CLINICAL ORAL IMPLANTS RESEARCH

Review Article

Clinical efficacy of immediate implant loading protocols compared to conventional loading depending on the type of the restoration: a systematic review

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Abstract

Background and objectives: Immediate loading has become a predictable option to restore all clinical situations. The aim of this systematic review was to assess whether immediate loading protocols achieve comparable clinical outcomes when compared to conventional loading protocols depending on the type of prosthetic restoration.

Methods: A protocol was developed aimed to answer the following focused question: "What are the effects of immediate implant loading protocols compared to conventional implant loading, in terms of implant failure, marginal bone levels, and biological and mechanical complications based on the type of restoration?" The next subanalysis were performed as follows: the extent, type, and material of the restoration and the type of occlusal contact in function. This systematic review only included randomized controlled trials (RCTs) with a follow-up of at least 6 months after implant loading.

Results: Thirty-seven final papers were included. The results from the meta-analyses have shown that the immediately loading implants demonstrated a statistically significant higher risk of implant failure [RR = 1.92; 95% CI (1.04; 3.54); $P = 0.036$], a statistically significant lower bone loss [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$] and a smaller increase in ISQ values [WMD = −1.096; 95% CI (−1.615; −0.577); $P < 0.001$, although both groups attained high survival rates (98.2% in the test and 99.6% in the control). Single teeth implants were greater risk of failure, when compared to immediately loaded full arch restorations (RR = 2 vs. 0.9), so as the occlusal pattern when compared to non-occlusal (RR = 1.9 vs. 1.4).

Conclusions: Immediate loading may impose a greater risk for implant failure when compared to conventional loading, although the survival rates were high for both groups.

The rehabilitation of partially and fully edentulous patients with implant-supported restorations has become a standardized and predictable therapy resulting in high survival and success rates for both implants and restoration (Weber et al. 2000; Leonhardt et al. 2002; Pjetursson et al. 2004; Rasmusson et al. 2005). These predictable clinical outcomes have been based on the achievement of a direct interface between the implant surface and the alveolar bone (osseointegration) during the healing after implant placement. Initially, it was assumed that to achieve osseointegration, implants needed to be submerged under the mucosa and left without any loading for a period of 3–6 months (Branemark et al. 1983). The rationale behind this healing period without loading was the avoidance of any micromotion on the implant, which may interfere the healing process leading to osseointegration, and instead, develop a connective tissue interface between the implant surface and the bone, which eventually caused the implant to fail due to its inability to withstand the masticatory forces (Schatzker et al. 1975; Roberts et al. 1984). In the last two decades, however, numerous clinical reports and clinical trials have demonstrated that, first, there is no need to submerge the implants under the mucosa during healing, since transmucosal implants have demonstrated similar outcomes when compared to submerged implants (Buser et al. 1991, 1997; Becker et al. 1997; Sanz et al. 2013). Secondly, with the advent of improved implant surface

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technology, faster and more predictable osseointegration can be attained, which allows a significant reduction of the standard implant loading protocols (from 12–24 weeks to 6–8 weeds) without affecting the predictability and success rates of the implants (Cochran et al. 2004).

In the full edentulous patient, this non-loading period is usually more troublesome, due to the functional and aesthetic disturbances associated with the need to use removable dentures (Borges Tde et al. 2011; Erkapers et al. 2011). The protocol of immediate loading was initially developed for the treatment of these patients, with the aim of improving their comfort through the attainment of immediate function and aesthetics (Goiato et al. 2013). Most of the early publications using this concept showed excellent results, mainly since the outcome was measured in terms of implant survival. Schnitman and coworkers followed during ten years 28 immediately loaded implants reporting a survival rate of 84.7% (Schnitman et al. 1997). Other reports, however, reported significantly lower survival rates when compared to conventional loading. Ottoni and coworkers, in 23 patients reported a 1-year survival rate of 56.53% in immediately loaded implants, compared with a survival rate 95.66% in implants with conventional loading. Interestingly, nine of the 10 immediate implants that failed in this study had low implant primary stability (measured torque of 20 Ncm) and therefore, these authors stated that a minimum primary stability was a requirement for immediately loaded implants (Ottoni et al. 2005). Besides the measurement of primary stability by torque control or other more sophisticated methods, several authors have recommended different strategies to increase implant stability, such as bicortical stabilization, under drilling of the implant osteotomy or the use of osteotomes to laterally condensate the available bone (Cannizzaro et al. 2008a; Donati et al. 2008). With increased implant stability and hence, the assurance of minimal micromovements at the bone-implant interface during healing, several clinical trials were conducted comparing immediately loaded implants with control implants using conventional loading, reporting similar implant survival rates (Capelli et al. 2010).

These results were corroborated in a recent systematic review where this intervention was compared with conventionally loaded implants reporting similar success rates. Immediate loading was defined as an implant put in function within 1 week after its placement (Esposito et al. 2013). In this review, however, limited information was reported on other relevant clinical outcomes, such as changes in marginal peri-implant crestal bone levels, changes in the peri-implant soft tissues or advent of biological and technical complications. Moreover, the influence of the type of restoration on the outcomes after immediate loading was not investigated (Esposito et al. 2013) and the authors reported that the literature evaluated had a potential risk of bias (Esposito et al. 2013).

It is, therefore, the aim of this systematic review to assess whether immediate loading protocols achieve comparable clinical outcomes (success rates, clinical outcome variables and the advent of technical and biological complications) when compared to conventional loading protocols depending on the type of the restoration used to rehabilitate the edentulous area.

Specifically, we aim to investigate the impact of:

- the extent of restoration (full-arch, partial, or single tooth prosthesis),
- type of restoration (provisional or definitive),
- material of the final restoration, and
- type of loading of the restoration (occlusal or non-occlusal)

Material and methods

Protocol development and eligibility criteria

Before the start of the systematic review a protocol was developed aimed to answer the following focused question (Needleman 2002): "What are the effects of immediate implant loading protocols compared to conventional implant loading, in terms of implant failure, marginal bone levels, and biological and mechanical complications based on the type of restoration?"

This question considered the following P.I.C.O. definitions:

- *Population:* Studies should include humans with at least one implant placed, older than 18 years and in good general health.
- *Intervention:* Immediate loading was considered the intervention of interest and was defined as an implant inserted in function within 1 week after its placement (Jung et al. 2011).
- *Comparison:* Conventional implant loading, also termed delayed loading, defined as implants loaded at least 2 months after the insertion (Esposito et al. 2013).
- *Outcomes:* The primary outcome was implant failure, measured as implant mobility and removal of stable implants dictated by progressive marginal bone loss (Capelli et al. 2010).

The following secondary outcomes variables were considered:

- Marginal bone levels changes (mm), measured as the change in bone levels from the implant shoulder to the first visible bone to implant contact (DIB – distance of implant to first bone contact) at the mesial and distal aspects of each implant.
- Advent of technical complications (number), including manifest mechanical damage of the implants, implant components and/or the suprastructures. Among these, fractures of the implants, fracture of screws or abutments, fractures of the luting cement (loss of retention), fracture or deformations of the framework or veneers, loss of the screw access hole restoration and screw or abutment loosening were included.
- Advent of biological complications, defined as those occurring directly related to the studied implants, ranging from peri-implant infections (mucositis and peri-implantitis) to temporary or permanent numbness of the lower lip.
- Clinical evaluation of the peri-implant tissue health status by means of probing pocket depths (PPD), interproximal tissue height and mid-facial mucosal level, bleeding on probing (BOP) and/or the plaque index (PI).
- Changes in implant stability measured as changes in *implant stability quotients* (ISQs), assessed at the time of implant installation and followed over time.
- Patient-related outcomes such as pain, discomfort, functional capacity, satisfaction.

This systematic review only included randomized controlled trials (RCTs) with a follow-up of at least 6 months after implant loading.

Types of prostheses

In addition to the P.I.C.O. question, the specific types of prostheses evaluated in this study were based on:

The number of missing teeth

The restorations for the rehabilitation of patients with missing teeth were divided according to the Glossary of Prosthodontics into "single-unit crowns" [SC] and "partial dental prosthesis" [partial PDP]. A partial PDP was defined as any dental prosthesis

that is cemented, screwed or mechanically attached or otherwise securely retained to dental implant abutments, as the primary support for the dental prosthesis. This may include replacement of 1–16 teeth in each dental arch (Terms 2005). A special subcategory was defined within this group for the treatment of full edentulous patients, which was termed "full-arch dental prosthesis" [FADP].

Fixed or removable restorations

In the treatment of full edentulous patients with FADP, a subgroup was made depending on the type of prosthesis:

- Implant-supported removable restorations, such as overdentures.
- Implant-supported fixed restorations.

The type of occlusion: occlusal or non-occlusal

"Non-occlusally loaded" implants were considered those implants that were immediately rehabilitated with provisional restorations without direct occlusal contacts with the opposing dentition, both in static or dynamic lateral movements. (Esposito et al. 2013).

Material of the restoration

The type of material of the final restoration was also evaluated in a subgroup meta-analysis to assess its possible influence. The following materials were considered: resin, metal-ceramic, metal-resin, gold-ceramic, or full-ceramic.

Search strategy

Three electronic databases were used as main tools in this search for studies, limited to human subjects and published until September 2013 that satisfied the inclusion criteria: (1) The National Library of Medicine (MEDLINE via Pubmed); (2) Embase; and (3) Cochrane Central Register of Controlled Trials.

The following search terms were used:

Population

(<[text words] Dental implant OR dental implant* OR oral implant OR oral implants> OR <[MeSH terms/all subheadings] "Dental Implants" OR "Dental implantation" OR "Dental Implant">)

Intervention

(<[text words] immediate loading OR immediate restoration OR immediate prostheses OR immediate overdenture OR immediate bridge OR immediate crown > OR <[MeSH terms/all subheadings] "Immediate Dental Implant loading" OR "Dental Implant Loading, Immediate" OR "Dental, complete, Immediate" OR "Denture, Partial, Immediate">)

Population and Intervention

Limits: Humans, randomized controlled trials

There were no language restrictions. All reference lists of the selected studies were checked for cross-references. The following journals were hand-searched: Journal of Clinical Periodontology, Journal of Periodontology, Journal of Periodontal Research; Clinical Oral Implants Research, International Journal of Oral & Maxillofacial Implants, British Journal of Oral and Maxillofacial surgery, European Journal of Oral Implantology, Implant Dentistry, International Journal of Oral and Maxillofacial Surgery, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of Dental Research, Journal of Dental Implantology, Journal of Prosthetic Dentistry, Journal of Oral and Maxillofacial Surgery and Clinical Implant Dentistry and Related Research.

Screening methods and data extraction

Two reviewers (ISS and ISM) did the primary search by screening independently the titles and abstracts and identified the studies appearing to meet the inclusion criteria, or those with insufficient data in the title and abstract to make a clear decision. These studies were selected for evaluation of the full manuscript, which was carried out independently by the same two reviewers who determined the final inclusion. Any disagreement was resolved by discussion with a third reviewer (EF). In order to prevent selection bias, the reviewers were blind to the name of the authors, institutions, and journal titles. All studies that met the inclusion criteria underwent a validity assessment. The reasons for rejecting studies at this or at subsequent stages were recorded. Special attention was paid to duplicate publications in order to avoid a likely bigger impact of the same data in the overall result.

Data extraction

Two reviewers (ISS and ISM) independently extracted the data using specially designed data extraction forms. Any disagreement was discussed and a third reviewer (EF) was consulted when necessary. The inter-reviewer reliability of the data extracted was calculated by determining the percentage of agreement, the correlation coefficients and using Kappa analysis. Authors of studies were contacted for clarification when data were incomplete or missing. Data were excluded until further clarification could be available if agreement could not be reached. When the results of a study were published more than once or if the results were presented in different publications, the most complete data set was included only once.

Quality assessment

The quality assessment of the included studies was undertaken independently and in duplicate by two reviewers (ISS and ISM) who were blinded to the name of the authors, institutions, and journal titles. Quality assessment was carried out following the recommendations by Cochrane for assessing risk of bias (Higgins et al. 2009). Studies were defined as low risk of bias if these six criteria were clearly met in the study: random allocation, definition of inclusion/exclusion criteria for selecting the population, measures to blind the patient and examiner, selection of a representative population group, use of identical treatment between groups except for the intervention and detailed reporting of the follow-up. When missing one of these criteria, the study was classified as moderate potential risk of bias. Missing two or more of these criteria resulted in a high potential risk of bias (Ten Heggeler et al. 2011).

Data analysis

To summarize and compare the selected studies, the data on the primary outcome (implant failure) was pooled and analyzed using risk ratios (RR) and 95% confidence intervals (95% CI). The data on secondary outcomes were analyzed depending on the type of variable. For dichotomous variables (e.g., technical or biological complications) the estimates of the effect were expressed as risk ratios (RR) and 95% confidence intervals. For continuous variables (marginal bone changes, peri-implant health status, ISQs) weighted mean differences (WMDs) and 95% CI were used.

The statistical heterogeneity among studies was assessed using the Q-test according to Dersimonian and Laird as well as the I2 index (Higgins et al. 2003) that assesses the percentage of variation in the global estimate attributable to heterogeneity (I2 = 25%: low; I2 = 50%: moderate; I2 = 75%: high heterogeneity).

The study-specific estimates were pooled using both the fixed effect model (Mantel–Haenzel–Peto test) and the random effect model (Dersimonian-Laird test). If a significant heterogeneity was found, the random effect model results were presented. In addi-

tion, and whenever possible, a subgroup analysis was carried out on the selected outcome variables using the following explanatory variables: (1) extent of restoration (full-arch, partial or single implant supported prosthesis), (2) type of restoration (provisional or definitive), (3) material of the final restoration, and (4) type of loading of the restoration (occlusal or non-occlusal).

Forest Plots were created to illustrate the effects in the meta-analysis of the global estimation and the different sub-analysis. STATA® (StataCorp LP, Lakeway Drive, College Station, Texas, USA) intercooled software was used to perform all analyses. Statistical significance was defined as a P value <0.05.

Results

Search results

Figure 1 depicts the study flow chart. The electronic search delivered 479 titles. After the evaluation of titles and abstracts, 385 studies were discarded (agreement = 86.4%; kappa = 0.45; $P < 0.001$) resulting in 94 studies, which after the addition of eight additional articles found on the manual search, resulted in 102 studies that were subjected to full text analysis. After this analysis, 37 final papers were included reporting data from 29 different investigations, since three groups of papers reported the results of the same material at different time points and two groups of papers reported different outcomes at the same time point. In the first series, two articles reported the same data at 12 months (Turkyilmaz et al. 2006a,b) and one article at 24 months (Turkyilmaz & Tumer 2007). In the second series, three articles reported the same data at different time points (Turkyilmaz 2006c; Turkyilmaz et al. 2010, 2012). In the third series, three articles reported the same data at different time points (Testori et al. 2007; Galli et al. 2008; Capelli et al. 2010). In the fourth series, two articles reported different outcomes at 12 months (Guncu et al. 2008a,b) but one of them did not report any variable of interest for this review (Guncu et al. 2008a). In the fifth series, two articles reported the same data at 12 months (Shibly et al. 2010, 2012). Therefore, 37 papers were included, reporting results of 29 studies, which were included in the meta-analyses that assessed the primary outcome.

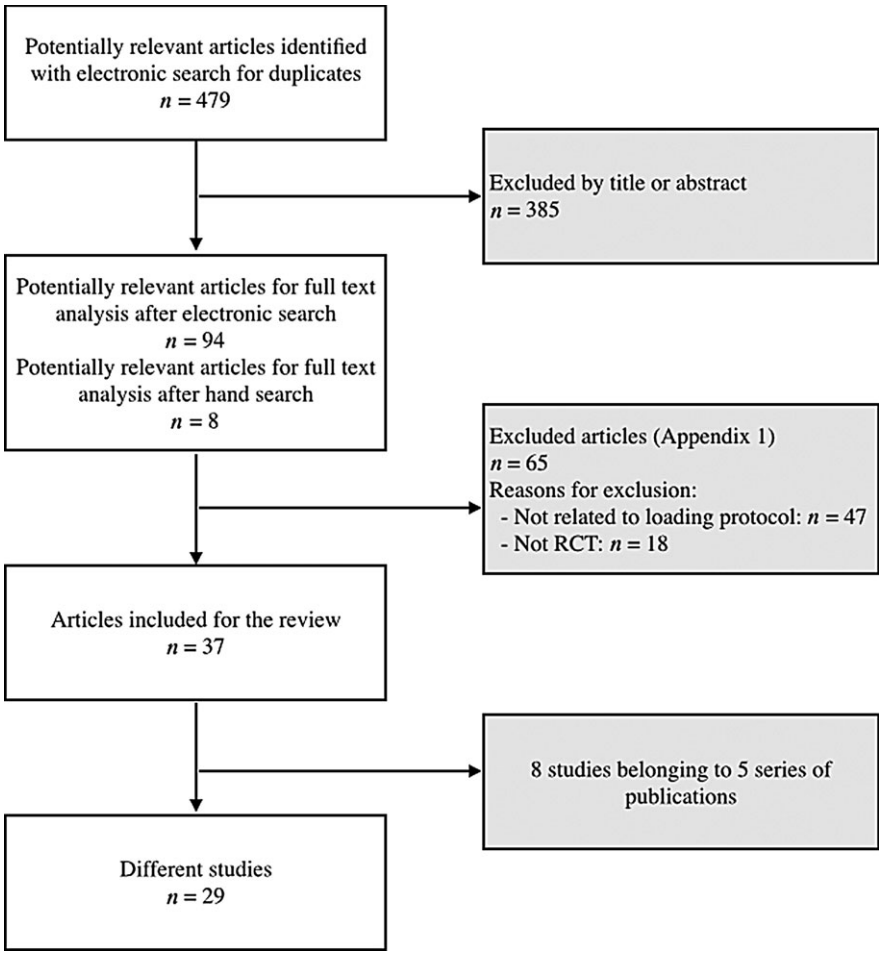

Fig. 1. Flow-chart.

Study design

The methodological characteristics of the selected studies are shown in Table 1. From the 29 investigations, four had a split-mouth design, one was a multi-centre study with a parallel design and the rest were parallel trials. Among the parallel studies, two studies had two experimental groups that met the inclusion criteria, so their data were divided into two for the comparisons with the same control group (Donati et al. 2008; Margossian et al. 2012). The minimum study length was 6 months and the maximum 84 months. Industry support was reported in eight investigations, in one there was institutional support and in six self-support was reported. The rest of the studies did not report the source of founding.

Study population

This systematic review pooled data of 1396 patients at baseline, 742 in the experimental group and 654 in the control, with a total of 2739 implants placed (1436 in the test and 1303 in the control). The mean follow-up period was of 25.8 months, with a minimum of 6 months in two studies (Oh et al. 2006; Tozum et al. 2007) and a maximum of 84 months in one study (Turkyilmaz et al. 2012). At the end of the study, 1365 patients were followed (720 in the test and 645 in the control) with a total of 2669 remaining implants (1389 in the test and 1280 in the control). The study with the smallest sample followed five patients per group (Assad et al. 2007), while the one with the biggest sample studied 82 patients per group (Degidi et al. 2009b).

In 14 studies, the data on age were presented by group, whereas in 13 studies the data on age were presented for the whole study population. Similarly, the gender distribution was mostly reported for the total sample, except in five studies (Assad et al. 2007; Hall et al. 2007; Danza et al. 2010; Barewal et al. 2012; Margossian et al. 2012) In regards to smoking, nine studies included smokers patients in their inclusion criteria (Romanos & Nentwig 2006; Hall et al. 2007; Cannizzaro et al. 2008a,b; Donati et al. 2008; Schincaglia et al. 2008; Capelli et al. 2010; Grandi et al. 2012a,b), while seven studies only included non-smoker patients (Guncu et al. 2008b; Danza et al. 2010; den Hartog et al. 2011; Barewal et al. 2012; Elsyad et al. 2012; Margossian et al. 2012). In the remaining studies, smoking data were not reported (Table 1).

Table 1. **Methodological characteristics of the selected studies**

References	Country	Study design (RCT)	Support	Follow up	Mean age (range) Test/Control *Global	Smoking habit Test/Control *Global	bs patient (implants) Test/Control	Final patient (implants) Test/Control	Study outcomes measured
Chiapasco et al. (2001)	Italy	Parallel	NR	24	59.3 (50–73)/57.6 (44–66)	NR	10 (40)/10 (40)	10 (39)/10 (39)	Survival, BL, Biol comp, PPD, G infl, PI, IS
Romeo et al. (2002)	Italy	Parallel	NR	24	63.2 (42–73)*	NR	10 (40)/10 (40)	10 (39)/10 (39)	Survival, BL, Biol comp, PPD, G infl, PI, IS
Testori et al. (2003)	Italy	Parallel	Self	24	56/54.2	NR	14 (52)/18 (49)	14 (50)/18 (48)	Survival, Tech compl, Biol comp, IS
Oh et al. (2006)	USA	Split mouth	Industry and University	6	45.2/47.3	NR	12 (12)/12 (12)	9 (9)/12 (12)	Survival, PPD, G infl, PI, Pat bas, ML, PAP
Romanos & Nentwig (2006)	Germany	Split mouth	Self	25,3	50.75*	50%*	12 (36)/12 (36)	12 (36)/12 (36)	Survival, BL, PPD, G infl, PI, IS
Turkyilmaz et al. (2006a,b) and Turkyimaz & Tumer (2007)	Turkey	Parallel	NR	24	62*	NR	10 (20)/10 (20)	10 (20)/10 (20)	Survival, BL, Tech comp, IS
Turkyilmaz et al. 2006a,b, 2009, 2012	Turkey	Parallel	NR	84	63 (50–76)*	NR	13 (26)/13 (26)	12 (24)/12 (24)	Survival, BL, PPD, G infl, PI, IS
Assad et al. (2007)	Egypt	Parallel	NR	24	NR (48–63)*	NR	5 (20)/5 (20)	5 (20)/5 (20)	Survival, BL, PPD, PI
Hall et al. (2007)	New Zeland	Parallel	Industry	12	43 (23–71)*	21.4%/42.8%	14 (14)/14 (14)	12 (12)/14 (14)	Survival, BL, Tech comp, Biol comp, PPD, PI, ML, PAP
Capelli et al. (2007, 2008, 2010)	Italy	Parallel	NR	60	51.6 (27–74)/51.3 (34–73)	17.3%/7.6%	25 (52)/27 (52)	24 (52)/26 (52)	Survival, BL, Biol comp, ML
Tozum et al. (2007)	Turkey	Parallel	Self	6	53 (42–65)*	NR	9 (18)/8 (16)	9 (18)/8 (16)	Survival, BL, IS
Cannizzaro et al. (2008a)	Italy	Parallel	Self	36	40.1 (18–62)/37.4 (19–64)	40%/45%	20 (52)/20 (56)	19 (52)/20 (56)	Survival, Tech comp, Biol comp, Pat bas, IS
Cannizzaro et al. (2008b)	Italy	Parallel	Self	12	62 (45–65)/56 (42–69)	47%/53%	15 (90)/15 (87)	15 (89)/15 (84)	Survival, BL, Tech comp, Biol comp, Pat bas, IS
Crespi et al. (2008)	Italy	Parallel	NR	24	45.5 (24–62)/48.8 (27–68)	NR	20 (20)/20 (20)	20 (20)/20 (20)	Survival, BL, Biol comp
Donati et al. 2008 (1)	Italy	Three armed	Industry	12	45.45*	23.2%*	50 (50)/57 (57)	49 (49)/55 (55)	Survival, BL, PPD, PI, PAP
Donati et al. 2008 (2)	Italy	Three armed	Industry	12	45.45*	23.2%*	54 (54)/57 (57)	49 (49)/55 (55)	Survival, BL, PPD, PI, PAP
Schincaglia et al. (2008)	Italy	Parallel	NR	12	51.87 (31–75)/49.2 (35–68)	7%/13%	15 (15)/15 (15)	15 (14)/15 (15)	Survival, BL, Tech compl, Biol compl, PPD
Guncu et al. (2008a,b)	Turkey	Split mouth	NR	12	41.09 (30–55)/41.09 (30–55)	0%/0%	12 (12)/12 (12)	12 (11))/12 (12)	Survival, BL, PPD, G infl, PI, IS
De Rouck et al. (2009)	Belgium	Parallel	Self founding	12	55/52	NR	24 (24)/25 (25)	24 (23)/25 (23)	Survival, BL, PPD, G infl, PI, Pat bas, ML
Degidi et al. (2009a)	Italy	Parallel	NR	36	31.5 (18–55)*	NR	30 (30)/30 (30)	30 (30)/30 (30)	Survival, BL, Tech compl, Biol compl, PPD, G infl, PAP, IS
Degidi et al. (2009b)	Italy	Parallel	National and university	60	54 (18–78)*	NR	82 (264)/73 (286)	82 (261)/73 (286)	Survival, BL, Tech compl,
Shibly et al. (2010, 2012)	USA	Parallel	Self and Industry founding	24	NR (25–94)*	NR	30 (30)/30 (30)	26 (26)/29 (28)	Survival, BL, PAP
Danza et al. (2010)	Italy	Parallel	NR	12	NR	0%/0%	23 (20)/22 (20)	23 (20)/22 (20)	Survival, BL, PPD, G infl
Prosper et al. (2010)	Italy	Parallel	NR	60	58.3 (26–72)*	NR	36 (60)/35 (60)	36 (58)/35 (58)	Survival, BL, G infl, PI
den Hartog et al. (2011)	Netherlands	Parallel	Industry	18	38.4 (18–66)/41.1 (18–67)	0%/0%	31 (31)/31 (31)	31 (30)/31 (31)	Survival, BL, PPD, G infl, PI, Pat Bas, ML, PAP
Elsyad et al. (2012)	Egypt	Parallel	NR	36	62.2/64.6	0%/0%	18 (36)/18 (36)	15 (28)/15 (30)	Survival, BL, PPD, G infl, PI, IS
Grandi et al. (2012a,b)	Italy	Multicenter Parallel	NR	12	51.8 (39–65)/55.3 (43–65)	30%/25%	40 (81)/40 (80)	40 (81)/40 (80)	Survival, BL, Tech compl, Biol compl,

Table 1. (Continued)

References	Country	Study design (RCT)	Support	Follow up	Mean age (range) Test/Control *Global	Smoking habit Test/Control *Global	bs patient (implants) Test/Control	Final patient (implants) Test/Control	Study outcomes measured
Margossian et al. 2012 (1)	France	Three armed	NR	24	NR	0%/0%	40 (105)/37 (98)	40 (105)/37 (98)	Survival, BL, Tech compl, IS
Margossian et al. 2012 (2)	France	Three armed	NR	24	NR	0%/0%	40 (104)/37 (98)	40 (97)/37 (98)	Survival, BL, Tech compl, IS
Meloni et al. (2012)	Italy	Split mouth	Industry	12	46 (28–70)/46 (28–70)	NR	20 (20)/20 (20)	20 (20)/20 (20)	Survival, BL, Tech compl, Biol compl, PPD, G infl
Barewal et al. (2012)	USA	Parallel	Industry	36	NR (20–82)*	0%/0%	8 (8)/15 (15)	7 (7)/14 (14)	Survival, BL, IS

(1) and (2) mean that in the same study, two different test groups were compared to the same control group (three armed study).
BL, Bone Level; Tech compl, Technical complications; Biol comp, Biological complications; PPD, Probing pocket depth; G infl, Gingival Inflammation; PI, Plaque index; IS, Implant stability; Pat bas, Patient based outcomes; ML, Mucosal Level; PAP, Papilla index.
*Data for all the sample, not divided by groups

Interventions

The groups were defined according to the loading time after implant placement. Table A1 depicts the data according to the characteristics of the interventions. In the experimental group (immediate loading), different definitions were used, although the most commonly used protocol (17 studies) was implant loading in the same day of implant placement. Other studies placed the prosthesis within 24 h (Testori et al. 2003; Donati et al. 2008; Schincaglia et al. 2008; den Hartog et al. 2011; Meloni et al. 2012), within 2 days (Romeo et al. 2002; Capelli et al. 2010), 3 days (Chiapasco et al. 2001) or 5 days (Tozum et al. 2007) or 7 days (Turkyilmaz & Tumer 2007; Turkyilmaz et al. 2012). The time of loading in the control group also varied among the studies. The majority of the studies (18) loaded the implants between 3 and 4 months after its placement, but different protocols were used in some studies, as loading after 2 months in three investigations (Testori et al. 2003; Capelli et al. 2010; Grandi et al. 2012a,b), after 2–3 months in one study (Cannizzaro et al. 2008b), after 3–6 months in another study (Danza et al. 2010) or after 4–8 months in three studies (Chiapasco et al. 2001; Hall et al. 2007; Degidi et al. 2009a,b).

Type of prostheses

Table A1 also depicts data according to the type of restoration.

Number of missing teeth

All the possible combinations were included. Full edentulous patients were restored with FAPD mandible overdentures in seven studies (Chiapasco et al. 2001; Romeo et al. 2002; Assad et al. 2007; Turkyilmaz & Tumer 2007; Elsyad et al. 2012; Turkyilmaz et al. 2012) and with a fixed FAPD in one study (Cannizzaro et al. 2008b). Single implants were used in 12 studies for replacing any tooth in the maxilla or in the mandible depending on the investigation. Partially edentulous patients were included in seven studies, while one study included both single and partially missing teeth (Capelli et al. 2010) and another included any possible combination (Degidi et al. 2009b).

Fixed or removable restorations

All the prostheses used in the selected studies were fixed except the seven studies reporting FAPD using mandibular overdentures. In the experimental group, all studies used a provisional prosthesis to immediately load the implants, except the seven studies using FAPD mandibular overdentures and one study restoring single mandibular molars with definitive restorations (Guncu et al. 2008b).

Type of occlusion

The most commonly used protocol was to give occlusal contacts in centric relation (19 studies), whereas contacts in centric relation and lateral movements were avoided in nine studies. In one study, occlusal contacts were used for complete edentulous patients, while non-occlusal contacts were used for single or partial restorations (Degidi et al. 2009b). In one study, the type of occlusion used was not reported (Shibly et al. 2010).

Effect of intervention

Main outcome: Implant failure

The mean survival rates were high for both groups (98.2% in the test and 99.6% in the control). In 13 of the 29 included studies (31 comparisons), there was no implant failure in any study group. The remaining studies, except two (Cannizzaro et al. 2008b; Barewal et al. 2012) reported that implant failures were higher in the immediately loaded group (1.9–25%) when compared to the conventionally loaded group (0–6.7%) (Table 2).

The results from the meta-analyses are presented in Table 3. The overall effect of immediately loading resulted in a statistically significant higher risk of implant failure when compared to the conventionally loading [RR = 1.92; 95% CI (1.04; 3.54); $P = 0.036$] (Fig. 2). The subgroup analysis resulted in a higher risk of failure for immediately loaded implants with fixed prosthesis [RR = 1.98; 95% CI (1.02; 3.83); $P = 0.042$] and with metal-ceramic restorations [RR = 3.05; 95% CI (1.18; 7.88); $P = 0.021$]. More risk of failure, although without reaching statistical significance was identified in the immediate loading group for single implant restorations [RR = 2.21; 95% CI (0.95; 5.13); $P = 0.064$] and when using of a provisional restoration [RR = 1.94; 95% CI (0.98; 3.81); $P = 0.053$].

Marginal bone level changes

Measurements of crestal bone level changes were reported in all studies except 3 (Testori et al. 2003; Oh et al. 2006; Cannizzaro et al. 2008b). Most studies used periapical x-rays for assessing the interdental bone levels, except three that used orthopantomographies (Chiapasco et al. 2001; Romeo et al. 2002; Romanos & Nentwig 2006; Chaddad et al. 2008) and one that used CT-scans (Elsyad et al. 2012). When attempting to combine all studies in the meta-analyses, a statistically significant heterogeneity was found (I2 = 59.1%; $P = 0.01$) (data not reported); and therefore, the final meta-analyses included only the studies using periapical x-rays and

Table 2. **Survival rates**

References	Survival test (%)	Survival Control (%)	*P*-value
Chiapasco et al. (2001)	97.5	97.5	>0.05
Romeo et al. (2002)	97.5	97.5	>0.05
Testori et al. (2003)	96.2	98	NR
Oh et al. (2006)	75	100	NR
Romanos & Nentwig (2006)	100	100	>0.05
Turkyilmaz et al. (2006a,b) and Turkyimaz & Tumer (2007)	100	100	>0.05
Turkyilmaz et al. (2006a,b, 2009, 2012)	100	100	>0.05
Assad et al. (2007)	100	100	>0.05
Hall et al. (2007)	92.3	100	>0.05
Capelli et al. (2007, 2008, 2010)	98.1	100	1.0
Tozum et al. (2007)	100	100	>0.05
Cannizzaro et al. (2008a)	100	100	>0.05
Cannizzaro et al. (2008b)	98.9	96.6	>0.05
Crespi et al. (2008)	100	100	>0.05
Donati et al. (2008) (1)	98	100	NR
Donati et al. (2008) (2)	94.2	100	NR
Schincaglia et al. (2008)	93.3	100	NR
Guncu et al. (2008a,b)	91.7	100	NR
De Rouck et al. (2009)	95.8	92	NR
Degidi et al. (2009a)	100	100	>0.05
Degidi et al. (2009b)	98.9	100	0.196
Shibly et al. (2010, 2012)	86.7	93.3	NR
Danza et al. (2010)	100	100	>0.05
Prosper et al. (2010)	96.7	96.7	>0.05
den Hartog et al. (2011)	96.8	100	>0.05
Elsyad et al. (2012)	93.3	100	NR
Grandi et al. (2012a,b)	100	100	>0.05
Margossian et al. (2012) (1)	100	100	>0.05
Margossian et al. (2012) (2)	93.3	100	NR
Meloni et al. (2012)	100	100	>0.05
Barewal et al. (2012)	100	93.3	NR

(1) and (2) mean that in the same study, two different test groups were compared to the same control group (three armed study).

Table 3. **Meta-analyses on implant failure expressed as risk ratio (RR), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n* (excluded)*	RR	95% CI	*P*-value	*I*-squared (%)	*P* value
Overall		18 (13)	1.924	1.044; 3.545	**0.036**	0.0	0.896
Missing teeth	Full	4 (4)	0.924	0.248; 3.447	0.906	0.0	0.557
	Partial	3 (5)	2.159	0.575; 8.112	0.254	12.9	0.317
	Single	10 (3)	2.217	0.956; 5.139	0.064	0.0	0.932
	Any	1 (0)	7.581	0.393; 146.078	0.180	–	–
Occlusion	Occlusal	12 (8)	1.902	0.866; 4.177	0.109	0.0	0.713
	Non-occlusal	4 (5)	1.466	0.387; 5.548	0.573	0.0	0.754
	Variable	1 (0)	7.581	0.393; 146.078	0.180	–	–
	Not reported	1 (0)	2.000	0.396; 10.108	0.402	–	–
Definitive/ provisional	Definitive	4 (4)	1.837	0.435; 7.757	0.408	0.0	0.824
	Provisional	14 (9)	1.943	0.989; 3.817	0.053	0.0	0.752
Fixed/ Removable	Fixed	15 (9)	1.982	1.025; 3.833	**0.042**	0.0	0.808
	Removable	3 (4)	1.606	0.316; 8.162	0.568	0.0	0.676
Material	Resin	3 (4)	1.606	0.316; 8.162	0.568	0.0	0.676
	Metal-ceramic	8 (5)	3.059	1.187; 7.883	**0.021**	0.0	0.861
	Metal ceramic or metal-resin	1 (0)	0.322	0.034; 3.039	0.323	–	–
	Gold-ceramic	2 (0)	5.094	0.589; 44.077	0.139	0.0	0.714
	Full-ceramic	2 (0)	1.310	0.143; 11.965	0.811	0.0	0.473
	Not reported	2 (3)	1.291	0.341; 4.887	0.707	0.0	0.353

*Number of excluded studies due to the absence of implant failure in any of the study groups.
Bold text indicates statistically significant differences.

combining mesial and distal sites (Table 4). This meta-analysis resulted in statistically significant higher bone loss in the control group (conventional loading) [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$] (Fig. 3). This statistical significance was, however, lost when analyzing mesial and distal sites independently.

In the subgroup analyses, in spite of the high heterogeneity shown among studies, a statistically significant higher bone loss was found in control group in studies with: parallel designs [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$], full-arch restorations [WMD = 0.067; 95% CI (0.004; 0.129); $P = 0.037$], partial restorations [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$], in presence of occlusal contacts [WMD = 0.052; 95% CI (0.007; 0.097); $P = 0.025$], in absence of occlusal contacts [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$], when provisional restoration were used for the immediate loading [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$], with fixed prosthesis [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$] and when the type of material for the definitive prosthesis was not reported [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$]. Higher bone loss, although without reaching statistical significance was identified in the conventional loading group for single implants [WMD = 0.136; 95% CI (−0.005; 0.277); $P = 0.059$], for metal-ceramic restorations [WMD = 0.047; 95% CI (−0.001; 0.095); $P = 0.056$] and when metal-ceramic or metal-resin restorations where used [WMD = 0.070; 95% CI (−0.000; 0.140); $P = 0.051$].

Technical complications

Technical complications were reported in 11 studies. The most common were fractures of the provisional restorations, porcelain chipping, and loosening of the abutment/prosthesis. These complications were all solved without affecting the outcome of the implants or the restorations. Three articles reported that there were no technical complications for none of the groups and one article (Degidi et al. 2009b) was excluded from the analysis because the statistical unit was the implant and not the prosthesis.

Results from meta-analyses are reported in Table A2. There were not statistical significant differences between groups for this outcome for the overall studies or for any of the subgroup comparisons [RR = 1.321; 95% IC: 0.842; 2.074); $P = 0.226$].

Biological complications

Biological complications were reported in 12 studies. The most common was progressive bone loss or peri-implant inflammation, which was reported in eight studies, whereas three investigations reported no biological complications, neither for the test nor for the control.

In the multiple meta-analysis performed, no statistical significant differences were found between groups in overall analysis (Table A3) or for any of the subgroup comparisons [RR = 1.094; 95% IC (0.488; 2.453); $P = 0.826$].

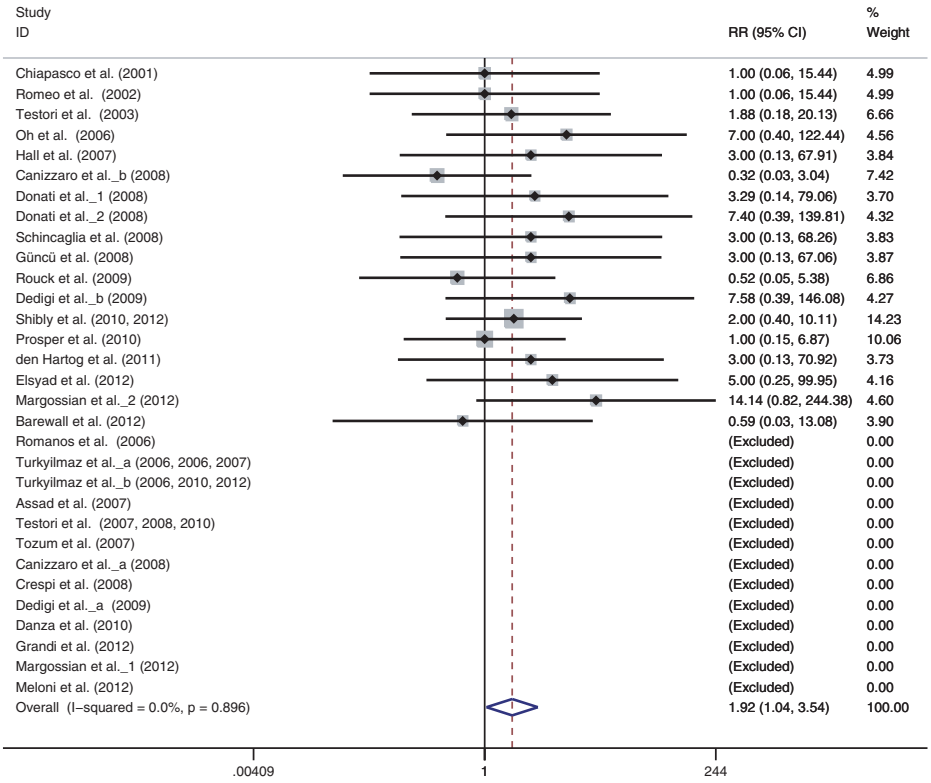

Fig. 2. Forest plots of individual studies on failure risk.

Table 4. **Meta-analyses on bone level changes expressed as weighted mean difference (WMD), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n*	WMD	95% CI	*P*-value	I^2 (%)	*P* value
Overall		14	0.046	0.043; 0.049	**0.000**	39.4	0.065
Overall (only mesial)		7	0.042	−0.072; 0.156	0.472	0.0	0.591
Overall (only distal)		7	0.086	−0.023; 0.195	0.122	0.0	0.959
Missing teeth	Full	4	0.067	0.004; 0.129	**0.037**	0.0	0.930
	Partial	4	0.046	0.043; 0.049	**0.000**	76.8	**0.005**
	Single	5	0.136	−0.005; 0.277	0.059	33.7	0.196
	Single and Partial	1	0.060	−0.142; 0.262	0.58	–	–
Occlusion	Occlusal	9	0.052	0.007; 0.097	**0.025**	60.8	**0.009**
	Non-occlusal	5	0.046	0.043; 0.049	**0.000**	0.0	0.910
Definitive/ provisional	Definitive	4	0.088	−0.037; 0.212	0.168	0.0	0.663
	Provisional	10	0.046	0.043; 0.049	**0.000**	53.7	**0.022**
Fixed/Removable	Fixed	11	0.046	0.043; 0.049	**0.000**	52.4	**0.021**
	Removable	3	0.054	−0.084; 0.193	0.440	0.0	0.815
Material	Resin	3	0.054	−0.084; 0.193	0.440	0.0	0.815
	Metal-ceramic	7	0.047	−0.001; 0.095	**0.056**	69.6	**0.003**
	Metal ceramic or metal-resin	1	0.070	−0.000; 0.140	0.051	–	–
	Full-ceramic	1	−0.010	−0.306; 0.286	0.947	–	–
	Not reported	2	0.046	0.043; 0.049	**0.000**	0.0	0.400

Only periapical radiographs included.
Positive results: control group had more bone loss than test groups.
Bold text indicates statistically significant differences.

Probing pocket depth

Regarding peri-implant health, PPD was recorded in 15 studies, although the data pooled in the meta-analysis were not possible in four studies due to how data were reported (e.g., data expressed in figures or mean and standard deviation by site) (Chiapasco et al. 2001; Assad et al. 2007; Donati et al. 2008; Danza et al. 2010). Moreover, there was no consistency on when the baseline visit was considered, which varied from the time of loading, to 1 year after loading. The mean changes in PPD in the test group were 0.1 mm with a range from −0.62 to 0.73 mm. The standard deviations (SD) also ranged from 0.37 to 0.89 mm. The mean changes in the control group were also 0.1 mm with a range from −0.49 (decrease in PPD) to 0.56 mm. The SD in this group ranged from 0.38 to 0.99 mm.

Results from meta-analyses are reported in Table A4. In the overall analyses, results revealed that the increase in PPD was greater in the control group, but without reaching statistical significance [WMD = −0.046; 95% CI (−0.166; 0.075); $P = 0.458$]. None of the subgroup analysis showed significant differences between groups.

Gingival inflammation

Mucosal inflammation was reported in 13 studies although the data of one study could not be used since it only reported median values and ranges (Chiapasco et al. 2001). Reporting mucosal inflammation was not consistent and four different indexes were used: modified bleeding index by Mombelli et al. (1987) (Romeo et al. 2002; Oh et al. 2006; den Hartog et al. 2011; Meloni et al. 2012), sulcus bleeding index by Muhlemann & Son (1971) (Romanos & Nentwig 2006; Turkyilmaz et al. 2012), gingival index by Loe & Silness (1963) (Guncu et al. 2008b; Elsyad et al. 2012) and percentage of sites with positive bleeding on probing (BOP) (De Rouck et al. 2009; Degidi et al. 2009a; Danza et al. 2010; Prosper et al. 2010). Due to these differences the meta-analysis was performed for the studies that used the same index but without doing any subgroup analysis (Table A5).

For the modified bleeding index (Mombelli et al. 1987), there was an improvement for both groups and the mean change varied from −0.09 to −0.43 in the test and from −0.15 to −0.55 in the control. The meta-analysis showed that there were not statistical significant differences between groups [WMD = −0.000; 95% CI (−0.226; 0.225); $P = 0.997$].

For the sulcus bleeding index (Muhlemann & Son 1971), there was a slight increase in gingival inflammation, which varied from 0 to 0.08 in the test and from 0.16 to 0.2 in the control. The meta-analysis showed that the increase was higher in the control group but without statistical significant differences [WMD = −0.163; 95% CI (−0.416; 0.090); $P = 0.208$].

For the gingival index (Loe & Silness 1963), in spite of the high heterogeneity among studies, the test group showed a mean change that varied from −0.34 to 0.62, whereas the control group showed an improvement that varied from −0.36 to −1.05. This difference was not statistical significant according to the

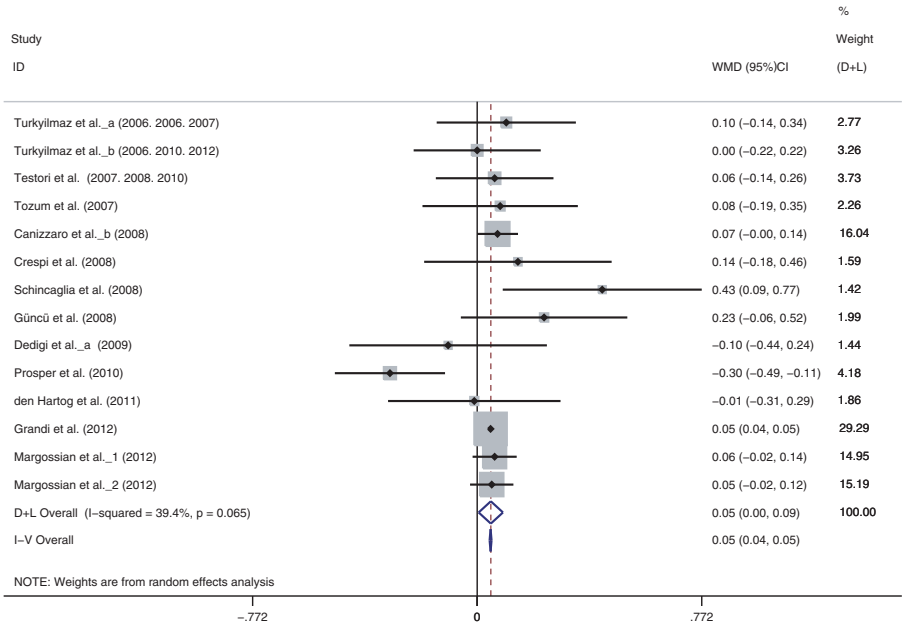

Fig. 3. Forest plots of bone level changes for individual studies.

meta-analysis [WMD = 0.838; 95% CI (−0.779; 2.455); $P = 0.310$].

Finally, in the case of BOP (%), there was a statistical higher increase in the control group [WMD = −1.999; 95% CI (−2.405; −1.593); $P = 0.000$].

The forest plot for each index is presented in Fig. A1.

Plaque index

Regarding plaque accumulation 13 studies reported it, but the data for the change in plaque scores could only be obtained from 10 investigations since in one study only median values were reported (Chiapasco et al. 2001) in another study only figures were used (Assad et al. 2007) and in another study it was reported by site (Donati et al. 2008). Similarly, due to the lack of consistency in how this parameter was assessed, three different indexes were used: modified plaque index by Mombelli et al. (1987; Romeo et al. 2002; Oh et al. 2006; Hall et al. 2007; Prosper et al. 2010; den Hartog et al. 2011; Elsyad et al. 2012), plaque index by Silness & Loe (1964; Romanos & Nentwig 2006; Guncu et al. 2008b; Turkyilmaz et al. 2012) and percentage of sites with presence of plaque (De Rouck et al. 2009). Meta-analysis was performed for the studies that used the same index but without doing any subgroup analysis (Table A5).

For the modified plaque index (Mombelli et al. 1987), the mean change in the test varied from −0.17 to 4 and in the control from −0.48 to 1. The meta-analysis, with high heterogeneity among studies, showed that there was a higher increase in the test but without statistical significant differences [WMD = 0.632; 95% CI (−0.186; 1.449); $P = 0.130$]. For the plaque index (Silness & Loe 1964) the mean change varied from −0.51 (decrease) to 0.12 in the test and from −0.32 to 0.6 in the control. There was a higher increase in this outcome in the control group without statistical significant differences [WMD = −0.302; 95% CI (−0.779; 0.175); $P = 0.214$]. In the case of percentage of sites with plaque, meta-analysis could not be performed, as only one study used that index. The mean change in this variable was 0% in the test and 2% in the control.

The forest plot for each index is presented in Fig. A2.

Soft tissue status

Regarding soft tissue alterations, the mucosal level was only registered in five studies, using a manual periodontal probe in three of them (Oh et al. 2006; Capelli et al. 2010; den Hartog et al. 2011), a manual periodontal probe with an acrylic stent in one investigation (De Rouck et al. 2009) and a calliper to measure cast models in another (Capelli et al. 2010). The changes varied from a gain of 0.06 to a loss of 0.67 in the test and from a gain of 0.09 to a loss of 0.67 in the control. The mean change did not exceed 1 mm and no meta-analysis was performed for this outcome due to the big heterogeneity in the way this parameter was reported.

For assessing the level of the interproximal papilla two methods were used: the Jemt index (Jemt 1997) in five publications (Oh et al. 2006; Hall et al. 2007; Degidi et al. 2009a; Shibly et al. 2010; den Hartog et al. 2011) and the changes in height in millimeters (Donati et al. 2008). When the Jemt index was used the change in the test group ranged from −0.31 to 0.8 and in the control from −0.11 to 0.3. When assessed by changes in papilla height in millimeters there was gain that ranged from −0.24 to −0.32 mm in the test and of −0.53 mm in the control. No meta-analysis was performed due to the high heterogeneity on how it was reported.

Implant stability quotient

Changes in implant stability were assessed by two methods: the Periotest® device (Chiapasco et al. 2001; Romeo et al. 2002; Romanos & Nentwig 2006; Elsyad et al. 2012) and resonance frequency analysis using the Ostell® device (Testori et al. 2003; Tozum et al. 2007; Turkyilmaz & Tumer 2007; Cannizzaro et al. 2008a,b; Guncu et al. 2008b; Degidi et al. 2009a; Margossian et al. 2012; Turkyilmaz et al. 2012). One article reported data for the Ostell® but it could not be used in the meta-analysis since the data were only reported as figures (Barewal et al. 2012).

From the studies using Periotest® meta-analysis could not be performed since two studies reported only medians and ranges (Chiapasco et al. 2001; Romanos & Nentwig 2006) while the other reported means and standard deviations (Romeo et al. 2002; Elsyad et al. 2012). In all the cases, there was a decrease in the Periotest® values in both groups.

In the studies reporting ISQ values measured with the Ostell® device the mean change varied from −2.6 to 7.6 in the test and from −2.8 to 5.7 in the control group. The meta-analysis results are reported in Table 5. In the overall evaluation, the change in ISQ values was significantly higher in the control than in the test group [WMD = −1.096; 95% CI (−1.615; −0.577); $P = 0.000$]. The forest plots are represented in Fig. A3. In the subggroup analysis, similar significant outcomes occurred in the studies with parallel designs [WMD = −1.098; 95% CI (−1.617; −0.579); $P = 0.000$], for full arch restorations [WMD = −1.032; 95% CI (−1.585; −0.480); $P = 0.000$], for partial restorations [WMD = −1.632; 95% CI (−3.145; −0.102); $P = 0.037$], for occlusal contacts [WMD = −1.187; 95% CI (−1.720; −0.655); $P = 0.000$], for provisional restorations when performing the immediate loading [WMD = −1.133; 95% CI (−1.615; −0.609); $P = 0.000$], for fixed prosthesis [WMD = −1.130; 95% CI (−1.654; −0.607); $P = 0.000$], for metal−ceramic restorations [WMD = −1.599; 95% CI (−3.113; −0.085); $P = 0.038$] and for metal-ceramic or metal-resin as final prosthesis material

Table 5. **Meta-analyses on ISQ values expressed as weighted mean difference (WMD), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n*	WMD	95% CI	*P*-value	*I*-squared (%)	*P* value
Overall		8	−1.096	−1.615; −0.577	**0.000**	8.6	0.364
Missing teeth	Full	4	−1.032	−1.585; −0.480	**0.000**	0.0	0.829
	Partial	2	−1.632	−3.145; −0.102	**0.037**	83.5	**0.014**
	Single	2	1.240	−9.781; 12.261	0.825	0.0	0.917
Occlusion	Occlusal	6	−1.187	−1.720; −0.655	**0.000**	7.2	0.370
	Non-occlusal	2	0.625	−1.685; 2.936	0.596	0.0	0.879
Definitive/ provisional	Definitive	4	0.687	−2.956; 4.329	0.712	0.0	0.995
	Provisional	4	−1.133	−1.657; −0.609	**0.000**	54.9	0.084
Fixed/Removable	Fixed	5	−1.130	**−1.654; −0.607**	**0.000**	40.4	0.152
	Removable	3	0.685	−3.074; 4.444	0.721	0.0	0.967
Material	Resin	3	0.685	−3.074; 4.444	0.721	0.0	0.967
	Metal-ceramic	3	−1.599	−3.113; −0.085	**0.038**	67.6	**0.046**
	Metal-ceramic or Metal-resin	1	−1.070	−1.629; −0.511	**0.000**	–	–
	Not reported	1	1.900	−14.700; 18.500	0.822	–	–

ISQ, only for studies using Ostell.
Test-control. Negative value: control greater ISQ increase than test.
Bold text indicates statistically significant differences.

[WMD = −1.070; 95% CI (−1.629; −0.511); P = 0.000].

Patient-related outcomes

Patient related outcomes were evaluated in five studies. Four of them registered the general, function and/or aesthetic satisfaction (Oh et al. 2006; Cannizzaro et al. 2008b; De Rouck et al. 2009; den Hartog et al. 2011) and one the pain, edema, and medication after the treatment (Cannizzaro et al. 2008a). No meta-analysis was performed for this outcome due to the high heterogeneity in how it was reported. Nevertheless, patients preferred immediate loading rather than the conventional loading in terms of general and aesthetic satisfaction as well as in regards to post-operative outcomes, such as pain, edema or the need of medication.

Quality assessment

From the 29 investigations, only five were considered to have a low risk of bias (Cannizzaro et al. 2008a,b; Danza et al. 2010; den Hartog et al. 2011; Meloni et al. 2012) and eight a moderate risk of bias (Donati et al. 2008; Guncu et al. 2008b; De Rouck et al. 2009; Degidi et al. 2009a; Capelli et al. 2010; Shibly et al. 2010; den Hartog et al. 2011; Elsyad et al. 2012). The remaining articles were in a high risk of bias (Table 6).

Discussion

Immediate implant loading protocols have been proposed to reduce the time interval between implant surgery and the delivery of the prosthetic rehabilitation with the objective of improving patient comfort and satisfaction. These protocols, however, are not

Table 6. **Quality assessment of selected studies**

References	Sequence Generation	Allocation Concealment	Blinding (single, double)	Reasons for drop out clearly specified	Free of selective reporting?	Free of other bias?	Risk of bias
Chiapasco et al. (2001)	NR	NR	NR	Yes	Yes	Yes	High
Romeo et al. (2002)	NR	NR	NR	Yes	Yes	Yes	High
Testori et al. (2003)	NR	NR	NR	Yes	Yes	Yes	High
Oh et al. (2006)	NR	NR	Single	Yes	Yes	Yes	High
Romanos & Nentwig (2006)	NR	NR	NR	Yes	Yes	Yes	High
Turkyilmaz et al. (2006a,b) and Turkyimaz & Tumer (2007)	NR	NR	NR	Yes	Yes	Yes	High
Turkyilmaz et al. (2006a,b, 2010, 2012)	Yes	NR	NR	Yes	Yes	Yes	High
Assad et al. (2007)	NR	NR	NR	Yes	Yes	Yes	High
Hall et al. (2007)	NR	Yes	NR	Yes	Yes	Yes	High
Capelli et al. (2007, 2008, 2010)	Yes	Yes	No	Yes	Yes	Yes	Moderate
Tozum et al. (2007)	NR	NR	NR	Yes	Yes	Yes	High
Cannizzaro et al. (2008a)	Yes	Yes	Double	Yes	Yes	Yes	Low
Cannizzaro et al. (2008b)	Yes	Yes	Double	Yes	Yes	Yes	Low
Crespi et al. (2008)	NR	NR	NR	Yes	Yes	Yes	High
Donati et al. (2008) (1)	Yes	NR	Single	Yes	Yes	Yes	Moderate
Donati et al. (2008) (2)	Yes	NR	Single	Yes	Yes	Yes	Moderate
Schincaglia et al. (2008)	Yes	NR	Single	Yes	Yes	Yes	Moderate
Guncu et al. (2008a,b)	Yes	Yes	NR	Yes	Yes	Yes	Moderate
De Rouck et al. (2009)	Yes	NR	Single	Yes	Yes	Yes	Moderate
Degidi et al. (2009a)	Yes	Yes	NR	Yes	Yes	Yes	Moderate
Degidi et al. (2009b)	NR	NR	NR	Yes	Yes	Yes	High
Shibly et al. (2010, 2012)	Yes	NR	Double	Yes	Yes	Yes	Moderate
Danza et al. (2010)	Yes	Yes	Double	Yes	Yes	Yes	Low
Prosper et al. (2010)	NR	NR	NR	Yes	Yes	Yes	High
den Hartog et al. (2011)	Yes	Yes	Single	Yes	Yes	Yes	Low
Elsyad et al. (2012)	Yes	NR	Single	Yes	Yes	Yes	Moderate
Grandi et al. (2012a,b)	NR	NR	NR	Yes	Yes	Yes	High
Margossian et al. (2012) (1)	NR	Yes	NR	Yes	Yes	Yes	High
Margossian et al. (2012) (2)	NR	Yes	NR	Yes	Yes	Yes	High
Meloni et al. (2012)	Yes	Yes	Single	Yes	Yes	Yes	Low
Barewal et al. (2012)	Yes	NR	Single	No	Yes	Yes	High

(1) and (2) mean that in the same study, two different test groups were compared to the same control group (three armed study).

used frequently by most clinicians and for all clinical indications, due to uncertainty whether similar outcomes can be achieved when compared with the standard loading protocols. It is, therefore, important to understand the risks and possible deleterious effects of this therapeutic implant strategy. This systematic review, based on 37 publications reporting results from 29 different RCTs comparing immediate versus conventional loading protocols and evaluating data from 1365 patients with a total of 2669 implants, was aimed to assess the scientific evidence behind this treatment protocol. The results from the meta-analyses have shown that the immediate loaded implants, when compared to conventionally loaded implants attained high survival rates in both groups (98.2% in the test and 99.6% in the control) and in fact, in 13 out of the 29 included studies (31 comparisons) no implant failure was reported in any of the study groups. Immediately loaded implants, however, demonstrated a statistically significant higher risk of implant failure [RR = 1.92; 95% CI (1.04; 3.54); $P = 0.036$], a statistically significant lower bone loss [WMD = 0.046; 95% CI (0.043; 0.049); $P = 0.000$] and a smaller increase in ISQ values [WMD = −1.096; 95% CI (−1.615; −0.577); $P < 0.001$] when compared with implants under conventional loading. With both interventions the advent of technical and biological complications, as well as the peri-implant health status (PPD, gingival inflammation and plaque levels) were similar.

These results are, however, not in full agreement with those recently published in a similar systematic review that reported similar survival and success rates for implants immediately loaded when compared to those conventionally or early loaded (Esposito et al. 2013; Stafford 2013). These discrepancies can be explained since in the present review only studies directly comparing immediate to conventional loading were included, thus excluding studies including early loading protocols. Likewise, this systematic review analyzed publications with a minimum follow-up time of 6 months and a maximum of 84 months, and whenever possible the longest follow-up period was chosen to assess the rate of events such as biological or technical complications. The Cochrane systematic review (Esposito et al. 2013) only included studies with a follow-up of 4 to 12 months on the basis that this time was considered enough to detect implant and/or prosthesis failure.

Although recently published reviews have also focused on the impact of immediate loading on selected prosthesis designs and clinical indications (Knoernschild 2012; Goiato et al. 2013; Papaspyridakos et al. 2013), to our knowledge, this is the first systematic review addressing the impact of different indications and types of restorations in regards to the outcome of immediate loading protocols. We have assessed the possible influence depending on the extent of the restoration (full-arch, partial or single tooth prosthesis), the type of restoration (provisional or definitive), the type of loading (occlusal or non-occlusal) and the material used to fabricate the final restoration. In regards to the *extent*, when evaluating the results of immediately loaded implants in comparison to conventionally loaded implants, single teeth implants seem to be in greater risk of failure, when compared to immediately loaded full arch restorations in fully edentulous patients (RR = 2 vs. 0.9). There is also more crestal bone loss for single restorations (WMD:0.14 mm vs. 0.06 mm) and a greater increase in ISQs values over time (1.24 vs. −1.02). Similarly, partially edentulous restorations had greater risk of implant failure when compared to fully edentulous (RR = 2.15 vs. 0.92). These outcomes are also different from those reported in a recent publication, which did not find significant differences regarding implant survival and marginal bone level changes when immediately loaded single implants in the esthetic zone were compared with conventionally loaded implants (Knoernschild 2012). The better results in the full arch restorations reported in this review can be explained by the cross-arch stabilization attained in this prosthesis, what may limit the extent of micromotion at the bone-implant interface during healing. In single tooth and short span bridges occlusal forces may impact directly with the implant and hence be more susceptible to implant failure. This fact may also explain why there is greater bone loss and greater ISQ values change in the single tooth restorations.

When analyzing the outcome of immediately loaded implants in comparison to conventionally loaded implants in regards to the *type of loading* (occlusal versus non-occlusal contacts) provided at the time of restoration delivery (within one week after implant placement), the occlusal pattern resulted in a slight greater risk of implant failure (RR = 1.9 vs. 1.4) and smaller change in ISQs values (WMD = 0.625 vs. −1.187) than the non-occlusal pattern. These results indicate that in presence of occlusal contacts there is a slight increase in the risk of implant failure but at the same time the change in ISQs values over time is reduced. These outcomes should be expected since the presence of occlussal contacts may lead to micromotion at the bone-implant interface if not adequately controlled and ultimately cause fibrous encapsulation. The outcomes presented evaluating the impact of occlusal contacts on ISQ values, however, are not in agreement with the results from experimental animal studies reporting increased bone apposition on the implant surface and increase the bone to implant contact when subjected to active loading (Nkenke et al. 2005; Barros et al. 2009; Degidi et al. 2009a,b,c). These potential histological advantages, however, do not always translate to improved clinical outcomes. In fact, several clinical trials have attempted to evaluate the impact of occlusal versus non-occlusal immediate loading. No definitive conclusion as to the most effective method of loading could be established (Cannizzaro et al. 2010; Margossian et al. 2012; Vogl et al. 2013).

When assessing the impact of the *prosthesic design* the risk of implant failure was similar when comparing definitive and provisional restorations (RR = 1.8 vs. 1.9) and when comparing fixed and removable restorations (RR = 1.9 vs. 1.6). In regards to the *material* in which the prosthesis was fabricated, the RR for metal-ceramic (3.05) and gold-ceramic (5.09) was higher when compared to resin (1.6) and full ceramic (1.3). Similarly, greater increases in ISQ values were found for the immediately loaded implants using a definitive prosthesis (WMD = 0.687 vs. −1.133), a removable prosthesis (WMD = 0.685 vs. −1.139) and resin material when compared to those using metal-ceramic prosthesis (WMD = 0.685 vs. −1.59). No relevant differences were found when assessing the impact of the prosthesis design and material of fabrication on the changes in bone crestal levels. The overall evaluation seems to indicate that the best results using immediately loaded implants are attained when using removable resin definitive prosthesis. The studies that reported on this type of prosthesis design all used mandibular overdentures (Chiapasco et al. 2001; Romeo et al. 2002; Tozum et al. 2007; Turkyilmaz & Tumer 2007; Elsyad et al. 2012; Turkyilmaz et al. 2012). In this indication, implants were placed in the interforaminal region where bone quality and quantity is often optimal, what has a direct impact on the primary stability of the implants (Yoon et al. 2011). In fact, different authors have identified the initial implant

stability, as a key factor for success with immediately loaded implants, since this stability will allow the withstand of occlusal forces during the early phases of healing without causing a significant alteration of the osseointegration process (Javed & Romanos 2010). From the publications analyzed, however, it was not possible to identify a minimum insertion torque or ISQ value required for immediate loading. The majority of the publications reported that the minimum implant stability accepted for inclusion were insertion torque values ranging from 20 Ncm (Donati et al. 2008; Schincaglia et al. 2008) to 48 Ncm (Cannizzaro et al. 2008b). Most studies utilized 30–35 Ncm as the minimum insertion torque (Grandi et al. 2012a,b; Margossian et al. 2012; Meloni et al. 2012). Other studies also used ISQ values to asses not only the implant rotational stability (insertion torque) but also the axial stability. These studies established a minimum value of 60 ISQ (Guncu et al. 2008b; Degidi et al. 2009a; Margossian et al. 2012).

The clinical applicability of the evidence reported in this systematic review must be interpreted with caution. The data were extracted from 29 publications from which, only five were judged to have a low risk of bias. Moreover, due to the absence of any implant failure in both studied groups, 13 studies were excluded from the meta-analysis to assess the risk for implant failure. This fact may overestimate the risk of using immediately loaded implants when considering this primary outcome variable, but it also needs to be appreciated the high survival rates attained (98.2%), which were similar when compared to the conventional loading protocol (99.6%). With respect to the analyzed secondary outcomes; the overall WMD for the changes in crestal bone levels, was in both groups inferior to 0.05 mm, which may be too small to be considered clinically relevant. Similarly, the WMD for ISQ value changes, although statistically significant for some prosthesis designs, were also clinically irrelevant.

Unfortunately, this systematic review failed to answer one relevant question, what is the influence of implant stability on the outcome of this protocol, since most of the studies did not report data on the initial stability of the failed implants. Similarly, no analysis could be performed to assess whether there is a minimum insertion torque needed to perform successful immediate loading. There is therefore, a need to conduct well designed clinical trials addressing these questions.

In conclusion, the results from this systematic review and meta-analysis have shown that immediate loading may impose a greater risk for implant failure when compared to conventional loading, although the survival rates were high for both groups. Immediately loaded implants demonstrated less crestal bone resorption during healing and a similar impact on peri-implant soft tissues, as well as advent of biological and technical complications, when compared to delayed loaded implants, what indicates that once osseointegration has occurred both treatment protocols behaved similarly. Immediately placed implants, however, showed a clear advantage in terms of patient's preference, due to improved function and comfort.

Conflict of interest – source of founding

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Appendix 1

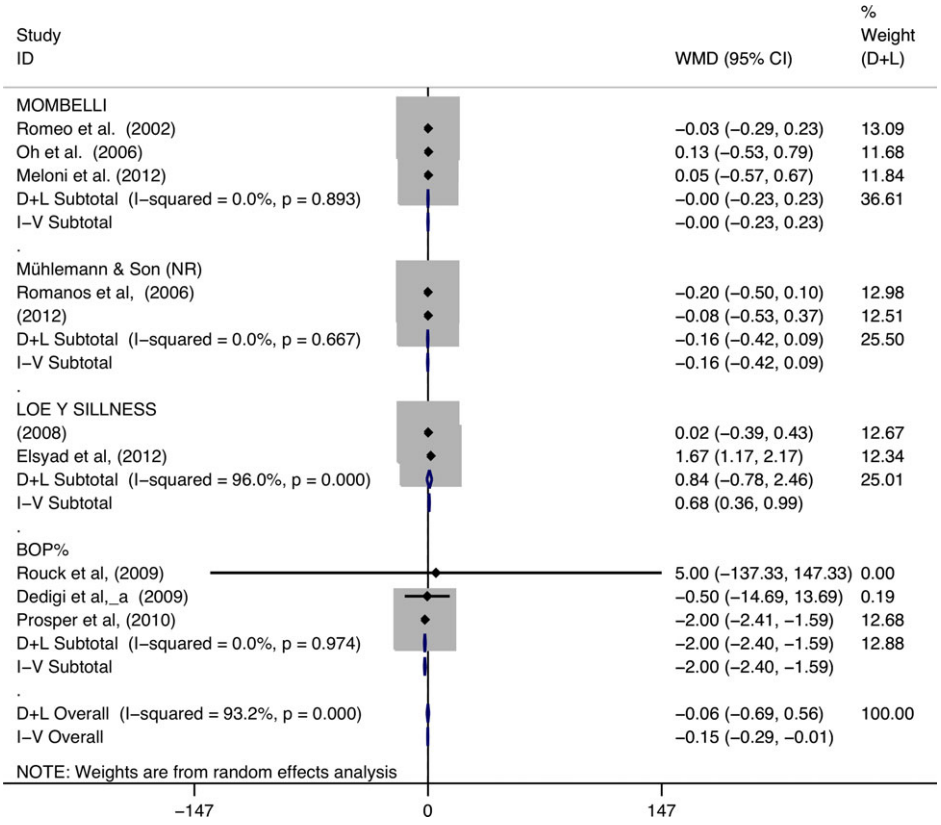

Fig. A1. Forest plot on individual studies for changes in gingival inflammation.

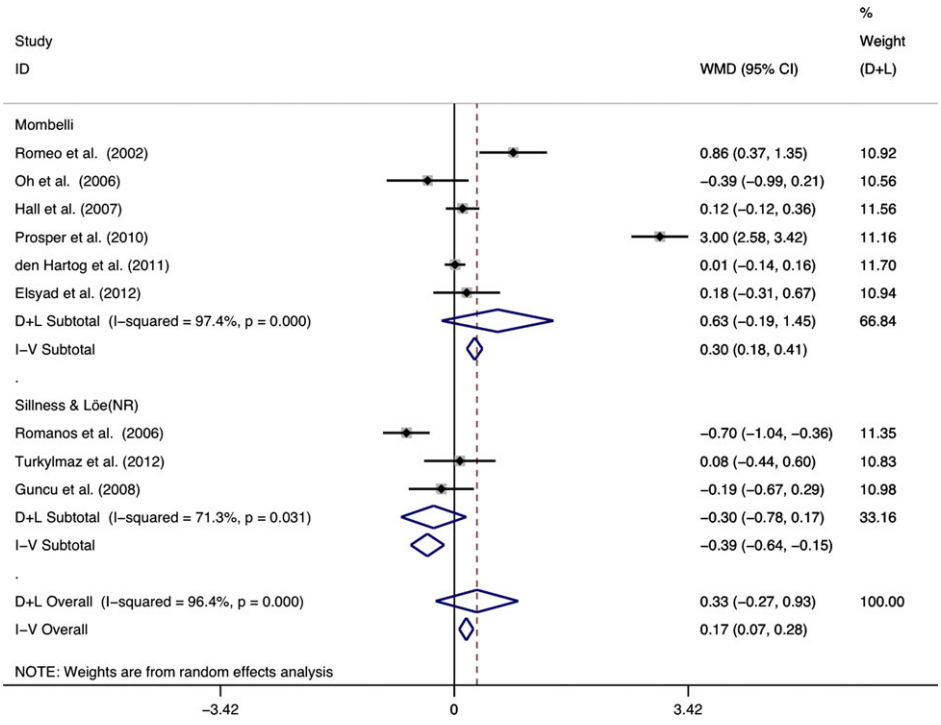

Fig. A2. Forrest plot on individual studies for changes in plaque index.

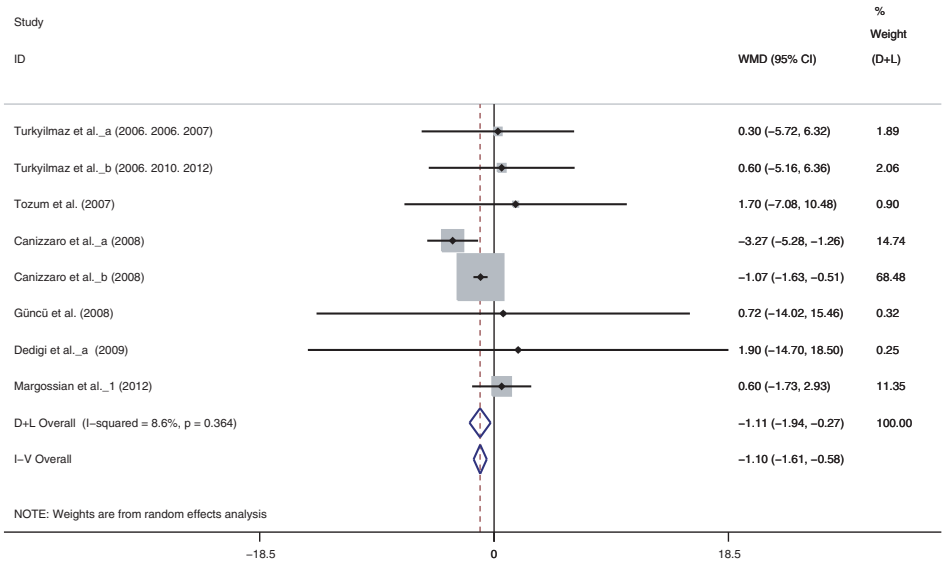

Fig. A3. Forest plot on individual studies for changes in ISQs values.

Table A1. **Definition of group and prosthetic characteristics**

References	Definition test	Definition control	Type of implants	Number of missing teeth	Position of implants	Occlusal/non occlusal in test	Definitive or provisional test	Fixed or removable	Definitive prosthesis (material)
Chiapasco et al. (2001)	Immediate (3 days)	Conventional (4–8 months)	Ti Unite MKIII, Nobel Biocare	Full	Mandible Interforaminal	Occlusal	Definitive	Removable	Resin, Bar supported Overdenture
Romeo et al. (2002)	Immediate (2 days)	Conventional (3–4 months)	Straumann SP	Full	Mandible Interforaminal	Occlusal	Definitive	Removable	Resin, Bar supported Overdenture
Testori et al. (2003)	Immediate (24 h)	Early loaded (2 months)	Osseotite and Osseotite NT (cylindrical and tapered)	Partial	Mandible and Maxilla anterior and posterior	Non occlusal	Provisional	Fixed	Metal resin
Oh et al. (2006)	Immediate (same day)	Delayed (4 months)	TSV Zimmer	Single tooth	Single tooth premaxilla	Occlusal	Provisional	Fixed	Metal Ceramic
Romanos and Nentwig (2006)	Immediate (same day)	Conventional (3 months)	Ankylos Implants	Partially	Posterior Mandible	Occlusal	Provisional	Fixed	Metal Ceramic
Turkyilmaz et al. (2006a,b) and Turkyimaz & Tumer (2007)	Immediate (1 week)	Delayed (3 months)	Ti Unite MKIII, Nobel Biocare	Full Lower	Interforminal	Occlusal	Definitive	Removable	Resin
Turkyilmaz et al. (2006a,b, 2010, 2012)	Immediate (1 week)	Delayed (3 months)	Ti Unite MKIII, Nobel Biocare	Full Lower	Interforminal	Occlusal	Definitive	Removable	Resin
Assad et al. (2007)	Immediate (same day)	Conventional (4 months)	Paragon dental implants; Core-Vent Corporation	Full Lower	Interforaminal	Occlusal	Definitive	Removable	Resin
Hall et al. (2007)	Immediate (same day)	Conventional (6.5 months)	Tapered Southern Implants	Single	Single tooth 15–25	Non occlusal	Provisional	Fixed	Metal ceramic
Capelli et al. (2007, 2008, 2010)	Immediate (2 days)	Early loaded (2 months)	3i Osseotite Tapered FNT Implants	Single and Partially edentulous upper and lower	Upper and lower	Non occlusal	Provisional	Fixed	Metal Ceramic
Tozum et al. (2007)	Immediate (5 days)	Delayed loaded (3 months)	Ti Unite MKIII, Nobel Biocare	Full Lower	Interforminal	Occlusal	Definitive	Removable	Resin
Cannizzaro et al. (2008a)	Immediate (same day)	Delayed (3 months mandible, 4 months maxillae)	Zimmer Tapered SP	Partial	Partially edentulous (maxilla or mandible)	Occlusal	Provisional	Fixed	Metal ceramic
Cannizzaro et al. (2008b)	Immediate (same day)	Delayed (2–3 months)	Zimmer Tapered SP	Full	Maxillary Full Arch	Occlusal (Reduced Occlusal surface, no cantilevers)	Provisional	Fixed	Metal-Ceramic (73%T, 40%C) or Metal-R esin (27%T, 60%C)
Crespi et al. (2008)	Immediate (same day)	Delayed (3 months)	Outlink, Sweden & Martina	Single	Maxillary Incisor, Maxillary Canine, Maxillary Premolar	Occlusal	Provisional	Fixed	Metal Ceramic
Donati et al. (2008) (1)	Immediate (24 h)	Delayed (3 months)	Osseospeed Astra Tech	Single	15–25 and 35–45	Occlusal	Provisional	Fixed	Gold Ceramic
Donati et al. (2008) (2)	Osteotomes Immediate (24 h)	Delayed (3 months)	Osseospeed Astra Tech	Single	15–25 and 35–45	Occlusal	Provisional	Fixed	Gold Ceramic
Schincaglia et al. (2008)	Immediate (24 h)	3–4 months	Ti Unite MKIII, Nobel Biocare	Single	Mandibular molar	Occlusal	Provisional	Fixed	Metal Ceramic
Guncu et al. (2008a,b)	Immediate (1 week)	3 months	Ti Unite MKIII, Nobel Biocare	Single (bilateral)	Mandibular molar	Occlusal	Definitive	Fixed	Metal Ceramic

Table A1. (Continued)

References	Definition test	Definition control	Type of implants	Number of missing teeth	Position of implants	Occlusal/non occlusal in test	Definitive or provisional test	Fixed or removable	Definitive prosthesis (material)
De Rouck et al. (2009)	Immediate implant+immediate restoration (same day)	2 stage surgery at 3 months	Ti Unite Replace, Nobel Biocare	Single	Single implant (15–25)	Non occlusal	Provisional	Fixed	NR
Degidi et al. (2009a)	Immediate (same day)	5 months	Xive Plus. Dentsply	Single	Single Implant (12 or 22)	Non occlusal	Provisional	Fixed	NR
Degidi et al. (2009b)	Immediate (same day)	6 months	Biohorizons	Any combinations	All combinations: single to full arch	Non occlusal for partial edentulous and occlusal for full edentulous	Provisional	Fixed	Metal Ceramic
Shibly et al. (2010, 2012)	Immediate (same day)	3 months	Groovy Replace tapered, Nobel Biocare	Single	Any single site	NR	Provisional	Fixed	NR
Danza et al. (2010)	Immediate (same day)	3–6 months	Alpha bio	Partial (1–3)	Posterior maxilla and mandible (1–3 implants)	Occlusal	Provisional	Fixed	NR
Prosper et al. (2010)	Immediate (same day)	3 months	Bioactive covering winsix (6.5 y 7.5 diameter)	Partial (1–2)	Mandibular molars	Occlusal	Provisional	Fixed	Metal Ceramic
den Hartog et al. (2011)	Immediate (24 h)	3 months	Groovy Replace tapered, Nobel Biocare	Single	Anterior maxilla (14–24)	Non occlusal	Provisional	Fixed	Full ceramic
Elsyad et al. (2012)	Immediate (same day)	3 months	Implant direct scre plant	Full	Mandibular overdenture	Occlusal	Definitive	Removable	Resin
Grandi et al. (2012a,b)	Immediate (same day)	2 months (1 stage)	NR	Partial	Fixed partial in maxilla and mandible	Non occlusal	Provisional	Fixed	NR
Margossian et al. (2012) (1)	Immediate (same day)	4 months	3i fullosseotite certain	Partial	Partial edentulism in the mandible	Non occlusal	Provisional	Fixed	Metal Ceramic
Margossian et al. (2012) (2)	Immediate (same day)	4 months	3i fullosseotite certain	Partial	Partial edentulism in the mandible	Occlusal	Provisional	Fixed	Metal Ceramic
Meloni et al. (2012)	Immediate (24 h)	3–4 months	Groovy Replace tapered, Nobel Biocare	Single (bilateral)	Single implant mandibular molar	Non occlusal	Provisional	Fixed	Metal Ceramic or full ceramic
Barewal et al. (2012)	Immediate (same day)	3 months	Astra osseospeed	Single	Single mandibular or maxillar implant	Occlusal	Provisional	Fixed	Full ceramic

(1) and (2) mean that in the same study, two different test groups were compared to the same control group (three armed study).

Table A2. **Meta-analyses on technical complications expressed as risk ratio (RR), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n* (excluded)*	RR	95% CI	*P*-value	*I*-squared (%)	*P* value
Overall		8 (3)	1.321	0.842; 2.074	0.226	0.0	0.917
Study design	Parallel	7 (3)	1.344	0.845; 2.140	0.212	0.0	0.864
	Split mouth	1 (0)	1.000	0.156; 6.420	1.000	–	–
Missing teeth	Full	2 (0)	1.314	0.779; 2.216	0.306	0.0	0.920
	Partial	3 (2)	1.626	0.507; 5.209	0.413	0.0	0.860
	Single	3 (1)	1.020	0.254; 4.103	0.978	3.0	0.917
Occlusion	Occlusal	4 (2)	1.200	0.335; 4.291	0.780	0.0	0.497
	Non-occlusal	4 (1)	1.340	0.842; 2.074	0.235	0.0	0.974
Definitive/provisional	Definitive	1 (0)	1.333	0.737; 2.414	0.342	–	–
	Provisional	7 (3)	1.305	0.652; 2.612	0.453	0.0	0.854
Fixed/Removable	Fixed	7 (3)	1.305	0.652; 2.612	0.453	0.0	0.854
	Removable	1 (0)	1.333	0.737; 2.414	0.342	–	–
Material	Resin	1 (0)	1.333	0.737; 2.414	0.342	–	–
	Metal-ceramic	4 (2)	1.248	0.423, 3.687	0.688	0.0	0.623
	Metal-ceramic or metal-resin	1 (0)	1.250	0.415; 3.766	0.692	–	–
	Metal-ceramic or Full-ceramic	1 (0)	1.000	0.156; 6.420	1.000	–	–
	Not reported	1 (1)	5.000	0.250; 99.954	0.292	–	–

Table A3. **Meta-analyses on biological complications expressed as risk ratio (RR), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n* (excluded)*	RR	95% CI	*P*-value	*I*-squared (%)	*P* value
Overall		8 (3)	1.094	0.488; 2.453	0.826	0.0	0.941
Missing teeth	Full	3 (0)	1.636	0.389; 6.889	0.502	0.0	0.758
	Partial	1 (1)	1.000	0.229; 4.373	0.993	–	–
	Single	3 (2)	1.006	0.242; 4.186	0.993	0.0	0.625
	Single and Partial	1 (0)	0.360	0.015; 8.435	0.526	–	–
Occlusion	Occlusal	4 (2)	1.287	0.460; 3.605	0.631	0.0	0.856
	Non-occlusal	4 (1)	0.845	0.231; 3.098	0.800	0.0	0.734
Definitive/provisional	Definitive	2 (0)	1.000	0.144; 6.926	1.000	0.0	1.000
	Provisional	6 (3)	1.115	0.459; 2.710	0.809	0.0	0.808
Fixed/Removable	Fixed	6 (3)	1.115	0.459; 2.710	0.809	0.0	0.808
	Removable	2 (0)	1.000	0.144; 6.926	1.000	0.0	1.000
Material	Resin	2 (0)	1.000	0.144; 6.926	1.000	0.0	1.000
	Metal-ceramic	3 (2)	1.015	0.297; 3.469	0.980	0.0	0.644
	Metal ceramic or metal-resin	1 (0)	3.000	0.350; 25.678	0.316	–	–
	Metal-ceramic or Full-ceramic	1 (0)	1.000	0.156; 6.420	1.000	–	–
	Not reported	1 (0)	0.333	0.014; 7.870	0.496	–	–

Table A4. **Meta-analyses on probing pocket depth (PPD) expressed as weighted mean difference (WMD), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Subgroup	*n*	WMD	95% CI	*P*-value	*I*-squared (%)	*P* value
Overall		11	−0.046	−0.166; 0.075	0.458	0.0	0.763
Missing teeth	Full	3	0.010	−0.208; 0.229	0.926	0.0	0.579
	Partial	1	−0.200	−0.487; 0.087	0.172	–	–
	Single	7	−0.026	−0.192; 0.140	0.759	0.0	0.665
Occlusion	Occlusal	6	−0.062	−0.227; 0.103	0.463	0.0	0.578
	Non-occlusal	5	−0.027	−0.202; 0.148	0.760	0.0	0.606
Definitive/provisional	Definitive	4	−0.016	−0.225; 0.193	0.880	0.0	0.630
	Provisional	7	−0.060	−0.207; 0.087	0.423	0.0	0.576
Fixed/Removable	Fixed	8	−0.070	−0.213; 0.074	0.342	0.0	0.642
	Removable	3	0.010	−0.208; 0.229	0.926	0.0	0.579
Material	Resin	3	0.010	−0.208; 0.229	0.926	0.0	0.579
	Metal-ceramic	4	−0.150	−0.340; 0.040	0.121	0.0	0.628
	Full-ceramic	1	−0.030	−0.537; 0.477	0.908	–	–
	Metal-ceramic or Full-ceramic	1	0.040	−0.381; 0.461	0.852	–	–
	Not reported	2	0.061	−0.238; 0.360	0.691	41.3	0.763

Test-control. Negative value: control greater PPD increase than test.

Table A5. **Meta-analyses on gingival inflammation and plaque levels expressed as weighted mean difference (WMD), with 95% confidence interval (CI) and evaluation of heterogeneity**

Analyses	Index	*n*	WMD	95% CI	*P*-value	*I*-squared (%)	*P* value
Gingival inflammation	Mombelli	3	−0.000	−0.226; 0.225	0.997	0.0	0.893
	Mühlemann & Son	2	−0.163	−0.416; 0.090	0.208	0.0	0.667
	Löe & Sillness	2	0.838	−0.779; 2.455	0.310	96.0	**0.000**
	BOP (%)	3	−1.999	−2.405; −1.593	**0.000**	0.0	0.974
Plaque index	Mombelli	6	0.632	−0.186; 1.449	0.130	97.4	**0.000**
	Löe & Sillness	3	−0.302	−0.779; 0.175	0.214	71.3	**0.031**

Bold text indicates statistically significant differences.