The Effectiveness of Immediate, Early, and Conventional Loading of Dental Implants: A Cochrane Systematic Review of Randomized Controlled Clinical Trials

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Purpose: *To test whether there is a difference in success rates between immediately, early, and conventionally loaded implants.* ***Materials and Methods:*** *All randomized controlled clinical trials (RCTs) of root-form osseointegrated oral implants having a follow-up of 6 months to 1 year comparing the same osseointegrated root-form oral implants loaded immediately (within 1 week); early (between 1 week to 2 months); or conventionally (after 2 months) were eligible. An exhaustive search was conducted with no language restriction on January 15, 2007. Outcome measures were prosthesis failures, implant failures, and marginal bone levels measured on intraoral radiographs. Screening of eligible studies, quality assessment, and data extraction were conducted in duplicate. Authors were contacted for any missing information. Results were expressed as random effects models using weighted mean differences for continuous outcomes and risk ratios for dichotomous outcomes with 95% confidence intervals. The statistical unit of the analysis was the patient.* ***Results:*** *Twenty RCTs were identified, and 11 trials including a total of 300 patients were included. Six trials compared immediate versus conventional loading, 3 early versus conventional loading, and 2 immediate versus early loading. None of the meta-analyses revealed any statistically significant differences.* ***Conclusions:*** *It is possible to successfully load dental implants immediately or early after their placement in selected patients, although not all clinicians may achieve optimal results. A high degree of primary implant stability (high value of insertion torque) seems to be 1 of the prerequisites for a successful immediate/early loading procedure. More well-designed RCTs are needed. Priority should be given to trials comparing immediately versus early loaded implants. These trials should be reported according to the CONSORT guidelines (www.consort-statement.org).* Int J Oral Maxillofac Implants 2007;22:893–904

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This review is based on a Cochrane systematic review titled "Interventions for replacing missing teeth: Different times for loading dental implants" published in The Cochrane Library, 2007, Issue 2 (see www.thecochranelibrary.com for information). Cochrane systematic reviews are regularly updated as new evidence emerges and in response to feedback. If you wish to comment on this review, please send your comments to the Cochrane website or to Marco Esposito. The Cochrane Library should be consulted for the most recent version of the review. The results of a Cochrane Review can be interpreted differently depending on one's perspective and circumstances. Please consider the conclusions presented carefully. They are the opinions of the review authors and are not necessarily shared by the Cochrane Collaboration.

Conflict-of-interest statement: *Marco Esposito is among the authors of 2 of the included studies, and 2 of the excluded studies; however, he was not involved in the quality assessment of these trials. Marco Esposito is working as independent methodological consultant for various implant-related projects for some of the companies whose implants were used in both the included and excluded trials; however, implant brands were not under evaluation in this review.*

Missing teeth and supporting oral tissues have traditionally been replaced with dentures or partial prostheses to restore the ability of patients to eat and speak and improve appearance. However, patients are not always satisfied with the function of removable dentures, and it is not always possible to place a fixed prosthesis if the number of remaining abutment teeth is insufficient. Since the 1970s, osseointegrated dental implants have offered an alternative.[1] They are surgically inserted into the jawbones to support a dental prosthesis and are retained because of the intimacy of bone growth onto the implant surface (osseointegration). Dental implants have undoubtedly been one of the most significant scientific breakthroughs in dentistry over the past 30 years.

Primary implant stability and lack of micromovement are considered 2 of the main factors necessary for the achievement of predictably high success rates for osseointegrated oral implants.[2] A successfully osseointegrated oral implant is anchored directly to bone; however, in the presence of movement, a soft tissue interface may encapsulate the implant,[3] causing its failure. To minimize the risk of soft tissue encapsulation, it has been recommended that implants be kept load-free during the healing period (3 to 4 months in mandibles and 6 to 8 months in maxillae).[1]

In general, removable prostheses are used during the healing period; however, many patients find these provisional prostheses rather uncomfortable. It would therefore be beneficial if the healing period could be shortened without jeopardizing implant success. In 1990 the first longitudinal clinical trial supporting immediate or early loading in the mandibles of selected patients was published.[4] Immediate and early loading of implants is now common, particularly in mandibles of good bone quality.[5] Some authors also advocate the use of specific implant surface preparations to reduce the healing time.[6] Immediately and early loaded implants may be at a greater risk of failure than conventionally loaded ones.[7] To decrease the risk of early failure with immediately loaded implants, various "clinical tricks" have been suggested, such as underpreparation of the implant site to achieve high primary stability,[8] the use of nonoccluding temporary prostheses during the first 2 months of healing,[9] and progressive loading of the prostheses. While the success of immediately loaded implants in mandible has been documented, for instance, in earlier versions of the present Cochrane Review,[10,11] less evidence is available regarding the effectiveness of immediately loaded maxillary implants.

It would be useful to know whether there are differences in success rates between immediately or early loaded implants compared with conventionally loaded implants in different clinical indications (full and partial edentulism, mandibles and maxillae) and whether certain surface modifications are able to promote faster bone healing (for the role of the surface characteristics the reader is referred to another Cochrane systematic review[12]). It is likely that the effect of loading at different times would become apparent during the first 6 months to 1 year of loading, and therefore it was decided to make all comparisons at 6 months to 1 year after loading, preferably at 1 year. Other systematic reviews have been published on the same topic[13,14]; however, these versions did not focus on the highest level of evidence (randomized controlled clinical trials [RCTs]); therefore, the results are subject to a higher potential level of bias and should be interpreted with great caution.

The aim of this review was to test the null hypothesis of no difference in success rates between the same osseointegrated implants loaded immediately, early, or conventionally, against the alternative hypothesis of a difference.

Readers not familiar with the terminology and the methodology of the systematic review format are referred to the Glossary of Terms in the Cochrane Collaboration and to the Cochrane Handbook for Systematic Reviews of Interventions.[15]

MATERIALS AND METHODS

Inclusion Criteria and Outcome Measures

The entire protocol for this review was conceived a priori, internally and externally refereed, and published electronically on the Cochrane database, where it was open to public criticism a priori. To minimize bias,[15,16] only RCTs of osseointegrated dental implants were considered. To be included, RCTs had to compare the same osseointegrated implants loaded at different times for a period of at least 6 months to 1 year of loading. For the purpose of this review immediate loading was defined as an implant put in function within 1 week after its placement; early loading as those implants put in function between 1 week and 2 months, and conventionally loading as those implants loaded after 2 months. The following comparisons were planned: *(1)* immediately versus conventionally loaded implants; *(2)* early versus conventionally loaded implants; *(3)* immediately versus early loaded implants. Both occlusally and nonocclusally immediately loaded implants were considered immediately loaded implants in this review.

RCTs presenting any of the following outcome measures were evaluated:

1. Prosthesis failure (either planned prostheses that could not be placed because of implant failure or loss of the prosthesis secondary to implant failure).
2. Implant mobility and removal of stable implants dictated by progressive marginal bone loss or infection. Implant mobility of individual implants could be assessed manually or with instruments such as Periotest (Siemens, Munich, Germany) or resonance frequency (Osstell; Integration Diagnostics, Göteborg, Sweden).
3. Radiographic marginal bone level changes on intraoral radiographs made with a parallel technique.

Search Strategy for the Identification of Studies

For the identification of studies included or considered for this review, a detailed search strategy was developed for each database to be searched. These were based on a search strategy developed for MEDLINE (OVID). The search strategy, which was revised appropriately for each database, used a combination of controlled vocabulary and free text and has been described elsewhere.[17]

The following databases were searched:

- The Cochrane Oral Health Group's Trials Register (to January 15, 2007)
- The Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2007, Issue 1)
- MEDLINE (1966 to January 15, 2007)
- EMBASE (1980 to January 15, 2007)

The most recent electronic search was undertaken on January 15, 2007. There were no language restrictions. To minimize publication bias[15] the authors of all identified RCTs and more than 55 oral implant manufacturers were contacted. Personal contacts were used, and an Internet discussion group (implantology@yahoogroups.com) was contacted in an attempt to identify unpublished or ongoing RCTs.

Details of the journals being handsearched by the Cochrane Oral Health Group's ongoing program are given at http://www.ohg.cochrane.org. The following journals were handsearched for this review: *British Journal of Oral and Maxillofacial Surgery, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Implant Dentistry, International Journal of Oral & Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of the American Dental Association, Journal of Biomedical Materials Research, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Oral Implantology, Journal of Oral and Maxillofacial Surgery, Journal of Periodontology,* and *Journal of Prosthetic Dentistry*. Where these have not already been searched as part of the Cochrane Journal Handsearching Programme, the journals were handsearched by 1 review author.

The bibliographies of all identified RCTs and relevant review articles were checked for studies outside the handsearched journals.

Review Methods

The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by 2 review authors. For studies appearing to meet the inclusion criteria, or for which insufficient data were available in the title and abstract to make a clear decision, the full report was obtained. The full reports obtained from all methods of searching were assessed independently by 2 review authors to establish whether the studies met the inclusion criteria. Disagreements were resolved by discussion. Where resolution was not possible, a third review author was consulted. All studies meeting the inclusion criteria then underwent validity assessment and data extraction. Reasons for exclusion of studies rejected at this or subsequent stages were recorded.

Quality Assessment

The quality assessment of the included trials was undertaken independently and in duplicate by 2 review authors as part of the data extraction process. Three main quality criteria were examined:

1. Allocation concealment: Allocation concealment was recorded as *adequate (A)*, *unclear (B)*, or *inadequate (C)*, as described elsewhere.[15] Allocation concealment was considered adequate if it was centralized (eg, allocation by a central office unaware of subject characteristics); if randomization was pharmacy-controlled; if prenumbered or coded identical containers were administered serially to participants; if allocation was kept in a locked unreadable computer file that could be accessed only after the characteristics of an enrolled patient had been entered; or if sequentially numbered, sealed, opaque envelopes were used. Other approaches similar to the aforementioned ones were also considered acceptable as long as the person who generated the allocation scheme did not administer it. Some innovative schemes may provide adequate concealment without the use of the aforementioned techniques. Any procedure that was entirely transparent before allocation, such as an open list of ran-

dom numbers, was considered inadequate. Ideally the surgeon should have been made aware of group allocation just prior to treatment delivery. Articles or authors that stated that allocation concealment procedures were implemented but did not provide details on how this was accomplished were coded as "unclear."
2. Blind outcomes assessment: A score of *A (Yes)*, *B (No)*, or *C (Unclear)* was recorded with respect to this criterion.
3. Completeness of follow-up: A score of *A* or *B* was recorded. A score of *A* was recorded if there was a clear explanation for withdrawals or dropouts in each treatment group or if there were no dropouts. If clear explanations for dropouts were given, the risk of bias of the assessment of reasons for dropping out was evaluated. A score of *B* was recorded if clear explanations for any dropouts or withdrawals were not provided.

After taking into account the additional information provided by the authors of the trials, studies were categorized as either *(a)* low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met or *(b)* high risk of bias (plausible bias that seriously weakens confidence in the results) if 1 or more criteria were not met.[15]

Further quality assessment was carried out to assess sample-size calculations, definition of exclusion/inclusion criteria, and comparability of control and test groups at entry. The quality assessment criteria were pilot tested using several articles.

Data Extraction

Data were extracted by 2 review authors independently using specially designed data extraction forms. The data extraction forms were piloted on several papers and modified as required before use. Any disagreement was discussed, and a third review author was consulted where necessary. All authors were contacted for clarification or missing information. Data were excluded until further clarification was available or if agreement could not be reached.

For each trial the following data were recorded: year of publication; country of origin; source of study funding; details regarding the participants, including demographic characteristics and criteria for inclusion; details regarding the type of intervention; details of the outcomes reported, including method of assessment; and time intervals.

Data Synthesis

For dichotomous outcomes, the estimates of effect of an intervention were expressed as risk ratios (RR) together with 95% confidence intervals (CI). For continuous outcomes, weighted mean differences (WMD) and standard deviation (SD) were used to summarize the data for each group. The statistical unit was the patient rather than the implant.

Meta-analyses were done only if there were studies of similar comparisons reporting the same outcome measures. Risk ratios for dichotomous data and mean differences for continuous data were combined using a random-effects model. Data from split-mouth studies were combined with data from parallel group trials with the method outlined by Elbourne et al,[18] using the generic inverse variance method in RevMan (Cochrane Collaboration, Manchester, UK). The techniques described by Follmann et al[19] were to be used to estimate the standard error of the difference for split-mouth studies where the appropriate data were not presented and could not be obtained.

The significance of any discrepancies in the estimates of the treatment effects from the different trials was to be assessed by means of Cochran's test for heterogeneity and the I^2 statistic, which describes the percentage total variation across studies due to heterogeneity rather than chance. Clinical heterogeneity was to be assessed by examining the types of participants and interventions for all outcomes in each study. It was planned to undertake sensitivity analyses to examine the effect of the study quality assessment on the overall estimates of effect. In addition, the effect of including unpublished literature on the review's findings was also to be examined, but there were insufficient trials to undertake this analysis.

RESULTS

Description of Studies

Of the 20 potentially eligible trials,[6–9,20–34] 9 trials were excluded, including an unpublished trial by Göthberg et al (2007). One trial[20] was excluded because insufficient data were presented; 4 trials,[6,9,33] including the unpublished trial, were excluded because of additional confounding factors; 2 trials[27,29] were excluded because they made comparisons outside the scope of the review; and 2 trials[7,31] were excluded because they were not RCTs. Of the 11 included trials, 5 were conducted in Italy (Milan, Pavia, Como, Rimini, and Monza),[8,21,24,32,34] 3 in New Zealand (Otago),[22,23,28] 1 in Sweden (Falun),[25] 1 in Germany (Frankfurt),[26] and 1 in the United States (Ann Arbor).[30] Ten trials had a parallel-group study design, and 1 had

a split-mouth study design.[26] All trials were conducted at university dental clinics, with the exception of 3 studies[8,32,34] which were conducted in private practices and 1 conducted in a specialist public clinic.[25] Eight trials received support from industry.[22,23,25,26,28,30,32,34] All studies included only adults.

Characteristics of Interventions

Immediate loading was compared with conventional loading in 6 trials.[8,21,24,26,28,30] Early loading was compared with conventional loading in 3 trials.[22,23,25] Immediate loading was compared with early loading in 2 trials.[32,34]

The main inclusion and exclusion criteria used by the authors of the included RCTs are described in Tables 1 and 2. All trials, with 2 exceptions,[32,34] used quite strict inclusion criteria and included mainly ideal patients.

Characteristics of Outcome Measures

Data on prosthesis and implant failures were given in all trials. Radiographic bone level changes were also given in all trials, with 1 exception.[30] However, in 6 trials peri-implant bone level measurements were not included in the present analyses because they were performed on panoramic radiographs,[21,24,26] because data were unusable as presented,[25] or because 1-year data from ongoing trials were not yet available.[32,34]

Methodological Quality of Included Studies

The final quality scoring after the incorporation of additional information kindly provided by the authors of the trials is summarized in Table 3. Nine studies were judged to be at high risk of bias and 2 studies[8,23] at low risk of bias.

Sample Size

A priori sample size calculation was performed in 2 trials.[32,34] Both were based on the outcome of another RCT of similar design,[7] and it was calculated that 26 patients per group were needed to complete the trial. Unfortunately, because of an independent decision of the clinicians in violation of the research protocol, only 25 patients were included in the immediately loaded group in 1 trial.[32] The other trial is still ongoing,[34] and only the preliminary results of the first 20 patients are available, but it is expected that the planned sample size will be achieved.

Baseline Comparability Between Treatment Groups

In general, the various groups were comparable at entry, with the exception of 1 trial[22] where the early loaded implants seemed to be shorter than those in the conventionally loaded groups, and another trial[32] in which more early loaded implants were placed in maxillae. The clinical significance, if any, of these findings is difficult to interpret.

Table 1 List of the Main Inclusion Criteria Used in the Included RCTs

• Completely edentulous mandible[21–24]
• Completely edentulous maxilla able to harbor 5 to 6 implants[25]
• Partially edentulous patients (both mandibles and maxillae)[8,32,34]
• Mandibles bilaterally edentulous distal to canines or premolars[26]
• Missing one single tooth in the anterior (premolar to premolar) maxilla, with adjacent teeth present, allowing the placement of at least 10 mm long with a 2.5 mm diameter[28]
• Missing a single tooth in the anterior (premolar to premolar) maxilla, allowing the placement of at least 10 mm long with a 3.7 mm diameter with a flapless procedure[30]
• At least 13 mm of residual anterior mandibular bone[21–23]
• At least 10 mm of residual anterior mandibular bone[24]
• At least 11 mm of residual posterior mandibular bone in height and 6 mm in width[26]
• Elderly patients (55 to 80 years)[22,23]
• Sufficient bone to allow placement of at least 13-mm-long implants and with a diameter of 3.7 mm[8]
• Sufficient bone to allow placement of at least 9.5-mm-long implants, and the bone thickness at implant sites had to be at least 5.5 mm[34]
• Minimal primary stability of 45 Ncm to be immediately loaded[8]
• Minimal primary implant stability of 30 Ncm for single implants and 20 Ncm for splinted implants to be immediately loaded[32]
• Minimal primary implant stability of 40 Ncm to be immediately loaded[34]

Table 2 List of the Main Exclusion Criteria Used in the Included RCTs

• Any evidence of current or previous smoking[22,23]
• Smoking more than 10 cigarettes per day[8,21,25]
• Smoking more than 20 cigarettes per day[24,28]
• Any systematic disease likely to compromise implant surgery[8,21–26,32,34]
• Previously grafted bone[22,23,25,28]
• Previously irradiated jaws[8,21–24,26,32] or jaws irradiated within the last year[34]
• Bone quality type 4 (very soft bone)[35] detected at the time of surgery[8,21–24] or on radiographs[28]
• History of bruxism[22,23] or severe clenching or bruxism[8,21,24,28,32,34]
• Severe maxillomandibular skeletal discrepancy[8,21,24]
• Failure to achieve primary implant stability[28]
• Previous history of failed implants[28]
• Less than 4 mm of keratinized mucosa[34]
• None specified[30]

Table 3 Results of Quality Assessment After Correspondence with the Authors

Study ID	Year	Allocation	Blinding of assessor	Clear explanation of withdrawals	Risk of bias
Chiapasco[21]	2001	No	Yes	Yes	High
Tawse-Smith[22]	2002	Unclear	Yes	Yes	High
Payne[23]	2002	Yes	Yes	Yes	Low
Romeo[24]	2002	No	Yes	Yes	High
Cannizzaro[8]	2003	Yes	Yes	Yes	Low
Fisher[25]	2004	Yes	No	Yes	High
Romanos[26]	2006	Unclear	No	Yes	High
Hall[28]	2006	Unclear	Yes	Yes	High
Oh[30]	2006	Unclear	Yes	Yes	High
Testori[32]	2007	Yes	Partly	Yes	High
Merli[34]	2007	Yes	Partly	Yes	High

Comparisons and Meta-analyses

In total 790 implants were originally placed in 300 patients. Of the placed implants, 253 (64 in maxillae) were immediately loaded, 230 (132 in maxillae) were early loaded, and 307 (90 in maxillae) were conventionally loaded. During the follow-up considered in this review (1 year of function for all trials, with the exception of 2 trials[30,34] for which the 6-month data were used), 20 implants failed. Six of the failed implants were immediately loaded, 8 were early loaded, and 6 were conventionally loaded. Of the 328 placed restorations, 12 (or 10, depending on the success criteria adopted) failed: 5 in the immediately loaded group, 5 (or 3, depending on the success criteria adopted) in the early loaded group, and 2 in the conventionally loaded group. The majority of prosthesis failures occurred in 2 trials: 3 (25%) immediately loaded prostheses failed in 1 trial[35] and 6 prostheses failed in another study.[22] Five of the failures (42%)—or 3 (25%) depending on the success criteria adopted—were loaded early.[22]

The meta-analysis for prosthesis failures, implant failures, and marginal bone level changes at 1 year (with the exception of 1 trial[30] for which 6-month data were used) are presented in Tables 4 to 11.

Immediate Versus Conventional Loading After 1 year of Function. Six trials were included.[8,21,24,26,28,30] Chiapasco et al[21] (parallel group design) compared 4 immediately loaded (2 to 3 days) Brånemark implants (Nobel Biocare, Göteborg, Sweden) with 4 conventionally loaded implants (4 to 8 months) supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Ten patients were originally included in each group. There were no withdrawals at 1 year. One implant failed in each group. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

Romeo et al[24] (parallel group design) compared 4 immediately loaded (2 days) Straumann sandblasted, large-grit, acid-etched (SLA) implants (Basel, Switzerland) with 4 conventionally loaded implants (3 to 4 months) supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Ten patients were originally included in each group. There were no withdrawals at 1 year. One implant failed because of peri-implantitis in the conventionally loaded group. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

Cannizzaro and Leone[8] (parallel group design) compared immediately loaded (same day) Zimmer Spline twist implants (Zimmer, Carlsbad, CA) with conventionally loaded implants (3.5 and 4.5 months in mandibles and maxillae, respectively) in partially edentulous patients for 2 years. Fourteen patients were originally included in each group. There were no withdrawals at 1 year. One single implant and the related crown failed at abutment connection in the conventionally loaded group. There were no statistically significant differences for prosthesis failures, implant failures, and marginal bone level changes between the different loading strategies.

Hall et al[28] (parallel group design) compared single immediately nonocclusally loaded (same day) Southern tapered implants with conventionally loaded implants (6 months) in the anterior maxilla (premolar to premolar) for 1 year. Fourteen patients were originally included in each group. One patient (with 1 implant in function) dropped out of the immediately loaded group because of emigration versus 2 patients from the conventionally loaded group at 1 year. One single implant and its related crown failed at abutment connection in the immediately loaded group. There were no statistically significant differences for prosthesis failures, implant fail-

Table 4 Immediate Versus Conventional Loading: Patients with Prosthesis Failures

Study or subcategory	Year	Log (relative risk)	SE	Relative risk (fixed) 95% CI	Weight (%)	Relative risk (fixed) 95% CI
Chiapasco	2001					Not estimable
Romeo	2002					Not estimable
Cannizzaro	2003	−1.1000	1.6000		32.11	0.33 (0.01, 7.66)
Hall	2006	0.9950	1.6450		30.37	2.70 (0.11, 67.98)
Oh	2006	1.9550	1.4800		37.52	7.06 (0.39, 128.48)
Romanos	2006					Not estimable
Total (95% CI)						
Test for heterogeneity: χ^2 = 2.02, df = 2 (*P* = .36), F = 0.8%						
Test for overall effect: Z = 0.75 (*P* = .45)				.01 0.1 1 10 100	100.00	1.98 (0.33, 11.70)

Favors immediate Favors conventional

Table 5 Immediate Versus Conventional Loading: Patients with Implant Failures

Study or subcategory	Year	Log (relative risk)	SE	Relative risk (fixed) 95% CI	Weight (%)	Relative risk (fixed) 95% CI
Chiapasco	2001	0.0000	1.3420		25.68	1.00 (0.07, 13.88)
Romeo	2002	−0.1086	1.6000		18.06	0.90 (0.04, 20.64)
Cannizzaro	2003	−1.1000	1.6000		18.06	0.33 (0.01, 7.66)
Hall	2006	0.9950	1.6450		17.09	2.70 (0.11, 67.98)
Oh	2006	1.9550	1.4800		21.11	7.06 (0.39, 128.48)
Romanos	2006					Not estimable
Total (95% CI)						
Test for heterogeneity: χ:^{2} = 2.30, df = 4 (*P* = .68), F = 0%						
Test for overall effect: Z = 0.54 (*P* = .59)				.01 0.1 1 10 100	100.00	1.44 (0.38, 5.46)

Favors immediate Favors conventional

ures, and marginal bone level changes between the different loading strategies.

Oh et al[30] (parallel group design) compared single immediately loaded (same day) Zimmer implants with conventionally loaded implants (4 months) in the anterior maxilla (premolar to premolar), placed with a flapless technique, for 6 months. Twelve patients were originally included in each group. There were no withdrawals at 1 year. Three single implants and the related crowns failed in the immediately loaded group. There were no statistically significant differences for prosthesis failures and implant failures between the different loading strategies.

Romanos and Nentwig[26] (split-mouth design) compared 3 immediately loaded (same day) Ankylos implants (Friadent, Mannheim, Germany) with 3 contralateral conventionally loaded (3 months) implants in mandibles partially edentulous distal to the canines or premolars for 2 years. Twelve patients were originally included. There were no withdrawals or failures at 1 year. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

For prosthesis failures, the meta-analysis found no significant difference, with a RR random effects of 1.98 (95% CI, 0.33 to 11.70), and no evident heterogeneity, although the meta-analysis was based only on 3 trials[8,28,30] (Table 4).

For implant failures, the meta-analysis (6 trials included) found no significant difference, with a RR random effects of 1.44 (95% CI, 0.38 to 122.48), and no evident heterogeneity (Table 5).

For marginal bone level changes, the meta-analysis found no significant difference, with WMD random effects of −0.02 (95% CI, −0.11 to 0.07). There was no evident heterogeneity, although only 2 trials[8,28] were included (Table 6).

Early Versus Conventional Loading After 1 Year of Function. Three trials were included.[22,23,25] Payne et al[23] (parallel group design) compared 2 early loaded (6 weeks) Straumann SLA implants with 2 conventionally loaded (12 weeks) implants supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Twelve patients were originally included in each group. Two withdrawals from the conventionally loaded group occurred at 1 year. No implant failed. There were no statistically significant differences for prosthesis failures, implant failures, and marginal bone levels between the different loading strategies.

Table 6 Immediate Versus Conventional Loading: Marginal Bone Level Changes

Study or subcategory	Year	Immediate loading N	Immediate loading Mean	Immediate loading SD	Conventional loading N	Conventional loading Mean	Conventional loading SD	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Cannizzaro	2003	14	−0.14	0.15	13	−0.12	0.08		99.35	−0.02 (−0.11, 0.07)
Hall	2006	12	−0.64	1.17	12	−0.78	1.58		0.65	0.14 (−0.97, 1.25)
Total (95% CI)		26			25				100.00	−0.02 (−0.11, 0.07)
Test for heterogeneity: χ^2 = 0.08, df = 1 (*P* = .78), F = 0%										
Test for overall effect: Z = 0.42 (*P* = .68)										

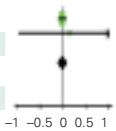
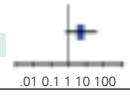


Table 7 Early Versus Conventional Loading: Patients with Prosthesis Failures

Study or subcategory	Year	Early loading (n/N)	Conventional loading (n/N)	RR (random) 95% CI	Weight %	RR (random) 95% CI
Payne	2002	0/12	0/10			Not estimable
Tawse-Smith	2002	6/24	1/24		100.00	6.00 (0.63, 39.67)
Fischer	2004	0/16	0/8			Not estimable



Tawse-Smith et al[22] (parallel group design) compared 2 early loaded (6 weeks) Southern or Steri-Oss implants with 2 conventionally loaded (12 weeks) implants supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Twelve patients were originally included in each of the 4 groups (Southern early loaded, Steri-Oss early loaded, Southern conventionally loaded, Steri-Oss conventionally loaded). No withdrawals were observed at 1 year. Seven Steri-Oss implants failed in 5 patients of the early loaded group; 1 Steri-Oss implant failed in the conventionally loaded group. No implants failed in the Southern groups. Most of the failed implants were placed by a surgeon with limited experience who only placed some Steri-Oss implants. There were no statistically significant differences for prosthesis failures, implant failures, and marginal bone levels between the different loading strategies.

Fischer and Stenberg[25] (parallel group design) compared 5 to 6 early loaded (9 to 18 days) Straumann SLA implants with 5 to 6 conventionally loaded (2.5 to 5.1 months) EstheticPlus implants in fully edentulous maxillae for 5 years. Sixteen patients were originally included in the early group and 8 in the conventionally loaded group. No withdrawals or prosthesis failures were reported at 1 year. One implant failed in the early loaded group versus 2 implants in 2 patients in the conventionally loaded group. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

Prosthesis failure was observed in only 1 trial.[22] No significant difference between groups was observed in this trial, with random effects of 5 (95% CI, 0.63 to 39.67; Table 7).

For implant failures, the meta-analysis of 2 trials[22,25] found no significant difference, with RR random effects of 1.15 (95% CI, 0.06 to 22.33). There was no evident heterogeneity; however, only 2 trials were included (Table 8).

For marginal bone level changes, the meta-analysis of 2 trials[22,23] found no significant difference, with WMD random effects of −0.04 (95% CI, −0.15 to 0.07). There was no evident heterogeneity, although only 2 trials were included (Table 9).

Immediate Versus Early Loading after 1 Year of Function. Two trials were included.[32,34] Merli et al[34] (parallel group design) compared immediately nonocclusally loaded (within 72 hours) Thommen implants (Waldenburg, Switzerland) with early nonocclusally loaded implants (6 weeks) placed with a flapless technique in partially edentulous patients for 1 year. This was a preliminary report providing the results of the first 20 patients (of 60 to be treated). Ten patients were included in the immediately loaded group and 10 in the early loaded group. There were no withdrawals or prosthesis or implant failures at 1 year. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

Testori et al[32] (parallel group design) compared immediately (within 48 hours) nonocclusally loaded Biomet/3i FNT implants (Palm Beach Gardens, FL)

Table 8 Early Versus Conventional Loading: Patients with Implant Failures

Study or subcategory	Year	Early loading (n/N)	Conventional loading (n/N)	RR (random) 95% CI	Weight %	RR (random) 95% CI
Payne	2002	0/12	0/10			Not estimable
Tawse-Smith	2002	5/24	1/24		51.07	5.00 (0.63, 39.67)
Fischer	2004	1/16	2/8		48.93	0.25 (0.03, 2.36)
Total (95% CI)		52	42		100.00	1.15 (0.06, 22.33)
Total no. of events: 6 (early loading), 3 (conventional loading)						
Test for heterogeneity: $\chi^2 = 3.76$, df = 1 ($P = .05$), F = 73.4%						
Test for overall effect: Z = 0.10 ($P = .92$)						

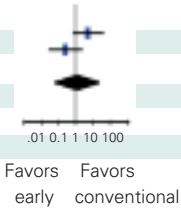


Table 9 Early Versus Conventional Loading (Marginal Bone Level Changes)

Study or subcategory	Year	Early loading N	Early loading Mean	Early loading SD	Conventional loading N	Conventional loading Mean	Conventional loading SD	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Payne	2002	12	0.27	0.18	10	0.35	0.22		39.91	−0.08 (−0.25, 0.09)
Tawse-Smith	2002	24	0.12	0.19	24	0.13	0.29		60.09	−0.01 (−0.15, 0.13)
Total (95% CI)		36			34				100.00	−0.04 (−0.15, 0.07)
Test for heterogeneity: $\chi^2 = 0.39$, df = 1 ($P = .53$), F = 0%										
Test for overall effect: Z = 0.69 ($P = .49$)										

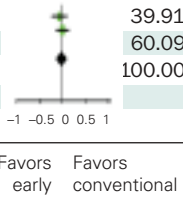


Table 10 Immediate Versus Early Loading: Patients with Prosthesis Failures

Study or subcategory	Year	Immediate loading (n/N)	Early loading (n/N)	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
Merli	2007	0/10	0/10			Not estimable
Testori	2007	1/25	0/27		100.0	3.23 (0.14, 75.83)

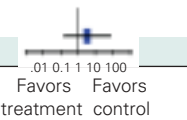
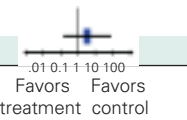


Table 11 Immediate Versus Early Loading: Patients with Implant Failures

Study or subcategory	Year	Immediate loading (n/N)	Control (n/N)	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
Merli	2007	0/10	0/10			Not estimable
Testori	2007	1/25	0/27		100.0	3.23 (0.14, 75.83)



with early loaded implants (2 months) in partially edentulous patients for 1 year. Twenty-five patients were originally included in the immediately loaded group and 27 in the early loaded group. There were no withdrawals at 1 year. One single implant and its related provisional crown failed after 2 months in the immediately loaded group. There were no statistically significant differences for prosthesis or implant failures between the different loading strategies.

Prosthesis failures were observed in only 1 trial.[32] There was no significant difference between the groups in this trial, with RR random effects of 3.23 (95% CI, 0.14 to 75.83; Table 10). Implant failures were also observed in only 1 trial.[32] Again, no significant difference was found between groups, with RR random effects of 3.23 (95% CI, 0.14 to 75.83; Table 11).

No subgroup analyses were conducted, as the maximum number of trials within any meta-analysis was 6, and the results of the largest 2 meta-analyses were nonsignificant, with no evidence of heterogeneity.

DISCUSSION

The question of whether implants can be loaded immediately or early after their insertion has relevant clinical implications, since such treatment can

drastically reduce the treatment period for the benefit of the patients. The main outcome for these types of studies is the success of the prosthesis, since implant loss may not always jeopardize prosthesis success.

No statistically significant differences for prosthesis success, implant success, or marginal bone levels were observed when different loading regimens were applied; however, the number of trials and patients included may be still insufficient to draw definitive conclusions. While in general the overall success was high, a couple of trials[22,30] reported higher failure rates. In 1 trial,[22] 7 of 24 Steri-Oss implants failed; there were failures in 5 of 12 patients. Since mandibular overdentures supported by 2 implants were used, the loss of a single implant could determine the failure of the entire treatment (prosthesis). However, the author of the study, acting as 1 of the referees of this review, argued that it is possible to have successful overdentures supported by only 1 implant, as observed in 2 of their patients. While this may be true, such circumstances may not be common, and many clinicians and patients may not be fully satisfied with the result. If an overdenture supported by a single implant is considered a failure, then the loss of 5 of 12 overdentures may have some important clinical implications. Conversely, it is likely that other confounding factors might have played a determinant role in the final outcome, such as the surgical skill of 1 operator who was responsible for almost all the failures or the presence of shorter implants in the early loaded group. In another study[30] of 6 months' duration, 3 of 12 single implants placed with a flapless procedure and immediately loaded failed, yielding a 25% failure rate, versus a failure rate of 0% in the conventionally loaded group.

It is worthwhile to briefly review the excluded studies, which contained relevant clinical information. In general, success rates were very high,[6,9,27,29,36] including the success rates of the unpublished studies by Göthberg and Cannizzaro, confirming the main conclusion of this review (ie, that immediate and early loading of dental implants are viable and successful treatment options). However, there was a single but relevant exception which deserves some additional comment.[7] In this trial of split-mouth design (not an RCT as described in the original article, but a controlled clinical trial using an alternation method to allocate sites to different implant interventions), single nonocclusally immediately loaded implants failed significantly more often than conventionally loaded dental implants. Ten of 23 immediately loaded implants failed versus only 1 of 23 of the conventionally loaded group. The authors were able to demonstrate a strong correlation between implant failures and the initial insertion torque of the implants. Nine of the 10 implants inserted with a torque of 20 Ncm failed versus only 1 of 10 placed with a torque of 32 Ncm in the immediately loaded group. The authors confirmed that they did not use a technique of "subpreparation" of the implant sites to increase insertion torque (primary stability) and that their patients did not follow any postoperative diet restriction regarding chewing on hard food. Since techniques to increase torque values at implant placement were used in a majority of the successful RCTs (although this was not always sufficiently described in the Materials and Methods sections), it can be concluded that a high degree of primary stability at implant insertion is a key prerequisite for a successful immediate or early loading procedure.

Another aspect which could be debatable is whether immediate "nonoccluding" loading (wherein a provisional restoration is placed on the implants but not placed in contact with the opposing dentition, also called "immediate provisionalization") should be considered an immediate loading procedure. The present researchers decided that from the patient's point of view this difference may not be very significant, since patients prefer to have their new teeth as soon as possible,[37] and since nonoccluding restorations are actually functionally used during chewing. The only RCT[29] that examined nonoccluding loading did not find any statistically significant difference or clinical trend toward difference between immediate occlusal loading and nonocclusal loading. The protocol of the present study included plans to make a subgroup analysis to investigate whether there could be different trends when comparing immediate occlusal versus non occlusal loading, but none of the planned subgroup analyses has been implemented yet because the number of included studies is still insufficient. No statistically significant differences were observed with which to elaborate reliable working hypotheses.

Generalization of the results of the included trials to ordinary clinical practice should be made with extreme caution. In the majority of the included trials, the inclusion criteria were strict, and only patients known to be ideal candidates for implant treatment were recruited. In general, operators were highly experienced, and it is important to observe that in a trial with less experienced operators prosthetic failures were higher—25% to 42% (depending on the success criteria adopted) in 1 study[22] and 44% in another.[7] However, it has been shown that in selected patients immediate loading of dental implants is possible with good success rates.

CONCLUSION

It is possible to successfully load dental implants immediately or early after their placement in selected patients, although not all clinicians may be able to achieve optimal results with immediate loading. A high degree of primary implant stability (high value of insertion torque) seems to be one of the prerequisites for a successful procedure.

More well-designed RCTs are needed to understand the predictability of the protocols for immediate and early loading. Such trials should be simply designed and reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (http://www.consort-statement.org).[38] It is suggested that priority be given to trials assessing the effectiveness of immediately versus early loaded implants to improve patient satisfaction and decrease treatment time.

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