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Review

Which is the best choice after tooth extraction, immediate implant placement or delayed placement with alveolar ridge preservation? A systematic review and meta-analysis

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ABSTRACT

A comprehensive literature search on implant placement protocols after tooth extraction (immediate, early, delayed, or later) was performed up to 2018. The screening process selected only randomized clinical trials (RCTs) from PubMed, Embase, Cochrane Library, Web of Science, Scopus, LILACS, and grey literature. A series of pairwise meta-analyses was carried out to evaluate implant performance in each protocol. The primary outcomes were implant survival and esthetic outcome, measured by pink esthetic score (PES), and the secondary outcomes were peri-implant bone resorption and implant complications. The outcomes were at least 1 year after implant surgery. A total of 5056 studies were found, of which 16 were included for qualitative analysis and 9 for quantitative analysis. The meta-analysis showed increased risk of implant failure by 3% in the immediate implant protocol. PES analysis showed no statistical significant difference between immediate or delayed protocols ($p = 0.16$). However, the subgroup analysis showed that the anterior region presented better results with immediate implants, while the molar region presented better results with delayed implants. The quantitative analysis showed no statistical difference in peri-implant bone resorption between the immediate and delayed implant protocols ($p = 0.42$). Due to the lack of studies with a low risk of bias, further RCTs are needed for definitive conclusions.

1. Introduction

Currently, dental implants are considered a reliable method for replacing missing teeth, with different protocols regarding the timing of implant placement suggested in the literature. These are as follows: type 1 (immediate implant placement), when the implant is installed immediately after tooth extraction; type 2 (early implant placement), when the implant is installed within 1–2 months after tooth extraction; type 3 (delayed implant placement), when the implant is installed within 3–4 months after tooth extraction; and type 4 (late or conventional placement), when the implant is installed more than 4 months after extraction (Chen and Buser, 2009).

Data concerning implant performance, including survival rates, success rates, and peri-implant bone loss are required to understand the potential advantages and disadvantages of the alternative timing protocols. Although immediate implant placement is an attractive technique, because it reduces the number of surgical procedures and increases patient satisfaction, it is still premature to conclude on the long-term results of this approach (Atieh et al., 2016).

Studies on animals (Araujo and Lindhe, 2005; Scala et al., 2014) and humans (Chappuis et al., 2013) have demonstrated that, after tooth extraction, the alveolar bone undergoes an inevitable physiological remodeling process that results in a variable reduction in bone dimensions. Probably, the bone reduction is correlated with the disruption of blood supply and the osteoclastic activity that occur after tooth extraction (Cardaropoli et al., 2003).

The purpose of this study was to synthesize information coming only from randomized clinical trials on various implant placement

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Table 1
PICOS criteria and framework for the systematic review.

		Search strategy (PubMed and Cochrane)	Search strategy (Embase)	Search strategy (Scopus)	Search strategy (Web of Science)	Search strategy (LILACS)
Patients or procedure (P) #1	Health patients requiring tooth extractions	–	–	–	–	–
Intervention (I) #2	Use of immediate implant placement, alveolar ridge preservation with grafting materials, and delayed implant or combined techniques for socket management after tooth extractions	((((((((((((Immediate Dental Implant Loading[MeSH Terms]) OR Dental Implants, Single-Tooth[MeSH Terms]) OR Dental Implants[MeSH Terms]) OR Dental Implantation, Endosseous[MeSH Terms]) OR Dental Implantation[MeSH Terms]) OR Alveolar Process [MeSH Terms]) OR Tooth Socket [MeSH Terms]) OR Alveolar Bone Loss[MeSH Terms]) OR Alveolar Bone Grafting[MeSH Terms]) OR ((((((osseointegrat*) AND implant*)) AND ((dental*) OR oral*))) OR (((((socket*) OR ridge*) OR alveolar)) AND ((augment*) OR preserv*)))))	('tooth implant'/exp OR 'tooth implantation'/exp OR 'alveolar bone'/exp OR 'alveolar bone grafting'/exp OR 'tooth socket'/exp OR 'single tooth implant'/exp OR 'alveolar ridge'/exp) OR ((osseointegrat* AND implant*) AND (dental* OR oral*)) OR ((socket* OR ridge* OR alveolar) AND (preserv* OR augment*))	(((((TITLE-ABS-KEY(osseointegrat*)AND TITLE-ABS-KEY(implant*))) AND((TITLE-ABS-KEY(dental*) ORTITLE-ABS-KEY(oral*)))) OR(((TITLE-ABS-KE(socket*) ORTITLE-ABS-KEY(alveolar*) OR TITLE-ABS-KEY(ridge*))) AND ((TITLE-ABS-KEY(augment*) OR TITLE-ABS-KEY(preserv*)))))	osseointegrat* AND implant* AND (dental* OR oral) OR ((socket* AND alveolar* AND ridge*) AND (augment* OR preserv*))	(tw:((osseointegrat$) (implant$) (dental$ OR oral$))) OR (tw:((socket$ OR alveolar OR ridge) (augment$ OR preserv$)))
Comparator or control group (C) #3	Different implant protocol	–	–	–	–	–
Outcomes (O) #4	Implant survival; implant esthetic outcome; peri-implant bone resorption expressed in mm; implant complications	–	–	–	–	–
Study design (S) #5	Studies in humans, including only RCT	(((((((((Randomized controlled trial[Publication Type]) OR controlled clinical trial [Publication Type]) OR randomized[Title/Abstract]) OR placebo[Title/Abstract]) OR "Clinical Trials as Topic"[Mesh:NoExp]) OR randomly[Title/Abstract]) OR trial[Title])) NOT ((animals [MeSH Terms]) NOT humans [MeSH Terms])))) NOT ((((((((((("Observational study"[Title]) OR Meta-analysis [Title]) OR retrospective[Title]) OR "Systematic review"[Title]) OR "Animal Study"[Title]) OR Rats[Title]) OR Mouse[Title]) OR Dogs[Title]) OR "Canine Model"[Title]) OR Rabbit[Title])	[Randomized controlled trial]/lim	((TITLE-ABS-KEY(randomized AND controlled AND trial) OR TITLE-ABS-KEY(controlled AND clinical AND trial) OR TITLE-ABS-KEY(randomized) OR TITLE-ABS-KEY(placebo) OR TITLE-ABS-KEY(randomly) OR TITLE(trial)))) AND NOT((TITLE(observational AND study) OR TITLE(meta-analysi) OR TITLE(retrospective)OR TITLE (systematic AND review) OR TITLE(animal AND study) OR TITLE(rats) OR TITLE(mouse) OR TITLE("Canine Model") OR TITLE(rabbit)))	(randomized clinical trial OR controlled clinical trial OR randomized OR placebo OR clinical trial OR randomly OR trial)	(tw:((tw:(randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR randomly OR trial))))AND NOT (ti:("Observational study" OR meta-analysis OR retrospective OR "systematic review" OR "animal study" OR rats OR mouse OR dogs OR "canine model" OR rabbit))
Language	No restriction					
Focused question	Which is the best choice after tooth extraction, immediate implant placement or alveolar ridge preservation technique with posterior implant placement?			#2 AND #5		

RCT, randomized clinical trial; MeSH terms, medical subject headings.

protocols (immediate, early, delayed, or later), evaluating implant performance in each case.

2. Materials and methods

The protocol for this systematic review was registered on PROSPERO (CRD42018102185). The PRISMA statement (Preferred Reporting Items for Systematic Review and Meta-Analysis) was used to ensure a higher methodological quality of the study (Moher et al., 2009). The PICOS strategy was used for the research question construction: (P) patients or population — health patients requiring tooth extractions; (I) intervention — immediate implant placement, early implant placement, delayed implant placement, alveolar ridge preservation with grafting materials, or combined techniques for socket management after tooth extraction; (C) comparison — different implant protocols; (O) outcomes — implant survival, implant esthetic outcome, peri-implant bone loss, implant complications; (S) study design — studies in humans, including only RCTs. There were no language or date restrictions. A broad electronic search of the MEDLINE/PubMed, EMBASE, Cochrane Library, Web of Science, Scopus, and Latin American and Caribbean Health Sciences Literature (LILACS) databases was conducted. The search strategy used both medical subject headings terms (MeSH) and free-text words. This search-specific PICOS framework strategy is shown in Table 1, to allow adequate reproduction of this study.

The search was limited to human studies, and the final electronic search was performed on July 22nd, 2018. The ClinicalTrials.gov trial registry platform was screened to find studies from the 'grey literature' (http://www.clinicaltrials.gov). The reference lists of the articles identified were then cross-checked. A manual search was performed in the following relevant journals: International Journal of Oral and Maxillofacial Surgery; Journal of Oral and Maxillofacial Surgery; Journal of Cranio-Maxillofacial Surgery; Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology; British Journal of Oral and Maxillofacial Surgery; Journal of Clinical Periodontology; Journal of Dental Research; Clinical Oral Implant Research; and International Journal of Oral and Maxillofacial Implants. Subsequently, the articles were imported into Endnote X9 software (Thompson Reuters, Philadelphia, PA, USA), where duplicates were automatically removed.

Controlled clinical trials, retrospective studies, duplicate studies, in vitro studies, studies with inadequate follow-up, studies focused only on histological analysis, and observational studies were excluded. Finally, articles were removed when the full text was not found or in cases of unpublished work where the authors could not be contacted to provide more information.

Titles and abstracts of the chosen studies were independently evaluated by two reviewers (JVC and FGR) who screened the titles and selected the abstracts for full-text inclusion. The full-text articles were obtained for those studies that the authors considered relevant or those where they were uncertain regarding the selection criteria. Any disagreement between the two review authors was resolved by a third author (PJM) The level of agreement between the review authors was calculated using the kappa statistic. A value of kappa between 0.40 and 0.59 was considered a fair agreement, between 0.60 and 0.74 a good agreement, and 0.75 or more an excellent agreement. Disagreement regarding inclusion was resolved by discussion. The primary outcomes were implant esthetic outcome and implant survival, at least 1 year after implant placement. The secondary outcomes were peri-implant marginal bone level changes and implant complications at least 1 year after implant placement.

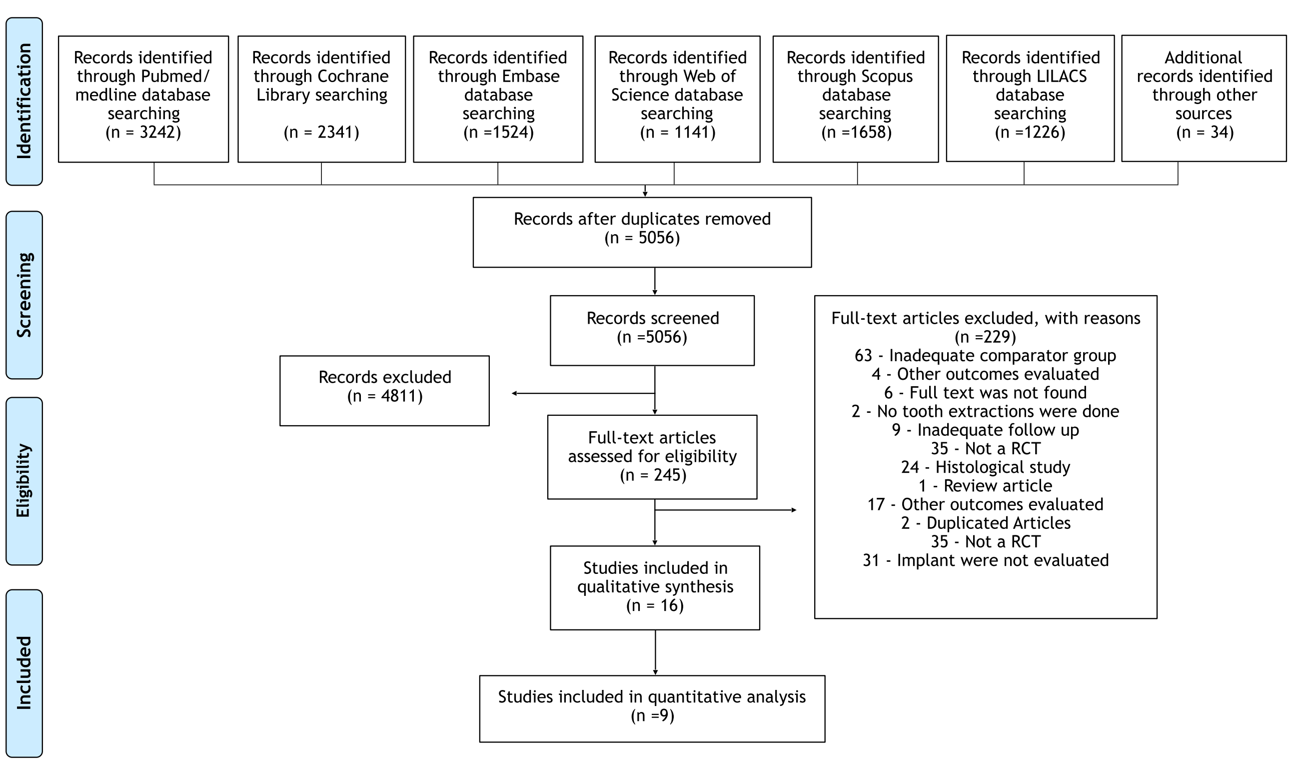

Fig. 1. PRISMA flow diagram of the screening and selection process.

The Cochrane Collaboration tool was used for assessing the risk of bias in the included studies (Higgins et al., 2011). Two review authors (JVC and FGR) assessed the risk of bias independently. The reviewers were blinded to information about the articles, such as the journal, the authors, the institution, and the direction magnitude of the results. Any disagreements between the authors were resolved by discussion.

Initially, a traditional pairwise meta-analysis was performed in this study using Review Manager (RevMan) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Statistical heterogeneity was measured by chi-square test (χ^2) and I-squared (I^2) tests. When $\chi^2 > 0.10$ and $I^2 < 50\%$, a fixed-effects model was used, thus ignoring heterogeneity. A random effects model was used to incorporate heterogeneity among studies and provide a more conservative pooled intervention effect when statistical heterogeneity was noted: $\chi^2 < 0.10$ and $I^2 > 50\%$. A *p*-value of 0.10 rather than the conventional level of 0.05 was used in this analysis to determine statistical significance, in accordance with Cochrane orientations.

3. Results

The PRISMA flow diagram of the screening and selection process is presented in Fig. 1. 11,165 studies were identified initially. After exclusion of duplicates, 5,056 records remained. After the eligibility process, 4,811 records were excluded and 245 full-text articles were obtained. After full-text reading of these studies, 16 randomized clinical trials (RCTs) fulfilled the inclusion criteria and were selected for qualitative analysis (Schropp et al., 2005, Schropp and Isidor, 2008, 2014; Lindeboom et al., 2006; Palattella et al., 2008; Block et al., 2009; Barone et al., 2012; Pang et al., 2014; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017). Finally, for quantitative analysis, 9 studies were included (Lindeboom et al., 2006; Block et al., 2009; Pellicer-Chover et al. 2014; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017). The reasons for exclusion are listed in Fig. 1. The value of kappa was 0.78, so agreement was considered to be excellent. None of the trials included in this review were assessed as being at low risk of bias for all the domains. 14 trials (Schropp et al., 2005, 2008, 2014; Lindeboom et al., 2006; Palattella et al., 2008; Barone et al., 2012; Pang et al., 2014; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017) were assessed as being at unclear risk of bias because each of these trials was at unclear risk of bias in one or more domains. The remaining two trials (Block et al., 2009; Checchi et al., 2017) were assessed as being at high overall risk of bias because each of these trials was at high risk of bias in one or more domains (Fig. 2).

3.1. Implant survival

The qualitative analysis included 16 studies (Schropp et al., 2005, 2008, 2014; Lindeboom et al., 2006; Palattella et al., 2008; Block et al., 2009; Barone et al., 2012; Pang et al., 2014; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) (Table 2), from which nine studies (Lindeboom et al., 2006; Block et al., 2009; Pellicer-Chover et al., 2014; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) were submitted for traditional meta-analysis. There were 580 implant surgeries in 444 patients. No relevant clinical heterogeneity was observed among the studies; the values of χ^2 and I^2 were 8.22 ($p = 0.41$) and 3%, respectively. Quantitative analysis showed that immediate implant intervention increased the risk of implant failure by 3% (risk difference 0.03; 95% confidence interval (CI) 0.0025–0.0647; $Z = 2.12$; $p = 0.03$). This is shown in Fig. 3.

3.2. Implant esthetic outcome

Nine studies were included in the qualitative analysis (Lindeboom et al., 2006; Pellicer-Chover et al., 2014; Cardaropoli

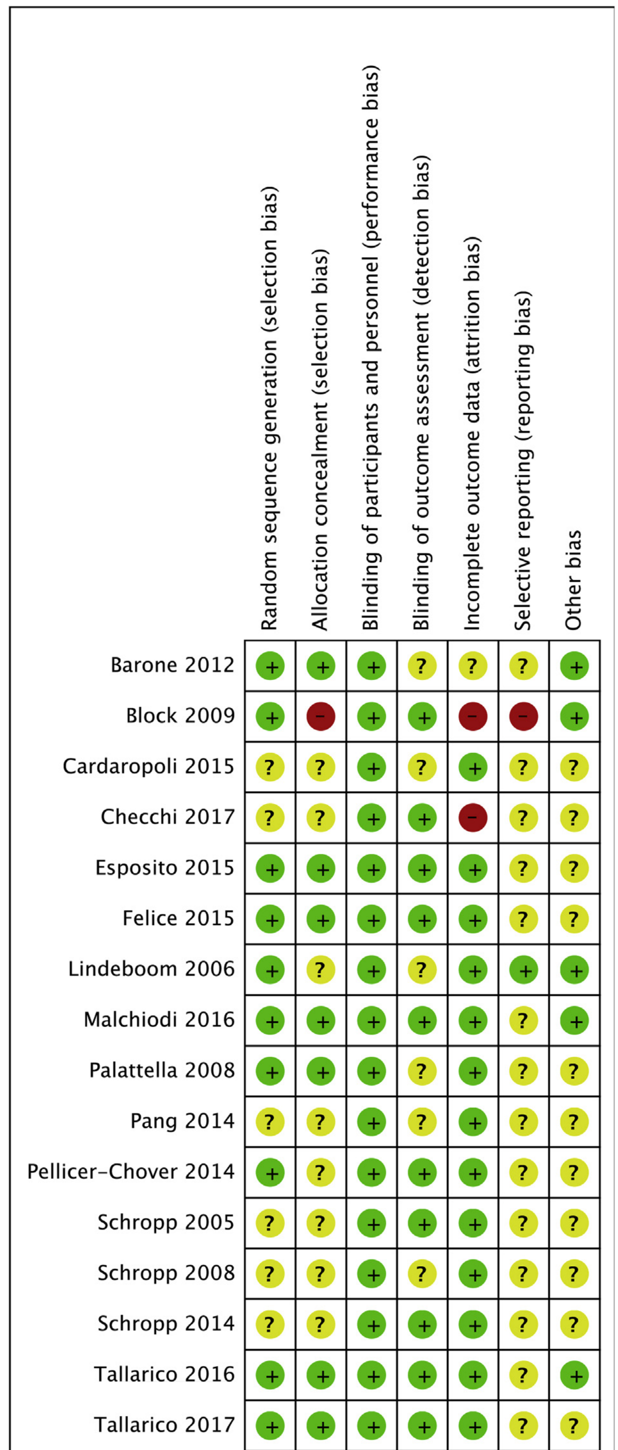

Fig. 2. Risk of bias summary: review authors' judgments.

Table 2
Primary outcomes.

Authors (year)	Comparison	Total number of patients	Drop-out	Follow-up	Number of implants per group	Survival				Success			
						Failure per group after at least 1 year	Implant survival rates (%)	p-value*	Meta-analysis	Evaluation method	PES (mean ± SD) OR success rates (%)	p-value*	Meta-analysis
Tallarico et al. (2017)	Immediate implant vs ARP-AXng + delayed implant	24	0	1 year	Immediate = 12; delayed = 12	Immediate (0); delayed (0)	Immediate (100); delayed (100)	–	Yes	PES	Immediate (10.6 ± 1.8); delayed (12.2 ± 1.2)	p = 0.019*	Yes
Checchi et al. (2017)	Immediate implant vs ARP-AXng + delayed implant	91	9	1 year	Immediate = 47; delayed = 44	Immediate (5); delayed (2)	Immediate (89.4); delayed (95.4)	p = 0.436	Yes	PES	Immediate (9.71 ± 2.71); delayed (10.86 ± 1.37)	p = 0.02*	Yes
Malchiodi et al. (2016)	Immediate implant + Xng vs delayed implant (no ARP)	40	0	1 year	Immediate = 20; delayed = 20	Immediate (0); delayed (0)	Immediate (100); delayed (100)	–	Yes	Albrektsson	Immediate (100%); delayed (100%)	–	No
Tallarico et al. (2016)	Immediate implant vs ARP-AXng + delayed implant	24	0	1 year	Immediate = 12; delayed = 12	Early (0); delayed (0)	Immediate (100); delayed (100)	–	Yes	PES	Immediate (10 ± 1.5); delayed (11.7 ± 1.2)	p = 0.081	Yes
Cardaropoli et al. (2015)	ARP-Xng + delayed implant vs delayed implant	41	0	1 year	ARP + delayed = 24; delayed = 24	ARP-Xng (0); delayed (0)	ARP + delayed (100); delayed (100)	–	No	Albrektsson	ARP-Xng (95.83%); delayed (91.66%)	p = 0.98	No
Esposito et al. (2015)	Immediate implant vs ARP-AXng + delayed implant	106	0	1 year	Immediate = 54; delayed = 52	Early (2); delayed (0)	Immediate (96); delayed (100)	p = 0.187	Yes	PES	Immediate (13.00 ± 1.5); delayed (12.80 ± 1.4)	p = 0.187	Yes
Felice et al. (2015)	Immediate implant vs ARP-Adb + delayed implant	50	2	1 year	Immediate = 25; delayed = 23	Immediate (2); delayed (0)	Immediate (92); delayed (100)	p = 0.490	Yes	PES	Immediate (12.78 ± 1.09); delayed (12.22 ± 1.13)	p = 0.09	Yes
Schropp et al. (2014)	Early implant vs delayed implant vs later implant	63	0	10 years	Early = 22; delayed = 22; later = 19	Early (2); delayed (1); later (0)	Early (91); delayed (95); later (100)	Not given	No	–	–	–	–
Pang et al. (2014)	ARP-Xng + delayed implant vs delayed implant	30	0	1 years	ARP + delayed = 15; delayed = 15	ARP-Xng (0); delayed (0)	ARP + delayed (100); delayed (100)	–	No	–	–	–	–
Pellicer-Chover et al. (2014)	Immediate implant vs delayed implant (no ARP)	15	0	1 year	Immediate = 68; delayed = 76	Immediate (0); delayed (0)	Immediate (100); delayed (100)	–	Yes	Buser	Immediate (100%); delayed (100%)	–	No
Barone et al. (2012)	ARP-Xng + delayed implant vs delayed implant	40	0	3 years	ARP + delayed = 20; delayed = 20	ARP-Xng (1); delayed (1)	ARP + delayed (95); delayed (95)	–	No	–	–	–	–
Block et al. (2009)	Immediate implant vs ARP-Alg + delayed implant	76	21	2 years	Immediate = 26; delayed = 29	Early (2); delayed (1)	–	p = 0.154	Yes	–	–	–	–
Palattella et al. (2008)	Immediate implant vs early implant	16	0	2 years	Immediate = 9; early = 9	Immediate (0); delayed (0)	Immediate (100); early (100)	–	No	–	–	–	–
Schropp and Isidor (2008)	Early implant vs delayed implant	45	0	5 years	Early = 23; delayed = 22	Immediate (4); delayed (1)	Early (91); delayed (95)	p = 0.154	No	–	–	–	–

(*continued on next page*)

Table 2 (*continued*)

Authors (year)	Comparison	Total number of patients	Drop-out	Follow-up	Number of implants per group	Survival				Success			
						Failure per group after at least 1 year	Implant survival rates (%)	p-value*	Meta-analysis	Evaluation method	PES (mean ± SD) OR success rates (%)	p-value*	Meta-analysis
Lindeboom et al. (2006)	Immediate implant vs delayed implant (no ARP)	50	0	1 year	Immediate = 25; delayed = 25	Immediate (2); delayed (0)	Immediate (92); delayed (100)	Not given	Yes	Albrektsson	Immediate (92%); delayed (100%)	–	No
Schropp et al. (2005)	Early implant vs delayed implant	46	0	2 years	Early = 23; delayed = 23	Immediate (2); delayed (1)	Early (91); delayed (96)	Not given	No	–	–	–	–

ARP-Alg, alveolar ridge preservation with allograft materials; ARP-Alp, alveolar ridge preservation with alloplastic materials; ARP-Xng, alveolar ridge preservation with xenograft materials; ARP-Fgg Xng, alveolar ridge preservation with xenograft materials and free gingival graft; ARP-Adb, alveolar ridge preservation with algae-derived bone substitute; PES, pink esthetic score; SD, standard deviation; *p < 0.05; vs, versus; immediate, when the implant is installed within the same session as the tooth extraction; early, when the implant is installed within 1–2 months after tooth extraction; delayed, when the implant is installed within 3–4 months after tooth extraction; later, when the implant is installed more than 4 months after tooth extraction.

et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) from which five (Esposito et al., 2015; Felice et al., 2015; Tallarico et al., 2016, 2017; Checchi et al., 2017) were combined in a meta-analysis (Table 2). There were 293 implant surgeries in 284 patients. Relevant statistical heterogeneity was observed among the studies; the values of χ^2 and I^2 were 24.48 ($p < 0.0001$) and 84%, respectively. The quantitative analysis showed no statistical difference in implant esthetic outcome between immediate or delayed implant placement, measured by the pink esthetic score (PES). On average, immediate implant reduced the score by 0.6 points on a scale from zero to 14 (mean difference −0.64; 95% confidence interval (CI) −1.54–0.25; $Z = 1.40$, $p = 0.16$). This is shown in Fig. 4.

Subgroup analysis (post hoc analysis) was carried out to explore the heterogeneity. Immediate implant revealed better results in the anterior alveolar bone site, with an average increase of 0.3 points on the PES scale. However, this was not statistically significant (mean difference 0.36; 95% confidence interval (CI) −0.06–0.77; $Z = 1.68$; $p = 0.09$). The molar region showed a statistically significant increase in PES score of 1.42 points (mean difference −1.42, 95% confidence interval (CI) −2.02 to −0.83; $Z = 4.68$, $p < 0.00001$). The subgroup analysis showed a statistically significant difference between groups ($p < 0.00001$) (Fig. 4).

A total of 11 studies (Schropp et al., 2008, 2014; Barone et al., 2012; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) evaluating peri-implant bone changes in different techniques after at least 1 year of follow-up were found (Table 3). There were 530 implant surgeries in 523 patients. The quantitative analysis (Fig. 5) showed no statistical difference in peri-implant bone resorption between immediate or delayed implant protocols, measured in mm (standard mean difference −0.31; 95% confidence interval (CI) −1.08–0.45; $Z = 0.80$; $p = 0.42$). Statistical heterogeneity was observed among the studies; the values of Chi-squared test χ^2 and I^2 were 36.45 ($p < 0.00001$) and 86%, respectively. Seven studies (Schropp and Isidor, 2008; Barone et al., 2012; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017) found no implant or prosthetic complications during the follow-up period; three studies (Schropp et al., 2014; Felice et al., 2015; Checchi et al., 2017) found some complications in both groups; and only one study (Esposito et al., 2015) found more complications for immediate post-extractive implants compared with the delayed protocol (Table 3).

4. Discussion

The gold standard protocol for implant rehabilitation after tooth extraction is still a matter of debate, with many systematic reviews (Quirynen et al., 2007; den Hartog et al., 2008; Atieh et al., 2010; Lang et al., 2012) attempting to clarify what is the best method to use. Originally, treatment with dental implants demanded a two-stage process. Over the last decade, immediate implant surgery has undoubtedly gained attention due to its similar results (Pellicer-Chover et al., 2014; Schropp et al., 2014; Malchiodi et al., 2016), with fewer surgical interventions and high levels of satisfaction with treatment (Schropp et al., 2004). However, the difficulty in achieving primary stability and the possibility of no bone formation around the implant as a result of micro-movements may be factors in reducing implant survival and esthetic results in the long term.

One Cochrane systematic review evaluating implant survival after immediate and delayed approaches showed more failures in immediate placement, but no statistically significant difference between the protocols ($p = 0.098$). However, the referred meta-

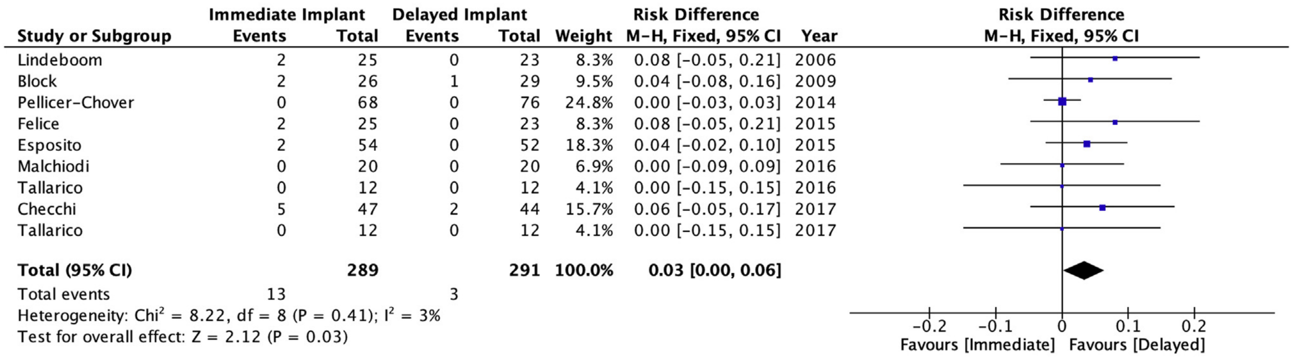

Fig. 3. Forest plot comparing implant survival in immediate and delayed protocols.

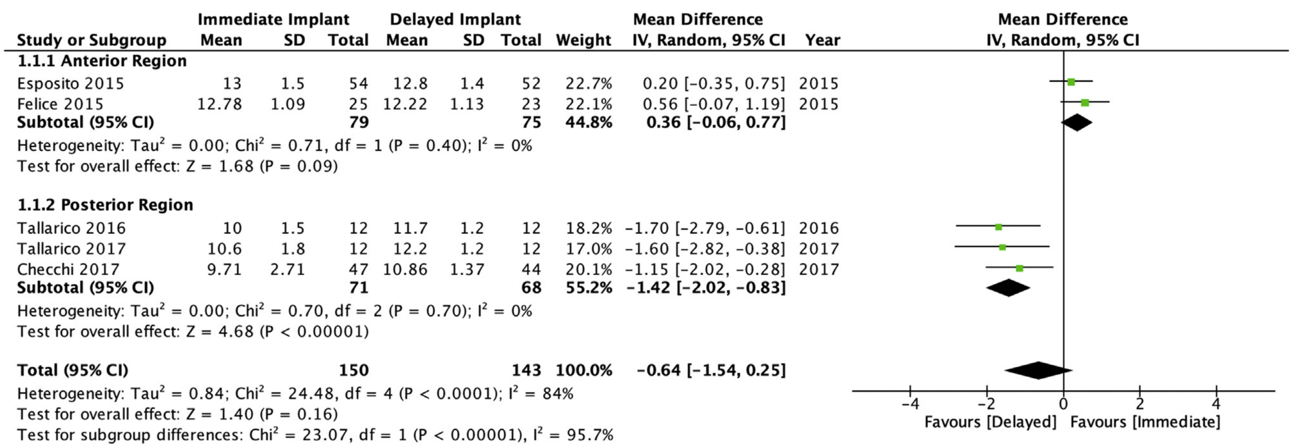

Fig. 4. Forest plot comparing esthetic score in immediate and delayed protocols.

analysis included only two RCTs (Lindeboom et al., 2006; Block et al., 2009), with a total of 110 patients. Our meta-analysis showed a statistically significant difference in favor of delayed protocol. Some occurrence of implant failure was observed when the immediate implant approach was used, increasing the risk of implant failure by 3%. This meta-analysis included a more robust analysis with nine studies (Lindeboom et al., 2006; Block et al., 2009; Pellicer-Chover et al., 2014; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) and a total of 444 patients.

Another systematic review (Atieh et al., 2010) concluded that the immediate approach was associated with high implant survival rates, although this difference was not statistically significant. The authors did not include only RCTs, and mixed retrospective and prospective studies in the analysis. Systematic reviews of RCTs are more likely to provide unbiased information than other study designs. The random process is the only way to prevent systematic differences between participants in immediate and delayed groups, regarding both known and unknown confounders. To our knowledge, our meta-analysis is the most comprehensive study on this topic, and includes only RCTs.

Three studies comparing implant survival in sites with and without alveolar ridge preservation technique were included (Barone et al., 2012; Pang et al., 2014; Cardaropoli et al., 2015). These studies found no differences between the groups; however, it seems that natural socket healing may not allow satisfactory esthetic and functional results, thus compromising results during the long period of follow-up (Barone et al., 2012). Just one of these studies (Cardaropoli et al., 2015) compared the success rates of the implants and showed a better result for those implants placed in sockets treated with the ARP technique.

The other primary outcome, implant esthetic outcome, is an important parameter to be analyzed. Implant survival does not necessarily mean good esthetic results, and so if a study has not tested success according to specific criteria, results could be misleading. Nine studies (Lindeboom et al., 2006; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) included in this systematic review evaluated implant success using three different methods: Albrektsson's criteria for success (Albrektsson et al., 1986); pink esthetic score (PES) (Furhauser et al., 2005); and Buser's criteria of success (Buser et al., 1999). The most used parameter, PES, allows reproducible evaluation of the esthetic appearance of single-tooth implant crowns. Comparing the different treatment protocols using a peri-implant self tissue esthetic scale would facilitate the measurement of implant success rate (Furhauser et al., 2005). We decided that the combination of Albrektsson's criteria, such as mobility testing, radiographic examination, and peri-implant bone loss, with the PES, might be the best way to describe implant success.

Our meta-analysis is the first published study to combine different articles that evaluated implant esthetic results by PES in immediate and delayed protocols. The results indicated that the immediate implant approach reduced overall PES score by 0.6 points, even though this reduction was not considered clinically or statistically significant. It is important to highlight that all five studies included in this synthesis (Esposito et al., 2015; Felice et al., 2015; Tallarico et al., 2016, 2017; Checchi et al., 2017) involved a

Table 3
Secondary outcomes (peri-implant bone level/implant and prosthetic complications).

Authors (year)	Comparison	Follow-up	Number of patients	Number of interventions per group	Peri-implant bone level				Complications	
					Method of evaluation	(Mean ± SD mm)	p-value*	Meta-analysis	Implant	Prosthodontics
Tallarico et al. (2017)	Immediate implant vs ARP-AXng + delayed implant	1 year	24	Immediate = 12; delayed = 12	Radiograph	Immediate (0.63 ± 0.31); ARP + delayed (0.23 ± 0.06)	p = 0.001*	Yes	No implants or prosthesis complications	
Checchi et al. (2017)	Immediate implant vs ARP-AXng + delayed implant	1 year	91	Immediate = 47; delayed = 44	Radiograph	Immediate (1.06 ± NR); ARP + delayed (0.63 ± NR)	p < 0.0001*	No	Ten complications occurred in 10 patients out of 47 from the immediate group (21.3%) vs four complications in four patients out of 44 in the delayed group (9.1%); p = 0.084	
Malchiodi et al. (2016)	Immediate implant + Xng vs delayed implant (no ARP)	1 year	40	Immediate = 20; delayed = 20	Radiograph	Immediate (0.68 ± 0.43); ARP + delayed (0.40 ± 0.26)	–	Yes	No implants or prosthesis complications	
Tallarico et al. (2016)	Immediate implant vs ARP-AXng + delayed implant	1 year	24	Immediate = 12; delayed = 12	Radiograph	Immediate (0.43 ± 0.37); ARP + delayed (0.10 ± 0.10)	p = 0.01*	Yes	No implants or prosthesis complications	
Cardaropoli et al. (2015)	ARP-Xng + delayed implant vs delayed implant	1 year	41	ARP + delayed = 24; delayed = 24	Radiograph	ARP-Xng (0.33 ± 0.28); delayed (0.35 ± 0.28)	p = 0.80	No	No implants or prosthesis complications	
Esposito et al. (2015)	Immediate implant vs ARP-AXng + delayed implant	1 year	98	Immediate = 52; delayed = 46	Radiograph	Immediate (0.23 ± 0.11); ARP + delayed (0.29 ± 0.15)	p = 0.036*	Yes	There were more complications for immediate postextractive implants compared with delayed implants	
Schropp et al. (2014)	Early implant vs delayed implant vs later implant	10 years	63	Early = 22; delayed = 22; later = 19	Radiograph	Early (1.15 ± 0.77); delayed (1.53 ± 1.06); later (1.42 ± 1.07)	–	No	Implant complications were no different from what was observed with implants placed according to the conventional protocol	
Felice et al. (2015)	Immediate implant vs ARP-Adb + delayed implant	1 year	46	Immediate = 23; delayed = 23	Radiograph	Immediate (0.15 ± 0.10); ARP + delayed (0.25 ± 0.15)	p = 0.009*	Yes	Three complications occurred in three patients in the immediate group (12.0%) versus two complications in two patients in the delayed group (8.7%); there were no statistically significant differences for complications between groups	
Pellicer-Chover et al. (2014)	Immediate implant vs delayed implant (no ARP)	1 year	13	Immediate = 6; delayed = 7	Radiograph	Immediate (0.54 ± 0.39); ARP + delayed (0.66 ± 0.25)	–	Yes	No implants or prosthesis complications	
Barone et al. (2012)	ARP-Xng + delayed implant vs delayed implant	3 years	38	ARP + delayed = 19; delayed = 19	Radiograph	ARP-Xng (1.02 ± 0.30); delayed (1.00 ± 0.20)	–	No	No implants or prosthesis complications	
Schropp and Isidor (2008)	Early implant vs delayed implant	5 years	45	Early implant = 23; delayed implant = 22	Radiograph	Early (1.22 ± 0.5); delayed (1.5 ± 0.7)	p = 0.08	No	No major implant or prosthetic complications	

ARP-Alg, alveolar ridge preservation with allograft materials; ARP-Alp, alveolar ridge preservation with alloplastic materials; ARP-Xng, alveolar ridge preservation with xenograft materials; ARP-Fgg Xng, alveolar ridge preservation with xenograft materials and free gingival graft; ARP-Adb, alveolar ridge preservation with algae-derived bone substitute; PES, pink esthetic score; SD, standard deviation; *$p < 0.05$; vs, versus; immediate, when the implant is installed within the same session as the tooth extraction; early, when the implant is installed within 1–2 months after tooth extraction; delayed, when the implant is installed within 3–4 months after tooth extraction; later, when the implant is installed more than 4 months after tooth extraction.

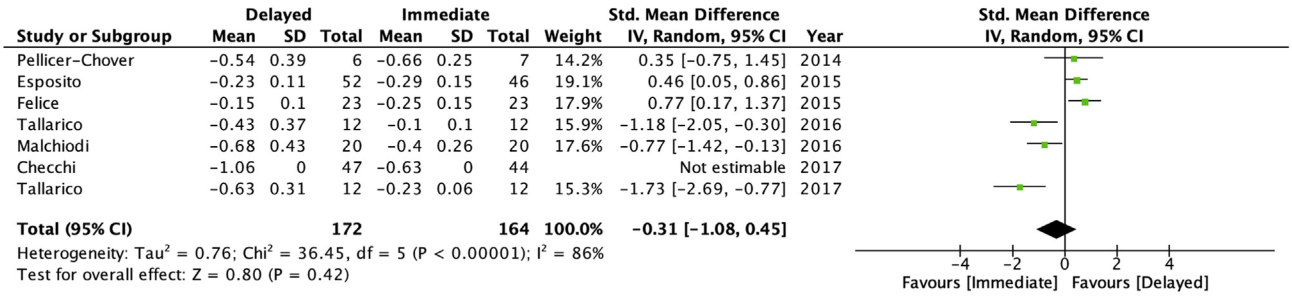

Fig. 5. Forest plot comparing peri-implant bone changes in immediate and delayed protocols.

short follow-up period of 1 year, so future research with longer follow-up periods is necessary to confirm these results.

Subgroup analysis was performed to investigate high statistical heterogeneity. When the studies were separated into anterior and posterior regions, the heterogeneity disappeared completely. A statistically significant subgroup effect meant that the covariate (alveolar region) considered in the subgroup analysis modified the treatment effect. The immediate implant placed in anterior alveolar bone showed better results in PES. Immediate implant in anterior sites are perhaps more able to preserve hard and soft tissues after tooth extraction, helping to avoid natural collapse in the sockets, and improving esthetic results.

11 RCTs (Schropp et al., 2008, 2014; Barone et al., 2012; Pellicer-Chover et al., 2014; Cardaropoli et al., 2015; Esposito et al., 2015; Felice et al., 2015; Malchiodi et al., 2016; Tallarico et al., 2016, 2017; Checchi et al., 2017) included in our systematic review described the complications associated with implants or prosthetic devices over at least 1 year of follow-up. While seven studies found no complications associated with implant or prosthesis rehabilitation in the immediate or delayed groups, three studies found some complications, without a statistically significant difference between immediate and delayed protocols. Only one study Esposito et al. (2015) found more complications associated with immediate placement than with delayed placement. In that study, eight minor complications occurred in patients from the immediate group (15%), with just one complication in the delayed group (2%). Similarly, Quirynen et al. (2007) concluded that there were only sporadic biological complications after implant surgery, and information on peri-implantitis was lacking.

A limitation of this systematic review was the lack of studies with low risk of bias. Because the results of some studies may be biased due to methodological flaws, it is appropriate to consider the results of this meta-analysis with caution.

In summary, the available literature suggests that immediate implants may be at higher risk of implant failure than delayed implants after 1 year of follow-up. Implant esthetic results do not appear to be affected by the type of protocol chosen. However, they might be improved when implants are placed immediately after tooth extraction in anterior sites, or when ARP techniques are used in delayed placement in the molar region. Due to the lack of studies with low risk of bias or with sufficient homogeneous methodology to permit a more precise analysis, further RCTs with larger sample sizes are needed for definitive conclusions.

Ethical approval

Not required.

Funding

None.

Conflicts of interest

None declared.

Patient consent

Not required.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.08.004.

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