Three-year Data from a Randomized, Controlled Study of Early Loading of Single-Stage Dental Implants Supporting Maxillary Full-Arch Prostheses

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Purpose: *The aim of this 3-year randomized controlled trial (RCT) was to compare biologic and technical treatment outcomes and patient satisfaction after early (≤ 14 days postimplantation) loaded implants with those of implants loaded after a healing period of 3 to 4 months in the edentulous maxilla.* ***Materials and Methods:*** *Twenty-four patients with completely edentulous maxillae were randomized into a test group (n = 16) and a control group (n = 8). All patients received 5 or 6 solid screw-type titanium implants with sandblasted, large-grit, acid-etched (SLA) surfaces. In total, 142 implants were placed and 139 implants were loaded with full-arch prostheses. Clinical assessments were obtained at loading and after 3, 6, 12, 24, and 36 months. Radiographs of implants and existing teeth were taken at loading; after 6, 12, 24, and 36 months; and at 12, 24, and 36 months, respectively.* ***Results:*** *The cumulative implant success rate 3 years after loading was 100%. At the 3-year examination the mean (P ≤ .005), distal (P ≤ .005), and mesial (P > .05) crestal bone levels were better in the test group. No significant differences between the test and control groups were noted for any other outcome measure. The most common adverse event in both groups was tooth-crown fracture.* ***Discussion:*** *A review of the literature, both printed and electronic, revealed no study fulfilling the criteria of an RCT dealing with the early loading of maxillary full-arch prostheses. This study fulfills those criteria.* ***Conclusion:*** *In this study population it has been concluded that the early (approximately 2 weeks) loading protocol is a viable alternative to the standard (3 to 4 months) protocol in the rehabilitation of a completely edentulous maxilla with a complete implant-supported fixed prosthesis.* (Controlled Clinical Cohort Study)
Int J Oral Maxillofac Implants 2006;21:245–252

Key words: *dental implants, early loading, edentulous maxillae, randomized controlled study*

Over the last few decades the utilization of bone-anchored dental implants has become an established treatment method in the replacement of missing teeth. The original concept for the best long-term documented implant systems included interim healing times of 6 and 3 months[1–4] for the maxilla and mandible, respectively. Following this standard protocol for restoration of the completely edentulous jaw with a full-arch prosthesis has produced favorable results.[5–8]

To minimize treatment time, the healing period prior to implant loading has been reduced, and the 1-stage surgical method whereby all the components are assembled during the same surgical procedure has been developed. The wearing of a transitional removable prosthesis during this healing period can hinder the patient's mental acceptance of implant treatment and increase the number of patient visits related to discomfort (ie, frequent prosthesis adjustments). In a study of 7 patients with immediately loaded implants and 7 with conventionally loaded implants, significantly fewer postoperative visits were seen in the immediately loaded group.[9] This investigation indicated that rehabilitation with functional implant loading immediately or as early as possible can be advantageous for both patients and operators.

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Editor's note: *As was the case in the decision to publish the 1-year data from this study, so has there been considerable disagreement concerning the management of the statistical analysis of the data presented in this 3-year report. The article has been accepted for publication recognizing the fact that there are multi-faceted problems with the interpretation of the results from this ongoing investigation which have been argued by statistical authorities representing both the author and this journal.*

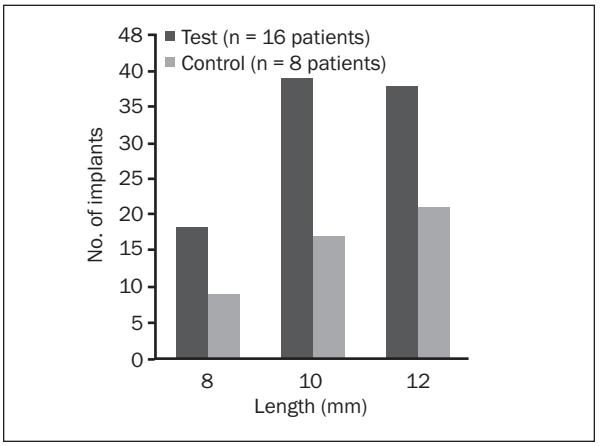

Fig 1 Distribution of 4.1-diameter implants by length.

The term *immediate/early,* which is sometimes seen in loading protocols, is confusing because it has been defined several ways. A report from a consensus meeting in Barcelona, Spain, in 2002 stated that *immediate* is used when the prosthesis is attached to the implants the same day the implants are placed and *early* when the prosthesis is attached at a second procedure but earlier than the conventional healing period of 3 to 6 months.[10] In the Cochrane Database of Systematic Reviews, Esposito and associates[11] used the term *immediate* when loading after 2 to 3 days and *early* when loading 6 weeks after implant placement. In a literature review of 95 articles on the early loading of dental implants, *early* is used when the prosthesis is attached to the implant within 3 weeks.[12] In 2003, at a consensus conference in Gstaad, Switzerland, one subject was the need to set loading protocols. The term *immediate* was defined as loading within 48 hours after implant placement; *early* was defined as loading between 48 hours and 3 months after implant placement.[13]

A systematic review of the incidence of biologic and technical complications in implant dentistry reported in prospective longitudinal studies has been presented by Berglundh and coworkers.[14] They concluded that implant loss was most frequently described (reported in about 100% of studies). Biologic complications were considered in 40% to 60% of the studies; technical complications in 60% to 80%. They concluded that data on the incidence of biologic and technical complications may be underestimated. Using an extensive search strategy to find randomized controlled trials (RCTs) showing differences in the clinical outcome between immediately or early loaded implants compared with conventionally loaded implants, Esposito and associates[11] found 3 articles. Two of these, dealing with overdentures, fulfilled their selection criteria. None of the 3 articles was concerned with full-arch implant-supported prostheses. They concluded that better-designed RCTs are needed to understand how predictable the protocols for immediate and early loading are. Gapski and associates[15] agreed; in the conclusion of their critical review of immediate implant loading literature, they stated that prospective, longitudinal, and randomized studies are certainly needed before this approach can be widely used.

To date the present authors have not found any RCTs that address the early loading of implants with a full-arch fixed prosthesis in the edentulous maxilla extending to a 1-year follow-up period. The purpose of this 3-year follow-up study was to compare biologic and technical treatment outcomes and patient satisfaction in early (< 14 days postimplantation) loaded implants with those in implants loaded after a healing period of 3 to 4 months.

MATERIALS AND METHODS

Twenty-four patients with completely edentulous maxillae were randomized into a test group and a control group. The test group comprised 16 patients, 10 female and 6 male, with a mean age of 65 years at the time of implant placement (range, 39 to 79 years). The control group comprised 8 patients, 6 female and 2 male, with a mean age of 62 years at the time of implant treatment (range, 40 to 76). The protocol for the study was approved by the research ethics committee at County Hospital, Falun, Sweden. All patients signed the informed consent. The inclusion criteria and randomization procedure have previously been described in detail in the 1-year report.[16]

Surgical and Prosthetic Procedures

A total of 142 implants (Straumann Dental Implant System, Waldenburg, Switzerland) were placed according to the standard protocol. All patients received 5 or 6 Straumann implants with sandblasted, large-grit, acid-etched (SLA) surfaces. Distribution of implant lengths for the 2 groups is shown in Fig 1. Implants with Octa abutments attached at the factory (Monotype) were used in the test group. Octa transfer copings were placed before the mucoperiosteal flaps were sutured. In the test group a maxillary full-arch prosthesis was connected to the implants within 14 days. No transitional prosthesis was used. The prosthesis was fabricated in cast titanium alloy with acrylic resin crowns. In the control group the same type of restoration was attached to the implants after a healing period that accorded with the standard protocol.

Table 1 Opposing Mandibular Dentition

	Support	No. of patients at treatment planning		No. of patients at 3-yr follow-up	
		Test	Control	Test	Control
Removable prosthesis					
Complete denture	Mucosa	0	1	0	0
Partial denture	Tooth	4	2	1	0
Conus construction	Tooth	1	0	0	0
Fixed prosthesis					
Complete	Tooth	1	0	1	0
	Implant	1	0	3	3
Partial	Tooth	2	3	5	3
	Implant	0	0	1	1
Single crown	Implant	0	0	1	0
Natural		6	2	3	1
None (edentulous)		1	0	1	0
Total		16	8	16	8

Table 2 Timetable of Follow-up Investigations

	Time postloading (mo)					
	0	3	6	12	24	36
Assessment						
Bone loss	×	×	×	×	×	×
Dental history		×	×	×	×	×
General health		×	×	×	×	×
Mobility	×	×	×	×	×	×
Oral hygiene		×	×	×	×	×
Pain	×	×	×	×	×	×
Peri-implant infection	×	×	×	×	×	×
Restoration	×	×	×	×	×	×
Soft tissue		×	×	×	×	×
Photographs taken	×			×	×	×
Radiographs taken			×	×	×	×
Existing teeth	×			×	×	×
Implants	×		×	×	×	×
Results assessment						
Patient satisfaction	×	×	×	×	×	×
Esthetics	×	×	×	×	×	×

0 = at loading.
Maintenance was performed on an as-needed basis.

Implants were loaded after 9 to 18 days in the test group and after 2.5 to 5.1 months in the control group. The mean lengths of the bilateral cantilever sections were 8.3 mm (range, 2 to 14 mm) in the test group and 9.6 mm (range, 5 to 16 mm) in the control group. Data regarding the opposing dentition for both groups are shown in Table 1. All surgical treatment and prosthetic and technical work was performed by 1 person within each profession. For detailed information regarding the surgical and prosthetic procedures, see Fischer and Stenberg.[16]

Follow-up Investigations

Bone loss, dental history, general health, mobility, oral hygiene, pain, peri-implant infection, restoration, and soft tissue condition were clinically evaluated by the prosthodontist (Table 2). The Sulcus Bleeding Index (SBI) and modified Plaque Index (mPI) were registered in accordance with Mombelli and associates.[17] The success of the implants was evaluated in accordance with Albrektsson and Zarb.[18]

Radiographic Examination. The periapical radiographs were taken using a standard technique. The

film was exposed using a paralleling technique so that the cervical implant threads were clearly visible. The radiographs were evaluated independently by a specialist in oral radiology (Dr Anders Frykholm, Stockholm, Sweden) according to the method of Buser and colleagues.[19]

Implant Stability. After removal of the prosthesis, percussion and manual manipulation of each implant was performed. Implant stability quotient measure (ISQ) was recorded for each implant as described by Meredith and coworkers.[20]

Occlusion. Occlusion (ie, vertical relation, need for guidance) was recorded at each follow-up.

Patients' Satisfaction. The patients were asked orally about comfort, appearance, ability to chew, ability to taste, and general satisfaction. They were asked to grade these subjectively as excellent, good, fair, or poor.

Esthetics. Esthetic appearance was evaluated and coded subjectively by the prosthodontist as excellent, good, fair, or poor.

Maintenance

At each follow-up appointment, the prosthesis was checked concerning fracture, component failure, or clinical signs of bruxism which could affect the outcome. If any of these conditions were seen, appropriate repair of the prosthesis was carried out. The most common adverse event in both groups was tooth-crown fracture.

Statistical Analysis

The investigation was devised as an observational study of 2 randomized groups. The statistical variables (response) were observed at the time of loading during a 3-year follow-up in a repeated-measures model.

There were multiple implants per patient. The effect of multiple implants is a correlation (in general, positive) of response values.

Multidimensional normal distribution was modeled with the multivariate analysis of variance (MANOVA) for repeated measurements using the Greenhouse-Geisser test strategy.[21] SPSS software (SPSS, Chicago, IL) was used to perform the statistical calculations.

The response of major interest is the marginal bone level (mesial, distal, and mean of mesial and distal). These variables are continuous. The Kolmogorov-Smirnov test was applied. This test does not reject the assumption of a multidimensional normal distribution. Therefore, the MANOVA model for repeated measures with the parameters Group, Time, and Time × Group is applicable for statistical analysis of the bone level measurements using the individual implant as the unit. The implant sample size of 94 in the test group and 45 in the control group was sufficient to generate a stable realization of the multidimensional normal distribution separately for the mesial, distal, and mean bone level measurements.

In the case of categorical (ordinal) correlated response, general estimation equations were applied using certified commercial software. The software used was Multiprocess Multilevel Modeling (EconWare, Los Angeles, CA). The model was a cumulative logit model with correlated response. The variables analyzed using this technique were the SBI and mPI.

For the other variables the sample size was the number of patients per group. The nonparametric Mann-Whitney test was used in the analysis of this data. Results were considered significant where P was less than or equal to .05.

RESULTS

Implants

Of the 142 implants placed, 139 were loaded with full-arch prostheses, 94 in the test group and 45 in the control group. Three implants, 1 in the test group and 2 in the control group, failed prior to loading. The cumulative success rate for surviving implants was 100% at 3 years postloading. The ISQ values for the test and control groups were 56.3 (range, 44 to 72) and 54.6 (range, 45 to 66), respectively.

Radiographic Findings

Bone level was measured from the implant shoulder to the first bone apposition level detected on the radiographs. An increase in the distance between the reference point (ie, the implant shoulder) and the bone level indicated bone loss around the implant. At the 3-year examination the mean ($P \leq .005$), distal ($P \leq .005$), and mesial ($P > .05$) crestal bone levels were better in the test group. The mesial, distal, and mean bone levels for each group from baseline up to 3 years are plotted in Figs 2a, 2b, and 2c along with the 95% confidence levels for the test and control groups. Changes in mean crestal bone levels at baseline and 1, 2, and 3 years postloading in both groups are shown in Table 3.

Clinical Evaluation

No significant differences were found ($P > .05$ in all cases) between the groups with respect to oral hygiene, SBI, mPI, gingival level, probing depth, width of attached mucosa midfacial of implant, attachment level, esthetics, opposing dentition, or satisfaction (with respect to comfort, appearance, ability to chew, ability to taste, and fit, as well as general satisfaction).

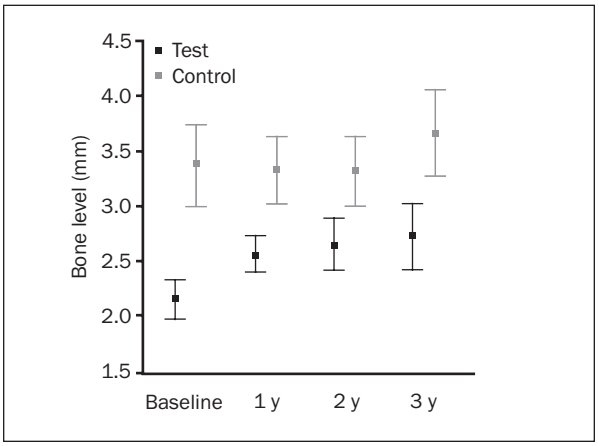

Fig 2a Mesial bone levels at baseline and at 1, 2, and 3 years postloading. The 95% confidence limits are indicated by bars.

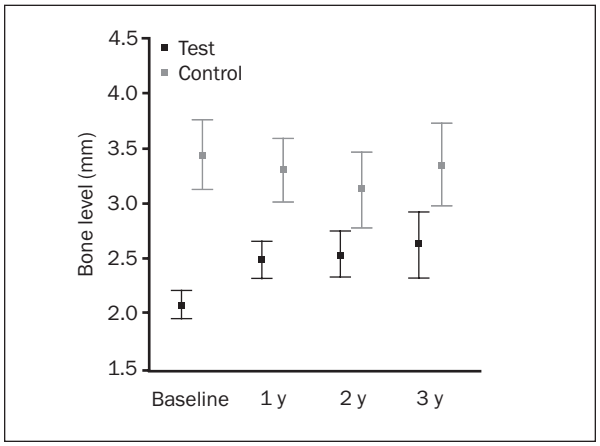

Fig 2b Distal bone levels at baseline and at 1, 2, and 3 years postloading. The 95% confidence limits are indicated by bars.

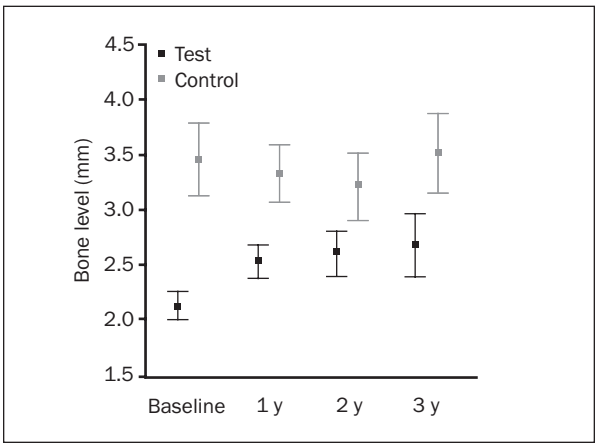

Fig 2c Mean bone levels at baseline and at 1, 2, and 3 years postloading. The 95% confidence limits are indicated by bars.

Table 3 Mean Crestal Bone Levels (in mm) at Baseline, 1, 2, and 3 Years Postloading

	Test	Control
Baseline		
Minimum	0.93	2.18
Maximum	4.95	6.76
Mean	2.13	3.46
1 year		
Minimum	1.18	1.90
Maximum	6.13	5.32
Mean	2.54	3.33
2 years		
Minimum	1.16	1.88
Maximum	6.70	5.79
Mean	2.60	3.21
3 years		
Minimum	1.16	2.13
Maximum	10.88	7.36
Mean	2.68	3.52

DISCUSSION

The need for prospective, longitudinal RCTs has been stated.[13,15] There is also an urgent need to implement more RCTs and to summarize their results in systematic reviews.[22] Quality assessment of 74 RCTs of oral implants was reported by Esposito and coworkers.[23] They concluded that the quality of RCTs in implant dentistry is poor and needs to be improved. In the 74 RCTs studied, descriptions of randomization and concealment allocation procedures were frequently missing (70%), as were reasons for withdrawals (23%). No attempt at blinding was reported in 72% of the studies. In the present parallel-group intervention, note was taken of these 3 domains.

In an article describing methods for comparing the results of different studies of oral and maxillofacial implants, Eckert and associates[24] presented a method for placing any single article within a "hierarchy of evidence," enabling an "estimate of confidence" in a particular therapy. Describing factors related to study design, they explained that studies that demonstrate efficacy are those that show that the treatment works. Such studies also produce the best possible results for a given therapy.[24] Efficacy studies often have inclusion and exclusion criteria and control for many variables, which limits the reader's ability to generalize results. In an effectiveness study the treatment is offered to a general population by an uncontrolled group of clinicians working according to broad guidelines and with a wider

group of patients. Some of these patients may have unfavorable traits or behaviors. In general, an effectiveness study rarely reaches a similar level of clinical success as an efficacy study.[24]

Judging the present study from the point of view of Eckert and associates,[24] it constitutes an efficacy study. Their suggestion that the best possible results will be obtained in this type of study was also confirmed. Weber and associates[25] described procedures to design implant studies so that data from such studies may be interpreted from a scientific and regulatory point of view to determine the safety and efficacy of a device while not overextending time, funds, and human resources in the process. Their design procedures were also taken into consideration in this study.

Outcome measures can be distinguished as either "true" or "surrogate" outcomes.[22] A true outcome can be defined as unequivocal evidence of tangible benefits for the patient. Examples are absence of irreversible pain and altered sensations, presence of implants or prostheses, implant stability testing, lack of radiographic peri-implant radiolucency, functionality, chewing ability, prosthesis stability, phonetics, patient satisfaction, preservation of marginal ridge, and esthetics. A surrogate outcome can be defined as a measure of the disease process; examples are marginal bone level changes in standardized periapical radiographs, superficial bleeding index and other inflammatory indexes, clinical attachment levels, probing depths, plaque assessments, crevicular fluid component and microbiologic analyses, time or number of visits or surgeries required for completion of the treatment, and for maintenance, patient discomfort associated with treatment and maintenance (pain swelling, bleeding, willingness to repeat the treatment).[22]

Several true and surrogate outcomes were measured in the present study. This RCT showed that early loading of titanium implants with an SLA implant surface within 2 weeks of implantation can be a viable treatment alternative in the completely edentulous maxilla. This is in accordance with the results from an RCT by Salvi and coworkers[26] and with those of a study by Nordin and associates.[27] These authors followed implants postplacement in the completely edentulous maxilla and in the edentulous posterior mandible and maxilla. Other clinical studies have also shown viable results using reduced healing times and the same type of implant surface.[28–30] Using titanium plasma-sprayed solid-screw Straumann implants, survival rates (96.6%) were obtained when loading with fixed prostheses in the edentulous maxilla following the delayed protocol.[31] A moderately roughened surface, such as that used in the present study (S_a between 1.0 and 2.0 μm), has shown stronger bone responses than smoother or rougher surfaces.[32]

Implants with oxidized surfaces have demonstrated a 10% higher success rate[33] compared with those with machined surfaces. The use of oxidized-surface implants helps to reduce the risk of stability loss in the posterior maxilla in the early healing period.[34] The implants in the present study had a surface texture somewhat similar to an oxidized surface, and this partly explains the high level of implant success. In a review article focusing on clinical knowledge of oral implant surfaces, Albrektsson and Wennerberg[35] summarized that SLA surface implants showed success rates from 97.5% to 100% in studies with follow-ups from 1 to 3 years. In this 3-year follow-up study of 24 patients the success rate was 100%.

Bone height measurements, as measured from reference points on radiographs, were performed for each implant. All prostheses were removed, and all implants were stability tested individually by percussion, rotational testing, and resonance frequency analysis (RFA). Thus the criteria for success were fulfilled.[18]

Some of the crestal bone level positions and crater-shaped bone defects at the 1- and 2-year follow-ups showed a bone gain. These observations are in accordance with those made in another study dealing with full-arch prostheses in the edentulous maxilla.[31] No explanation for this phenomenon can be found in the literature. One interpretation may be that radiography is too insensitive as a method for detecting less mineralized bone tissue zones.

In this study the ISQ values for the test and control group were 56.3 (range, 44 to 72) and 54.6 (range, 45 to 66), respectively, after 3 years. In a 1-year follow-up study by Olsson and coworkers[36] of early loading in totally edentulous maxillae, RFA showed a mean ± SD primary stability of 60.1 ± 3.6 ISQ, which increased to 62.8 ± 1.6 after 4 months on average. The higher ISQ values reported in the latter study can probably be explained by the use of a different type of implant, Brånemark System TiUnite (Nobel Biocare, Göteborg, Sweden). The configuration of the implants in that study also differed from the present investigation. In a study using ITI implants with an SLA surface the primary stability ISQ values (55.0 ± 6.8) were more similar to the values in this study.[37]

In a study by Glauser and associates[38] of 127 immediately loaded implants supporting single and partial fixed prostheses, 34% failed in the posterior maxilla and only 9% in other regions. In the current study no problems related to location were observed. This is probably a result of the fact that a

rigid full-arch prosthesis distributes high loading forces in the posterior region to all implants. A discussion of implant stability at placement and during the first year postloading with respect to early loading protocols has been presented by Fischer and Stenberg.[16]

Can the results of this study help clinicians in caring for their patients? This concept for judging a trial is termed generalizability or external validity.[22] In this study there are no compelling reasons, except for the quantity of bone tissue in the maxilla, why the results should not be applied to a particular patient. What was observed in this study was evidence of a difference when comparing treatment results using early (test group) and standard (control group) protocols. The results showed that the distal and mean crestal bone levels were better in the test group. Functional immediate or early loading can be advantageous for both patients and operators and thus a treatment of choice.

CONCLUSION

This randomized, controlled 3-year follow-up study showed that distal and mean crestal bone loss was higher in the delayed loading group. No other significant differences in treatment outcomes were found in this study of the early (within 2 weeks) and the standard (3 to 4 months) protocols for rehabilitation of the totally edentulous maxilla with a complete implant-supported fixed prosthesis.

ACKNOWLEDGMENTS

The authors are grateful to James Simpson and Madeleine Kings at Straumann. They sincerely thank dental technician Tord Rådberg, Falun, and staff members Eva Helin for radiographic examinations and Lisa Hallin for coordination of patients. This study was supported by Straumann, Basel, Switzerland.

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