

# Immediate Nonocclusal Versus Early Loading of Dental Implants in Partially Edentulous Patients: 1-year Results from a Multicenter, Randomized Controlled Clinical Trial

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**Purpose:** To compare the efficacy of immediate nonocclusal loading (test group) versus early loading (control group) in partially edentulous patients. **Materials and Methods:** Fifty-two patients in 5 Italian private practices were randomized to 1 of the treatments: 25 to the immediately loaded group and 27 to the early loaded group. To be immediately loaded, single implants had to be inserted with a torque of > 30 Ncm, and splinted implants had to be inserted with a torque of > 20 Ncm. Implants in the immediately loaded group were provided with full acrylic resin nonoccluding temporary restorations within 48 hours after placement. After 2 months, full occluding provisional restorations were provided. Implants in the early loading group were not submerged and were loaded after 2 months. At 8 months, provisional restorations were replaced with definitive metal-ceramic prostheses. Outcome measures were prosthesis and implant failures as well as biologic and prosthetic complications recorded by nonblinded assessors. The Fisher exact test was used to compare the proportion of implant failures. **Results:** Fifty-two implants were placed in the immediately loaded group and 52 in the early loaded group. No dropouts or complications occurred up to 14 months postinsertion. One single implant failed in the immediately loaded group 2 months after placement. There was no statistically difference for the tested outcome measures between the 2 procedures ( $P > .99$ ). **Conclusions:** The results of this randomized controlled clinical trial with 25 patients rehabilitated with immediately restored nonocclusally loaded implant-supported prostheses compared to 27 patients restored 2 months following placement suggest that there are no major clinical differences in implant survival between these 2 protocols. No biologic or prosthetic complications occurred. (Clinical Trial) *INT J ORAL MAXILLOFAC IMPLANTS* 2007;22:815–822

**Key words:** dental implants, early loading, immediate loading, partial edentulism

Osseointegrated dental implants traditionally have been placed in accordance with a 2-stage protocol.<sup>1</sup> This approach dictated that the implant be

submerged and left to heal for a period of 3 to 4 months in mandibles and 6 to 8 months in maxillae. Attempts to load the implant earlier were associated with increased failure rates.<sup>1</sup>

In general, removable prostheses have been used during the implant healing period. However, as many patients have found these temporary prostheses uncomfortable, it would be beneficial if the healing period could be shortened without jeopardizing implant success. In 1990 the first longitudinal clinical trial suggesting that implants could be loaded immediately or early in the mandibles of selected patients was published.<sup>2</sup> Nowadays, implants are commonly loaded immediately or early, particularly in mandibles of good bone quality.<sup>3</sup>

A Cochrane systematic review of randomized controlled clinical trials (RCTs) evaluating the efficacy of immediately and early loaded implants versus conventionally loaded implants concluded that, while it is possible to successfully load oral implants immedi-

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ately after placement in edentulous mandibles of adequate bone density and height, the predictability of this approach is not yet known.<sup>4</sup> In mandibles of adequate bone density and height, increased failure rates were not demonstrated in RCTs comparing immediately loaded implants to conventionally or early loaded implants.<sup>5-9</sup>

However, immediately loaded implants on occasion have been associated with clinically relevant increased failure rates.<sup>10,11</sup> In a recent RCT of split-mouth design, single nonoccluding immediately loaded implants showed significantly greater failure rates than conventionally loaded dental implants. Ten of 23 immediately loaded implants failed versus only 1 of 23 in the conventionally loaded group.<sup>10</sup> The authors demonstrated a strong correlation between implant failures and the initial insertion torque of the implants. Nine of the 10 implants inserted with a 20-Ncm torque failed, versus only 1 of 10 placed with a 32-Ncm torque in the immediately loaded group.<sup>10</sup> These findings support the hypothesis that implant stability and lack of micro-movement are 2 of the main factors necessary for achieving predictably high success rates.<sup>12</sup>

To decrease the risk of immediately loaded implants failing early, various "clinical tricks" have been suggested, such as underpreparation of the implant site to achieve high primary stability,<sup>7</sup> the use of a nonoccluding temporary prosthesis during the first 2 months of healing,<sup>13</sup> or progressive loading of the prosthesis. It is important to clinically evaluate whether predictable results can also be obtained when loading dental implants immediately in partially edentulous patients.

The aim of this RCT was to compare the efficacy of immediate nonocclusal loading (test group) versus early loading (control group) in partially edentulous patients. The null hypothesis was that there would be no difference in prosthesis and implant success rates, or number of complications, between the 2 procedures.

Immediate nonocclusal loading was defined as the seating within 48 hours after implant placement of a provisional prosthesis that would not be in occlusal contact for about 2 months. Early loading was defined as loading of both mandibular and maxillary implants after a 2-month healing period.

This report presents preliminary 14-month data. In the study protocol, it was planned to undertake this assessment and follow-up to the third year of function and to report additional outcome measures, such as peri-implant marginal bone-level changes on intraoral radiographs and soft tissue changes over time. The present article is reported according to the CONSORT statement for improving the quality of reports of parallel-group randomized trials ([www.consort-statement.org](http://www.consort-statement.org)).

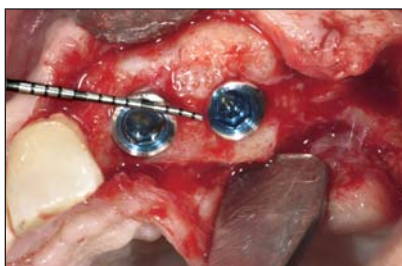
## MATERIALS AND METHODS

Any partially dentate patient requiring dental implants who was at least 18 years old was eligible for inclusion in this trial. Participants were informed of the nature of the study and provided their signed informed consent. For patients with multiple edentulous areas to be restored, the operator was free at the screening visit to select 1 area to be included in the trial. Patients were not accepted into the study if they met any of the following exclusion criteria: (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 augmentation, or (12) a gap between one of the bone walls and the surface of a postextraction implant of more than 1.5 mm.

Patients were recruited and treated in 5 private dental clinics located in northern Italy: Como (2 centers), Milan (2 centers), and Monza (1 center). One experienced surgeon at each center performed all the operations. Ethical or institutional review board approval was not sought.

Partially edentulous patients requiring dental implants were randomized to either the test group (nonocclusal immediate loading) or the control group (nonocclusal early loading). Patients were instructed to use chlorhexidine mouthwash 0.2% for 1 minute 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 hour prior to the intervention and 2 g 6 hours postoperatively. Patients allergic to penicillin were given clarithromycin 500 mg 1 hour prior to the intervention. Ibuprofen 600 mg was given 1 hour prior to intervention and then twice a day for 3 days.

A sedative premedication (Valium; Roche, Milan, Italy), was given to anxious patients 1 hour prior to the intervention. Local anesthesia was obtained using articaine with adrenaline 1:100,000 (Ultracain, D-S forte; Aventis Pharma Deutschland, Frankfurt, Germany). If teeth were 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 midcrestal incision was performed from the distal surface of the more mesial tooth to the mesial surface of the distal tooth. In the presence of a distal edentulous ridge, the incision was extended distally. Vertical releasing



**Fig 1a** Two implants placed in the left maxilla in a patient randomized to the immediately loaded group.



**Figs 1b and 1c** Impression-making phase of the same patient.

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 minimize patient discomfort. The buccal flaps were secured to the inner side of the cheek with silk sutures to minimize trauma to the flap during the surgical procedure. Teeth extractions were performed as atraumatically as possible to preserve the buccal alveolar bone using periostomes and small levers. Extraction sockets were carefully cleaned of any granulation tissue.

The choice of the implant diameter and length was left up to the surgeon. Osseotite tapered FNT implants (Biomet/3i, Palm Beach Gardens, FL) were inserted according to the manufacturer's instructions. The implant diameters used were 4, 5, and 6 mm; 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."<sup>14</sup> Resistance to implant insertion was objectively recorded with Osseocare equipment (Nobel Biocare, Göteborg, Sweden). In the protocol-formulation phase, it was decided that single implants with a torque resistance of  $\leq 30$  Ncm or splinted implants with a torque resistance of  $< 20$  Ncm that were randomized to the immediately loaded group should instead be treated as belonging to the early loaded group. In soft bone, underpreparation was performed using a shaping drill 1 size smaller than the final implant diameter. In general implants were placed at crestal level in healed edentulous ridges (Fig 1a) and slightly subcrestally in extraction sockets. In cases where a residual gap of  $\leq 1.5$  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 nonsubmerged technique was employed. Before abutment placement, an envelope containing the randomization code was opened, allowing the surgeon to know whether the patient 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 pickup impression copings was made for the implants to be immediately loaded using addition silicon (Elite Implant Impression Material; Zhermack, Badia Polesine, Rovigo, Italy; Fig 1b), and a transparent resin impression tray (Set Dental, Dental Trey, Fiumana-Predappio, Italy; Fig 1c). The vertical dimension was registered with a wax plate (Aluwax, Allendale, MI). Healing screws were placed.

Ice packs were provided to the patients, and a soft diet was recommended. Smokers were asked to avoid smoking for 48 hours postoperatively.

Models were made with class 4 precision plaster and mounted in standard articulators. Provisional restorations were manufactured using acrylic resin (Jet Kit, Wheeling, IL) and fixed on the analog with a temporary cylinder and a titanium screw. Patients of the immediately loaded group returned the following day for placement of the abutments (Fig 2) and provisional prostheses. Provisional restorations could also be cemented on the implant abutments (Fig 3a). The occlusal surface of the provisional restoration was ground to avoid any occlusal contact with the opposing dentition (Fig 3b). All provisional restorations of the immediately loaded group were placed within 48 hours. Sutures were removed 2 weeks after implant placement.

Two months after implant placement, individual implants were manually tested for stability, and acrylic resin was added to the immediately nonocclusally loaded restorations to put 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. Intraoral radiographs of the study implants were made (Fig 4).

Eight months after implant placement, individual implants were manually tested for stability. The final restorations were cemented (Figs 5a and 5b), intraoral radiographs were taken (Fig 6), and an alginate impression of the study implants was made.

Patients were recalled every 3 months for oral



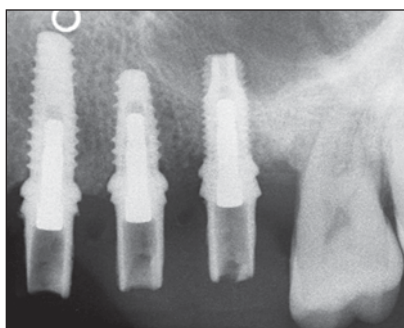
**Fig 2** Abutments were placed about 24 hours after the surgical phase.



**Fig 3a** (above) Occlusal view of the provisional full acrylic resin restoration.



**Fig 3b** (right) Buccal view. Articulating paper was applied to ensure that no occlusal contacts were present.



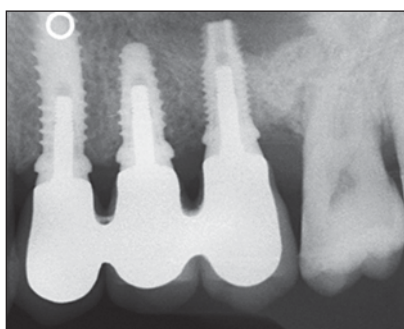
**Fig 4** Intraoral radiograph made 2 months after placement of the provisional restoration when the provisional prosthesis was put in full occlusion.



**Fig 5a** Occlusal view of the definitive metal-ceramic restoration placed after 8 months.



**Fig 5b** Buccal view of the definitive metal-ceramic restoration placed after 8 months.



**Fig 6** Intraoral radiograph at placement of the definitive prosthesis.

1. Prosthesis failure: the planned prosthesis could not be placed or was lost because of implant failures.
2. Implant failure: the presence of any mobility of an individual implant (assessed manually by rotating the implant) and/or any infection dictating implant removal at insertion of the provisional or definitive prostheses.
3. Any biologic or prosthetic complications. Possible biologic complications included 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), and fistulae. Examples of possible prosthetic complications were fracture of the implant, abutment screw, framework, or occlusal material.

hygiene maintenance and prosthetic controls up to the first year after implant placement. Thereafter, patients with excellent oral hygiene were recalled every 6 months, while all other patients continued to be recalled at 3-month intervals.

Outcome measures evaluated for the present study were:

These outcome measures were assessed by the treating clinicians, who were therefore not blinded. Additional outcome measures will be reported in future reports, including marginal bone level changes on intraoral radiographs made with the paralleling technique and soft tissue stability assessed by independent and blinded assessors. The final follow-up was planned to be at 3 years of loading.

**Table 1 Patient Distribution in the Various Centers**

	Immediate (n = 25)	Early (n = 27)
Como 1	9	6
Como 2	2	5
Milan 1	6	6
Milan 2	4	4
Monza	4	6

The sample size was chosen based on calculations of the number of patients likely to have at least 1 implant failure. In a recent study<sup>10</sup> of 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 2-group continuity-corrected chi-square test with a .050 2-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 dropouts.

A manually generated restricted randomization list was used to create 2 groups with equal numbers of patients. Only 1 investigator, who was not involved in the selection and treatment of the patients, was aware of the randomization sequence and had access to the randomization list, which was 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; 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 biostatistician with expertise in dentistry analyzed the data without knowledge of the group allocation. Differences in the proportion of failures and other complications between the groups were compared using the Fisher exact probability test. All statistical comparisons were conducted at the .05 level of significance.

**Table 2 Characteristics of Patients and Interventions**

	Immediate (n = 25)	Early (n = 27)
No. of female subjects	12	17
Mean age at implant insertion (range)	51.6 (27 to 74)	51.3 (34 to 73)
No. of smokers	9	4
Total no. of implants placed	52	52
No. of implants placed in mandibles	38	21
No. of implants placed in anterior areas (canine to canine)	3	3
No. of implants placed in fresh extraction sockets	6	9 (1 grafted)
No. of patients receiving single implants	7	10
No. of patients receiving 2 implants	10	9
No. of patients receiving 3 implants	7	8
No. of patients receiving 4 implants	1	0

## 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 since the centers decided to stop patient enrollment at the end of May 2005. All patients were treated according to the allocated interventions. No patient dropped out, all implants achieved the minimal implant stability required, and the data of all patients were evaluated in the statistical analyses.

Deviations from the operative protocol were as follows: while 4 centers used exclusively FNT implants, the Como 1 center also used some prototypes of tapered implants with identical surface characteristics by the same manufacturer (19 of 35 inserted implants). One patient from the immediately loaded group was provided with the definitive restoration after 2 months instead of the planned 8 months. Because of a cardiac disease, 1 patient from the early loaded group received the definitive prosthesis 14 months after implant placement; however, that patient's implants were assessed for stability 8 months after placement as planned.

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 last definitive prosthesis was inserted in January 2006, and the last patient was recalled in September 2006 for the 1-year follow-up, corresponding to 14 months after implant placement. Patient distribution in the various centers is shown in Table 1. Main baseline patient characteristics are presented in Table 2. Patients were generally

**Table 3 Implant Length and Diameter**

	Immediate (n = 52)	Early (n = 52)
Implant length		
8.5 mm	8	2
10 mm	18	16
11.5 mm	13	15
13 mm	11	17
15 mm	2	2
Implant diameter		
4 mm	38	33
5 mm	12	18
6 mm	2	1

healthy. Three patients suffered from hypertension and 1 from hepatitis C. These 4 patients were 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. The bone density, subjectively evaluated, and the maximum insertion torque (primary implant stability) appear in Table 4. There were no apparent significant baseline imbalances between the 2 groups.

No patient dropped out or was excluded from the trial, and all were followed up to 14 months following implant placement. A single implant and its provisional prosthesis, inserted with a primary stability of 50 Ncm in medium bone density, 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 among the 2 interventions (Fisher exact test,  $P > .99$ ).

No surgical or prosthetic complications were observed in any of the patients.

## DISCUSSION

Successfully 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.<sup>15</sup> To minimize the risk of soft tissue encapsulation, it has been recommended that implants be kept load-free by submerging them during the healing period.<sup>1</sup> This traditional approach requires longer treatment periods as well as a second surgical intervention to expose the implants. The present investigation was designed to evaluate

**Table 4 Bone Density Evaluated Clinically and with the Osseocare Device (Primary Implant Stability)**

	Immediate (n = 52)	Early (n = 52)
Tactile bone density		
Hard	1	2
Medium	43	40
Soft	8	10
Insertion torque		
20 Ncm	3	4
30 Ncm	6	14
40 Ncm	18	20
50 Ncm	22	14
60 Ncm	3	0

whether immediate nonocclusal loading in partially edentulous patients could provide satisfactory results, since such shorter treatment periods are highly appreciated and requested by many patients. The preliminary results are encouraging. Only 1 implant and its prosthesis were lost in the immediately loaded group over a 14-month period. It should be emphasized that the immediately loaded implants were not put in direct occlusion for 2 months, although they were used during chewing by patients. Another aspect which may explain the good results is that all implants achieved high primary stability at placement. To qualify for the immediate loading, the minimum required insertion torque was 20 Ncm for implants that were to be splinted and 30 Ncm for single implants. To achieve this in soft bone, underpreparation was performed using a shaping drill 1 size smaller than the final implant diameter.

A recent RCT<sup>10</sup> of split-mouth design in which single implants were either immediately occlusally loaded or conventionally loaded found a strong correlation between primary stability, measured as placement torque, and implant failures for immediately loaded implants. In fact, of 10 single implants placed with an insertion torque of 20 Ncm, 9 failed, whereas only 1 of 10 failed of implants inserted with a 32-Ncm torque. These clinical findings prove beyond any reasonable doubt that primary implant stability is a prerequisite for the success of immediate implant loading.

To the best of the authors' knowledge there are 2 other RCTs comparing immediate loading with conventional loading in partially edentulous patients. In 1 trial,<sup>7</sup> 14 patients were treated in each group, and immediately loaded implants were fully loaded the day of implant placement and followed for 2 years. Only 1 early failure was reported; that failure was in the conventionally loaded group. The other trial,

which was of split-mouth design,<sup>9</sup> included 12 patients. Three implants distal to the canines loaded the same day with temporary restorations were compared with 3 implants on the contralateral side conventionally loaded at 3 months. There were no failures up to 1 year of loading. Ongoing as-yet unpublished trials seem to confirm these preliminary results.

It can be concluded that immediate loading of dental implants can be successful if clinical precautions are taken. Such precautions may include underpreparation of the implant sites, particularly in the presence of soft bone; the use of implants favoring stronger and faster bone integration; achievement of high insertion torques (> 30 Ncm); and accurate control of loading. Some authors also advocate the use of specific implant surface preparations to reduce the healing time.<sup>16</sup>

The present trial included 5 centers in the north of Italy. The advantages of multicenter trials are 2-fold: more patients can be included, therefore increasing the precision of the results, and the results are more generalizable when more centers achieve similar results. However, the logistic organization of multicenter trials is more complex, and there is always the risk that some centers may inadvertently deviate in small ways from the protocol. This trial involved a group of experienced 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 1 of the centers of 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 placement in which group they were going to be included, since group allocation was concealed. Therefore, it is unlikely that this protocol violation significantly impacted the outcome of the present study.

With respect to the sample size calculation (ie, the number of patients needed to be included in the study to detect a predefined statistically significant difference), it was decided to randomize 30 patients in each group, with one center providing 20 patients and the other 4 centers providing 10 patients each. However, clinicians decided to stop enrollment at the end May 2005, although the planned number of patients had not been reached. The number of included patients may still be too low to detect any difference. To establish whether immediately loaded implants are reliable and effective procedures, a greater number of patients should be evaluated.

All patients asked to join the present trial agreed to be enrolled. All treated patients were accounted for with no exclusions. Assessment of the outcome measures presented in this report was carried out by the operators. It is recognized that there is a risk of bias when operators assess their own interventions,<sup>17</sup> but because this study was not commercially or institutionally funded, it was not feasible to have a blinded independent outcome assessor visit the various centers to evaluate the outcome measures or to have a second outcomes assessor in each center.

With respect to the generalizability (external validity) of these findings, it should be recognized that both techniques were tested in real clinical conditions and that patient inclusion criteria were broad. Therefore, the results can be easily generalized to a wider population. However, the operators were highly experienced, and this may limit extrapolation of the present results.

## CONCLUSIONS

Treatment goals were achieved with both of the loading protocols used; however, immediate nonocclusal loading achieved these goals in a shorter period of time. No statistically significant differences for failures were observed between the 2 interventions, and no complications occurred.

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