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Outcome of Early Dental Implant Placement Versus Other Dental Implant Placement Protocols: A Systematic Review and Meta-analysis

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Abstract

Background: The aim of this systematic review and meta-analysis was to compare the clinical efficacy of the early dental implant placement protocol with immediate and delayed dental implant placement protocols.

Methods: An electronic and manual search of literature was made to identify clinical studies comparing early implant placement with immediate or delayed placement. Data from the included studies were pooled and quantitative analyses were performed for the implant outcomes reported as the number of failed implants (primary outcome variable) and for changes in peri-implant marginal bone level, peri-implant probing depth, and peri-implant soft tissue level (secondary outcome variables).

Results: Twelve studies met the inclusion criteria. Significant difference in risk of implant failure was found neither between the early and immediate placement protocols (Risk difference=−0.018; 95% CI=−0.06, 0.025; $p=0.416$) nor between early and delayed placement protocols (Risk

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DISCLOSURES

All authors have no conflict of interest.

Key findings: The early implant placement protocol results in implant outcomes similar to immediate and delayed placement protocols, while this implant placement protocol was found to be superior to the immediate placement protocol in terms of the stability of peri-implant hard tissue.

difference=-0.008; 95%CI=-0.044, 0.028; $p=0.670$). Pooled data of changes in peri-implant marginal bone level demonstrated significantly less marginal bone loss for implants placed using the early placement protocol compared with those placed in fresh extraction sockets ($p=0.001$; Weighted Mean Difference=-0.14 mm; 95%CI=-0.22, -0.05). No significant differences were found between the protocols for the other variables.

Conclusion: The available evidence supports the clinical efficacy of the early implant placement protocol. Present findings indicate that the early implant placement protocol results in implant outcomes similar to immediate and delayed placement protocols and a superior stability of peri-implant hard tissue compared to immediate implant placement.

Keywords

Clinical Protocols; Dental Implantation/methods; Dental Implants; Meta-analysis; Time Factors; Tooth Extraction; Tooth Socket/surgery

INTRODUCTION

Replacement of missing teeth using implant-supported restorations is a widely accepted treatment approach.^{1, 2} The classic protocol for dental implant therapy was introduced by Per-Ingvar Brånemark in the 1980s.³ It Included a post-extraction healing period of at least six months before implant placement.^{3, 4} This recommendation was based on the belief that complete soft and hard tissue healing after tooth extraction is required to achieve successful osseointegration.⁴ However, the need for complete post-extraction healing before implant placement has been disproven,⁵⁻⁸ which has led to the protocol of immediate implant placement.

Immediate implant placement refers to the placement of implants into fresh extraction sockets immediately after extraction.⁹ Immediate implant placement offers advantages, such as minimizing the number of surgical interventions and shortening the overall treatment course.¹⁰ However, immediate implant placement has been shown to be associated with a risk of esthetic complications.^{11, 12} In addition, an increased risk of infection and insufficient volume of soft tissue are other challenges that clinicians may encounter with this protocol.¹³

Early implant placement, which refers to implant placement following complete soft tissue coverage of the extraction socket,⁹ was introduced as a viable treatment alternative. It has been suggested that the soft tissue healing allows for the resolution of local pathology and provides enhanced soft tissue volume.^{13,14} Several studies have shown promising clinical outcomes for implants placed according to the early placement protocol.¹⁴⁻¹⁷ However, it is necessary to compare the clinical outcomes of implants placed according to the early implant placement protocol with those of implants placed according to the immediate or the delayed implant placement protocols.

There are only two meta-analyses that compared efficacy of early implant placement with immediate or delayed implant placement.^{18, 19} Esposito and colleagues published a systematic review in 2010 and found only two randomized clinical trials that compared outcomes of early implant placement with immediate or delayed implant placement.¹⁸

Another meta-analysis published in 2012 by Sanz and colleagues performed quantitative analysis with data from only two clinical studies.¹⁹ Both studies concluded that more clinical studies are required to establish clear conclusions and clinical guidelines regarding the timing of implant placement.^{18, 19} Subsequently, there has been a considerable increase in the number of clinical studies investigating the efficacy of early implant placement. However, there is no systematic review to provide quantitative and qualitative overview of the recently available evidence on this topic. Hence, there is a need for an updated systematic review to provide a comprehensive basis for evidence-based decision making regarding the timing of implant placement.

Accordingly, this systematic review and meta-analysis aimed to compare the early implant placement protocol with delayed and immediate implant placement protocols in terms of implant outcomes (risk of implant failure), changes in peri-implant marginal bone level, peri-implant probing depth, and peri-implant soft tissue level.

MATERIAL AND METHODS

This review followed PRISMA guidelines for conducting and reporting systematic reviews and meta-analyses.²⁰

Focus Question

The focus question was defined as: “Are there differences in implant outcomes, changes in peri-implant marginal bone level, peri-implant probing depth, or peri-implant soft tissue level when comparing early dental implant placement protocol to immediate or delayed dental implant placement protocols in adult human subjects who required single or multiple dental implant placement?”

Eligibility Criteria According to PICO Framework

A PICO framework was utilized to answer the focused question using the following approach elements: 1) Population: studies in human subjects who required single or multiple implant placement were included; 2) Intervention: included studies had to have a test group consisting of patients who received dental implant treatment according to an early implant placement protocol; 3) Comparator: included studies had to have a comparator group consisting of patients who received dental implant treatment according to delayed or immediate implant placement protocols; 4) Outcome: included studies have to provide quantitative outcomes for at least one of the following variables: a) implant outcomes reported as the number of failed implants (primary outcome variable), b) changes in peri-implant marginal bone level, c) changes in peri-implant probing depth, or d) changes in peri-implant soft tissue level.

Implant placement following complete soft tissue coverage of the extraction socket⁹ (within 3–8 weeks of tooth extraction) was considered as the early implant placement. Delayed implant placement was defined as implant placement 12 weeks or more after tooth extraction.¹⁹ Immediate implant placement was defined as implant placement into fresh extraction socket immediately after tooth extraction.^{9, 19} All study designs with a control or comparison group were considered for inclusion in order to present all existing evidence.

Exclusion Criteria

Studies were excluded if they met any of the following exclusion criteria: 1) studies with a sample size of less than 5 patients in each group in order to exclude individual case reports/series; 2) studies with a minimum follow-up period of less than one year after implant placement; 3) studies that did not fulfill the above-mentioned definitions for population, intervention, comparator, or outcomes; 4) studies that did not clearly describe the timing of implant placement, experimental methodology, or outcome parameters; 5) studies including same patient population which reported same outcome variable as other included studies; 6) non-English citations, in vitro studies, animal studies, editorials, reviews, case reports, or case series.

Search Strategy

The following electronic databases were searched to identify relevant studies from the start of the database through March 2017: MEDLINE, Web of Science, EBSCO, and EMBASE. Details of the electronic search strategy are outlined in the Appendix. In addition, the reference lists of relevant narrative or systematic reviews and all included articles were also screened. The tables of contents of the following specialized scientific journals were also searched for relevant articles from January 2000 to March 2017: *Journal of Periodontology*, *Journal of Clinical Periodontology*, *Journal of oral implantology*, *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *International Journal of Oral and Maxillofacial Implants*, *Implant Dentistry*, and *Journal of the American Dental Association*.

Study Selection

Two investigators (S.B. and K.E.) independently screened results of the systematic literature search. Disagreements regarding the inclusion of the studies were resolved through discussion and consensus and by consulting a third author (G.I.).

Data Extraction

Data extraction was done by two reviewers (S.B. and C.C.), independently, using a pre-determined data extraction table. Details of the methodology for data extraction are presented in the Appendix.

Risk of Bias Assessment

Two reviewers (S.B. and C.C.) independently performed risk of bias assessment using the Cochrane Collaboration's tool for assessing risk of bias.^{21, 22} Details of methodology for the risk on bias assessment are presented in the Appendix.

Quantitative Analysis

Two sets of quantitative analyses were performed to compare early implant placement with immediate implant placement and to compare early implant placement with delayed implant placement. The primary outcome variable was implant outcomes reported as the number of failed implants. The secondary outcome variables were the mean changes in peri-implant marginal bone level, peri-implant probing depth, and mid-buccal soft tissue recession. For the dichotomous outcome variable (implant outcomes), the included studies had to report the

sample size in each group and the number of events (number of failed implants) for each group. For continuous outcome variables, the sample size in each group and the mean and standard deviation values for each group had to be reported. All statistical analyses were performed using a software package.[#]

Summary measures: Data from the included studies were pooled to estimate the effect size. The planned summary measures were risk difference for dichotomous outcomes and weighted mean differences and 95% confidence intervals (CI) for continuous outcomes.

Assessment of heterogeneity: Heterogeneity of effect across studies was assessed using Cochran-Q statistic and I^2 statistic tests.²² P value of >0.05 from Cochran-Q statistic and I^2 value of $<25\%$ were considered as an acceptable level of heterogeneity, where a fixed-effect meta-analysis model was utilized to pool data. Otherwise, a random effect model was used.

Meta-analysis: Fixed effect model was employed where the results Cochran-Q statistic and I^2 tests demonstrated no significant heterogeneity. Significant heterogeneities were detected only in comparison of changes in peri-implant marginal bone level between early and delayed placement protocols, as well as in comparison of peri-implant probing depths between the early and immediate implant placement protocols. Random effect models were used to perform the meta-analyses for both comparisons. Forest plots were generated to graphically represent individual and combined effect sizes.

Sensitivity Analysis

Sensitivity analyses were performed for the primary outcome variable to test the effects of the inclusion of studies with retrospective and cross-sectional designs on the conclusions of this meta-analysis. The effect size was estimated after excluding studies with retrospective and cross-sectional designs.

Publication Bias

Potential publication bias for the primary outcome variable was explored by the funnel plots, Egger's regression Test, and Begg's and Mazumdar rank correlation test.

RESULTS

Study Selection

A flow diagram of the literature search results is presented in Figure 1. The electronic and manual literature search identified a total of 2518 articles with 2399 of these citations excluded after titles and abstracts screening. The full-text of the remaining 119 citations was reviewed, among which 12 articles met the inclusion criteria (Table 1).^{23–34} Five studies compared the early placement protocol with the immediate placement protocol,^{23–27} and four studies compared the early placement protocol with the delayed placement protocol.^{31–34} The other three citations evaluated all three protocols.^{28–30}

[#]Comprehensive Meta-Analysis software (Version 3), Biostat Inc., Englewood, NJ, USA

Study Characteristics

Characteristics of the included studies are presented in Table 1A and 1B. Only one study was of a randomized clinical trial,²⁵ and five studies had a non-randomized controlled clinical design.^{23, 24, 26, 30, 34} The other studies had a retrospective^{27, 28, 31} or cross-sectional design.^{29, 32, 33} The majority of studies were conducted solely in academic settings.^{23–25, 27, 28, 30, 31} Five studies were supported by non-industry funding sources,^{27, 29, 30, 32, 33} and one study received support from industry in terms of materials.³⁴ The sources of funding were not reported in the other studies. The average follow-up period ranged from one-year post-placement to ten-years post-loading. The definition of early placement protocol varied between studies from implant placement 3–5 to 6–8 weeks after extraction.

One half of the studies included only implants that were placed in the maxilla^{25, 29, 30, 32–34}, while the other half included implants placed in both jaws.^{23, 24, 26–28, 31} Five studies included implants placed in the non-molar sites,^{23, 29, 32–34} and two studies included only implants that were placed in the incisor and canine positions.^{25, 30} Implant sites where teeth were extracted due to periodontal diseases were included in five studies,^{23, 25, 26, 32, 33} while these sites were excluded in four studies.^{28–30, 34}

Patients received a pre-operative antibiotic dose in six studies.^{23, 28–30, 32, 33} Some of the implants were placed using a flapless approach in two studies.^{23, 30} In one of these two studies, only implants in the immediate placement group were placed flapless.³⁰ In the other study, flapless implant placement was performed solely for two cases.²³ No grafting materials were used in four studies,^{29, 32–34} and barrier membranes were not used in three studies.^{29, 32, 33} Implants were left non-submerged in six studies^{23, 25, 28, 30, 32, 33} and submerged in three studies.^{24, 31, 34}

An immediate loading protocol was followed for all implants in two studies.^{23, 25} Implants placed according to the immediate placement protocol were immediately loaded if placement torque of equal or greater than 35 Ncm was achieved in one study.³⁰ A delayed loading protocol was followed in the other studies. In addition, the type of definitive restorations was solely single crowns in the majority of the studies.^{23, 25, 28–30, 32–34} The definitive restorations were cement-retained in five studies,^{28, 30, 32–34} whereas a mixture of screw-retained and cemented-retained restorations were used in three studies.^{25, 29, 31}

Risk of bias assessment

The results of risk of bias assessment are presented in Table 2 and the Appendix.

Quantitative Analyses—Meta-analyses were performed for the following outcome variables: 1) implant outcomes (primary outcome variable), 2) changes in marginal peri-implant bone level, 3) peri-implant probing depth, and 4) mid-buccal soft tissue recession. The following two sets of comparisons were done: a) early placement protocol vs. immediate placement protocol and b) early placement protocol vs. delayed placement protocol.

1. Implant outcomes (primary outcome variable)

- A. Early placement protocol vs. immediate placement protocol: The total number of implants and number of failed implants were reported in seven out of eight studies that compared early and immediate implant placement protocols. Hence, the meta-analysis included these seven studies.^{23–28, 30} In total, 194 implants were placed according to the early placement protocol and 371 implants were placed according to the immediate placement protocol. The number of failed implants was eight for the early placement protocol and 23 for the immediate placement protocol, resulting in overall implant survival rates of 95.88% (186/194) for the early placement and 93.80% (348/371) for the immediate placement protocols. No significant difference in the risk of implant failure was found between the two protocols (Figure 2A; Risk difference=−0.018; 95% CI=−0.06, 0.025; $p=0.416$; heterogeneity $I^2<0.001\%$; $\tau<0.001$; Fixed model).
- B. Early placement protocol vs. delayed placement protocol: Seven included studies compared early and delayed implant placement protocols. One of these studies did not report the number of failed implants.²⁹ Two other studies had a same patient population,^{32, 33} so only one of them was included in the analysis. Therefore, meta-analysis was done for five studies.^{28, 30–32, 34} The total number of implants was 150 for the early placement group and 177 for the delayed placement group. Three implants were failed in the early placement group compared to five implants in the delayed placement group. Therefore, the overall survival rates were 98.00% (147/150) for early placement and 97.17% (172/177) for delayed placement. There were no significant differences in the risk of implant failure between the two protocols (Figure 2B; Risk difference=−0.008; 95% CI=−0.044, 0.028; $p=0.670$; heterogeneity $I^2<0.001\%$; $\tau<0.001$; Fixed model).

2. Changes in peri-implant marginal bone level

- A. Early placement protocol vs. immediate placement protocol: Data on changes of peri-implant marginal bone level were reported in five studies comparing early and immediate implant placement protocols.^{23–25, 28, 29} The total numbers of implants in this comparison were 150 and 146 for early and immediate placement protocols, respectively. Meta-analysis showed a significant difference between early and immediate placement protocols ($p=0.001$), which favored the early placement protocol with a clinical magnitude of 0.14 mm less marginal bone loss (Figure 3A; Weighted Mean Difference (WMD)=−0.14; 95% CI=−0.22, −0.05; $I^2<0.001\%$; $\tau<0.001$; Fixed model).
- B. Early placement protocol vs. delayed placement protocol: Five studies comparing early and delayed placement protocols provided data on the changes in peri-implant marginal bone level.^{28, 29, 31, 33, 34} The total number of implants in the early placement group was 137 and 126 for the delayed placement group. Quantitative analysis demonstrated no significant difference between the two protocols (Figure 3B; WMD=−0.13; 95% CI=−0.38, 0.12; $p=0.319$; heterogeneity $I^2=74.68\%$; $\tau=0.24$; Random model).

3) Peri-implant probing depth

- A. Early placement protocol vs. immediate placement protocol: Three included studies reported the peri-implant probing depth measurements.^{23, 24, 28} In total, 106 and 111 implants in early and immediate placement protocols were included in this analysis, respectively. Meta-analysis showed no significant difference in the peri-implant probing depth between early and immediate implant placement protocols (Figure 4A; WMD=-0.22; 95% CI=-0.59, 0.15; $p=0.246$; heterogeneity $I^2=90.19\%$; $\tau=0.309$; Random model).
- B. Early placement protocol vs. delayed placement protocol: Only one study comparing early and delayed placement protocols reported data on the peri-implant probing depth.²⁸ Therefore, meta-analysis was not possible for this comparison. Annibali et al. reported that the mean peri-implant probing depth was 2.72 ± 0.05 mm for the early placement group and 2.6 ± 0.1 mm for the delayed placement group.²⁸

4) Mid-buccal soft tissue recession

- A. Early placement protocol vs. immediate placement protocol: Mid-buccal soft tissue recession data were reported in three studies.^{23, 25, 28} The total number of implants in the early and immediate placement protocols was 27 and 35 in this comparison, respectively. Meta-analysis showed a clinical magnitude of 0.22 mm less mid-buccal soft tissue recession favoring the early placement protocol. However, this difference did not reach statistically significant level (Figure 4B; WMD=-0.22; 95% CI=-0.44,0.01; $p=0.059$; heterogeneity $I^2=2.99\%$; $\tau=0.037$; Fixed model).
- B. Early placement protocol vs. delayed placement protocol: Data on mid-buccal soft tissue recession were provided only in one study comparing early and delayed placement protocols.²⁸ Hence, it was not possible to perform quantitative analysis for this comparison. The mean reported mid-buccal soft tissue recession was 0.79 ± 0.39 mm and 0.66 ± 0.5 mm for early and delayed placement protocols in this study, respectively.²⁸

Sensitivity Analyses and Publication Bias—The results of sensitivity analyses and publication bias assessment are presented in the Appendix.

DISCUSSION

Principal Findings

The results of this meta-analysis revealed that there were no statistically significant differences in the implant outcomes (risk of implant failure) between the early implant placement protocol and the immediate or the delayed implant placement protocols. However, it was found that the early implant placement protocol results in less marginal peri-implant bone loss compared with the immediate placement protocol. No other significant differences were found between the protocols.

Significantly lower marginal peri-implant bone loss was found for implants placed according to the early placement protocol compared with those placed immediately into fresh extraction sockets. The greater marginal peri-implant bone loss in the immediate placement group may be attributed to the horizontal and vertical resorption of the extraction socket walls that begin immediately after tooth extraction.^{35, 36}

Implant placement protocols were also compared based on the peri-implant probing depth and peri-implant soft tissue level. No significant differences were found between the early and immediate placement protocols for these two variables, indicating that peri-implant health and soft tissue stability can be achieved using both implant placement protocols. However, this conclusion is only based on three studies that reported data on these two variables for early and immediate placement protocols. Moreover, only one study compared early and delayed placement protocols with regard to these variables. Therefore, there is a need for future clinical studies to explore the effect of timing of implant placement on the health and stability of the peri-implant complex.

Agreements and Disagreements with Previous Systematic Reviews

The results of this meta-analysis are similar to those of previous systematic reviews and meta-analyses that indicated the timing of implant placement does not significantly affect the rate of implant failure.^{18, 19, 37} A meta-analysis published by Sanz and colleagues in 2011 reported similar survival rates for implants placed according to early and delayed placement protocols. It should be mentioned that meta-analysis was performed for only two studies.^{38, 39} Similar results were reported in a meta-analysis published by Esposito et al in 2010. They compared early implant placement protocol with immediate and delayed implant placement protocols, and meta-analysis was performed only based on the data from one study.¹⁸ Another systematic review published by Quirynen and colleagues on this topic in 2007 reported similar implant outcomes for early and immediate placement protocols. They found the implant failure rate was less than 5% for both immediate and early placement protocols with a tendency toward more implant failure for immediately loaded dental implants.³⁷

Esthetic outcomes of implants placed according to early or immediate placement protocols were also compared in a systematic review published by Chen & Buser in 2014.¹¹ They reported that implants placed according to immediate placement protocol had a higher frequency of midbuccal mucosa recession of greater than 1 mm compared to those placed according to early placement protocol.¹¹ Similarly, the present study found 0.22 mm less mid-buccal soft tissue recession in early placement group compared to immediate placement group.¹¹ It should be noted that, unlike the present systematic review, studies with no comparison group were included in Chen's review.

Clinical Implications

The present systematic review showed that early placement protocol results in similar implant outcomes (risk of implant failure) to immediate and delayed placement protocols, while this placement protocol was found to be superior to the immediate placement protocol in terms of stability of peri-implant hard tissue. It is prudent to consider that the risks and

benefits associated with each of the implant placement protocols can be more significant depending on the site and patient presentation. The clinical implications of losing 0.5mm of tissue in an esthetic implant location could be far detrimental to the quality of the result and patient satisfaction than losing 1mm in a molar location. It is therefore important to apply the results of this systematic review to each individual case independently. It is evident that each protocol has its own indications that makes it more predictable and suitable in different sites and patients.

It is also important to follow implant placement protocols as they continue to develop. Promising clinical outcomes have been reported for a modification of the early placement protocol where implants were placed 10 days after extraction.^{40–42} Schropp and colleagues have shown comparable clinical outcomes between this protocol and the delayed implant placement protocol after 5-years and 10-year follow-up periods.^{40–42}

Patient-centered outcomes have become essential element of quality healthcare. It should be noted implant placement protocols may result in different patient-centered outcomes as these placement protocols are different in terms of the number of interventions, morbidity, and cost of the overall treatment. Therefore, futures studies are need to compared the implant placement protocols with regards to patient-centered outcomes.

Limitations and Recommendations for Future Research

It is important to highlight the low number of randomized controlled trials in the literature attempting direct comparisons of different timing protocols. It has been argued that it is not feasible or ethical to perform randomized clinical studies to compare the different timings of implant placement.⁴³ One argument is that there are extraction site risk factors present in many cases, such as lack of buccal bone or presence of thin buccal bone, which make some extraction sites less preferable for one protocol.⁴³ Hence, it is challenging to apply similar standard case selection criteria that are suitable for different implant placement timing protocols.

It is useful to include non-randomized studies to provide evidence of the effect for interventions that are unlikely to be studied in randomized trials according to the recommendation of the Cochrane handbook.²² Hence, all study designs with a control or comparison group were considered for the inclusion in this study in order to present all existing evidence. However, the sensitivity analysis demonstrated excluding studies with retrospective and cross-sectional designs did not change the overall conclusion of the present meta-analysis.

Several clinical parameters such as hard or soft tissue grafting, presence of keratinized mucosa, loading protocol, and peri-implant maintenance therapy may affect the outcome of implant therapy. It should be mentioned that subgroup analyses for several clinical variables were initially planned in the study protocol. However, the sub-group analysis would not have enough power to detect a true effect when there are fewer than ten studies included in a meta-analysis.²² Hence, subgroup analyses were not performed. Well-designed large clinical trials are needed in future to directly compare the effects of the clinical variables of interests on the outcomes of implant therapy.

In addition, only studies published in the English language were included in this systematic review, and search of the gray literature was not performed. The lack of inclusion of gray literature and non-English citations is considered as a possible limitation of this study. Moreover, it is important to emphasize that conclusions of this meta-analysis might be affected by the quality of included studies. Risk of bias assessment demonstrated that most of included had more than two “No” or “unclear” domains. Therefore, the inclusion of these studies may consider as a possible limitation of this systematic review.

CONCLUSIONS

The current evidence supports the clinical efficacy of early implant placement protocol. The results indicate that an early placement protocol yields similar implant outcomes (risk of implant failure) to immediate and delayed placement protocols. Early implant placement protocol was found to be superior to the immediate placement protocol in terms of stability of peri-implant hard tissue. Well-designed clinical studies are still required to directly compare the effect of timing of implant placement on the peri-implant health and stability of peri-implant hard and soft tissues.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1-
Study selection flow diagram.

(A) Forest plot for the comparison of the changes in peri-implant probing depth between early and immediate placement protocols. (B) Forest plot for the comparison of the changes in peri-implant mid-buccal soft tissue recession between early and immediate placement protocols.

Table 1A.

included studies: study characteristics, patients characteristics, and extracted teeth features.

Study Characteristics				Patients characteristics				Extraction site features												
Design	Country	Setting	Funding	Follow-up period		Groups	Healing time after extraction	Patients (n)	Mean Age ± SD (yr)	M/F	Smokers (n) ^a	No. of implants			Location	Type of teeth	Perio included ^b			
				Min	Ave							B	Fo							
Immediate placement protocols																				
RCT	Italy	Acad	Unk	1 yr AP/AL	1 yr AP	E	4–8 wks	10	47.4	NR	0	8	8	Both	Non-Mol	Yes				
					I	0	7					7								
RCT	Austria	Acad	Unk	12 mo AP	12.4 mo AP	E	6–8 wks	36	62.4	14/22	NR	97	88	Both	All	NR				
					15.2 mo AP	I	0					31	59.2				12/19	93	85	
RCT	Italy	Acad	Unk	2 yr AP/AL	2 yr AP	E	8 wks	8	37.6 ± 11.6 ^c	4/4	0	9	9	Max	In, C	Yes				
					I	0	8					33 ± 5.5 ^c	2/6				0	9	9	
RCT	10 Countries	Acad & P	Unk	5 yr AL	5 yr AL	E	3–5 wks	143	43.7	68/75	NR	47	NR	Both	All	Yes				
					I	0	I					0	217				NR			
retro	Turkey	Acad	Non-ind	20 mo AP	61.9 mo AP	E	4 wks	19	56.1 ± 28.5	16/20	NR	24	24	Both	All	NR				
				25 mo AP	51.6 mo AP	I	0					17	26				26			
Immediate, and delayed placement protocols																				
retro	Italy	Acad	Unk	1 yr AL	32.91 mo AP	E	4–7 wks	11	41.3 ± 11.8	6/5	0	12	10	Both	1 st Mol	No				
					38.84 mo AP	I	0					19	38.31 ± 12.08				12/7	0	20	18
					42.66 mo AP	D	NR					17	42.41 ± 14.3				11/6	0	21	21
CS	Austria	NR	Non-ind	1 yr AP	54 mo AP ^f	E	6–8 wks	35	37 ± 17	NR	NR	35	35	Max	Non-Mol	No				
					56 mo AP ^f	I	0					26	26				26			
					58 mo AP ^f	D	> 6 mo					13	NR				NR	13	13	
RCT	Lithuania	Acad	Non-ind	1 yr AL	1 yr AL	E	6–8 wks	8	32.4 ± 9.1	15/10	0	8	8	Max	In, C	No				
					I	0	9					9	9							
					D	> 6 mo	8					8	8							
Delayed placement protocols																				
retro	Turkey	Acad	Unk	2 yr AL	30.11 mo AL	E	4–5 wks	42	53.32 ± 12.42	11/31	7	101	101	Both	All	NR				

Study Characteristics					Patients characteristics				Extraction site features							
Design	Country	Setting	Funding	Follow-up period		Groups	Healing time after extraction	Patients (n)	Mean Age $\pm$ SD (yr)	M/F	Smokers (n) ^a	No. of implants		Location	Type of teeth	Perio included ^b
				Min	Ave							B	Fo			
					33.27 mo AL	D	NR	45	50.47 $\pm$ 13.73	15/30	15	111	111			
CS	Belgium	Acad & P	Non-ind	17 mo AP	30 mo AP	E	6-8 wks	21	52	19/25	4	22	21	Max	Non-Mol	Yes
				18 mo AP	31 mo AP	D	> 6 mo	23			3	27	25			
CS	Belgium	Acad & P	Non-ind	17 mo AP	30 mo AP	E	6-8 wks	21	52	19/25	4	22	22	Max	Non-Mol	Yes
				18 mo AP	31 mo AP	D	> 6 mo	23			3	27	27			
RCT	Denmark	NR	Ind- assoc	10 yr AL	10 yr AL	E	4 wks	10	35	5/5	NR	10	9	Max	Non-Mol	No
						D	> 12 wks	10	31	5/5		10	10			

0 cigarette/day)

p periodontal diseases included in the study

data

ce, Germany, Italy, Japan, Switzerland, The Netherlands, USA

included in this systematic review

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on but reporting different outcome variables

er loading of implants; AP: after placement of implants; Ave: average; B: baseline; Both: both maxilla and mandible; C: canines; CT: CS: cross-sectional; D: delayed placement protocol; E: early placement protocol; F: female; Fo: follow-up (baseline - drop outs); I: immediate placement protocol; In: associated; M: male; Max: maxilla; Min: minimum; mo: months; Mol: molars; n: number; Non-ind: non-industry; non-M: non-molars; practice settings; Perio: periodontal disease; RCT: randomized controlled trial; Retro: retrospective; SD: standard deviation; Unk: unknown; wks: weeks; and yr: year.

Table 1B.

Characteristics of included studies: Implant features and surgical and prosthodontics considerations.

Study	Implant features		Surgical considerations				Prosthodontic considerations			
	Implant type	Pre-operative antibiotic	Flap	Grafting materials	Membrane	Type of healing	Loading protocol	Loading timing	Type of definitive restoration	Fixation mode
Studies comparing early and immediate placement protocols										
Carini et al.	*	Yes	Mixed	Auto & AP ^a	R ^a	Non-submerged	Immediate	24 h	Single crowns	NR
Mensdorff-Pouilly et al.	†, ‡	NR	Yes	Auto / AP ^a	Non-R ^a	Submerged	Delayed	> 3 mo	Single crowns, partial, and full arch restorations	NR
Palattella et al.	§	NR	Yes	NR	NR	Non-submerged	Immediate	48 h	Single crowns	Mixed
Polizzi et al.		NR	NR	Mixed	Mixed	NR	Delayed	NR	Single crowns, partial, and full arch restorations	NR
Soydan et al.	¶	NR	Yes	Auto & XG ^a	NR	NR	Delayed	2–4 mo	Single crowns, partial, and full arch restorations	NR
Studies comparing early, immediate, and delayed placement protocols										
Annibali et al.	# and **	Yes	Yes	XG ^a	R ^a	Non-submerged	Delayed	> 3 mo	Single crowns	Cemented
Hof et al. ^b	† ‡ and ‡ ‡	Yes	Yes	No	No	Mixed	Delayed	NR	Single crowns	Mixed
Juodzbals et al.	§§	Yes	E Yes	XG	R	NR	Delayed	> 3 mo	Single crowns	Cemented
			I No	XG ^a	R ^a	Non-submerged	Mixed			
			D Yes	No	No	NR	Delayed	> 4 mo		
Studies comparing early and delayed placement protocols										
Bekcioglu et al.	† ‡ and	NR	Yes	NR	NR	Submerged	Delayed	> 3 mo	Partial and full arch restorations	Mixed
Cosyn et al. ^c	‡ ‡	Yes	Yes	No	No	Non-submerged	Delayed	> 3 mo	Single crowns	Cemented

	Implant features	Surgical considerations				Prosthetic considerations				
		Pre-operative antibiotic	Flap	Grafting materials	Membrane	Type of healing	Loading protocol	Loading timing	Type of definitive restoration	Fixation mode
Study	Implant type									
Eghbali et al. ^c	† ‡	Yes	Yes	No	No	Non-submerged	Delayed	> 3 mo	Single crowns	Cemented
Goffredsen et al.	¶¶	NR	Yes	No	Non-R	Submerged	Delayed	> 6 mo	Single crowns	Cemented

^a It was not used for all implants

^b Not all experimental arms were included in this systematic review

^c Studies with the same population but reporting different outcome variables

AP: autologous graft; Auto: autologous graft; D: delayed placement protocol; E: early placement protocol; h: hours; I: immediate placement protocol; mo: months; Non-R: non-resorbable membrane; NR: not reported; R: resorbable membrane; XG: xenograft

^{*} TSA Advance, Phibo, Barcelona, Spain

[†] IMZ, Friatec AG, Mannheim, Germany

[‡] Bränemark, Nobelpharma AB, Gothenburg, Sweden

[§] SLA - Tapered effect, Institut Straumann, Waldenburg, Switzerland

^{||} Standard self tapping implants, Nobel Biocare AB, Goteborg, Sweden

[¶] Straumann, Waldenburg, Switzerland

[#] Nobel - Replace Straight, Nobel Biocare AB, Goteborg, Sweden

^{**} Pilot, Sweden & Martina, Padova, Italia

[†] MK III, Nobel Biocare AB, Gothenburg, Sweden

[‡] Nobel Replace Tapered, Nobel Biocare AB, Goteborg, Sweden

^{§§} SLA - SP tissue level, Straumann, Waldenburg, Switzerland

^{||} IV TiUnite, Nobel Biocare AB, Goteborg, Sweden

^{¶¶} Astra Tech ST, Astra Tech AB, Mölndal, Sweden

Table 2.

Summary of risk of bias assessment in included studies.

Study	Adequate sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data addressed	Free of selective outcome reporting
Annibali et al.	No	No	Unclear	Yes	Yes	Yes
Bekcioglu et al.	No	No	Unclear	Unclear	Yes	Yes
Carini et al.	Unclear	Unclear	Unclear	Unclear	Yes	Yes
Cosyn et al. ^a	No	No	Unclear	Yes	Yes	Yes
Eghbali et al. ^a	No	No	Unclear	Yes	Yes	Yes
Gotfredsen et al.	Unclear	Unclear	Unclear	Unclear	Yes	Yes
Hof et al.	No	No	Unclear	Yes	Yes	Yes
Juodzbals et al.	Unclear	Unclear	Unclear	Yes	Yes	Yes
Mensdorff-Pouilly et al.	Unclear	Unclear	Unclear	Unclear	Yes	Yes
Palattella et al.	Yes	Yes	Unclear	Unclear	Yes	Yes
Polizzi et al.	Unclear	Unclear	Unclear	Unclear	Yes	Yes
Soydan et al.	Unclear	Unclear	Unclear	Unclear	Yes	Yes

^aStudies with the same population but reporting different outcome variables