

Meta-Analysis Dental Implants

Immediate implant placement into fresh extraction sockets versus delayed implants into healed sockets: A systematic review and meta-analysis

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Abstract. The aim of this systematic review and meta-analysis was to compare the survival rate of the implants and the peri-implant tissue changes associated with implants inserted in fresh extraction sockets and those inserted in healed sockets. This review has been registered at PROSPERO under the number CRD42016043309. A systematic search was conducted by two reviewers independently in the databases PubMed/MEDLINE, Embase, and the Cochrane Library using different search terms; articles published until November 2016 were searched for. The searches identified 30 eligible studies. A total of 3,049 implants were installed in a total of 1,435 patients with a mean age of 46.68 years and a minimum of 6 months of follow-up. The survival rate of delayed implants (98.38%) was significantly greater than immediate implants (95.21%) ($p = .001$). For the marginal bone loss ($p = .32$), implant stability quotients values ($p = .44$), and pocket probing depth ($p = .94$) there was no significant difference between the analysed groups. The immediate implants placed in fresh sockets should be performed with caution because of the significantly lower survival rates than delayed implants inserted in healed sockets.

Key words: dental implants; fresh socket; healed socket; immediate implant; systematic review; meta-analysis.

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New designs and surface treatments have made it possible to insert dental implants immediately after tooth extraction. This is a variation of the conventional protocol for osseointegration established by Brane-

mark¹. Immediate insertion reduces the time required for osseointegration^{2,3}, which takes 3–6 months^{1,4} using the conventional protocol. The novel method also minimizes bone resorption by maintaining

the periodontal architecture,^{5,6} and it leads to better aesthetic results, particularly when the front teeth are lost.

Thus, immediate implant placement has been a focus of clinical practice for

implantodontists. The technique preserves the alveolar ridge, and it decreases the morbidity and rehabilitation time associated with tooth replacement; furthermore, it increases patient satisfaction with treatment^{7–9}. However, the literature presents no consensus regarding the advantages of immediate implant placement. On the contrary, the following disadvantages have been reported: (1) lower implant survival rates than delayed implants placed into the alveolar ridge after a healing time, (2) marginal bone loss, and (3) changes affecting the peri-implant soft tissues^{10,11}.

To standardize the nomenclature used to classify the time of implant installation, Hammerle et al.¹² published a classification based on morphologic, dimensional, and histologic changes that follow tooth extraction and on common practice derived from clinical experience. This systematic review and meta-analysis was performed according to this classification in which post-extraction implant placement in this context refers to immediate placement (type 1), early placement with soft tissue healing (type 2), early placement with partial bone healing (type 3), and late placement (type 4)^{12,13}.

Therefore, the aim of this study was to compare the implant survival rates and peri-implant tissue changes between implants inserted immediately after tooth extraction (fresh extraction sockets) and those inserted after a conventional healing period (healed sockets). The null hypotheses were as follows: (1) survival rates do not differ between implants inserted into fresh extraction sockets (immediate implants) and those inserted into healed sockets (delayed implants); (2) implants inserted into fresh extraction sockets do not differ significantly from those inserted into healed sockets in terms of the associated marginal bone loss or soft tissue changes.

Materials and methods

Registry protocol

This systematic review was structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist described by Moher et al.¹⁴ and in accordance with models proposed in the literature^{15–19}. The methods for this systematic review were registered with PROSPERO (CRD42016043309).

Research strategy and information sources

Two researchers (C.M.M. and C.A.A.L.) independently selected the articles to be

included in this review according to the inclusion and exclusion criteria described below. The PubMed/Medline, Embase, and Cochrane databases were searched for articles published until November 2016. The following search terms were entered using Boolean operators: “dental implants and immediate implant OR dental implants and immediate dental implant OR dental implants and immediately placed OR dental implants and immediately placed OR dental implants and immediately placed OR dental implants and immediately placed OR dental implants and immediately installed”.

The searches attempted to identify studies that compared immediate implant insertion after tooth extraction with implant insertion after a conventional healing period (2–4 months). This systematic review and meta-analysis are based on the classification of Hammerle et al.¹² that defines post-extraction implant placement according to installation time as the following: immediate placement (type 1), early placement with soft tissue healing (type 2), early placement with partial bone healing (type 3), and late placement (type 4)¹³.

Disagreement between examiners regarding which articles should be included was resolved by discussion, and a consensus was reached among all of the study authors. When necessary, careful analysis was performed by a third examiner (E.P. P.) and discussion continued until a consensus was reached.

As a complement to the above database searches, a search of grey literature and a manual search of journals dedicated to a specific area were performed. Specifically, the following journals were searched manually: *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Oral Implantology*, *Journal of Oral Rehabilitation*, *Journal of Periodontology*, and *Periodontology 2000*.

Study selection

Studies were initially selected through a reading of the titles and abstracts, and final study selection was performed through a reading of the full texts applying the inclusion and exclusion criteria.

The PICO approach (population, intervention, comparison, and outcome) was used to address the following question: “Do immediately inserted implants perform similarly to implants that are inserted

into a healed socket?” Patients (P) that had undergone osseointegrated implant insertion into fresh extraction sockets (I) or healed sockets (C) were evaluated. The primary outcome (O) evaluated was implant survival rate. Marginal bone loss, primary implant stability, and soft tissue changes were considered secondary outcomes.

Inclusion/exclusion criteria

To qualify for inclusion, studies were required to (1) be randomized controlled trials, (2) be prospective studies, (3) have been published in English, (4) have more than five implants in each group, and (5) involve a follow-up period of at least 6 months.

Studies were excluded from the present review if they were (1) duplicates, (2) retrospective, (3) case series, (4) carried out *in vitro*, or (5) using animals, (6) systematic reviews, (7) analyses of implant loading protocols (immediate load), or (8) simple evaluations of either delayed or immediate implants—without a comparison group.

Data synthesis

The data obtained from the selected studies were evaluated both qualitatively and quantitatively. The total number of immediate implants placed was calculated, as were the survival rate, marginal bone loss, and soft tissue changes associated with the implants. These values were compared with those obtained for implants inserted in healed sockets.

Quality analysis of the studies included

Two investigators (C.C.M. and C.A.A.L.) assessed the methodological quality of the studies according to the Jadad scale²⁰. The scale ranges from 0 to 5 with scores of 3 or more considered high quality. The Cochrane Collaboration’s tool for assessing risk of bias was used to assess the quality of the studies included in this review.

Additional analysis

The kappa coefficient was used to measure inter-rater agreement during article selection. Any disagreements were resolved by discussion and a consensus was reached among all of the authors.

Summary measures

Reviewer Manager 5.3 software (Nordic Cochrane Centre, Copenhagen, Denmark) was used to perform the meta-analysis; $p < .05\%$ were considered significant. Marginal bone loss, implant stability quotients (ISQs), and probing pocket depth were assessed as continuous outcome variables using the inverse variance (IV) method; they were recorded as mean differences (MDs) with a 95% confidence interval (CI). Implant survival rates were assessed as a dichotomous outcome using the Mantel-Haenszel method; they were recorded as risk ratios (RRs) with a 95% CI and the weight contribution of each study. The I^2 statistic was used to express the percentage of the total variation across studies due to heterogeneity, with 25% corresponding to low heterogeneity, 50% to moderate, and 75% to high. A funnel plot (plot of effect size versus standard error) was drawn. Asymmetry of the funnel plot may indicate publication bias and other biases related to sample size, although the asymmetry may also represent a true relationship between trial size and effect size²¹.

Results

General outcomes

The database searches covering 5,737 articles, including 3,473 from PubMed/Medline, 2,216 from Embase, and 48 from Cochrane. After duplicate articles were removed, 4,891 titles and abstracts had been analysed, and 52 qualified for the full text read. The inclusion and exclusion criteria were then applied; ultimately, 30 studies were eligible for data analysis^{8,10,11,22-48}, all of which had been published by November 2016. The studies are listed in Table 1 (qualitative analysis), Table 2 (quantitative analysis), and Table 3 (qualitative analysis). The details of the search strategy are presented in a flow diagram (Fig. 1).

Inter-rater agreement was calculated by obtaining a kappa value for the articles that had been selected after evaluation of their titles and abstracts as follows: PubMed/Medline (kappa = 0.93), Embase (kappa = 0.90), and Cochrane Library (kappa = 1).

Demographic data

The selected studies included a total of 1,435 patients (588 male and 657 female) with a mean age of 46.68 years and a mean follow-up period of 30.09 months (range 6–60 months).

Most of the selected studies evaluated implants that had been inserted in maxilla^{8,10,23,25,29,32,36,39,41-45,47}, and both dental arches^{22,26,28,30,31,34,35,37,40,46,48}; involved the anterior and posterior regions. Fourteen studies included patients who smoked^{10,24,26-30,33-35,38,46-48} and five studies included patients with periodontal compromised status^{27,28,31,40,46}.

Surgical and prosthetic data

The eligible studies included a total of 3,049 implants. Of these, 1,440 implants had been placed immediately after tooth extraction, while 1,609 had been placed into healed sockets. The most common type of dental implant connection, as observed in five studies, was an internal connection^{10,29,30,34,43}; the exception was the study performed by Davarpanah et al.²⁶ which used an external hexagon connection. The implants varied in diameter (3.25–9 mm) and length (8.5–17 mm). A single unit prosthesis was used in most of the studies^{8,10,11,22,23,25,26,29,34,36,41-45,47,48}.

Healing time and loading conditions

Among the studies evaluating implant placement in a healed socket, the alveolar ridge was allowed to heal for a mean period of 3 weeks or more following tooth extraction. In the studies evaluating immediate placement of implants, insertion was typically accompanied by immediate loading of the implants^{10,11,22-25,28,29,32-36,42,43}. This mainly occurred when implants were placed in the maxillary arch alone^{8,10,23,29,32,36,38,41-45,49}.

Implant survival and complication rates

Among the 3,049 dental implants inserted, 95 failures (3.11%) were recorded. Of these failures, 69 were immediate implants (72.63%), and 26 were delayed implants (27.37%). A meta-analysis was performed to evaluate the survival rates between fresh and healed sockets. A statistically significant difference was detected, showing that implants placed in healed sockets had more favourable outcomes ($p = .001$, RR 2.49, 95% CI 1.44–4.29) between the groups. The result of the χ^2 test for heterogeneity was 27.46 ($p = .19$, $I^2 = 20\%$) (Fig. 2).

Sub-analysis was performed to compare the influence of healing time of tissues. There was no significant difference for type 1 when compared with type 2 ($p = .47$; RR 1.45, 0.53–3.98). The result of the χ^2 test for heterogeneity was 1.16 ($p = .56$, $I^2 = 0\%$) (Fig. 3A). However,

Table 1. Characteristics of included studies ($n = 30$).

First Author, publication year	Study types	Mean age (Years)	Patients (n)	Arch/Region	Healing time and type ^a	Implants (n)	Implants – Diameter × Length (mm)	Prosthesis type	Follow-up
Aguirre-Zorzano et al. ²²	Prospective clinical study	48.5	56(19 M/37F)	Max, Mand/Post	NR	56(I)	3.4, 4.0, 4.5, 5.0 × 11, 13, 15, 17 mm	Single unit	23 months
Atieh et al. ¹¹	Controlled clinical trial	53.6	24 (9 M/15F)	Mand/Post	At least 16 weeks/type 4	22(H) 12 (I)	3–9 × 7–11 mm	Single unit	12 months
Block et al. ²³	Prospective Evaluation	43	55 (24 M/31F)	Max/Ant, Post	16 weeks/type 4	12(H) 26 (I)	3.25, 4 × 11.5, 13 mm	Single unit	24 months
Colomina ²⁴	Prospective longitudinal trial	57.5	13 (NR)	Mand/Ant, Post	8 and 24 weeks/type 2 and 4	29(H) 32(I)	NR	Full-arch	18 months

Table 1 (Continued)

First Author, publication year	Study types	Mean age (Years)	Patients (n)	Arch/Region	Healing time and type ^a	Implants (n)	Implants – Diameter × Length (mm)	Prosthesis type	Follow-up
Cooper et al. ²⁵	Prospective	43.5	94 (39 M/55F)	Max/Post	12 weeks/type 3	29(H) 45 (I)	3.5–5 × 11–17 mm	Single unit	60 months
Davarpanah et al. ²⁶	Prospective Clinical study	59.8	92 (36 M/56F)	Max, Mand/Ant, Post	8 weeks/type 2	49 (H) 68 (I)	4.0 × 8.5–15 mm	Single unit	18 months
De Bruyn and Collaert ²⁷	Prospective	65.2	36 (18 M/18F)	Mand/Ant, Post	At least 8 weeks/type 3	80 (H) 31(I)	3.75, 5 × 7–18 mm	Full-arch	36 months
Deng et al. ²⁸	Prospective	62	12 (8 M/4F)	Max, Mand/Ant, Post	NR	153(H) 32(I)	3.75, 5 × 10–13 mm	Full arch	12 months
Esposito et al. ²⁹	Pragmatic multicentre randomized controlled trial	49	106 (46 M/60F)	Max/Post	16 weeks/type 4	52(H) 54 (I)	4, 5, × 7, 8.5, 10, 11, 13, 15 mm	Single partial denture	12 months
Grandi et al. ¹⁰	Multicentre controlled cohort study	52	50 (21 M/29F)	Max/Post	16 weeks/type 4	52 (H) 25(I)	3.7, 4.3, 5 × 11.5, 13, 15 mm	Single unit	12 months
Han et al. ³⁰	Prospective single-center clinical	46.4	39 (26 M/13F)	Max, Mand/Ant, Post	At least 16 weeks/type 4	25(H) 30(I)	3.5, 4, 4.5, 5, 6, 7 × 7, 8.5, 10, 11.5 mm	Single unit, FPD, Full arch	12 months
Jo et al. ³¹	Prospective survival study	49	75 (42 M/33F)	Max, Mand/Ant, Post	NR	32(H) 90(I)	3.8, 5.5, 6.8 × 10, 13, 16 mm	Single unit, FPD	40 months
Kan et al. ³²	Prospective multicentre study	45.1	29	Max/Ant	NR	196(H) 23(I)	3.7, 4.3, 5 × 10, 13, 16 mm	Partial Fixed denture	12 months
Krennmair et al. ³³	Prospective study	61.5	24 (14 M/10F)	Mand/Ant	NR	15(H) 55(I)	3.8, 4.3 × 13, 16 mm	Full arch	24 months
Lindeboom et al. ⁸	Prospective randomized study	39.7	50 (25 M/25F)	Max/Post	12 weeks/type 3	41(H) 25(I)	3.8, 4.5, 5.5, 6.5 mm diameter	Single unit	12 months
Luongo et al. ³⁴	Prospective multicentre study	44.5	46 (23 M/23F)	Max, Mand/Ant, Post	NR	25(H) 10(I)	3.5, 4.0, 4.5 × 10, 11.5, 13 mm	Single unit	12 months
Oxby et al. ³⁵	Prospective clinical study	68	39 (22 M/17F)	Max, Mand/Ant, Post	NR	47(H) 72 (I)	3.5, 4.0, 4.5, 5.0 × 11, 13, 15, 17, 19 mm	Partial Fixed denture/Full-arch	55 months
						110 (H)			

Palattella et al. ³⁶	Prospective clinical study	35	16 (6 M/10F)	Max/Ant	8 weeks/type 2	9(I)	4.1, 4.8 × 10, 12 mm	Single unit	24 months
Pellicer-Chover et al. ³⁷	Prospective, randomized, single-blind, clinical preliminary trial	63.7	15 (6 M/9F)	Max,Mand/Ant, Post	24 weeks/type 4	9(H) 68 (I)	3.8 × 10.0 mm	Full arch	12 months
Peñarrocha-Oltra et al. ³⁸	Prospective Controlled Study	54.6	34 (15 M/19F)	Mand/Ant, Post	NR	76 (H) 107 (I)	3.8–5 × 8.5–15 mm	Full arch	21 months
Peñarrocha-Oltra et al. ³⁹	Nonrandomized Controlled Clinical Study	55.4	29(13 M/16F)	Max/Ant, Post	NR	76 (H) 105(I)	3.8, 4.25, 5.0 × 10, 11.5, 13, 15 mm	Full arch	12 months
Polizzi et al. ⁴⁰	Prospective Multicentre Study	NR	86(NR)	Max, Mand/Ant, Post	3 to 5 weeks/type 2	88(H) 217(I)	NR	Single unit, FPD, Full-arch	60 months
Raes, et al. ⁴¹	Prospective	43	96 (41 M/55F)	Max/Ant	At least 12 weeks/type 3	47(H) 48(I)	NR	Single unit	60 months
Raes and De Bruyn ⁴²	Prospective Clinical study	42.5	39 (22 M/17F)	Max/Ant, Post	At least 12 weeks/type 3	54(H) 16(I)	3.5 – 5.0 × 11 – 17 mm	Single unit	52 months
Ribeiro et al. ⁴³	Comparative study	45.4	64 (27 M/37F)	Max/Post	NR	23(H) 46(I)	3.5, 4.3, 5, 6 × 10, 11, 13, 15 mm	Single unit	27 months
Rieder et al. ⁴⁴	Randomized Clinical Trial	44.8	48 (24 M/24F)	Max/Ant	6 weeks/type 2	36(H) 24(I)	3.3, 4.1, 4.8 × 12 mm	Single unit	8 months
Siciliano et al. ⁴⁵	Controlled clinical trial	48.8	30 (14 M/16F)	Max/Post	24 weeks/type 4	24(H) 15(I)	6.5 mm	Single unit	12 months
Siebers et al. ⁴⁶	Longitudinal case control study	52.9	76 (34 M/42F)	Max, Mand/Ant, Post	16 to 24 weeks/type 4	15(H) 58(I)	NR	Single unit/FPD	48 months
Tsirlis ⁴⁷	Prospective	50	38 (NR)	Max, Mand/Ant	4 to 8 weeks/type 2	164(H) 28(I)	3.8; 6 × 13 mm	Single unit	24 months
van Kesteren et al. ⁴⁸	Prospective, randomized clinical study	52	24	Max,Mand/Ant, Post	12 weeks/type 3	15(H) 13 (I)	4.1 × 10, 12 mm	Single unit	6 months
						13 (H)			

NR = not reported; I = immediate; H = healed; M = male; F = female; Max = maxilla; Mand = mandible; Ant = anterior; Post = posterior; FPD = fixed partial denture.

^aClassification of healing time for implant placement in extraction sockets according to Hammerle et al.¹² at a consensus conference.

Table 2. Outcomes of included studies for quantitative analysis.

First Author	Survival rate (%)		Outcomes measurements	Outcome immediate	Outcome healed	Complications (n – implants)
	Immediate (F – S/T)	Healed (F – S/T)				
Aguirre-Zorzano et al. ²²	98.7%. (1 – 55/56)	100% (22/22)				Infectious process (1); Crown decenteration (11); Cement retained in peri-implant tissues (10); Periapical lesions (6)
Atieh et al. ¹¹	66.7%. (4 – 8/12)	83.3% (2 – 10/12)	Implant stability (ISQ units)	ISQi – 80.08 ± 5.07 ^a ISQf – 75.70 ± 10.52 ^a	ISQi – 78.83 ± 3.69 ^a ISQf – 76.75 ± 10.24 ^a	Veneer chipping (6 – 3 I/3H)
Block et al. ²³	84.62%. (4 – 22/26)	96.56% (1 – 28/29)	Marginal bone loss Cementum enamel junction	0.45 ± 1.22 mm ^b 2.82 mm ^b	0.54 ± 1.00 mm ^b 2.86 mm ^b	Screw loosening (11)
Colomina ²⁴	93.75% (2 – 30/32)	100% (29/29)				Cantilever fracture (15%); incorrect adjustment Screw loosening (23%)
Cooper et al. ²⁵	100% (45/45)	100% (49/49)	Median changes in the papillae Mucosal zenith	Mesial: -0.13 ± 1.61 mm Distal: -0.21 ± 1.61 mm ^c -0.05 ± 0.92 mm ^c	Mesial: 0.39 ± 1.52 mm Distal: 0.5 ± 1.35 mm ^c 0.78 ± 1.34 mm ^c	
Davarpanah et al. ²⁶	95.59% (3 – 65/68)	98.75% (1 – 79/80)				
De Bruyn and Collaert ²⁷	61% (12–19/31)	99.3% (1 – 152/153)				
Deng et al. ²⁸	87.5% (4 – 28/32)	100% (52/52)	Marginal bone loss	1.01 ± 0.29 mm ^b	1.24 ± 0.23 mm ^b	
Esposito et al. ²⁹	96% (2 – 52/54)	100% (52/52)	Marginal bone loss	0.13 mm ± 0.16 mm ^a	0.27 mm ± 0.14 mm ^a	(I) partial fracture of the provisional crown (4); loosening of the provisional crowns (2); prolonged postoperative discomfort during chewing that lasted 4 months (1); and prolonged postoperative pain resulting in implant mobility at 1 month after loading (1),(H) loosening of a provisional crown (1)
Grandi et al. ¹⁰	92% (2 – 23/25)	96% (1 – 24/25)	PES score	13.0 ^b	12.8 ^b	
Han et al. ³⁰	100% (30/30)	96.9% (1–31/32)	Marginal bone loss	0.35 mm ± 0.23 mm ^b	0.39 mm ± 0.16 mm ^b	
Jo et al. ³¹	97.7% (2–88/90)	93.8% (12–184/196)	Implant stability (ISQ units)	80.1 ± 3.3 mm ^b	80.5 ± 3.4 mm ^b	Fistula formation (10); Mobility (4); Bacterial contamination (3)
Kan et al. ³²	100% (23/23)	100% (15/15)				Unseating of provisional restorations (3) fractured a provisional crown (1) experienced gingival greying (1)
Krennmair et al. ³³	100% (55/55)	100% (41/41)	Marginal bone loss	0.26 ± 0.49 mm ^a	0.58 ± 0.48 mm ^a	Abutment screw loosening (4), acrylic teeth fractured (15), acrylic teeth repaired in office (9), acrylic denture base fracture (5), denture rebasing/reduction (22), denture cleaning (discolouration) (26), crew hole (acrylic repair) (8)

Lindeboom et al. ⁸	92% (2 – 23/25)	100% (25/25)	Pocket depth	4.79 ± 0.98 mm ^b	4.45 ± 0.96 mm ^b	
			Marginal bone loss (Mesial and Distal)	Mesial: 0.49 ± 0.11 mm Distal 0.53 ± 0.12 mm ^b	Mesial: 0.52 ± 0.16 mm Distal: 0.52 ± 0.14 mm ^b	
Luongo et al. ³⁴	100%. (10/10)	97.8% (1 – 46/47)	Implant stability (ISQ units)	ISQf = 64.5 ± 3.9 ^b	ISQf = 64.5 ± 4.4 ^b	H - Pain and swelling (1), abutment screw loosening (2), porcelain fracture (1)
			Marginal bone loss	0.22 ± 0.20 mm ^c	0.35 ± 0.22 mm ^c	
Oxby et al. ³⁵	100% (72/72)	100% (110/110)	Probing depth	2.23 ± 0.65 mm ^c	1.95 ± 0.74 mm ^c	I - Exposed abutments and implant necks (2)
Palattella et al. ³⁶	100% (9/9)	100% (9/9)	Movement of mucosal margin	-0.8 ± 0.7 mm ^b	-0.6 ± 0.6 mm ^b	
			Marginal bone loss	0.54 ± 0.51 mm ^b	0.46 ± 0.54 mm ^b	
Pellicer-Chover et al. ³⁷	100% (68/68)	100% (76/76)	Implant Stability (ISQ units)	ISQf = 72 ± 3 ^b	ISQf = 73 ± 2 ^b	
			Gingival retraction	0.43 ± 0.56 mm ^a	0.15 ± 0.26 mm ^a	
			Probing depth	1.39 ± 0.44 mm ^b	1.59 ± 0.52 mm ^b	
			Marginal bone loss	0.54 ± 0.39 mm ^a	0.66 ± 0.25 mm ^a	
Peñarrocha-Oltra et al. ³⁸	96.8% (4 – 101/105)	99% (88/88)	Marginal bone loss	0.62 ± 0.23 mm ^a	0.55 ± 0.26 mm ^a	
Peñarrocha-Oltra et al. ³⁹	98.13% (2 – 105/107)	H – 98.69% (1 – 75/76)	Marginal bone loss	0.80 ± 0.18 mm ^a	0.62 ± 0.20 mm ^a	Mucositis (7) fractured a definitive prosthesis (2)
Polizzi et al. ⁴⁰	93.55% (14–203/217)	93.62% (3–44/47)				Fistula formation (8); Soft tissue penetration (8); Paraesthesia (2)
Raes, et al. ⁴¹	97.9% (1–47/48)	98.2% (1–53/54)	OHIP-14	a	a	
Raes and De Bruyn ⁴²	94% (1 – 15/16)	100% (23/23)				PES failure (5); WES failure (10)
Ribeiro et al. ⁴³	93.5% (3 – 43/46)	100% (36/36)	PES scores	8.47 ± 2.08 mm ^a	6.62 ± 3.24 mm ^a	Mobility or pain (4)
Rieder et al. ⁴⁴	95.8% (1–23/24)	100% (24/24)		7.93 ± 3.21 mm ^b	8.10 ± 3.25 mm ^b	
				PPD – 4.07 mm ^a	PPD – 2.88 mm ^a	
Siciliano et al. ⁴⁵	100% (15/15)	100% (15/15)	Probing depth			
Siebers et al. ⁴⁶	93.1% (4 – 54/58)	99.3% (1 – 163/164)	Marginal bone loss	0.75 ± 1.05 mm ^b	0.875 ± 0.62 mm ^b	
Tsirlis ⁴⁷	100% (28/28)	100% (15/15)	probing depth	0.3 ± 0.2 mm ^b	0.4 ± 0.37 mm ^b	
van Kesteren et al. ⁴⁸	92.3% (1 – 12/13)	100% (13/13)	Mean reduction in ridge	Grafted –0.70 ± 0.39/non-grafted –0.96 ± 0.55 mm ^a	0.41 ± 0.41 mm ^a	
			Apicocoronal position	–0.05 mm ^a	–0.28 mm ^a	
			Midbuccal soft tissue	0.20 ± 1.04 mm ^a	0.49 ± 0.57 mm ^a	

F = failure; S = survival; T = total; ISQi = implant stability quotient initial; ISQf = implant stability quotient final.

^a Statistically significant difference between analysed groups.

^b No statistically significant difference between analysed groups.

^c Not performed statistical analyses.

Table 3. Outcomes of included studies for qualitative analysis.

First Author, publication year	Loaded	Grafting procedures	Smokers/Diabetics	Periodontal compromised	Infections	Antibiotics/mouth rinse
Aguirre-Zorzano et al. ²²	Immediate	Y	N/N	N	1 (Imed)	Y/Y
Atieh et al. ¹¹	Immediate	N	N/N	N	NR	Y/Y
Block et al. ²³	Immediate	Y	N/N	N	N	Y/-
Colomina ²⁴	Immediate	N	Y/N	N	N	Y/Y
Cooper et al. ²⁵	Immediate	N	N/N	N	NR	NR
Davarpanah et al. ²⁶	Immediate and Delayed	Y	Y/N	N	1 (Imed)	NR
De Bruyn and Collaert ²⁷	Immediate and Delayed	N	Y/N	Y	Y	N/Y
Deng et al. ²⁸	Immediate	N	Y/N	Y	NR	Y/Y
Esposito et al. ²⁹	Immediate or Delayed	Y	Y/N	N	N	Y/Y
Grandi et al. ¹⁰	Immediate	Y	Y/N	N	NR	Y/Y
Han et al. ³⁰	Immediate	Y	Y/N	NR	N	Y/Y
Jo et al. ³¹	Immediate and Delayed	N	NR	Y	N	NR
Kan et al. ³²	Immediate	Y	N/N	N	NR	Y/Y
Krennmair et al. ³³	Immediate	N	Y/N	N	NR	Y/Y
Lindeboom et al. ⁸	Non-loaded	Y	N/N	N	NR	Y/Y
Luongo et al. ³⁴	Immediate	Y	Y/N	N	N	Y/Y
Oxby et al. ³⁵	14–53 days	N	Y/N	N	N	Y/-
Palattella et al. ³⁶	Immediate	N	N/N	N	NR	Y/Y
Pellicer-Chover et al. ³⁷	12 weeks (Max) 10 weeks (Mand)	N	N/N	N	N	Y/Y
Peñarrocha-Oltra et al. ³⁸	Immediate or Delayed (2 months)	N	N/N	N	NR	Y/Y
Peñarrocha-Oltra et al. ³⁹	Immediate or Conventional	N	Y/N	N	N	Y/Y
Polizzi et al. ⁴⁰	NR	Y	NR	Y	Y	NR
Raes, et al. ⁴¹	Immediate	N	N/N	N	N	Y/Y
Raes and De Bruyn ⁴²	Immediate	Y	N/N	N	NR	NR
Ribeiro et al. ⁴³	Immediate	N	N/N	N	NR	Y/Y
Rieder et al. ⁴⁴	Immediate and Delayed	Y	N/N	N	N	N/Y
Siciliano et al. ⁴⁵	–	N	N/N	N	N	Y/Y
Siebers et al. ⁴⁶	4–6 months	N	Y/N	Y	NR	NR
Tsirlis ⁴⁷	Delayed	Y	Y/N	N	N	N/N
van Kesteren et al. ⁴⁸	No prosthesis	Y	Y/N	N	NR	NR

Y = yes; N = no; NR = not reported.

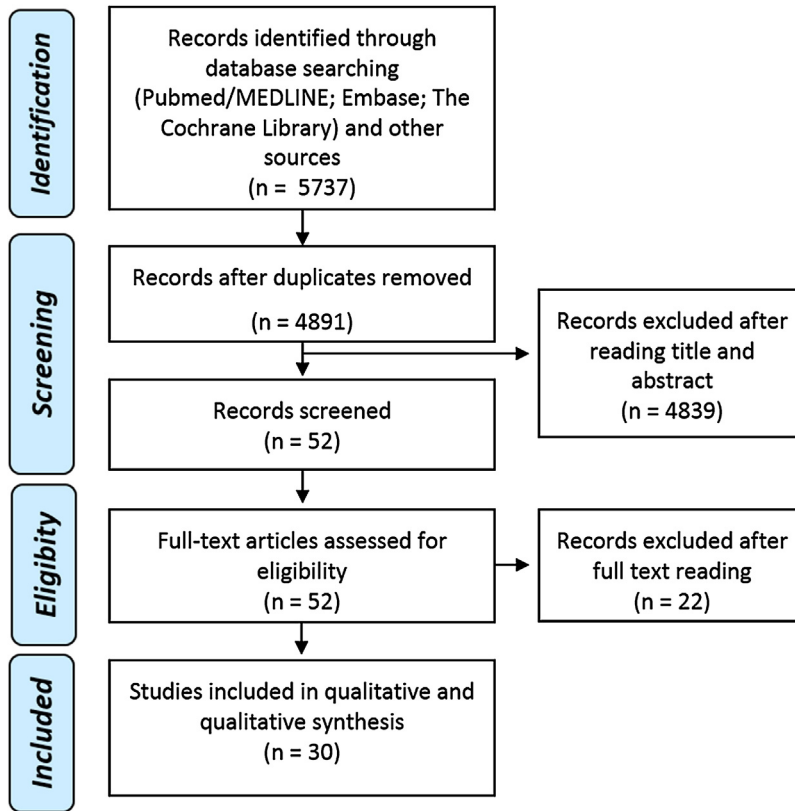


Fig. 1. Flow diagram about the literature search and results.

type 1 showed significantly higher failures rates when compared with type 3 ($p = .005$; RR 5.25, 1.67–16.49) (Fig. 3B) and type 4 ($p = .02$; RR 2.86, 1.22–6.70) (Fig. 3C). The result of the χ^2 test for heterogeneity was 7.74 ($p = .26$, $I^2 = 22\%$) and 3.81 ($p = .70$, $I^2 = 0\%$), respectively.

Some authors described complications affecting the appearance of the implants: infectious process^{22,31,38,40}, abutment exposure³⁵, cement breakage or provisional fractures^{22,29,32–34,39}, chipping of the ceramic veneer^{11,34}, gingival darkening³², and loosening of the screws^{11,24,33,34,39}.

Marginal bone loss

Among the studies that analysed bone tissue changes, five evaluated implants inserted into the maxilla^{8,23,29,36,38}, two analysed implants inserted into the mandible^{33,38}, and four involved both dental arches^{28,34,37,47}. Thus, 11 studies^{8,23,28,29,33,34,36–39,47} were included in a meta-analysis evaluating peri-implant bone loss. No statistically significant difference was observed between immediate and delayed implantation ($p = .32$), with a mean difference of -0.04 (95% CI -0.13 to 0.04). The result of the χ^2 test for

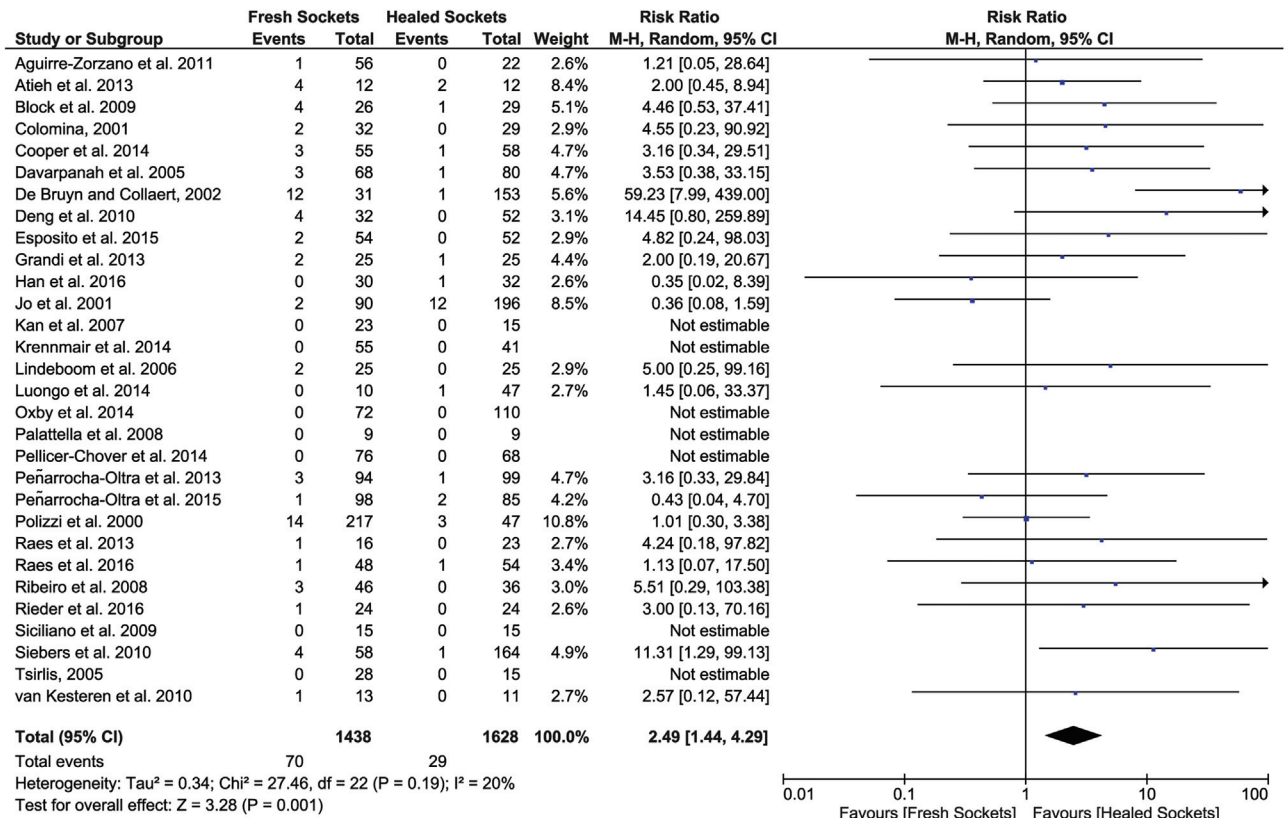


Fig. 2. Forest plot for the event ‘implants survival rates’ for eligible studies.

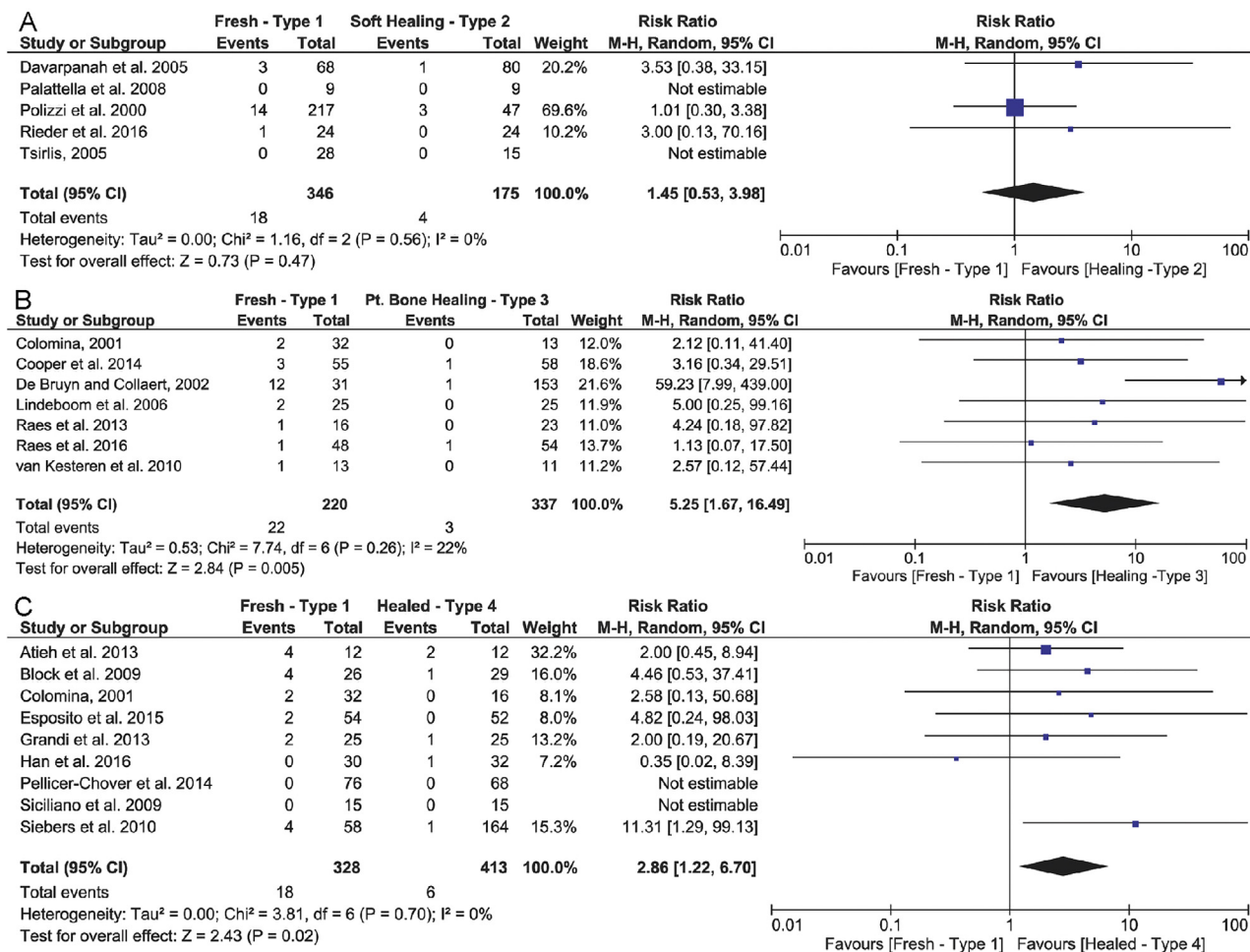


Fig. 3. Forest plot for the event ‘implants survival rates’ for different healing time. (A) type 1 vs. type 2; (B) type 1 vs. type 3; (C) type 1 vs. type 4.

heterogeneity was 152.34 ($p < .00001$, $I^2 = 91%$) (Fig. 4).

Implant stability

Four studies^{8,11,30,36} evaluated implant stability of the implants after a period of osseointegration. The values were reported as an ISQs and ranged from 64.5 ± 3.9 to 80.1 ± 3.3 ISQ units for immediate implants and from 64.5 ± 4.4 to 80.5 ± 3.4 ISQ units for delayed implants.

Quantitative analysis showed no statistically significant difference in implant stability between the two groups ($p = 0.44$, MD -0.46 , 95% CI -1.62 to 0.70). The χ^2 heterogeneity was 0.38 ($p = 0.94$, $I^2 = 0%$) (Fig. 5A).

Peri-implant soft tissue changes

Five studies reported values for probing pocket depth values in the two groups.^{33,34,37,45,47} These varied from

0.30 mm (± 0.20 mm) to 4.79 mm (± 0.98 mm) for fresh extraction sockets (immediate implants) and from 0.40 mm (± 0.37 mm) to 4.45 mm (± 0.96 mm) for healed sockets (delayed implants). Only Siciliano et al.⁴⁵ reported a statistically significant difference in probing pocket depth between the two groups; showing that delayed implants were significantly more favourable in this regard (2.88 mm for fresh extraction socket vs. 4.07 mm for healed sockets).

Quantitative analysis revealed no statistically significant difference in probing pocket depth between the two groups. Specifically, a mean difference between the groups of 0.01 mm ($p = .94$, 95% CI -0.22 to 0.24) was calculated. The χ^2 test for heterogeneity was 9.03 ($p = .03$, $I^2 = 67%$) (Fig. 5B).

Assessment of study quality

The Jadad scale used to assess the quality of the evidence indicated that only eight

studies were of high quality (Table 4). That is, there was a high risk of bias concerning randomization and blinding of patients and surgeons. The Cochrane criteria indicated high risk of bias for the randomization, allocation, and blinding (participants and personal/outcome assessment) of the studies. However, the high risk of bias concerning the blinding of participants and personnel could be justified by the difficulty of blinding the surgeon and patients, but the blinding of outcome assessment could be performed in these studies. Most of studies were adequate for addressing incomplete outcome data and selective reporting, and all studies were free of other sources of bias (Fig. 6).

Publication bias

The funnel plot of studies included in the failures rates of implants showed symmetry (Fig. 7), indicating possible absence of publication bias.

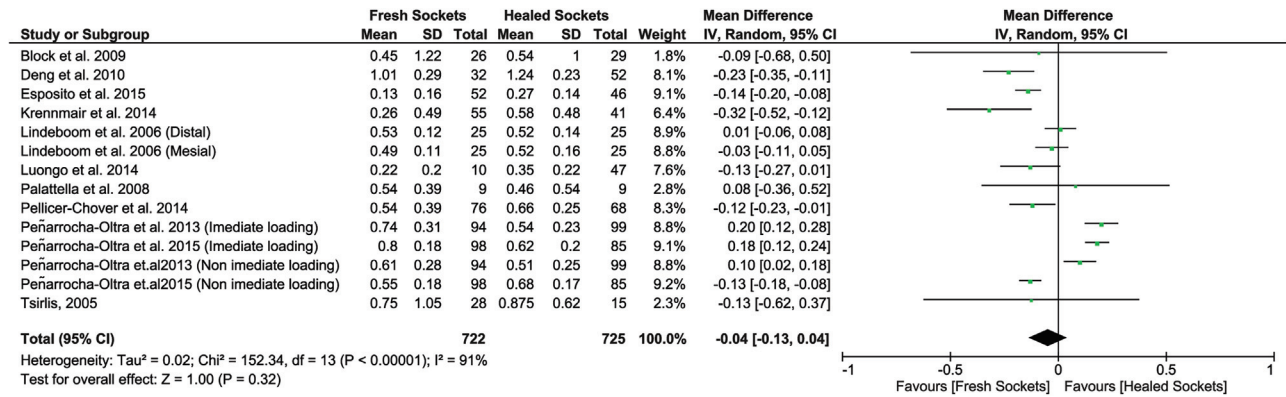


Fig. 4. Forest plot for the event “marginal bone loss”.

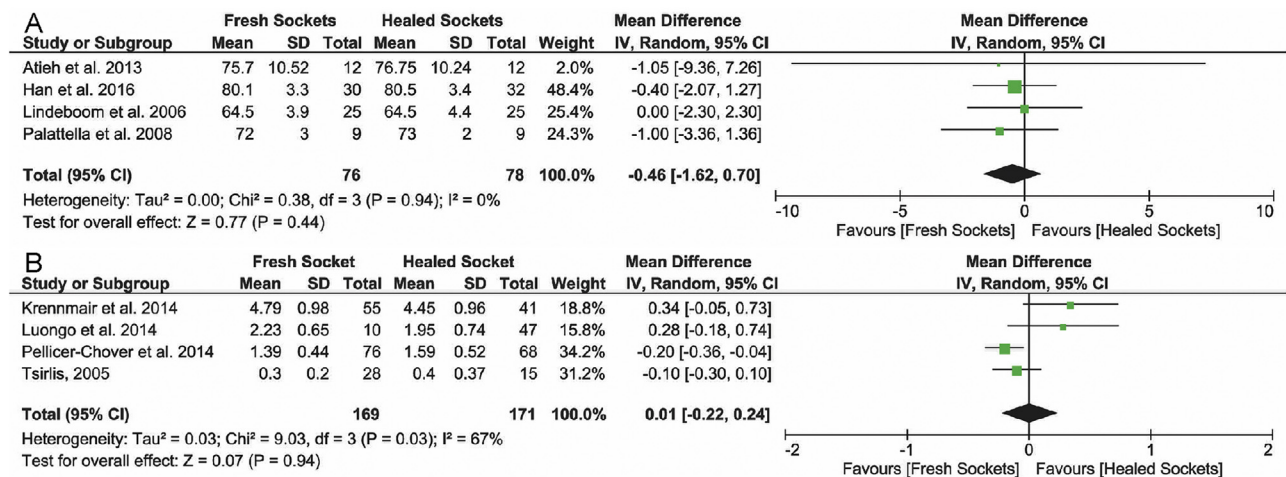


Fig. 5. Forest plot for the event. (A) ‘implant stability quotient’; (B) ‘probing depth’.

Discussion

The aim of this study was to find evidence in the literature supporting the immediate placement of osseointegrated implants into fresh sockets (after tooth extraction). We compared the survival rate and the associated peri-implant tissue changes of the immediately placed implants with those of the implants that had been placed into healed sockets.

We found that, among the 95 failures described in the eligible studies, 69 occurred in fresh extraction sockets and 26 occurred in healed sockets. Quantitative analysis revealed that, even though the immediately placed implants had higher survival rates,^{32,35,37,49} the implants placed in healed sockets showed statistically superior results. Therefore, we reject our first null hypothesis, which states that survival rates do not differ significantly between groups; in this regard, we concur

with the results found in the literature^{8,28,42,43,48}.

Among periodontally compromised patients, the difference in implant survival rates is even more marked. For instance Deng et al.²⁸ reported survival rates of 87.5% for immediately placed implants and 100% for implants inserted in healed sockets. This discrepancy was likely to be due to the bone remodelling process that occurs along the alveolar ridge; this process can be divided into five steps, and it is completed, on average, 16 weeks after tooth extraction^{50,51}. Specifically, 16 weeks is the average time period after which the eligible studies considered the alveolar ridge sufficiently healed to allow insertion of osseointegrated implant^{38,39}. A similar phenomenon can be seen in fresh extraction sockets, wherein the newly formed bone tissue is only able to guarantee high levels of stability after this 16-week healing period. That is,

healed sockets ensure greater primary stability⁵².

In the present review, although some studies worked with full arch prosthetics^{28,33,35,37-39} most involved the fabrication of single and fixed partial dentures^{8,10,11,22,23,25,26,29,32,34,36,42,43,45,48}.

We suspect that this is because immediate implant placement is still controversial, and because outcomes are more predictable after the fabrication of single and fixed partial dentures. Specifically, there is less interference during analysis of the results, because a smaller number of teeth are involved; moreover, it is easier to manufacture this type of prosthesis. Nonetheless, because immediate implant insertion has clear advantages in the case of edentulous patients, many clinical studies have involved this group of patients^{53,54}.

Our literature review revealed also that there has been a trend towards allowing immediate loading after implant

Table 4. Quality assessment of the selected studies using JADAD scale.

Quality assessment	Pen																															
	Aguirre-Zorza 2011	Ateih 2013	Block 2009	Colomina 2001	Cooper 2014	Davarpanah 2005	De Bruyn 2002	Deng 2010	Esposito 2015	Grandi 2013	Han 2016	Jo 2001	Kan 2007	Kremmair 2014	Lindeboom 2006	Luongo 2014	Oxby 2014	Palanella 2008	Pellicer-Chover 2014	Oltra 2015	Oltra 2013	Polizzi 2000	Rates 2016	Rates 2013	Ribera 2008	Rieder 2016	Sciliano 2009	Siebers 2010	Tsirilis 2005	van Kesteren 2010		
1. Was the study described as random?	N	N	Y	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	Y	Y	N	N	Y	N	N	N	Y	N	N	N	N	Y	
2. Was the randomization scheme described and appropriate?	N	N	Y	N	N	N	N	N	Y	N	N	N	N	Y	Y	N	N	Y	Y	N	N	Y	N	N	N	Y	N	N	N	N	Y	
3. Was the study described as double-blind?	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
4. Was the method of double blinding appropriate?	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
5. Was there a description of dropouts and withdrawals?	L	L	H	L	L	L	L	L	H	L	L	L	L	L	L	L	L	H	H	L	L	H	L	L	L	H	L	L	L	L	L	
Jadad score	1	1	4	1	1	1	0	0	3	1	1	1	1	0	3	1	1	3	3	1	1	3	0	1	1	5	1	1	1	0	3	
Quality of study	L	L	H	L	L	L	L	L	H	L	L	L	L	L	H	L	L	H	H	L	L	H	L	L	L	H	L	L	L	L	L	

Y = Yes; N = No; L = low; H = high.

placement^{10,11,22,23,28,29,32-36,38,39,42,43,45,48,49}. This strategy avoids a period of edentulism and immediately puts the implants to work. For this reason, the literature showed increased satisfaction among of patients who experienced tooth loss and were rehabilitated using immediately placed implants^{5,10,40,55-57}.

The studies performed by Luongo et al.³⁴ and Krennmair et al.³³ paired immediate implant placement with immediate loading among implants that used single and full-arch prosthetics, respectively. These studies demonstrated no significant radiographic evidence of bone resorption, and the condition of the gingival tissue was suitable for immediate implant placement.

Bone density at the receptor site, and the primary stability achieved at the time of implant insertion, can influence stress distribution in the peri-implant bone tissue; this can compromise the longevity of the osseointegrated implants⁵⁸⁻⁶⁰. In the case of immediate implants, this should be considered during each patient's rehabilitation planning.

With this in mind, although the mandible is a more compact bone, a larger number of immediate implants were inserted in the maxilla, because it is of greater aesthetic concern^{8,23,25,32,36,39,42,43,45}. However, even though the bone is of lower density, the literature reveals a high rate of success among dental implants inserted in the maxilla, regardless of whether bone grafting was performed. Furthermore, different bone grafting techniques, as well as, surface treatment of the implants to facilitate osseointegration, has increased rates of success, which has in turn increased the viability and predictability of using immediate dental implants^{58,61-63}.

Marked variation in the dimensions of the implants (diameter and length) was noted; these measurements directly influenced the survival rate of the implants. Therefore, we recommended using implants with the largest possible allowed by the bone height and thickness of the bone tissue in the region.⁶⁴ In particular, some of the studies showed that, when long implants were inserted into an average of 6-8 mm into of baseline bone tissue, they were exposed to vital cells. This increased direct contact between such cells and the implant surface, which in turn improved the primary stability of the implants^{33,56,65-67}. Consequently, the survival rate of the osseointegrated implants also increased.

Interestingly, in some eligible studies^{10,26,28,29,34-36,38,39,45,48} the

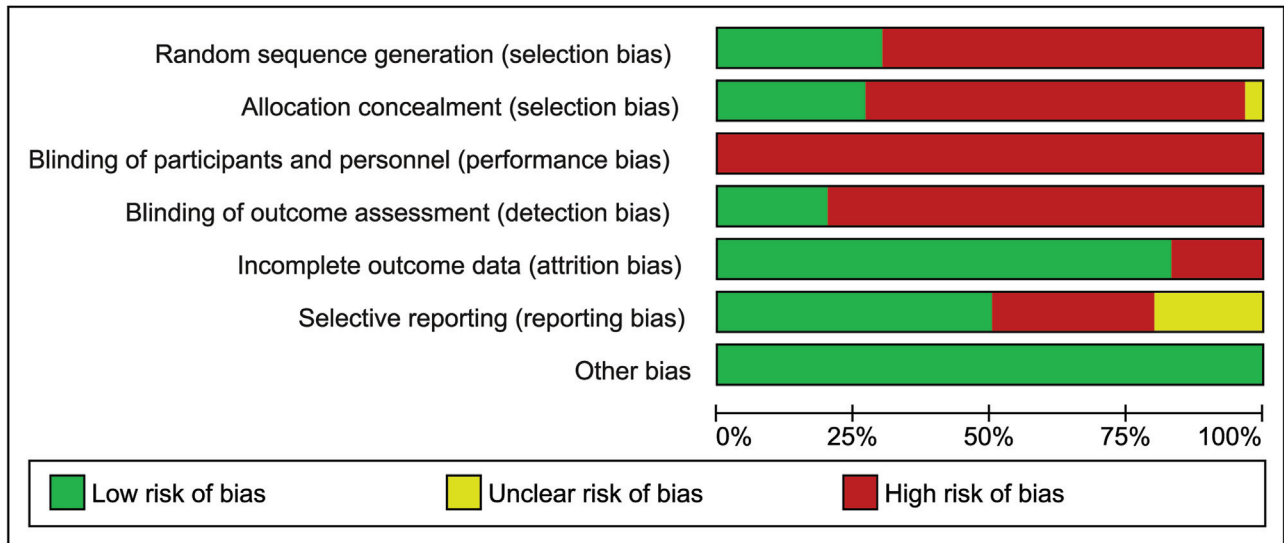


Fig. 6. Assessing risk of bias in included studies by Cochrane Collaboration’s tools.

authors used implants that had undergone different surface treatments; that is, some were double acid-etched, whereas others were thermo-etched or plasma-sprayed. In this regard, the literature suggests that modifying the implant design and surface may accelerate the osseointegration process and influence the success of dental implants^{68,69}. Using fresh extraction sockets in a dog model, Calvo-Guirado⁷⁰ showed that surface-conditioned implants presents 8% more bone apposition and 1.07 mm less crestal bone resorption than surface non-conditioned implants after 12 weeks of healing. However, despite this

encouraging result, there is still no consensus regarding whether any given surface modification is better than another⁷¹, or what is the most effective surface treatment for the immediate implants.

We accepted our second null hypothesis: that implants inserted into fresh extraction sockets do not differ significantly from those inserted into healed sockets in terms of the associated marginal bone loss or soft tissue changes. In this regard, it is important to analyse changes to the marginal bone tissue, because immediate implant insertion involves bone remodelling that occurs after tooth extraction; this can

generate unavoidable horizontal and vertical dimensional changes in the alveolar ridge^{72–74}. However, when we performed a quantitative analysis on studies that reported these kinds of data^{10,28,34,36–39,49}, there was no significant difference in bone loss between the two groups.

With regard to ISQ analysis using devices such as the Osstell, no significant differences were found between the two groups. Specifically, even though immediate implants had the lowest ISQ values, the latter remained within limits previously established in the literature (54–74 ISQ units)⁷⁵. Importantly, only the final ISQ

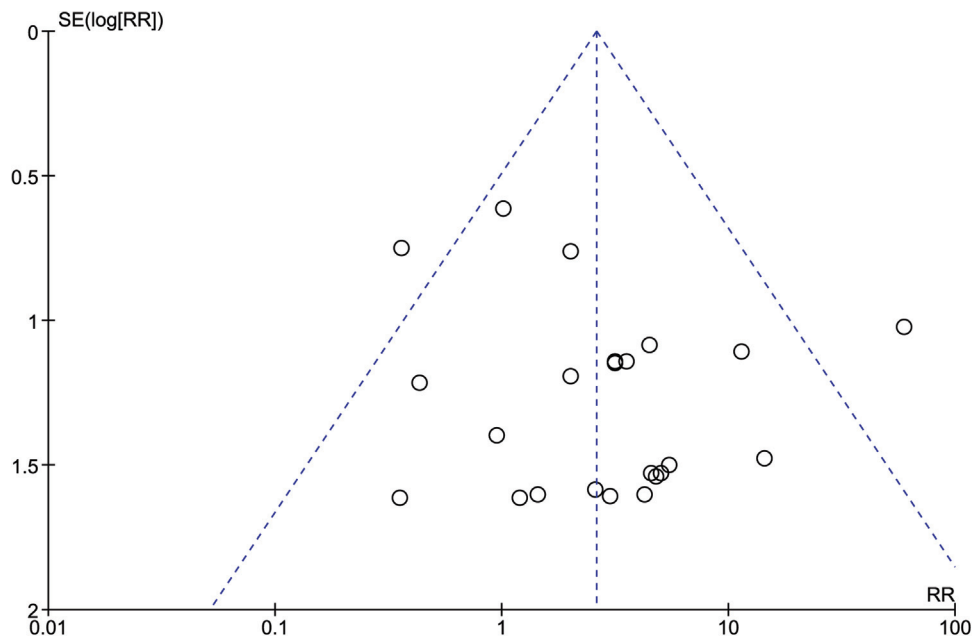


Fig. 7. Funnel plot for the studies reporting the outcome event ‘implants survival rates’ for eligible studies.

values were used in the quantitative analysis in the present study. This may be why no statistically significant differences were found between the two groups.

A quantitative analysis was also performed on the studies that reported probing pocket depth^{33,34,37,45}. No significant differences occurred between the two groups in this regard. Pocket probing depth may be increased by gaps that form between the implant and alveolar walls after implant placement in a fresh extraction socket. Such gaps can lead to major dimensional changes in the hard and soft tissue surrounding the implants; these can in turn impede the initial torque and primary stability at the time of insertion⁵⁵. In the case of implants inserted in healed sockets, a completely different clinical situation was seen.

For these reasons, the primary stability of implants placed in fresh sockets mainly depends on the quantity and quality of the remaining apical bone. In delayed implants, the alveolar ridge cicatrizes for a mean period of 4–6 months. At the time of implantation, alveolar bone regeneration has reached its peak, resulting in increased primary stability and low values for dimensional change^{34,58,61}. Interestingly, the differences between the two groups were most significant in the first postoperative year; they tended to stabilize over the following year^{38,76}.

Most studies did not include patients with systemic diseases and harmful habits (smoking)^{8,11,22,23,29,32,36,37,42,43,45,49} that could have affected the outcome. Nonetheless, among the eligible studies, two groups of the authors^{28,46} inserted implants in periodontally compromised patients. Siebers et al.⁴⁶ reported survival rates of 99.4% for delayed implants and 93.1% for immediate implants, while Deng et al.²⁸ observed survival rates of 87.5% for immediate implants and 100% for delayed implants. Importantly, Deng et al. reported all implant failures in the maxillary arch, a region that possesses a greater number of risk factors, including decreased bone density and increased shear forces^{59,77,78}. Thus, it must be emphasized that immediate implants are more susceptible to failure in patients with systemic conditions such as periodontal disease⁷⁹.

Immediate implants may be preferred in certain clinical situations: specifically, when bone conditions are optimal, with sufficient height and thickness to guarantee good primary stability at the time of implant insertion. This must be associated with careful planning and execution of the surgical and prosthetic procedures; in this

way, surgeons can reduce the number of risk factors present during insertion of the implants into fresh extraction sockets.

A possible limitation of this study is that some eligible studies have a short-term follow-up period (less than 12 months) and this could influence the implants survival rates. Additionally, an expressive variation in dimensions (diameter/length) of the implants was observed among the eligible studies. Although some studies have shown the placement of wide diameter implants, there was no possible specifically analysis. The authors did not report failure rates according to the diameter of implants, and the dimension of implants was selected by the surgeon according to each clinical situation.

Finally, given the high level of bias among our selected studies, which was due to lack of randomization, allocation and blinding for most studies further randomized controlled clinical studies with larger follow-up period are needed. The lack of bias occurred because it is difficult to blind patients and surgeons to the treatment group. It is only possible to blind those responsible for the analysis. For this reason the quality of the evidence is reduced.

In conclusion, immediate implant insertion should be performed with caution because implant survival rates are significantly lower than with implants inserted into healed sockets.

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Competing interests

None.

Ethical approval

Not applicable.

Patient consent

Not applicable.

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