

Immediate Loading with Single Implant Crowns: A Systematic Review and Meta-analysis

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Purpose: A systematic review and meta-analysis of studies that specifically compared immediate to conventional loading of single implant crowns was conducted and the overall treatment effect was estimated. **Materials and Methods:** MEDLINE, the Cochrane Controlled Trials Register, and bibliographies of relevant primary and review articles were searched. Randomized and nonrandomized controlled studies that compared immediate with conventional loading of single implant crowns were selected according to strict criteria. From the 105 articles screened, five studies with 248 implants were analyzed. The meta-analysis was prepared in accordance with the Quality of Reporting of Meta-analyses (QUOROM) statement. Descriptive and outcome data were extracted using specially designed data extraction forms. The data were entered into MIX software for meta-analysis using a fixed effects model, relative risk, and 95% confidence interval (CI). **Results:** Immediate loading of single implant crowns was associated with a significantly higher risk of implant failure (relative risk: 5.07, 95% CI: 2.00 to 12.84, $P < .001$). Pooling of randomized controlled trials showed similar results, although the difference was not statistically significant. Immediate nonocclusal loading was also associated with worse outcomes when compared to conventional loading (relative risk: 4.76, 95% CI: 1.74 to 13.02, $P = .002$). **Conclusions:** This systematic review and meta-analysis shows that better outcomes are currently achieved using conventional loading of single implants with crowns, as opposed to immediately loaded ones, which are at a higher risk of failure. Further adequately powered clinical trials are needed. Caution with immediate loading of implants with crowns as a standard of care for single tooth replacement is recommended. *Int J Prosthodont* 2009;22:378–387.

In the late 1960s, Brånemark and coworkers described a protocol leading to the successful osseointegration of oral implants.^{1,2} They recommended a healing period of 8 to 12 months after tooth extraction

before placing implants, followed by submerged and unloaded healing periods of 3 to 6 months. This treatment sequence is known historically as the two-stage submerged procedure^{2,3} and was designed to eliminate implant micromovement after implant surgery, which was thought to likely result in either failure to osseointegrate or fibrous tissue encapsulation of the implant.⁴ In addition, coverage of an implant with the two-stage procedure was originally proposed to prevent infection and epithelial downgrowth.²

The high success and survival rates reported for various implant systems using this protocol for single tooth replacement meant that the two-stage submerged procedure was initially considered the standard of care for oral implants.^{5–11} However, in meeting many patients' desires for a shorter treatment time, clinicians have attempted to load implants immediately or soon after placement. The application of immediate loading protocols to single implant crowns was initially seen as more challenging than multiple implants in

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partially and totally edentulous arches since they lack mutual or cross-arch stabilization.¹²⁻¹⁴ However, improvements in surgical techniques and implant designs have enhanced primary stability of implants, increasing the acceptance of modifying the loading protocols for single implant crowns.

Immediate loading may be defined as either non-functional, consisting of immediate provisionalization with nonoccluding provisional crowns, or functional, where the provisional or definitive crown is placed in occlusion. The reduced loading that accompanies immediate provisionalization might be thought to produce a more predictable outcome compared with immediate functional loading. However, a study comparing these two loading protocols could find no statistically significant difference in treatment outcomes.¹⁵

Immediately loaded single implants in the anterior region have the advantage of shortened treatment time and optimization of esthetics and function, and several studies have shown high survival rates.¹⁶⁻²³ As a result, today, the immediate implant loading protocol in a single-tooth restoration is a popular and accepted treatment modality among clinicians. However, many studies only report short-term outcomes for this approach and there is a trend indicating greater variability in survival rates for immediately loaded single-tooth implants, compared with conventionally loaded implants.^{24,25} Furthermore, although an updated Cochrane review²⁶ showed no statistically significant differences between the different loading protocols for both partially and fully edentulous situations, the authors recommended proper patient selection and high primary stability as requirements for successful immediate and early loading protocols. Therefore, there is still a further need to critically review the immediate loading protocols with respect to the restoration of single implant crowns. Meta-analysis is an analytic method where both independent and different studies are integrated, and their results are pooled together mathematically into a single common result. This should enhance the precision of estimates of treatment effects and consequently lead to improvements in policy making and clinical strategies.

The aim of this study was to perform a systematic review and meta-analysis of available studies that specifically compared immediate loading of single implant crowns to conventional loading in order to provide an estimate of an overall treatment effect.

Materials and Methods

This current systematic review was conducted according to procedures suggested by the Quality of Reporting of Meta-analyses (QUOROM) statement.²⁷ The PICO formula approach was also used to develop

a clear question, with the objectives and the inclusion criteria organized into a single focused format.²⁸ The acronym stands for P (population or patient), I (intervention being investigated), C (comparisons), and O (outcomes). Thus, for the present study:

- Population: patients that need single implants.
- Intervention: immediate loading of single implants in the anterior esthetic zone.
- Comparison: conventional loading of single implants in the anterior esthetic zone.
- Outcome: implant survival.

Search Protocol

A computer search of electronic databases, primarily MEDLINE via Ovid database (from 1969 to November 1, 2007), and the Cochrane Central Register of Controlled Trials was performed for articles written in English. Keywords included "immediate loading," "immediate provisionalization," "conventional loading," "single implant," "dental implants," and "endosseous implants," used alone or in combination under the publication type "randomized controlled studies" and "controlled trials."

Manual searches of the bibliographies of all retrieved papers and related reviews selected from the electronic search were also performed. Furthermore, manual searching was applied to the following journals for the years 2001 to 2007: *International Journal of Prosthodontics*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Prosthetic Dentistry*, *Implant Dentistry*, *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *Journal of Clinical Periodontology*, and *Journal of Periodontology*. The search and screening process was carried out by two independent reviewers, with disagreements resolved by a third examiner.

Study Selection

For the selection of papers, appropriate inclusion and exclusion criteria pertaining to the question in focus were established prior to the literature search. To be eligible for inclusion in the meta-analysis, studies had to be randomized controlled clinical trials or controlled clinical trials that compared the immediate loading of single implants with crowns in anterior regions (including premolars) to conventional loading. A sample size with a minimum of 10 single implants in the immediate loading group was required. Investigations in which all or part of the study population were restored with either implant-supported overdentures or implant-supported partial or full-arch prostheses were excluded.

Trials were also excluded if the test (immediately loaded) and control (conventionally loaded) groups consisted of differing implant systems or configurations, or when the number of implants placed, the duration of follow-up, or the withdrawal and/or failure rates were not reported. The review was restricted to peer-reviewed publications dealing with endosseous, solid titanium screw-shaped implants. Only data from clinical (human) studies with a minimum follow-up period of 6 months were evaluated.

Implant survival was defined as the presence of the implant at the time of the evaluation. Immediate loading was defined as occlusal or nonocclusal restoration of implants on the same day the implants were placed²⁹ or within the first 48 hours following implant placement,³⁰ and conventional loading referred to placing the restoration in a second procedure after a healing period of 3 to 6 months.³⁰ Early loading was not included in this review as its definition in the literature is imprecise—periods ranging from 1 to 8 weeks²⁶ or from 48 hours to 12 weeks³⁰ after implant insertion have been labeled early loading.

Data Extraction

Using a data extraction form, the following was extracted from the papers that were selected for evaluation: year of publication, patient inclusion and exclusion criteria, implant loading time, patient demographics, number of implants per treatment arm, implant survival rate, the time of outcome evaluation, and whether the immediate provisional restoration was placed in or out of occlusion.

Statistical Analysis

Data analysis was performed using a meta-analytic software package called MIX (Meta-analysis with Interactive eXplanations [available at www.mix-for-meta-analysis.info]),^{31,32} with the relative risk for dichotomous outcomes being presented with 95% confidence intervals (CIs). In the language of meta-analysis, homogeneity implies a mathematical compatibility between the results of each individual trial. Narrowing the inclusion criteria increases homogeneity but also excludes the results of more trials and thus risks the exclusion of significant data. The Cochran Q test was used to test for heterogeneity to assess the significance of the discrepancies in the estimates of treatment effects from the different trials. Where statistically significant ($P < .10$) heterogeneity is detected, a random effects model should be used to assess the significance of treatment effects,³³ this being a measure that incorporates clinical heterogeneity of the overall estimate in the analysis. Where no statistically significant

heterogeneity is found, analysis using a fixed effects model is appropriate. In this study, a fixed effects model was used throughout the analysis, since statistically significant heterogeneity was not found. However, since tests for heterogeneity have relatively low power,³⁴ the threshold for P values was set higher ($P < .10$).

Sensitivity analyses were performed to investigate two variables: study design and the type of occlusal loading (functional versus nonfunctional). A forest plot, which is a graphic display that shows the strength of evidence in quantitative scientific studies, was used to show the point estimate of the results of each individual study and the estimate of the overall result. In a typical forest plot, the weight of each study contributing to the meta-analysis is proportional to the area of each square, with its CI represented by a horizontal line running through the square. A diamond shape shows the overall estimate.

The authors also considered publication bias, which can take several forms. Studies with statistically significant treatment effects are more likely to be accepted for publication, are more likely to be published in English, and may appear in multiple publications, compared to trials that show neutral or negative effects.^{35–37} The possibility of publication bias was evaluated using the funnel plot,³⁸ Begg and Mazumdar's rank correlation test,³⁹ and Macaskill et al's regression test.⁴⁰ The funnel plot method plots each trial's effect size against some other measure of its size, such as the precision, the overall sample size, or the standard error. In the absence of bias, the plot should resemble a symmetric inverted funnel.³⁸ An asymmetric funnel plot leads to doubts over the appropriateness of a meta-analysis.

Results

Systematic Review

The electronic search retrieved 105 articles concerning immediately loaded single implants (Fig 1). The hand search did not provide any additional relevant studies. Screening of the full texts led to the exclusion of 93 articles, leaving 12 trials^{19,22,41–50} for more detailed analysis. Of these, seven studies were excluded for the following reasons: two trials^{42,43} compared early loading with conventional loading; one trial⁴¹ reported on five unsplinted single implants, the remainder being implant-supported fixed partial dentures (FPDs); one study⁴⁴ only considered splinted implants supporting FPDs; one paper⁴⁵ compared immediate versus early loading for partially edentulous patients; one article⁴⁶ was a retrospective noncontrolled study; and the final excluded paper⁴⁷ compared different implant systems in the test and control groups and did not report implant failure as an outcome measure.

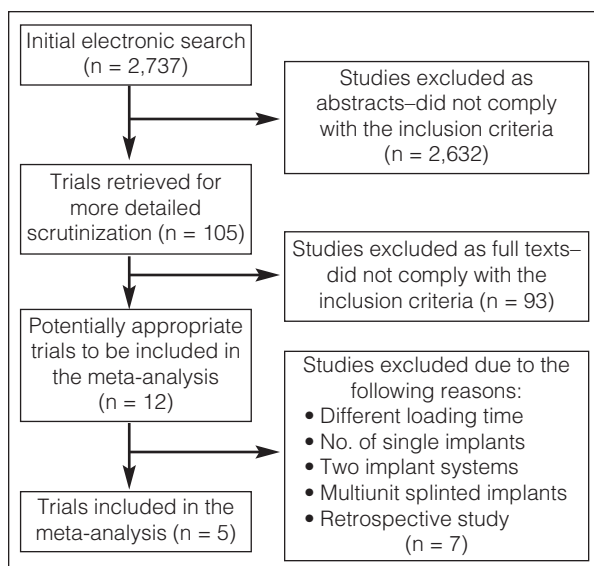


Fig 1 Process of the search strategy.

The remaining five trials^{19,22,48–50} fulfilled the inclusion criteria and were published in peer-reviewed journals (Table 1). Two of the trials^{22,49} were randomized, and the rest were controlled clinical trials. The longest follow-up within the included studies was 24 months^{48,50} and the shortest was 6 months.⁴⁹ Four trials^{19,22,48,50} reported immediate nonocclusal loading and only one⁴⁹ placed the transitional crown immediately into occlusion.

Four trials^{19,22,48,49} were limited to single implant restorations and only one⁵⁰ had both single and multiunit implant restorations. For the latter paper,⁵⁰ only data pertaining to single implants were extracted and included in the current analysis. A total of 248 implants were included in this meta-analysis, with an overall implant failure rate of 20/248 (8.1%).

Five implant systems were used in these studies: XiVE (Dentsply/Friadent), Brånemark (Nobel Biocare), Southern (Southern Implants), Zimmer (Zimmer Dental), and Frialit-2 (Dentsply/Friadent).

Details of the Included Trials

In the study performed by Ericsson et al,¹⁹ 14 immediately loaded (within 24 hours) single-tooth Brånemark implants were compared with eight conventionally loaded (3 months after implantation) single-tooth implants. All implants were placed anterior to the molars in both arches. The evaluation period was 18 months, during which two implants failed in the immediately loaded group. No statistically significant differences for implant failures or changes in marginal bone level were detected between the two groups.

Ottoni et al⁴⁸ performed a split-mouth trial of 46 immediately and conventionally loaded single-tooth Frialit-2 implants placed at or anterior to the second premolar in the maxilla or mandible. Patients were followed up for 24 months. Ten out of the 23 immediately loaded implants failed versus one out of 23 in the conventionally loaded group. Failure of immediately loaded implants was negatively correlated with initial insertion torque; nine of the 10 failed immediately loaded implants had an insertion torque of ≤ 20 Ncm. The authors recommended that only implants that required an insertion torque > 32 Ncm (indicating better quality bone) should be considered for immediate loading in single-tooth situations. There were no statistically significant differences between the two groups in regard to marginal bone level loss.

Oh et al⁴⁹ compared 12 immediately loaded (at placement) single-tooth Zimmer implants with 12 single-tooth implants conventionally loaded after 4 months. All implants were placed in the anterior maxilla using a flapless technique and evaluated for 6 months after loading. Three implants failed in the immediately loaded group; there were no statistically significant differences in implant failures between the two groups.

Degidi et al⁵⁰ evaluated a total of 1,005 XiVE dental implants placed in 371 patients for 24 months. Of these, 32 single-tooth implants were immediately loaded (within 1 to 2 hours) and 96 single-tooth implants were conventionally loaded. Only one implant failed in the immediately loaded group versus two implants in the control group. There were no statistically significant differences for implant failure or marginal bone levels between the two groups.

Hall et al²² compared 14 immediately loaded (at placement) single Southern tapered implants with 14 conventionally loaded (after 6 months) implants. All implants were placed in the anterior maxilla and followed up for 1 year. One participant in the test group failed to return for the 1-year recall but confirmed that the implant was still in function. Two control participants did not return for the 1-year recall visit. One implant failed in the immediately loaded group. There were no statistically significant differences for implant failure, mucosal response, or marginal bone level changes between the test and control groups.

In four studies,^{19,22,48,50} participants were assessed against generally similar and strict requirements. The inclusion criteria for these studies included a good general and oral health condition, sufficient bone volume, no evidence of smoking or bruxing, no need for hard tissue augmentation, patient availability for a postoperative control program, and adequate primary stability. However, the exclusion criteria were not clear in one paper.⁴⁹ Favorable mucosal responses were demonstrated for immediately loaded implants in two

Table 1 Characteristics of the Included Studies

Study/design	No. of implants	Implant system	Time to loading	Occlusion of immediate provisional crown	Implant location	Allocation concealment	Follow-up period	Survival rate (%)
Degidi et al ⁵⁰								
CT	128	XiVE	Within 1 to 2 h After 6 mo	No contacts	Unclear from text	Not used	24 mo	96.7 97.9
IL	32							
DL	96							
Ericsson et al ¹⁹								
CT	22	Brånemark	Within 24 h After 3 mo	Minimal or no contacts	Anterior (maxilla, mandible)	Not used	18 mo	85.5 100
IL	14							
DL	8							
Hall et al ²²								
RCT	28	Southern Implants	At placement After 26 wk	No contacts	Anterior maxilla	Adequate	12 mo	92.9 100
IL	14							
DL	14							
Oh et al ⁴⁹								
RCT	24	Zimmer	At placement After 4 mo	In occlusal contact	Anterior maxilla	Unclear from text	6 mo	75 100
IL	12							
DL	12							
Ottoni et al ⁴⁸								
CT	46	Frialit-2	At placement Delayed (not specified)	No contacts	Anterior (maxilla, mandible)	Not used	24 mo	56.5 95.7
IL	23							
DL	23							

CT = controlled trial; RCT = randomized controlled trial; IL = immediate loading; DL = delayed loading.

studies,^{48,49} as the provisional crown preserved the gingival contour and interdental papilla during the healing phase, resulting in excellent esthetic outcomes.²² There were no differences in marginal bone loss between the immediate and conventional loading approaches, at least in the short-term.^{19,22,48–50}

All of the included studies had a higher failure rate for the immediately loaded group. However, this was not statistically significant in any study. Various reasons were given for the increased failure rates. Flapless placement and immediate functional loading were claimed to contribute to the relatively high failure rates in the immediately loaded group.⁴⁹ Immediate loading of implants placed in fresh extraction sockets,⁵⁰ improper oral hygiene maintenance,¹⁹ and an insertion torque of less than 32 Ncm⁴⁸ were also suggested as reasons for a higher failure rate among immediately loaded single implants.

Meta-analysis

In the assessment of publication bias, the funnel plot showed a symmetric funnel shape, hence substantiating the validity of the meta-analysis (Fig 2). However, the quantitative assessments using Begg and Mazumdar's rank correlation test ($P = .81$) and Macaskill et al's test ($P = .48$) were not supportive of publication bias.

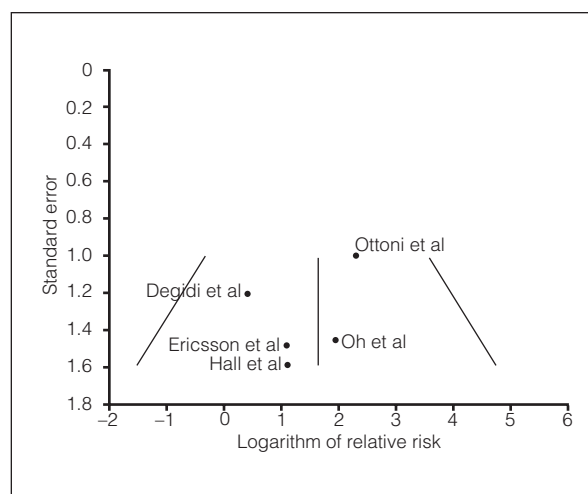
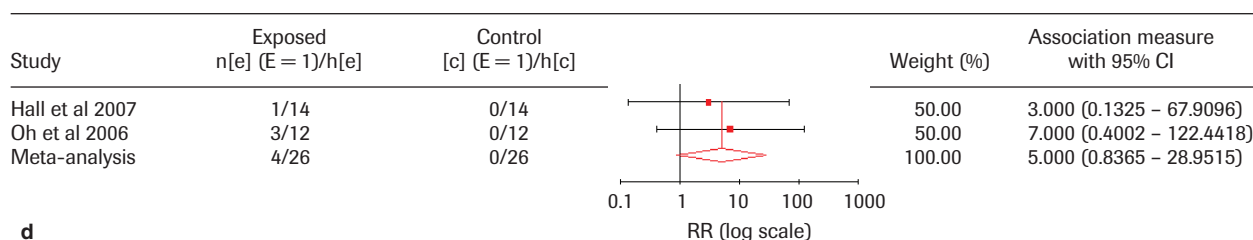
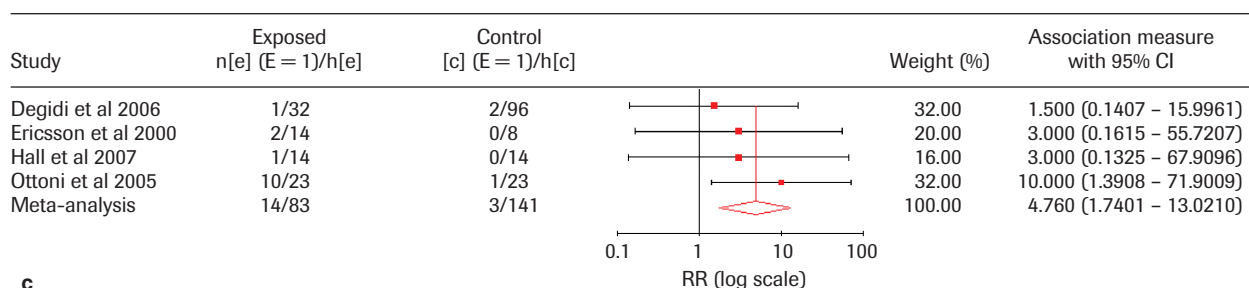
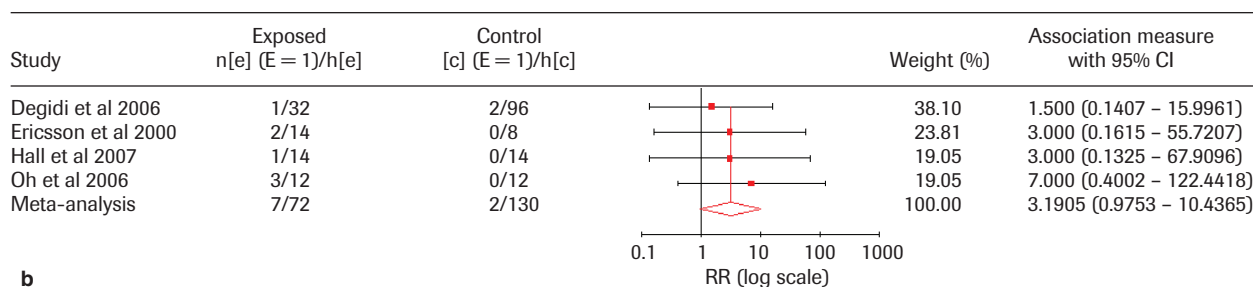
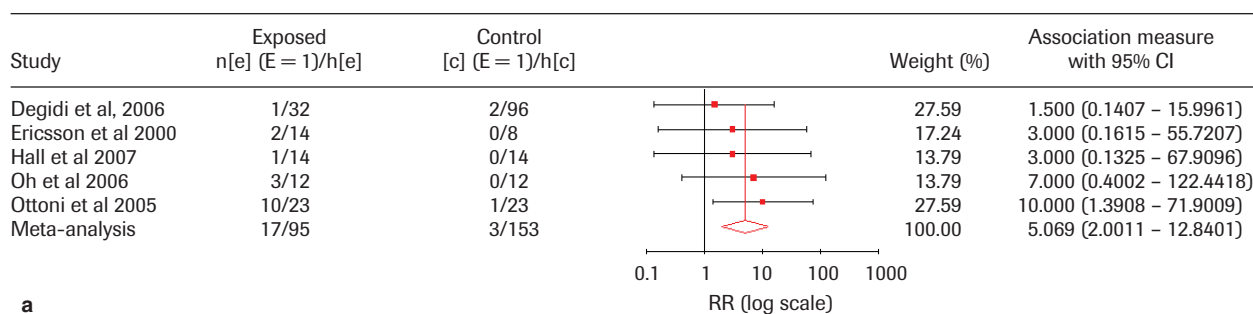


Fig 2 Funnel plot for assessment of publication bias.

Information on the implant failure rate was reported in all the studies included in the meta-analysis. The fixed effects model was used since the test result for heterogeneity ($\chi^2 = 1.75$, $P = .78$) indicated neither significant heterogeneity within studies, nor between-study variability ($I^2 = 0\%$, 95% CI: 0% to 79.2%). Overall, there was a significantly lower risk of implant failure in



Figs 3a to 3d Forest plots of (a) all trials reporting implant failures, (b) homogenous trials reporting implant failures, (c) studies reporting on immediate nonfunctional loading protocol, and (d) all randomized clinical trials. The boxes represent the relative risk (RR) estimates with the horizontal lines representing 95% CIs for the point estimate in each study. The size of the boxes represents the weight given to the study. The right column shows the numeric values for each study and summary measure.

conventionally loaded groups compared with immediately loaded implants (relative risk: 5.00, 95% CI: 2.00 to 12.84, $P < .001$) (Fig 3a).

Despite the lack of significant heterogeneity, one study was considered as an obvious outlier⁴⁸ due to a very high failure rate among the immediate loading group. Using the fixed effects model, an analysis of the

remaining four studies showed a smaller difference between the two groups, although still marginally significant in favor of the conventional group (relative risk: 3.19, 95% CI: 0.98 to 10.44, $P = .055$) (Fig 3b).

A sensitivity analysis was performed for the four studies^{19,22,48,50} that reported an immediate, nonocclusal loading protocol. The fixed effects model was

again used as the test for heterogeneity between the four studies and was not statistically significant ($\chi^2 = 1.64$, $P = .65$). There was a statistically significant difference between the different loading strategies, with a higher risk of implant failure in the immediately loaded implants even when the provisional crown was placed in nonocclusal contact (relative risk: 4.76, 95% CI: 1.74 to 13.02, $P = .002$) (Fig 3c).

Further sensitivity analysis of the two randomized controlled trials (RCTs)^{22,49} in this review revealed a better outcome for the delayed loading group, although the difference was not statistically significant (relative risk: 5.00, 95% CI: 0.86 to 28.95, $P = .07$) (Fig 3d). The test result for heterogeneity was also not significant ($\chi^2 = 0.16$, $P = .69$).

Discussion

This systematic review and meta-analysis was performed to evaluate the clinical effectiveness of immediate loading of single implant crowns in the anterior esthetic region. The eligibility criteria for accepting publications were restricted to provide more accurate and comprehensive information from the literature. The effect sizes of five trials^{19,22,48-50} that compared immediate to conventional single implant loading were combined using a fixed effects model. A statistically significant difference was demonstrated between the two loading strategies, with implant failure occurring more often after immediate loading (relative risk: 3 to 5 times). Since the secondary analyses made little or no difference to the overall results, we can assume that the review's conclusions are valid.

An interesting finding was the higher failure risk of immediate nonocclusal loading when compared to conventional loading. Several authors stated that limitation of occlusal forces is a critical factor for successful immediate loading.^{18,51,52} However, claims that immediate provisionalization provided better primary stability were not supported by the results of this study. The authors suggest that nonoccluding immediate restorations are actually functionally loaded during mastication. Additional properly designed studies are still needed to conclusively determine the influence of occlusion-related factors.

Several excellent review articles have been published on immediate and early implant loading protocols, including an updated Cochrane review and meta-analysis²⁶ restricted to RCTs including both partially and fully edentulous participants, a critical review⁵¹ that reported the advantages and disadvantages of immediate and early loading protocols and the key factors needed for a successful outcome, and finally a comprehensive literature review²⁴ that included a wide range of study designs and discussed different loading

protocols in various clinical applications, including single implants. The systematic review presented in this article differs from previous work in a number of ways. First, the authors focused on immediate loading for single implants. They consider that this reduced heterogeneity in the data and increased the validity of their findings. Second, studies that used an early loading protocol were excluded since this was considered to be poorly defined. The authors feel that this results in a more objective assessment of the effect of immediate loading. Third, the criteria for this review were stringent, being restricted to studies with control groups in order to ensure that only studies of the highest quality were included.

One of the limitations of this review and subsequent meta-analysis is that the search terminated in November 2007. However, the findings were substantiated when a subsequent search using the same strategy was conducted up to July 1, 2008. Six additional trials⁵³⁻⁵⁸ were identified. However, none of them were found eligible to be included in the present meta-analysis. The reasons for their elimination are summarized in Table 2.

The present meta-analysis must be interpreted with caution due to the small number of studies that met the restricted eligibility criteria; only five RCTs or controlled trials were included,^{19,22,48-50} with an overall sample size of only 248 implants. The selected studies had differing inclusion and exclusion criteria and short-term follow-up periods. The analysis was not adjusted for variations in duration of follow-up. Furthermore, the search strategy did not include the EMBASE database. Searching EMBASE as well as MEDLINE can add up to 30% more references, mainly from European journals. However, omission of these additional studies does not appear to bias the results of the meta-analysis.⁵⁹ Moreover, it was considered unnecessary to search other databases, since hand searching did not uncover any additional papers.

The present analysis was restricted to published data. It is possible that studies with negative results, which showed no trend in favor of either intervention, may remain unpublished, forming part of the "gray" literature that also includes conference proceedings, graduate theses, company reports, and guidelines. Although the results in the "gray" literature may be of a lower quality than peer-reviewed published literature, it has been suggested that the exclusion of such results from meta-analyses may result in an overestimation of the effect size by an average of 12%.⁶⁰ This meta-analysis was also limited to English language publications for practical reasons; although this might limit the number of studies retrieved, it is not thought to bias the effect size.⁶¹ The authors acknowledge the fact that κ tests were not used to evaluate the level of agreement between the reviewers. Any disagreements were usually resolved by discussion.

Table 2 Reasons for Exclusion of Newly Retrieved Trials

Study	Reason for exclusion
Turkylmaz et al ⁵³	Compared early and delayed loading protocols
Güncü et al ⁵⁴	Limited to mandibular molar sites
Zöllner et al ⁵⁵	Compared immediate and early loading protocols
Galli et al ⁵⁶	Only seven single implants in the test group
Susarla et al ⁵⁷	Retrospective cohort study
Donati et al ⁵⁸	The use of modified implant placement procedure, which is beyond the scope of this review

Funnel plots were used to consider whether publication bias was present³⁸ and a degree of asymmetry was observed. However, smaller studies tend to have greater effects than larger ones, which could also contribute to the observed asymmetry of the funnel plot, even in the absence of publication bias.³⁸ Statistical tests, such as Begg and Mazumdar's rank correlation test³⁹ and Macaskill et al's regression test,⁴⁰ were employed to provide a more formal assessment of publication bias than the inspection of funnel plots. Although such tests indicated no obvious evidence for the existence of publication or related bias, this cannot be completely excluded due to the small study size and the low power of these statistical tests.

It is important to keep in mind that a meta-analysis only serves to increase the power and hence the precision of an estimate; it does not increase the validity or believability of the results. In addition, the results of meta-analyses based on a small number of studies should be taken with caution, regardless of the significance of the result.⁶²

Although the findings of this systematic review and meta-analysis are clearly not robust enough to guide clinical practice, they do demonstrate better outcomes with a conventional loading protocol for single implant crowns. Therefore, the authors suggest caution with the recommendation of immediate loading of implants with crowns as a standard of care for single tooth replacement.

Conclusion

This systematic review and meta-analysis has shown that better outcomes are currently achieved with conventional loading of single implants with crowns, as opposed to immediately loaded implants, which carry a higher risk of failure. More definitive data from clinical trials of sufficient power are still needed to understand the effect of the timing of loading, to identify appropriate indications, and to investigate the factors that may compromise the success of single implants with crowns.

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