Dental Implant Outcomes in Grafted Sockets: a Systematic Review and Meta-Analysis

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ABSTRACT

Objectives: To assess the treatment outcomes of the dental implants placed in the grafted sockets.
Material and Methods: A search protocol was developed to evaluate the treatment outcomes of dental implants placed in the grafted sockets in terms of implant survival rates (primary outcome), marginal-bone-level (MBL) changes, clinical parameters (i.e., bleeding on probing, probing depth), occurrence of peri-implant diseases, and aesthetic outcomes (secondary outcomes). Randomized controlled clinical trials (RCTs), controlled clinical trials, and prospective studies with at least 12 months of follow-up and a minimum of 10 patients having at least one dental implant inserted into the grafted socket were conducted. MEDLINE (PubMed) was searched for relevant articles published until 1st April 2019. A meta-analysis was performed using the random-effects model on the selected qualifying articles.
Results: The present analysis included 7 RCTs. The survival rate of the implants inserted into the grafted sockets ranged from 95 to 100% after 1 to 4 years of follow-up. MBL loss was found to be significantly greater for the implants placed in the non-grafted healed sites than for those placed in the previously grafted sockets (weighted mean difference = -1.961 mm, $P < 0.0001$). In terms of MBL changes, no difference was detected between immediately inserted implants versus implants placed in previously grafted sockets. None of the included studies reported on the clinical parameters or occurrence of peri-implant diseases
Conclusions: Implants inserted into the previously grafted sockets showed high survival rates and lower marginal-bone-level loss than the implants inserted into the non-grafted sites.

Keywords: alveolar bone atrophy; alveolar bone grafting; dental implants; tooth socket.

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INTRODUCTION

Extraction of a natural tooth inevitably results in significant three-dimensional alveolar bone resorption, particularly within the first 6 months [1,2]. As a consequence, alveolar ridge resorption can complicate the placement of implants into prosthetically driven positions. Therefore, to limit the post extraction dimensional changes, alveolar ridge preservation therapies, which intend to preserve the ridge volume in the envelope existing at the time of extraction, have been proposed [3].

The results of previous systematic reviews indicate that alveolar ridge preservation is effective at minimizing bone reduction [4-6]. In particular, alveolar ridge preservation performed immediately after tooth extraction were shown to result in significantly less vertical and horizontal contraction of the alveolar crest compared to the spontaneous healing [5]. Additionally, the beneficial effect of alveolar ridge preservation was more pronounced in the prevention of horizontal bone resorption, followed by the prevention of resorption in the vertical mid-buccal and vertical mid-lingual bone [4,6].

With regard to clinical outcomes of implants placed in grafted sites, the implant survival rates following lateral bone augmentation or sinus-floor elevation with the lateral approach were reported to be high and comparable to the ones placed into native bone [7,8]. Likewise, based on previous clinical studies, implants placed simultaneously with guided bone regeneration procedures exhibited clinical performance (with respect to survival rates, marginal-bone-height, and peri-implant soft tissue parameters) similar to that of implants in non-grafted sites [9-11]. Moreover, lateral bone augmentation procedures were found to be associated with peri-implant tissue stability after short-term (1 to 3 year) and long-term (> 3 year) follow-ups [12].

Until now, however, there has been limited evidence regarding the clinical outcomes of implants inserted following ridge preservation. Hence, the aim of this systematic review is to assess the existing evidence regarding the clinical outcomes of implants placed into previously grafted extraction sockets.

MATERIAL AND METHODS

Protocol and registration

The methods of the analysis, inclusion and exclusion criteria were specified in advance and documented in a protocol. The review was registered in PROSPERO, an international prospective register of systematic reviews.

The review protocol was developed according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement [13].

Focus question

The following question was developed according to the population, intervention, comparison, and outcome (PICO) study design (Table 1):

What are the clinical and radiographic treatment outcomes of the dental implants placed into the grafted sockets?

Information sources

The electronic databases MEDLINE (PubMed) was searched for relevant articles published until 1st April 2019.

In MEDLINE (PubMed), the search was limited to humans, and English language. Also, a filter concerning "Article Type" was applied: controlled clinical trial, randomized controlled trial, evaluation studies, clinical study, clinical trial, comparative study, multicenter study, observational study, twin study, validation studies.

Table 1. The focus question development according to the PICO study design

Component	Description
Population (P)	Patients, older than 18 years and in good general health, requiring the placement of one or more implants in grafted sockets
Intervention (I)	Implant placement in grafted sockets
Comparison (C)	Implant placement in non-grafted sockets
Outcomes (O)	**Primary**: implant survival. **Secondary**: marginal-bone-level changes (mm), clinical parameters (i.e., bleeding on probing (%), probing depth (mm), occurrence of biological complications (i.e., peri-implant mucositis and/or peri-implantitis), aesthetic outcomes (pink aesthetic score [PES], white aesthetic score [WES], PES/WES, Jemt's score)
Focus question	What are the clinical and radiographic treatment outcomes of the dental implants placed into the grafted sockets?

In addition, a hand search was performed including reference lists of all full-text articles and the following scientific journals: "Clinical Oral Implants Research", "Clinical Implant Dentistry and Related Research", "European Journal of Oral Implantology", "Implant Dentistry", "International Journal of Oral & Maxillofacial Implants", "International Journal of Periodontics and Restorative Dentistry", "Journal of Clinical Periodontology", "Journal of Oral Implantology", "International Journal of Oral and Maxillofacial Surgery", "Journal of Periodontology", "Journal of Prosthetic Dentistry", "Open Dentistry Journal", "Journal of Implants and Advanced Clinical Dentistry".

Search

The following search terms were used: (dental Implants [Mesh] OR implant) AND (bone regeneration [Mesh] OR socket preservation [Mesh] OR socket graft [Mesh] Or ridge preservation [Text word] OR augmentation [Text word]).

Selection of studies

During the first literature-selection stage, the titles and abstracts of all identified studies were screened for eligibility by two independent reviewers (AR and AC).

Inclusion and exclusion criteria

The following inclusion criteria were applied:

- Randomized controlled clinical trials, controlled clinical trials, and prospective studies with at least 12 months of follow-up with a minimum of 10 patients, older than 18 years old, having at least one implant inserted into the grafted socket;
- Grafting interventions performed prior to implant placement that aimed at preserving extraction sockets (i.e., procedures aimed at preserving the ridge volume within the envelope existing at the time of extraction [3]) were included;
- Studies with screw-type titanium implants that were placed into the healed sites (type IV implant placement [14]);
- Studies reporting on the specified primary or secondary treatment outcome.

At the second stage, the full texts of potentially eligible articles were reviewed and evaluated according to the following exclusion criteria:

- Animal studies;
- Retrospective studies, case reports, and cross-sectional studies;
- Studies in which lateral ridge augmentation procedures and/or alveolar ridge contour augmentation and/or maxillary sinus floor elevation and/or augmentation of extraction [2] sockets were performed;
- Studies reporting on lateral and/or vertical bone augmentation procedures;
- Articles published in language other than English.

Differences between reviewers were resolved by discussion and consensus. The level of inter-examiner agreement for the first- and second literature-selection stages was expressed by Cohen's kappa-score.

Data extraction and data items

From the selected articles fulfilling the inclusion criteria, the following data were retrieved into pre-defined tables:

- General information: study design, follow-up period, number of patients, patient-related information, including age, gender, smoking status, history of periodontitis (Table 2).
- Socket grafting procedures and implant related information: material used for socket grafting, Control group characteristics, use of systemic antibiotics, number of implants, time of implant placement, implant type, time of loading, maintenance program (Table 3).
- Treatment outcomes: implant survival, radiographic outcomes (i.e., marginal-bone-level [MBL] changes), clinical parameters (i.e., bleeding on probing [BOP], probing depth (PD)), occurrence of biological complications (i.e., peri-implant mucositis and/or peri-implantitis), aesthetic outcomes (pink aesthetic score [PES], white aesthetic score [WES], PES/WES, Jemt's score), additional findings (Table 4).

Quality assessment

The Cochrane Collaboration's tool for assessing risk of bias was used in the case of controlled clinical trials [15] (Table 5). In six categories (random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, other potential risk of bias) a rating of low, unclear or high risk of bias was performed.

Data synthesis

A meta-analysis integrates the quantitative findings from separate but similar studies and provides a numerical estimate of the overall effect of interest. All meta-analyses were performed on randomized

Table 2. Characteristics of the included studies

Study	Year of publication	Study design	Follow-up period	No. of patients	Patient age (years)	Gender (male/female)	Smoking status	History of periodontitis
Tallarico et al. [27]	2017	RCT	1.5 year	24 patients. Test: 12; Control: 12	53.9 (range 37 to 67)	8/16	No smokers were included	Untreated periodontitis was an exclusion criteria
Tallarico et al. [28]	2016	RCT	1 year	24 patients. Test: 12; Control: 12	Test: 56.2 (range 42 to 67); Control: 51.6 (range 37 to 67)	8/16	No smokers were evaluated	Untreated periodontitis was an exclusion criteria
Cardaropili et al. [29]	2015	RCT	1 year	41	47.2 (SD 12.9)	24/17	NR	Periodontitis patients excluded
Barone et al. [30]	2012	RCT	3 years	40 patients. Test: 20; Control: 20	Range 26 to 69	16/24	Smokers included. 12 participants (30%) (6 in each group) were smokers	NR
Marconcini et al. [31]	2018	RCT	4 years	42 patients. Test 1: 15; Test 2: 14; Control: 13	52.8 (SD 2.31)	17/25	NR	NR
Felice et al. [32]	2015	RCT	1 year	50 patients. Test: 25; Control: 25	Test: 53.08 (range 39 to 72); Control: 51.32 (range 32 to 71)	25/25	Test: non-smokers (16); up to 10 cigarettes/day (9); more than 10 cigarettes/day (0) Control: non-smokers (14); up to 10 cigarettes/day (8); more than 10 cigarettes/day (3)	Untreated periodontitis was an exclusion criteria
Esposito et al. [33]	2015	RCT	1 year	106 patients. Test: 52; Control: 54	Test: 50 (range 30 to 72); Control: 48 (range 28 to 70)	46/60	Three groups: non-smokers; up to 10 cigarettes/day; more 10 cigarettes/day	Untreated periodontitis was an exclusion criteria
Esposito et al. [34]	2017	RCT	1 year	210 patients. Test: 70; Control 1: 70; Control 2: 70	Test: 55.8 (SD 11.6); Control 1: 55.3 (SD 11); Control 2: 53.5 (SD 13.4)	Test: 37/33 Control 1: 34/36 Control 2: 36/34	Three groups: non-smokers; up to 10 cigarettes/day; more 10 cigarettes/day	Untreated periodontitis was an exclusion criteria

RCT = randomized clinical trial; NR = not reported; SD = standard deviation.
All papers included systemically healthy patients.

Table 3. Socket preservation procedures and implant characteristics

Study	Socket grafting materials	Control group	Systemic antibiotics	No. of implants	Time of implant placement	Implant type	Loading protocol	Maintenance program
Tallarico et al. [27]	Corticocancellous porcine bone (GENOSS, OsteoBiol®) + portice derma (OsteoBiol®)	Immediate implants placed into the sockets grafted with corticocancellous porcine bone (GENOSS, OsteoBiol®) + portice derma (OsteoBiol®)	Prophylactic preoperatively; 4 days postoperatively[a]	24 implants. Test: 12; Control: 12	4 months	Osstem® 7 mm wide	4 months: definitive restorations	-
Tallarico et al. [28]	Corticocancellous porcine bone + extracellular resorbable membrane. GENOSS, OsteoBiol® + portice derma (OsteoBiol®)	Immediate implants placed into the sockets grafted with corticocancellous porcine bone (GENOSS, OsteoBiol®) + portice derma (OsteoBiol®)	Prophylactic preoperatively; 4 days postoperatively[a]	24 implants. Test: 12; Control: 12	4 months	Osstem® 7 mm wide	4 months: definitive restorations	Recall visits every 6 months, up to 1 year.
Cardaropoli et al. [29]	Deproteinized bovine bone graft (Geistlich Bio-Oss®) + absorbable collagen membrane (Geistlich Bio-Gide®)	Implants placed in naturally healed sites	No	48 implants. Test: 24; Control: 24	4 months	4 to 5 mm diameter, conical shape. (Biomet/3i)	4 months	NR
Barone et al. [30]	Corticocancellous porcine bone particles (OsteoBiol®) + collagene membrane (OsteoBiol®)	Implants placed in naturally healed sites	Prophylactic preoperatively; 4 days postoperatively[a]	40 implants. Test: 20; Control: 20	4 months	3.3 to 5 mm diameter, 10 to 13 mm length (Sweden & Martina®)	4 months	Oral hygiene every 3 months
Marconcini et al. [31]	Test 1: Collagenated corticocancellous porcine bone particles (OsteoBiol®) + collagene membrane (OsteoBiol®) Test 2: cortical porcine bone (OsteoBiol®) + collagene membrane (OsteoBiol®)	Implants placed in naturally healed sites	Prophylactic preoperatively; 4 days postoperatively[a]	42 implants. Test 1: 15; Test 2: 14; Control: 13	3 months	Diameter: NR; BT Evo; Biotech	Two-stage surgery 4 month	Personalized maintenance programme and recall visits
Felice et al. [32]	Algae-derived frios algipore (Dentsply Friadent®) + Geistlich Bio-Gide®	Immediate implant placement bone-to-implant gaps filled with algae-derived bone substitute	Prophylactic preoperatively; 4 days postoperatively[a]	50 implants. Test: 25; Control: 25	4 months	Diameter: 3.8/4.5/5.5 mm, length: 8/9.5/11/13/15 mm Xive S plus, Dentsply®	Immediate restoration (> 35 N); 4 months (< 35 N); 4 months definitive crown	Oral hygiene and recall visit every 6 months
Esposito et al. [33]	Deproteinized bovine bone graft (Bio-Oss®) + absorbable collagen membrane (Geistlich Bio-Gide®)	Immediate implant placement 35 implants (40%) bone-to-implant gaps were filled with anorganic bovine bone	Prophylactic preoperatively; 4 days postoperatively[a]	106 implants. Test: 54; Control: 52	4 months	Diameter: 4/5 mm Length: 7/8.5/10/11.5/13/15 mm (MegaGen®)	Immediate restoration (> 35 N); 4 months (< 35 N); 4 months definitive crown	NR
Esposito et al. [34]	Collagenated corticocancellous porcine bone particles (OsteoBiol®) + resorbable membrane derived from equine pericardium (OsteoBiol®)	Control 1: immediate placed implants. Control 2: immediate-delayed placed implants after 6 weeks post extraction	Prophylactic preoperatively; 4 days postoperatively[a]	210 implants. Test: 70; Control 1: 70 Control 2: 70	4 months	Diameter: 3.5/4.3/5 mm; length: 8.5/10/11.5/13/15 mm (Nobel Biocare®)	Two-stage surgery; Loading with prov. Crowns 4/6 months after surgery	Oral hygiene and recall visit every 6 months

[a]Prophylactic preoperatively 2 g amoxicillin or 600 mg clindamycin (in case of allergy); 4 days postoperatively 1 g amoxicillin or 300 mg clindamycin twice a day.

Table 4. Treatment outcomes

Study	Implant survival (%)	Radiographic bone assessment	Clinical parameters[a]	Peri-implant diseases	Aesthetic outcomes[b]	Other findings
Tallarico et al. [27]	Test: 100%; Control: 100%	MBL changes. Test: 0.23 (SD 0.06) mm; Control: 0.63 (SD 0.31) mm; P = 0.001	NR	NR	PES score. Test group: 12.2 (SD 1.2); Control group: 10.6 (SD 1.8); P = 0.019	-
Tallarico et al. [28]	Test: 100%; Control: 100%	MBL changes. Test: 0.23 (SD 0.06) mm; Control: 0.63 (SD 0.31) mm; P = 0.01	NR	NR	PES score. Test group: 11.7 (SD 1.2); Control group: 10.7 (SD 1.5); P = 0.081	-
Cardaropoli et al. [29]	Test: 100%; Control: 100%	MBL changes. Test: 0.33 (SD 0.28) mm Control: 0.35 (SD 0.27) mm; P = 0.8	NR	NR	NR	During implant placement additional bone grafting was necessary in 14 implants in Test group (58.33%), P < 0.05. MBL > 1 mm during the first year: Test: 1 implant; Control: 2 implants (P = 0.98)
Barone et al. [30]	Test: 95%; Control: 95%	MBL changes. 1 year: Test: 0.75 (SD 0.3) mm; Control: 0.76 (SD 0.3) mm; P = 0.82 2 years: Test: 0.83 (SD 0.2) mm; Control: 0.84 (SD 0.2) mm; P = 0.66 3 years: Test: 1 (SD 0.2) mm; Control: 1.02 (SD 0.3) mm; P = 0.52	NR	NR	NR	During implant placement additional bone grafting was necessary in 13 implants in the Test group and 10 in the Control group (P = 0.02)
Marconcini et al. [31]	Test 1: 100%; Test 2: 100%; Control: 100%	MBL changes. Test 1: 1.14 (SD 0.23) mm; Test 2: 1.13 (SD 0.29) mm; Control: 1.95 (SD 0.07) mm. Significantly higher in control group (P < 0.001)	NR	NR	PES score. Test 1: 9.42 (SD 0.75); Test 2: 8.53 (SD 1.18); Control: 6.07 (SD 1.89). Significantly higher in Test 1 compared to Test 2 and Control groups (P = 0.02)	During implant placement additional bone grafting was necessary in 6 implants in the Control group
Felice et al. [32]	Test: 100%; Control: 92%	MBL changes. Test 0.19 (SD 0.1) mm; Control 0.13 (SD 0.09) mm; P < 0.001	NR	NR	PES score. Test group: 12.22; Control group: 12.78; P = 0.09	-
Esposito et al. [33]	Test: 100%; Control: 96%	MBL changes. Test: 0.27 (SD 0.14) mm; Control: 0.13 (SD 0.16) mm. Significantly higher for the test implants (P < 0.036)	NR	NR	PES score. Test group 12.8 (SD 1.4); Control group: 13 (SD 1.5); P = 0.615	-
Esposito et al. [34]	Test: 98%; Control 1: 94%; Control 2: 94%	MBL loss. Test: 0.31 (SD 0.16) mm; Control 1: 0.25 (SD 0.17) mm; Control 2: 0.29 (SD 0.14) mm. Significantly higher for the test implants (P < 0.0001)	NR	NR	PES score. Test group: 11.78 (SD 1.1); Control 1: 12.52 (SD 1.08); Control 2: 12.49 (SD 0.96); P < 0.0001	-

[a]Clinical parameters: probing depth, bleeding on probing, mucosal recession.
[b]Aesthetic outcomes: papilla index, PES (pink aesthetic score).
MBL = marginal-bone-level; PES = pink aesthetic score (mean value); SD = standard deviation; NR = not reported.

Table 5. Assessment of the risk of bias for included controlled clinical studies

Study	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Summary assessment
Tallarico et al. [27]	Low	Low	Low	Low	Low	Low	Low
Cardaropoli et al. [29]	Low	Unclear	Unclear	Low	Low	Low	Unclear
Barone et al. [30]	Unclear	Low	Low	Low	Low	Low	Low
Marconcini et al. [31]	Low	Low	Unclear	Low	Low	Unclear	Low
Felice et al. [32]	Low	Unclear	Unclear	Low	Low	High	Unclear
Esposito et al. [33]	Low	Low	Low	Low	Low	Unclear	Low
Esposito et al. [34]	Low	High	Low	Low	Low	Unclear	Low

controlled clinical trials that reported the clinical outcomes of non-surgical periodontitis treatment utilizing different adjunctive antiseptics.

Thus, each study provided estimates of outcome measures. The goal was to obtain global estimates of these measures and to test whether they differed significantly. Global estimates of a proportion can be obtained by simply pooling together the data from each study. However, a test for significance cannot be applied to such pooled data, as these studies are heterogeneous with respect to study population and treatment protocol. Therefore, individual trials were pooled, and the weighted mean differences for the MBL changes, together with their 95% confidence intervals (CIs), were calculated. Under the fixed-effects model, it is assumed that all studies come from a general population and that the size is not significantly different among the different trials. This assumption was tested by the heterogeneity test using the Cochran Q statistics. We considered that in our case the random-effects model (the Der Simonian and Liard method) [16] was more appropriate to use since it took into account both the random variation within the studies and the variation among different studies. Later findings indicated the fixed-effects model might be invalid. Indeed, the random-effects model tended to give a more conservative estimate (i.e, with a wider CI), but the results from the 2 models usually agreed well.

RESULTS

Search results

The initial electronic search resulted in the identification of 115 titles. Following the evaluation of titles and abstracts, 99 publications were excluded (Cohens kappa = 0.927). The remaining 16 full-text articles were evaluated. The reasons for exclusion were as follows: (i) studies included < 10 patients in the Test group [17-19], did not assess the outcomes of dental implants [20,21], follow-up period < 1 year [22-26]. Finally, 8 articles were included into the analysis (Figure 1).

Characteristics of the included studies

The included studies are described in Tables 1 to 3. Two of the studies involved the same patient sample that was evaluated at different follow-up periods [27,28], therefore, a total of 7 original clinical investigations were included. All of them were designed as randomized controlled trials with a follow-up period ranging from 1 to 4 years. Control group participants in 3 of the studies had implants placed into naturally healed sites [29-31]. In the remaining 4 investigations Control group participants were treated with immediately placed implants [27,32-34] or were inserted 6 weeks post extraction [34]. Additionally, in the latter 4 investigations, immediate implants were inserted either into grafted sockets [27] or the gap between the implant and the bone was filled with a bone-fill material [32-34].

This systematic review pooled data collected from 512 patients (243 men, 270 women). All investigations included systemically healthy patients with a mean age range of 42.7 to 55.8 years. Smokers were included in 4 of the studies [30,32-34]. Smoking habit was an exclusion criteria in one investigation [27] and patient smoking status was not reported in two of the studies [29,31]. In 5 of the 7 studies, untreated periodontitis [27,32-34] or a history of periodontitis [29] was an exclusion criteria. Patients' periodontal status was not reported in two studies [30,31] (Table 2).

Socket grafting in all seven studies involved guided bone regeneration concept with the use of bone substitute material covered with a barrier membrane (Table 3). As a bone substitute, either xenogenous (six studies) or alloplastic (one study) bone-filler particles were used. As a barrier membrane, either collagen membranes (in five studies), porcine derma (one study) or a pericardium membrane (one study)

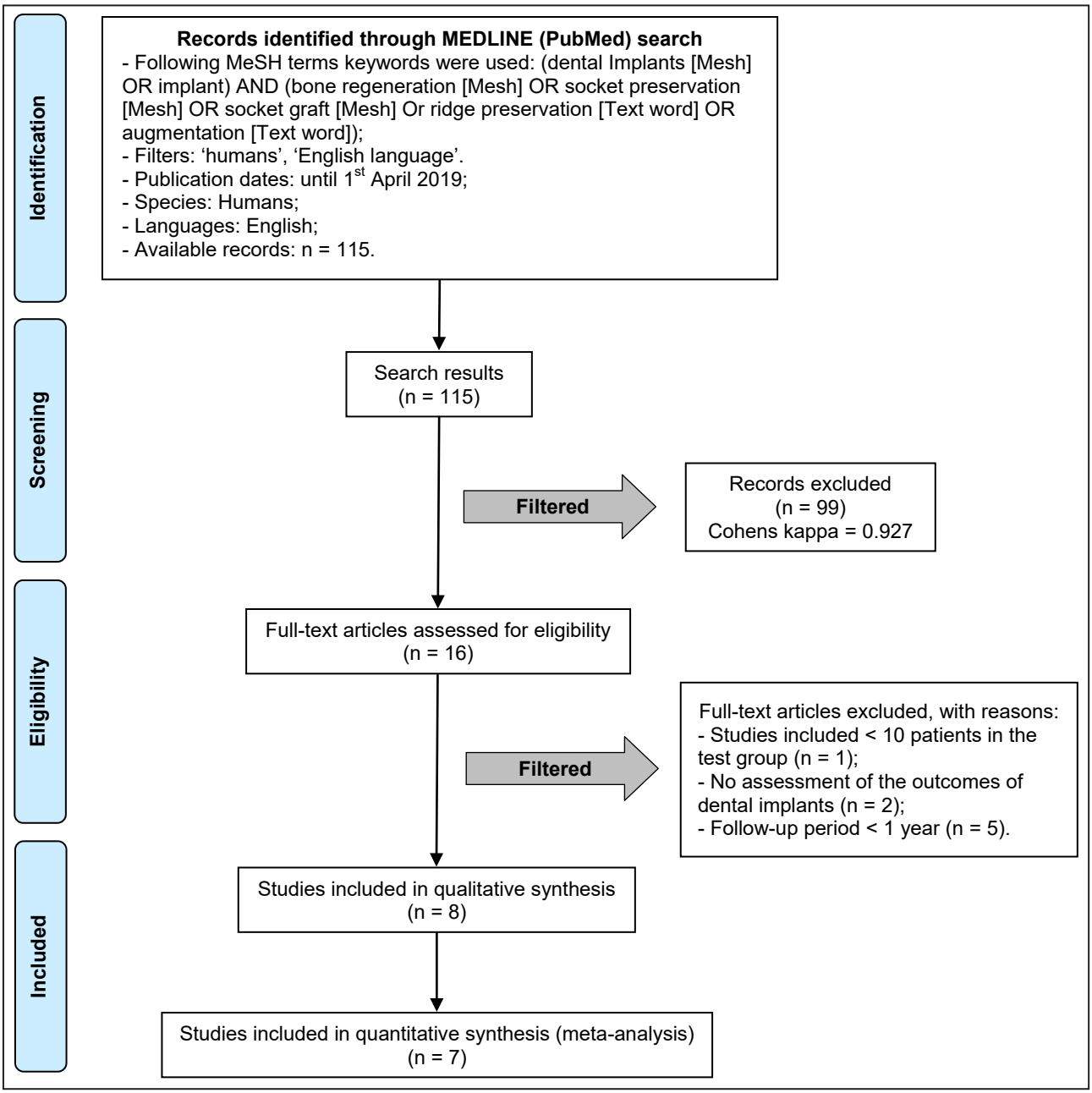


Figure 1. PRISMA 2009 flow diagram.

were used. In all but one study [29], all patients received prophylactic antibiotics preoperatively and continuously 4 to 6 days postoperatively (Table 4).

Of the total of 520 implants included, 232 were inserted into the previously grafted sockets (3 to 7 months following the grafting) (test), fifty-seven were inserted into the naturally healed sites, and 231 were placed immediately (or 6 week post extraction) after tooth extraction (controls). The diameter of the implants ranged from 3.3 to 5.5 mm, and one investigation included only implants with a diameter of 7 mm [27]. In 5 of the studies, patients were enrolled into either a personalized or regular maintenance program with 3- to 6-month intervals [27,30,32,34].

The assessment of risk of bias in the included randomized trials is presented in Table 5. A low risk of bias was noted in 5 studies according to 4 (3 studies), 5 (2 studies) or all 6 domains (1 study) [27,30,31,33,34]. The remaining 2 studies were judged to have an unclear risk of bias based on 2 ('allocation concealment' and 'blinding') domains [29,32].

The reported clinical outcomes of the implants

Implant survival, which was defined as a primary outcome, ranged from 95 to 100% for the Test group implants and from 92 to 100% for the implants in the Control groups (Table 4).

The mean MBL changes were reposted in all 7 investigations included. Two of them revealed no significant difference between the implants placed into the naturally healed sites or the previously grafted sockets [29,30]. In contrast, a single study reported higher MBL loss for the implants placed into the naturally healed sites versus grafted sockets [31]. In five investigations where immediate implants were the Control group, three of them found significantly higher MBL resorption for the implants placed into previously grafted sockets, compared to the immediately inserted ones [32-34]. Contradictory findings were reported by Tallarico et al. [27], where immediately placed implants experienced significantly higher rates of the MBL loss.

A pink aesthetic score (PES) was reported in five of the included studies [27,31-34]. In two of them, no difference was noted between the implants placed into the grafted sockets or immediately placed ones [32,33], whereas one study reported significantly higher PES scores for the immediately inserted implants [34]. Conversely, two investigations found superior soft tissue measurements for the implants placed into the healed, previously grafted sockets, compared to the immediately placed ones [27] and implants placed into the naturally healed sites [31]. Additionally, it has to be pointed out that none of the included studies reported the clinical parameters (i.e., BOP, PD) or the occurrence of peri-implant diseases (i.e., peri-implant mucositis or peri-implantitis). Moreover, three of the investigations revealed that additional bone grafting procedures were more often necessary around the implants placed into the naturally healed sites, compared to the previously grafted post extraction sockets [29-31]. Two of these studies found this difference to be statistically significant [29,30].

Meta-analysis

A meta-analysis was conducted to assess MBL changes in the following groups:

- Implants placed in the grafted sockets (n = 73 implants) vs. implants inserted into the non-grafted bone (n = 57 implants).
- Implants placed in the grafted sockets (159 implants) vs. immediately placed implants (231 implants).

The results showed significantly higher marginal bone loss for the implants in previously non-grafted healed sites than for the ones placed in the grafted sockets (weighted mean difference (WMD) = -1.961, 95% confidence interval [CI] [-3.793 to -0.13]; degrees of freedom [df] = 3; heterogeneity test [Q] = 54.36; $P < 0.0001$) (Figure 2).

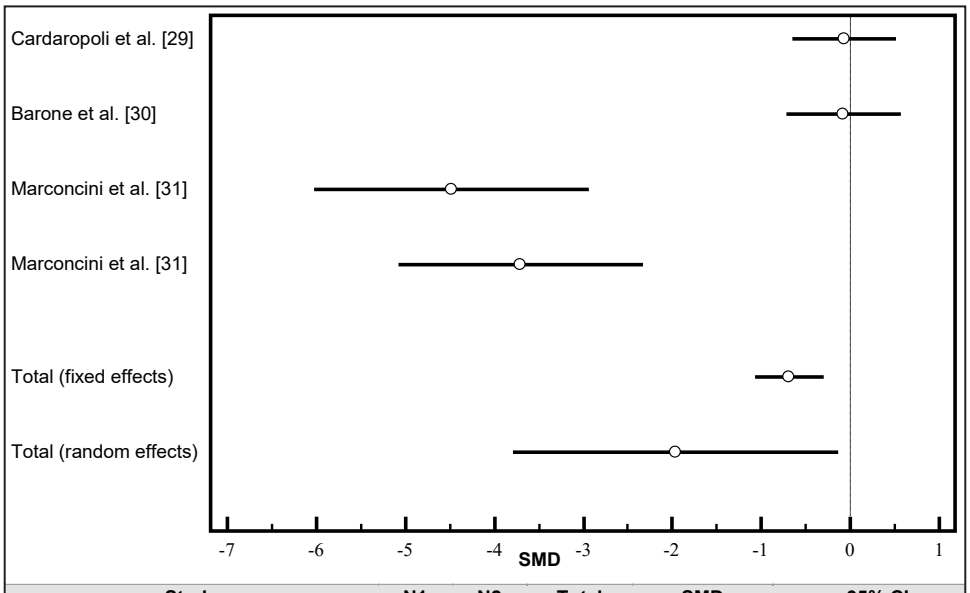
The comparison between implants in the grafted sockets vs. immediate implant placement (or 6 weeks post extraction) demonstrated no significant difference between the two implant groups (WMD = 0.194, 95% CI [-0.342 to 0.731]; df = 4; Q = 28.29; $P < 0.0001$) (Figure 3).

DISCUSSION

The aim of the present systematic review was to investigate the clinical performance of the implants placed in the previously grafted sockets. The included clinical studies presented methodological differences in terms of the variables assessed to measure the outcomes, and the Control groups (immediate implant placement vs. implants in the healed non-grafted sites).

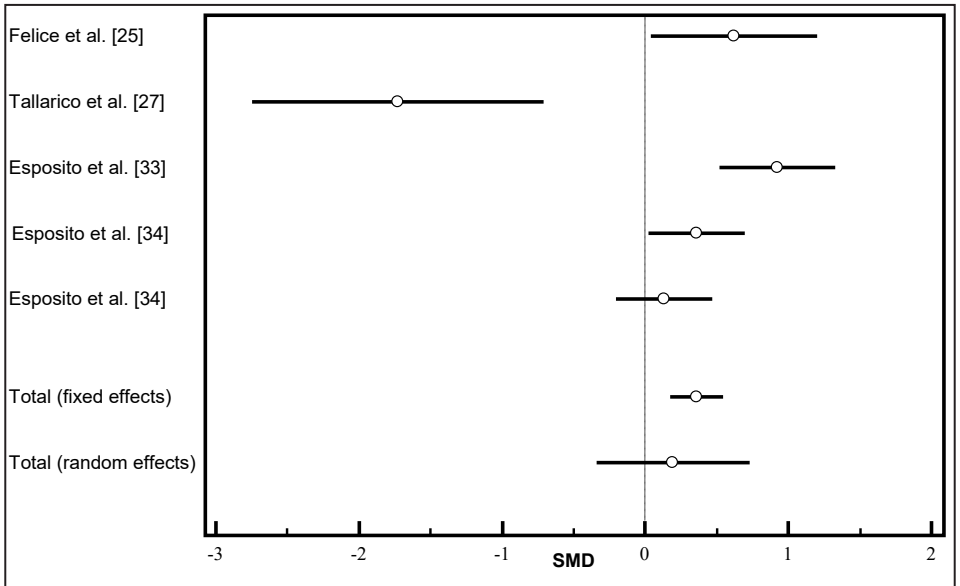
Based on the included 7 randomized clinical trials, the implants' survival rates ranged between 95% and 100% after 1 to 4 years of implant placement, with no significant differences between implants placed into previously augmented sockets and those inserted into the spontaneously healed sites. These findings corroborate the survival rates noted for the implants placed into the laterally augmented alveolar ridge sites (78.2 to 100%) [35] and for implants inserted into the laterally augmented sinuses (88.6 to 100%) [8]. Furthermore, the implant-survival rates following socket grafting were within the range of those previously reported for implants placed in pristine sites (93.2 to 100%) [7].

The present meta-analysis points toward significantly higher MBL loss for the implants in previously non-grafted healed sites than for implants placed in grafted sockets. Furthermore, the 3 studies included in the meta-analysis revealed that additional bone-grafting procedures were often required during implant placement at the sites without previous socket grafting [29-31]. These findings are comparable with the results of the previous meta-analysis, in which implant placement without bone augmentation resulted in significantly higher radiographic marginal bone loss compared to at the sites where dehiscence-type defects were augmented using a xenograft bone substitute and a collagen membrane [36]. However, out of three studies included in the present quantitative analysis, significant differences in terms on the MBL changes were reported in the investigation with the longest follow-up period (4 years [31] versus 1 [29] and 3 years [30]). Therefore, the follow-up period might be a critical factor in the treatment outcomes.



Study	N1	N2	Total	SMD	95% CI
Cardaropoli et al. [29]	24	24	48	-0,0715	-0,653 to 0,51
Barone et al. [30]	20	20	40	-0,0769	-0,717 to 0,564
Marconcini et al. [31]	15	13	28	-4,485	-6,025 to -2,944
Marconcini et al. [31]	14	13	27	-3,704	-5,079 to -2,329
Total (fixed effects)	73	70	143	-0,689	-1,077 to -0,301
Total (random effects)	73	70	143	-1,961	-3,793 to -0,13
Q = 54.3627; df = 3; P < 0.0001					

Figure 2. Forest plot of odds ratio (95% CI) for marginal bone level changes between the implants placed in the grafted sockets and implants inserted in previously non-grafted sites. CI = confidence interval; SMD = standardized mean difference; N1 = implants placed in the grafted sockets; N2 = implants inserted in previously non-grafted sites; df = degrees of freedom; Q = heterogeneity test.



Study	N1	N2	Total	SMD	95% CI
Felice et al. [25]	25	25	50	0.621	0.0374 to 1.204
Tallarico et al. [27]	12	12	24	-1.73	-2.748 to -0.711
Esposito et al. [33]	52	54	106	0.923	0.517 to 1.329
Esposito et al. [34]	70	70	140	0.361	0.0245 to 0.699
Esposito et al. [34]	70	70	140	0.132	-0.202 to 0.467
Total (fixed effects)	229	231	460	0.36	0.172 to 0.548
Total (random effects)	229	231	460	0.194	-0.342 to 0.731
Q = 28.2905; df = 4; P < 0.0001					

Figure 3. Forest plot of odds ratio (95% CI) for marginal-bone-level changes between the implants placed in grafted sockets and immediate implant placement. CI = confidence interval; SMD = standardized mean difference; N1 = implants placed in grafted sockets; N2 = immediate implant placement; df = degrees of freedom; Q = heterogeneity test.

Further comparison of the MBL changes between implants in the grafted sockets vs. immediate implant placement demonstrated no significant difference between the two approaches. Similar results were obtained in a previous systematic review, in which implant placement into fresh extraction sockets versus delayed implants into healed sockets resulted in comparable MBL changes [37]. However, among the 4 investigations included in the present meta-analysis, an inconsistency regarding the treatment outcomes was noted. Specifically, while Tallarico et al. [27] found significantly higher MBL loss for the immediately inserted implants over those placed into the healed and previously grafted sockets, the remaining investigations reported significantly higher MBL for the implants in the latter group (i.e., with delayed implants in the previously grafted sockets) [32-34].

The soft-tissue changes around the implants were assessed by PES score in 5 of the included studies [27,31-34]. Again, inconsistency existed among the results of the included studies. In particular, while 2 studies found superior PES scores for the implants placed into the healed, previously grafted sockets [27] and implants placed into the naturally healed sites [31] as compared to the immediately placed ones, Esposito et al. [34] contrarily presented significantly better soft-tissue outcomes for the immediately inserted implants. The latter study corroborates the results of the previous 3-year clinical investigations, which found superior soft-tissue outcomes (PES scores) for the immediately placed and immediately restored implants, as compared to the conventionally restored implants installed in to the healed sites [38]. The authors noticed that superior aesthetic outcomes could be expected in young patients (≤ 30 years) with implants in central incisor/cuspid areas and in the presence of bone recontouring [38].

Contradictory findings exist regarding the timing of implant placement and soft-tissue treatment outcomes. A recent prospective clinical investigation reported no significant difference in PES values between the immediate and conventional implant placement after 1- and 8 years of follow-up [39]. This observation is supported by the 2 included studies in the present analysis that revealed comparable soft-tissue outcomes for the immediate and delayed implant placement [32,33].

Recently, a meta-analysis has found the comparable prevalence of peri-implant mucositis and peri-implantitis as well as implant loss for dental implants placed in either native or augmented sites (including vertical and/or horizontal ridge augmentation) at both the patient and implant levels [40]. In the present analysis, however, none of the studies reported the clinical parameters or the occurrence of biological implant complications, which prevents comparison with the previous investigations.

CONCLUSIONS

In terms of survival rates, placing dental implants in previously grafted sockets is a predictable treatment option. Differences could be found for the peri-implant marginal-bone-level changes when compared with the implants placed into the non-grafted sites. Other objective quantitative methods must be considered in future studies to assess the peri-implant tissue changes that occur over time using different treatment approaches, in terms of the timing of grafting procedures and of implant placement.

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