested under real clinical
conditions; therefore, the results can be
easily generalized to a wider population.

Immediately loaded implants were not
put in direct occlusion for 2 months,
although they were actually loaded during chewing. It could be debated whether immediate ‘non-occluding’ loading (i.e. a provisional restoration placed on the implants and not in contact with the opposite dentition, also called ‘immediate provisionalization’), as opposed to ‘occlusal’ loading (the restoration in full occlusal contact with the opposite dentition), should be considered to be a real immediate loading procedure and whether this could have an influence on the outcomes evaluated in the present trial. From a patient’s viewpoint, the difference may not be significant because patients do prefer to have their new teeth as soon as possible (Schropp et al. 2004). In addition, non-occluding restorations are actually functionally used during chewing. The only RCT that investigated this hypothesis (Lindeboom et al. 2006) did not find any statistically significant difference or clinical trend by comparing immediate occlusal loading vs. non-occlusal loading. Actually, one more implant was lost in the non-occluding group when compared with the fully occluding group. Marginal bone loss was virtually identical in the two groups after 1 year in function and was in the range of 0.2–0.3 mm. From a clinical point of view, it might still be tempting to suggest the use of provisional restorations in non-occlusal contact, particularly in those situations where the clinician fears that problems might arise, but the evidence does not support this clinical tip.

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 (Table 6).

When interpreting the finding of virtually no clinically detectable changes in vestibular soft-tissue levels after placement of the definitive restorations, it is possible that some changes may have occurred during the first 8 months when the provisional restorations were used.

To the best of the authors’ knowledge, only one ongoing unpublished RCT has compared immediate loading with early loading in partially edentulous patients (Merli et al. 2008); however, bone-level data are not yet available.

A recent Cochrane review (Esposito et al. 2007) was able to include only two RCTs (Cannizzaro & Leone 2003; Hall et al. 2006) in a meta-analysis comparing bone-level changes of patients with immediate vs. conventionally loaded implants. Both studies included initially 14 patients in each group and reported bone losses after 1 year in function in the range of 0.1 mm for both groups (Cannizzaro & Leone 2003) or 0.6 mm (immediate loading)/0.8 mm (conventional loading) (Hall et al. 2006). Both studies are in agreement with the findings of the present trial, showing no differences in bone loss between the two loading strategies. However, they also showed lower marginal bone loss than what was observed in the present trial. The possible explanations for the bone loss differences observed in the present trial (1.1 mm) and the other two trials (0.1–0.8 mm) are purely speculative and may be attributed to different implant designs and/or different ways of measuring bone-level changes. Any direct comparisons between different trials may lead to biased conclusions and should be avoided or carefully worded.

Conclusions

No statistically significant differences in marginal bone and buccal soft-tissue level

Table 5. Mean radiographic peri-implant marginal bone levels between groups and time periods

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>2 months Mean (SD)</th>
<th>8 months Mean (SD)</th>
<th>14 months Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate loading</td>
<td>0.03 (0.09)</td>
<td>0.56 (0.50)</td>
<td>0.95 (0.56)</td>
<td>1.14 (0.58)</td>
</tr>
<tr>
<td>Early loading</td>
<td>0.07 (0.16)</td>
<td>0.67 (0.47)</td>
<td>1.04 (0.52)</td>
<td>1.18 (0.54)</td>
</tr>
</tbody>
</table>

*All changes from baseline statistically different (P<0.001).

Table 6. Comparison of mean changes in peri-implant marginal bone levels at different time periods between groups

<table>
<thead>
<tr>
<th></th>
<th>Baseline – 2 months Mean (SD)</th>
<th>Baseline – 8 months Mean (SD)</th>
<th>Baseline – 14 months Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate loading</td>
<td>0.52 (0.48)</td>
<td>0.92 (0.55)</td>
<td>1.10 (0.58)</td>
</tr>
<tr>
<td>Early loading</td>
<td>0.60 (0.46)</td>
<td>0.97 (0.50)</td>
<td>1.11 (0.54)</td>
</tr>
</tbody>
</table>

*Analysis of covariance for 14 months with baseline as a covariate.

Table 7. Comparison of mean clinical crown length values between groups and time periods

<table>
<thead>
<tr>
<th></th>
<th>Baseline/8 months Mean (SD)</th>
<th>14 months Mean (SD)</th>
<th>Mean Difference (SD)</th>
<th>P-value comparing 8 with 14 months</th>
<th>P-value comparing immediate vs. early loading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate loading</td>
<td>8.50 (1.37)</td>
<td>8.63 (1.49)</td>
<td>0.13 (0.40)</td>
<td>0.11</td>
<td>0.24</td>
</tr>
<tr>
<td>Early loading</td>
<td>7.97 (1.74)</td>
<td>7.98 (1.72)</td>
<td>0.01 (0.37)</td>
<td>0.93</td>
<td></td>
</tr>
</tbody>
</table>
changes were observed when comparing immediately non-occlusally loaded with early loaded implants in partially edentulous patients followed for 14 months. The timing of loading does not appear to have a significant clinical impact on marginal peri-implant bone or soft-tissue levels.

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