

Comparing success of immediate versus delay loading of implants in fresh sockets: A systematic review and meta-analysis

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Abstract

Background and aims: The replacement of teeth with *osseointegrated implants* is one of the significant advances in the field of restorative dentistry. The time interval between tooth extraction and the implant can be very short or long. This systematic review and meta-analysis aimed to collect and evaluate articles related to determining the effect of immediate loading of dental implants are placed in the fresh socket initial stability on the clinical success of the implant compared to delay loading procedure.

Materials and Methods: In this study, all the available articles indexed in leading databases, including PubMed, ISI Web of Science, Embase, PsycINFO, PROSPERO, and Scopus were searched. The full text of the articles meeting the primary criteria to be included in this research was obtained and appraised. Data of studies were extracted if they were scored as a high or moderate level of evidence.

Results: A total of 2,258 published articles were found through electronic database searching. After screening the titles and abstracts, and full-text of articles 16 studies met the inclusion criteria and were included in the analysis. The results of this study revealed that regarding the success rate, although there was no significant difference between immediate and delay loading of dental implants, immediate procedure showed a lower incidence of bone loss in single implants.

Conclusion: Based on the results of this study, immediate loading of dental implant, under certain conditions, is a successful treatment process and is effective in reducing treatment time. Thus, immediate loading represents a valid alternative to the traditional delayed loading rehabilitation.

Introduction

The replacement of teeth with osseointegrated implants is one of the significant advances in the field of restorative dentistry [1]. The time interval between tooth extraction and the implant can be very short or long [2]. Sometimes implants place in empty cavities on the same day as the tooth is extracted, but it usually takes between 3 to 6 months for the gingival tissue to heal so that implant surgery can be performed with great success. However, if the time interval between tooth extraction and the implant is more than one year, there is a possibility of gingival resorption and failure of the implant method [3]. The implant delay method is the implant placement protocol after removing the damaged teeth and placing the implants, followed by an extraction socket with a recovery period of several months to one year. Long-term preservation of hard and soft tissue after the loss of one or more teeth is one of the most challenging goals of implant treatment. Immediate implant procedures, on the other hand, involve implant placement immediately after tooth extraction and may have several advantages over delayed methods, including reducing the number of surgical procedures, decreasing the overall treatment time, and reducing complications [4–6]. Despite the clinical benefits of the implant method for tooth replacement, the long time-interval between tooth extraction and the implant is considered as a disadvantage and may influence the decision to choose this treatment modality [7].

The stability of the implant is among the most imperative and convenient elements when predicting implant anchorage, and imposes two types including primary and secondary stabilities. The primary stability is defined as the biomechanical stability of the implant, while secondary stability is the development of new bones around the implant surface with a biological fixation [8–10]. The use of immediate loading of implants to reduce post-implantation recovery time has been suggested in many studies; thus, if initial stability is provided, the success rate of this treatment modality is comparable to the standard method of implant placement [11]. Many researchers have reported the success of the instant loading method using fixed cross-arch prostheses [12, 13]. The remarkable results of these studies led to further research on reducing treatment time in multi-unit and then single-unit implants restorations in the maxillary sites, and finally led to the introduction of immediate loading using a temporary prosthesis in a single maxillary implant [14, 15]. In addition to reducing treatment time, another important advantage of immediate loading of dental implants is the preservation of soft and hard tissue, because the whole surgery and loading process is done in one session [16]. But in the standard method, 2 to 3 sessions of surgery are required, which causes additional trauma to the soft and hard tissues. On the other hand, the implantation of a temporary prosthesis mechanically keeps the gingiva of the buccal surface, and reducing the need for additional soft tissue surgery [17].

Recently, immediate loading of dental implants following the extraction of teeth has become more frequent, due to the need for fewer surgical interventions, a shorter period of treatment time, decreased soft and hard tissue loss, as well as patient's

psychological satisfaction. This systematic review and meta-analysis aimed to collect and evaluate articles related to determining the effect of immediate loading of dental implants are placed in the fresh socket on the clinical success of the implant compared to delay procedure.

Methods

Study design

This systematic review and meta-analysis was conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [18], PRISMA [19] guidelines, and the Quality of Reporting of Meta-analyses (QUOROM) statements.

Search strategy

In this study, all the available articles indexed in leading databases, including PubMed, ISI Web of Science, Embase, PsycINFO, PROSPERO and Scopus using “Immediate Load*” or “Immediate Restor*” or “Immediate Functional Load*” or “Immediate Nonfunctional Load*” and “Immediate Implant*” or “Fresh Socket” or “Immediate Placemen” or “Delayed Implant*” or “rehabilitat*” or “bridge*” or “conventional implant*” and “Dental Implant” keywords or a combination of them, from 1980 to 2020 with no language limitations were initially collected.

Inclusion criteria

Studies that fulfilled defined criteria, including clinical or prospective interventional studies with a follow-up period of at least 12 months, use of at least 10 implants in each group, and details of implants used (length-diameter-type) and implant stability status, as well as expressing a clear success rate or survival rate or information to help calculate them, were included.

Exclusion criteria

Studies that fulfilled defined criteria, including unclear information about patients, implants, follow-up time and study design, animal studies, case presentation or retrospective studies, other types of implant protocols such as delayed implant placement, absence of control group, and review studies, were excluded.

Study selection

From the available literature, related articles were selected and used for further and detailed evaluation. The selected articles were evaluated from two aspects, including scientific principles of study and methodological quality. Articles were independently evaluated by two authors and in case of any disagreement, the article was reviewed by a third person. Then, among the articles whose scientific principles were approved, those with high and moderate validity were selected. Then, all selected articles were categorized based on the type of methods studied and studies with similar conditions were placed in a group. Selected articles were divided into three categories, including 1st, studies that compared immediate loading of dental implants in one group compared to another group with delay loading procedure; 2nd, studies comparing immediate loading with delayed loading in cases of immediate implantation; and 3rd, studies in which immediate full-jaw loading of implants was compared in one group with another group with delay procedure.

Methodological quality assessment

Since only interventional and prospective studies were included in the final evaluations, the standard appraisal checklist was used to assess the accuracy of the methodology. Quality assessment is a structured list of traits or items that are extracted or determinable from a published paper in order to evaluate the accuracy of study results and the data reported in the study. In this article, the quality of selected studies was assessed using a ten-item guideline of Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (Rob 2) [20].

Statistical analysis

First, the statistical information presented in each article was extracted based on comparisons made for each group. This information included sample size, method of comparison of the mean and standard deviation (SD) or any other statistical information provided by the author. The risk differences (RD) and standardized mean differences (SMD) were estimated as interested effect sizes to investigate differences in success rate and crestal bone values between immediate and delayed implants,

respectively. We pooled estimates of each study were pooled using a random-effects model [21]. Both I^2 statistic and Chi-square test were used to assess the heterogeneity, which was clarified using an unrestricted maximum likelihood mixed-effects meta-regression analysis [22]. According to results of the heterogeneity test, either Der Simonian-Laird's random-effects method or Mantel-Haenszel's fixed-effects method were used to pool the estimations of RD and SMD and 95% confidence intervals [23]. Review manager 5.3 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen) was used to provide pooled estimations, with corresponding 95% CI and plots. We used Q-statistic, T^2 -statistic, and I^2 statistics to determine the heterogeneity between the studies. The Q-statistic defines the statistical significance for heterogeneity, while T^2 and I^2 statistics estimate the effect of inhomogeneity. Also, the inverse method was used to estimate the variance and weight for each study (a split on the intra-group variance of each study plus between groups of studies variance). To perform a meta-analysis, Stata version 11.0 and Review manager 5.3 softwares were used. Funnel plot, Beggs and Eggers tests were also used to check for the presence or absence of any potential publication bias [24, 25]. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 2,258 published articles were found through electronic database searching. After screening the titles and abstracts, and full-text of articles 16 studies met the inclusion criteria and were included in the analysis (Table 1).

Table 1
Characteristics of included studies

ID	Population	N of Implant		Follow-up (Month)	Crestal bone (mm)		Success rate N (%)		Methodological quality*
		Immediate	Delay		Immediate	Delay	Immediate	Delay	
Hui et al., 2001 [26]	24 patients, Mean age 37 years	13	11	15	0.6	0.6	13 (100)	11 (100)	7
Tsirlis et al., 2005 [27]	38 patients, age range 20–60 years	28	15	24	0.75 ± 1.05	0.87 ± 0.62	28 (100)	15 (100)	8
Palattella et al., 2008 [28]	16 patients, Mean age 35 years	10	10	24	0.54 ± 0.51	0.46 ± 0.54	10 (100)	10 (100)	9
Ribeiro et al., 2008 [29]	64 patients, Mean age 45.4 years	46	36	27	-	-	43 (93.5)	36 (100)	6
Cooper et al., 2010 [30]	139 patients, Mean age 45.1 years	58	65	12	1.3 ± 2.5	0.4 ± 1.43	55 (94.5)	64 (98.3)	7
Alberti et al., 2012 [31]	70 patients, Mean age 45 years	25	45	12	-	-	25 (100)	45 (100)	8
Atieh et al., 2013 [32]	70 patients, age range 53.6–51.5 years	12	12	12	0.41 ± 0.57	0.54 ± 0.51	10 (83.3)	8 (66.7)	5
Bruyn et al., 2013 [33]	113 patients, age range 42–45 years	55	58	36	1.6 ± 2.4	0.4 ± 1.5	52 (94.6)	57 (98.3)	8
Vandeweghe et al., 2013 [34]	38 patients, Mean age 49 years	23	15	26	0.88 ± 0.31	1.28 ± 0.23	23 (100)	15 (100)	7
Felice et al., 2015 [35]	50 patients, Mean age 40 years	25	25	12	0.13	0.19	23 (92)	25 (100)	6
Zou et al., 2015 [36]	32 patients, Mean age 41.6 years	17	15	60	-	-	16 (96.4)	14 (91.8)	8
Esposito et al., 2015 [37]	106 patients, Mean age 48 years	54	52	12	0.23	0.29	51 (94)	52 (100)	7

ID	Population	N of Implant		Follow-up (Month)	Crestal bone (mm)		Success rate N (%)		Methodological quality*
		Immediate	Delay		Immediate	Delay	Immediate	Delay	
Slagter et al., 2016 [38]	32 patients, Mean age 41.6 years	20	20	12	0.56 ± 0.39	0.51 ± 0.43	20 (100)	20 (100)	8
Simonpieri et al., 2017 [39]	42 patients, Mean age 55.8 years	237	97	48	-	-	233 (98.3)	94 (96.9)	8
Checchi et al., 2017 [40]	91 patients, Mean age 55.8 years	47	44	12	-	-	42 (89.4)	42 (95.4)	6
Chan et al., 2019 [41]	38 patients, Mean age 55.8 years	18	20	24	1.1 ± 0.45	1.3 ± 0.74	16 (90)	20 (100)	7

*This tool includes five bias areas: (1) the randomization process, (2) deviation from intended interventions, (3) missing outcome data, (4) the outcome measures, and (5) selection of the reported result. The response decisions for a complete risk-of-bias judgment are include low risk of bias, with some concerns or high risk of bias.

The selection process was presented in a PRISMA flow chart (Fig. 1).

Success Rate

A total of 16 studies with 963 patients (443 male and 520 female) were included in the meta-analysis. The results of Cochrane Q and I^2 statistics showed that 16 studies were not heterogeneous with $P = 0.77$ and $I^2 = 39.23\%$, so overall RD was obtained using a fixed-effects model. The summary estimate of RD was -0.03 [95%CI: (-0.05, <-0.001)] which showed that success rate was significant between immediate and delay loading of dental implants (Figs. 2).

To assess the presence or absence of publication bias in printing, a Funnel plot was used which showed that there was no publication bias effect ($P = 0.80$, Fig. 3). Besides, sensitivity analysis showed that the overall RD was not changed substantially when individual studies were removed.

Crestal Bone

A total of 8 studies with 664 patients (347 male and 317 female) were included in the meta-analysis for crestal bone. The results of Cochrane Q with $P < 0.001$ and $I^2 = 83\%$ showed that 8 studies were extremely heterogeneous, so overall MD was obtained using a random-effects model (Fig. 4). The pooled estimate of MD was -0.09 [95%CI: (-0.24, 0.43)] which revealed that crestal bone was not significant between the immediate and delay loading of dental implants (Figs. 4).

Moreover, the small study effects using Egger's tests showed that there was publication bias effect ($P = 0.04$, Fig. 5).

Discussion

In the present study that was aimed to determine the effect of immediate loading of implants are placed in the fresh socket on the clinical success of the implant compared to delayed implant placement, significant results in term of success rate were obtained. In the past, Osseo integrated implants, which is the most important factor for the success of any implant-based prosthesis, was defined as success rate [42]. Thus, immediate implant placement is considered as a predictable treatment process and concept because many studies have indicated a high success rate for this technique [43–45].

Formerly, some studies reported a high success rate of the immediate loading of dental implant compared to delay procedure, but in some studies, which a very low success rate were reported. Thomé *et al.*, reported the success rate of immediate implant placement as 99.6% [46]. Another retrospective study was conducted by Perelli *et al*, and showed that immediate loading of dental implant had a survival rate of 92.0% [47]. While Chaushu *et al*, who compared the immediate and non-immediate loading of dental implants, reported the survival rate for the immediate loading of dental implant was 82.4% compared to 100% for non-immediate procedure [48].

Given that the criteria for implant success have changed in recent decades, implant treatment has shifted from a bone-driven protocol to a restorative-driven protocol [49]. The results of this systematic review on immediate loading of dental implant showed not only less bone resorption but also an increase in marginal bone surface area may happen in the first year of implant. Therefore, at least it can be stated that immediate loading of dental implant, as much as the standard method of implant placement in the ridge, is effective in preserving bone in the short term [50].

Another important issue is the preservation of dental papillae. The main key in this case is the amount and level of bone in the proximal of the adjacent tooth [51]. The results of previous studies showed that immediate loading of dental implants could not have significant results in preventing papillary defect [52–55]. This result can be interpreted as that papillary preservation depends on the presence of interdental bone rather than on the surgical procedure and prosthetic protocol. In these studies, there was no significant difference in papillary height after 1.5 years of follow-up between immediate and delay loading of dental implants.

In the past, it was believed that placing the implant in the socket of a fresh socket would prevent bone remodeling and preserve the shape of the ridge [56]. But later on animal as well as human studies have ruled this out [57–60]. These studies have shown that regardless of the method of implant placement, remodeling will occur after tooth extraction and will lead to transverse and vertical bone resorption. On the other hand, bone resorption on the buccal side is much more significant than on the lingual side. This can be explained by the fact that the buccal bone crest is mainly composed of bundle bone, which loses its function and resorbs by extracting the tooth.

Another issue with the immediate loading of dental implants is the use of implants with a surface treatment that can have a higher rates r than bone-to-implant contact (BIC). On the other hand, the use of tapered implants in immediate implantation is more successful than the cylindrical type in achieving primary stability. However, in terms of the placement of the torques, no general agreement has been reached on their minimum amount in these studies [61, 62]. In general, by examining these studies, can say that immediate loading of dental implants can be problematic due to the presence of infection at the implant site, and the treatment protocol needs further and more detailed investigation in these cases. Besides, achieving primary stability in immediate loading of dental implant is the most important success factor. Immediate loading procedure also should not be done, especially in cases where the buccal bone defect has reached the crest area. Because in these cases it is necessary to use a bone graft with a membrane on the surface of the ridge and the prosthesis can no longer be placed on the surface of the implant. Another concern is the placement of the prosthesis in the occlusion. It is recommended that in an immediate implant, all the effort should be made to keep the temporary prosthesis out of the occlusion in all movements [63].

Bassir SH *et al.*, 2019 shown that early implant placement protocol (risk difference = -0.018; 95% confidence interval [CI] = -0.06, 0.025; P = 0.416) like immediate placement protocols (risk difference = -0.008; 95% CI = -0.044, 0.028; P = 0.670) [64]. However, our study shows that immediate implantation, is a successful treatment process.

Review studies comparing the success of immediate and delayed implants have emphasized that in the short term there is no difference between the two implantation methods; but in terms of aesthetics and patient satisfaction and maintaining alveolar height, immediate implantation was better than delayed implantation. On the other hand, studies related to immediate implants, especially if followed by immediate loading had more failure rate [65]. These results are consistent with the information obtained from this study, with the difference that the mentioned studies considered immediate implant and immediate loading more successful in the anterior of the mandible, but in the studies included in this meta-analysis, this method was also evaluated as successful in the posterior the mandible and maxilla.

Different views were previously expressed on placement of implants after tooth extraction, which means that immediate implantation is a more complex treatment and delayed implants allow for better primary stability and better prosthesis placement.

However, around 30% of immediate implants cases are aesthetically pleasing to patients, and survival rate of immediate implants are high and comparable to those in a recovered ridge [66, 67]. Also, another study that immediate implants do not prevent horizontal and vertical resorption after tooth extraction. On the other hand, bone width reconstruction after immediate implant placement prevents transverse bone resorption, however, vertical resorption of the buccal bone will continue. Interestingly, these studies provided strong evidence that bone regeneration, even in cases of immediate implants is more successful than delayed implants [68].

In a systematic review study [69], although a large number of articles reported a limited amount of bone loss or even an increase in its level in immediate implantation, these results should be interpreted with caution. Because few of these studies have been reviewed radiographically. However, in this study, only studies that expressed the exact amount of bone loss or increase based on radiography in millimeters were included in this meta-analysis.

In fresh socket, the gap between the implant surface and the bone wall is an important issue in the healing process. As the width of this cavity increases, the amount of BIC decreases and the most coronal part of the BIC migrates towards the apical part [70]. However, the authors state that implants with immediate loading will have a higher BIC than the delayed method, and less bone resorption will occur in these cases. In our study, it was also found that the rate of analysis was lower in the immediate implant group. However, in most of these studies, including this study, the difference between the two groups was not statistically significant. In general, randomized clinical trial studies with more samples are recommended so that long-term evaluation of results both in terms of success and bone resorption is possible .and meta-analysis can be performed with more robust studies.

Conclusion

Based on the results of this study, immediate loading of dental implant, if the conditions are available, may consider as a successful treatment process and is effective in reducing treatment time. These conditions include patient selection, bone quality and quantity, implant number and design, implant primary stability, occlusal loading and clinician's surgical ability, of which primary stability is undoubtedly the most important When compared with delay loading, immediate procedure could achieve comparable implant survival rates. Thus, immediate loading represents a valid alternative to the traditional delayed loading rehabilitation.

Declarations

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Ethics deceleration

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

For this type of study, formal consent is not required.

Informed consent

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Alghamdi, H.S., *Methods to Improve Osseointegration of Dental Implants in Low Quality (Type-IV) Bone: An Overview*. Journal of functional biomaterials, 2018. **9**(1): p. 7.

2. Pal, U.S., et al., *Evaluation of implants placed immediately or delayed into extraction sites*. National journal of maxillofacial surgery, 2011. **2**(1): p. 54-62.
3. Do, T.A., et al., *Risk Factors related to Late Failure of Dental Implant-A Systematic Review of Recent Studies*. Int J Environ Res Public Health, 2020. **17**(11).
4. Testori, T., et al., *Immediate Versus Delayed Loading of Postextraction Implants: A Long-Term Retrospective Cohort Study*. Implant Dentistry, 2017. **26**(6): p. 853-859.
5. Pera, P., et al., *Immediate Versus Delayed Loading of Dental Implants Supporting Fixed Full-Arch Maxillary Prosthesis: A 10-year Follow-up Report*. Int J Prosthodont, 2019. **32**(1): p. 27-31.
6. Tealdo, T., et al., *Immediate versus delayed loading of dental implants in edentulous patients' maxillae: a 6-year prospective study*. Int J Prosthodont, 2014. **27**(3): p. 207-14.
7. Al-Quran, F.A., R.F. Al-Ghalayini, and B.N. Al-Zu'bi, *Single-tooth replacement: factors affecting different prosthetic treatment modalities*. BMC oral health, 2011. **11**: p. 34-34.
8. Meredith, N., *Assessment of implant stability as a prognostic determinant*. Int J Prosthodont, 1998. **11**(5): p. 491-501.
9. Papaspyridakos, P., et al., *Success criteria in implant dentistry: a systematic review*. J Dent Res, 2012. **91**(3): p. 242-8.
10. Gómez-Polo, M., et al., *Does Length, Diameter, or Bone Quality Affect Primary and Secondary Stability in Self-Tapping Dental Implants?* J Oral Maxillofac Surg, 2016. **74**(7): p. 1344-53.
11. Tettamanti, L., et al., *Immediate loading implants: review of the critical aspects*. ORAL & implantology, 2017. **10**(2): p. 129-139.
12. Vanden Bogaerde, L., et al., *Early function of splinted implants in maxillas and posterior mandibles, using Brånemark System Tiunite implants: an 18-month prospective clinical multicenter study*. Clin Implant Dent Relat Res, 2004. **6**(3): p. 121-9.
13. Tarnow, D.P., S. Emtiaz, and A. Classi, *Immediate loading of threaded implants at stage 1 surgery in edentulous arches: ten consecutive case reports with 1- to 5-year data*. Int J Oral Maxillofac Implants, 1997. **12**(3): p. 319-24.
14. Degidi, M., et al., *Immediate functional loading of edentulous maxilla: a 5-year retrospective study of 388 titanium implants*. J Periodontol, 2005. **76**(6): p. 1016-24.
15. Ostman, P.O., M. Hellman, and L. Sennerby, *Direct implant loading in the edentulous maxilla using a bone density-adapted surgical protocol and primary implant stability criteria for inclusion*. Clin Implant Dent Relat Res, 2005. **7** Suppl 1: p. S60-9.
16. Singh, M., et al., *Immediate dental implant placement with immediate loading following extraction of natural teeth*. National journal of maxillofacial surgery, 2015. **6**(2): p. 252-255.
17. Chen, J., et al., *Immediate versus early or conventional loading dental implants with fixed prostheses: A systematic review and meta-analysis of randomized controlled clinical trials*. The Journal of Prosthetic Dentistry, 2019. **122**(6): p. 516-536.
18. Stroup, D.F., et al., *Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group*. Jama, 2000. **283**(15): p. 2008-12.
19. Panic, N., et al., *Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses*. PLoS One, 2013. **8**(12): p. e83138.
20. Zeng, X., et al., *The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review*. J Evid Based Med, 2015. **8**(1): p. 2-10.
21. Borenstein, M., et al., *A basic introduction to fixed-effect and random-effects models for meta-analysis*. Res Synth Methods, 2010. **1**(2): p. 97-111.
22. Kelley, G.A. and K.S. Kelley, *Statistical models for meta-analysis: A brief tutorial*. World J Methodol, 2012. **2**(4): p. 27-32.
23. DerSimonian, R. and N. Laird, *Meta-analysis in clinical trials*. Control Clin Trials, 1986. **7**(3): p. 177-88.
24. Begg, C.B. and M. Mazumdar, *Operating characteristics of a rank correlation test for publication bias*. Biometrics, 1994. **50**(4): p. 1088-101.
25. Egger, M., et al., *Bias in meta-analysis detected by a simple, graphical test*. Bmj, 1997. **315**(7109): p. 629-34.
26. Hui, E., et al., *Immediate provisional for single-tooth implant replacement with Brånemark system: Preliminary report*. Clinical Implant Dentistry and Related Research, 2001. **3**(2): p. 79-86.
27. Tsirlis, A.T., *Clinical evaluation of immediate loaded upper anterior single implants*. Implant Dentistry, 2005. **14**(1): p. 94-103.

28. Palattella, P., F. Torsello, and L. Cordaro, *Two-year prospective clinical comparison of immediate replacement vs. immediate restoration of single tooth in the esthetic zone*. Clinical Oral Implants Research, 2008. **19**(11): p. 1148-1153.
29. Ribeiro, F.S., et al., *Success rate of immediate nonfunctional loaded single-tooth implants: immediate versus delayed implantation*. Implant Dentistry, 2008. **17**(1): p. 109-117.
30. Cooper, L.F., et al., *Comparison of Radiographic and Clinical Outcomes Following Immediate Provisionalization of Single-Tooth Dental Implants Placed in Healed Alveolar Ridges and Extraction Sockets*. International Journal of Oral & Maxillofacial Implants, 2010. **25**(6).
31. Di Alberti, L., et al., *Clinical and radiologic evaluation of 70 immediately loaded single implants in the maxillary esthetic zone: preliminary results after 1 year of functional loading*. International Journal of Oral & Maxillofacial Implants, 2012. **27**(1).
32. Atieh, M.A., et al., *Immediate single implant restorations in mandibular molar extraction sockets: a controlled clinical trial*. Clinical oral implants research, 2013. **24**(5): p. 484-496.
33. De Bruyn, H., et al., *Three-years clinical outcome of immediate provisionalization of single Osseospeed™ implants in extraction sockets and healed ridges*. Clinical Oral Implants Research, 2013. **24**(2): p. 217-223.
34. Vandeweghe, S., et al., *Immediate loading of screw-retained all-ceramic crowns in immediate versus delayed single implant placement*. International Journal of Prosthodontics, 2013.
35. Felice, P., et al., *Immediate non-occlusal loading of immediate post-extractive versus delayed placement of single implants in preserved sockets of the anterior maxilla: 1-year post-loading outcome of a randomised controlled trial*. Eur J Oral Implantol, 2015. **8**(4): p. 361-72.
36. Zou, D., et al., *Autologous Ilium Grafts: Long-Term Results on Immediate or Staged Functional Rehabilitation of Mandibular Segmental Defects Using Dental Implants after Tumor Resection*. Clinical implant dentistry and related research, 2015. **17**(4): p. 779-789.
37. Esposito, M., et al., *Immediate loading of post-extractive versus delayed placed single implants in the anterior maxilla: outcome of a pragmatic multicenter randomised controlled trial 1-year after loading*. Eur J Oral Implantol, 2015. **8**(4): p. 347-58.
38. Slagter, K.W., et al., *Immediate Single-Tooth Implant Placement in Bony Defects in the Esthetic Zone: A 1-Year Randomized Controlled Trial*. J Periodontol, 2016. **87**(6): p. 619-29.
39. Simonpieri, A., et al., *Four-year post-loading results of full-arch rehabilitation with immediate placement and immediate loading implants: A retrospective controlled study*. Quintessence Int, 2017. **48**(4): p. 315-324.
40. Checchi, V., et al., *Wide diameter immediate post-extractive implants vs delayed placement of normal-diameter implants in preserved sockets in the molar region: 1-year post-loading outcome of a randomised controlled trial*. Eur J Oral Implantol, 2017. **10**(3): p. 263-278.
41. Chan, H.L., et al., *A randomized controlled trial to compare aesthetic outcomes of immediately placed implants with and without immediate provisionalization*. Journal of clinical periodontology, 2019. **46**(10): p. 1061-1069.
42. Karthik, K., et al., *Evaluation of implant success: A review of past and present concepts*. J Pharm Bioallied Sci, 2013. **5**(Suppl 1): p. S117-9.
43. Soydan, S.S., et al., *Are success and survival rates of early implant placement higher than immediate implant placement?* Int J Oral Maxillofac Surg, 2013. **42**(4): p. 511-5.
44. Lang, N.P., et al., *A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year*. Clin Oral Implants Res, 2012. **23** Suppl 5: p. 39-66.
45. Cosyn, J., et al., *The effectiveness of immediate implant placement for single tooth replacement compared to delayed implant placement: A systematic review and meta-analysis*. Journal of Clinical Periodontology, 2019. **46**(S21): p. 224-241.
46. Thomé, G., et al., *Retrospective Clinical Study of 453 Novel Tapered Implants Placed in All Bone Types: Survival Rate Analysis Up to 2 Years of Follow-Up*. Int J Oral Maxillofac Implants, 2020. **35**(4): p. 757-761.
47. Perelli, M., et al., *The Long-Term Evaluation of Two-Unit Fixed Partial Dentures on Short, Threaded Implants: Delayed Versus Immediate Loading*. Int J Periodontics Restorative Dent, 2020. **40**(4): p. e157-e162.
48. Chaushu, G., et al., *Immediate loading of single-tooth implants: immediate versus non-immediate implantation. A clinical report*. Int J Oral Maxillofac Implants, 2001. **16**(2): p. 267-72.

49. Roblee, R.D., S.L. Bolding, and J.M. Landers, *Surgically facilitated orthodontic therapy: a new tool for optimal interdisciplinary results*. *Compend Contin Educ Dent*, 2009. **30**(5): p. 264-75; quiz 276, 278.
50. Adell, R., et al., *Marginal tissue reactions at osseointegrated titanium fixtures (I). A 3-year longitudinal prospective study*. *Int J Oral Maxillofac Surg*, 1986. **15**(1): p. 39-52.
51. Buser, D., W. Martin, and U.C. Belser, *Optimizing esthetics for implant restorations in the anterior maxilla: anatomic and surgical considerations*. *Int J Oral Maxillofac Implants*, 2004. **19 Suppl**: p. 43-61.
52. Kan, J.Y., K. Rungcharassaeng, and J. Lozada, *Immediate placement and provisionalization of maxillary anterior single implants: 1-year prospective study*. *Int J Oral Maxillofac Implants*, 2003. **18**(1): p. 31-9.
53. Yuenyongoram, P., et al., *Facial Gingival Changes with and without Socket Gap Grafting following Single Maxillary Anterior Immediate Tooth Replacement: 1-Year Results*. *J Oral Implantol*, 2020.
54. Cornelini, R., et al., *Immediate restoration of implants placed into fresh extraction sockets for single-tooth replacement: a prospective clinical study*. *Int J Periodontics Restorative Dent*, 2005. **25**(5): p. 439-47.
55. Velasco-Ortega, E., et al., *Survival rates and bone loss after immediate loading of implants in fresh extraction sockets (single gaps). A clinical prospective study with 4 year follow-up*. *Med Oral Patol Oral Cir Bucal*, 2018. **23**(2): p. e230-e236.
56. Paolantonio, M., et al., *Immediate implantation in fresh extraction sockets. A controlled clinical and histological study in man*. *J Periodontol*, 2001. **72**(11): p. 1560-71.
57. Araújo, M.G., et al., *Ridge alterations following implant placement in fresh extraction sockets: an experimental study in the dog*. *J Clin Periodontol*, 2005. **32**(6): p. 645-52.
58. Araújo, M.G. and J. Lindhe, *Ridge alterations following tooth extraction with and without flap elevation: an experimental study in the dog*. *Clin Oral Implants Res*, 2009. **20**(6): p. 545-9.
59. Lee, J.S., et al., *Ridge regeneration of damaged extraction sockets using rhBMP-2: an experimental study in canine*. *J Clin Periodontol*, 2015. **42**(7): p. 678-87.
60. Botticelli, D., T. Berglundh, and J. Lindhe, *Hard-tissue alterations following immediate implant placement in extraction sites*. *J Clin Periodontol*, 2004. **31**(10): p. 820-8.
61. Klokkevold, P.R., et al., *Osseointegration enhanced by chemical etching of the titanium surface. A torque removal study in the rabbit*. *Clin Oral Implants Res*, 1997. **8**(6): p. 442-7.
62. Lazzara, R.J., et al., *A human histologic analysis of osseotite and machined surfaces using implants with 2 opposing surfaces*. *Int J Periodontics Restorative Dent*, 1999. **19**(2): p. 117-29.
63. Wennerberg, A., et al., *A 1-year follow-up of implants of differing surface roughness placed in rabbit bone*. *Int J Oral Maxillofac Implants*, 1997. **12**(4): p. 486-94.
64. Bassir, S.H., et al., *Outcome of early dental implant placement versus other dental implant placement protocols: A systematic review and meta-analysis*. *J Periodontol*, 2019. **90**(5): p. 493-506.
65. Quirynen, M., et al., *How does the timing of implant placement to extraction affect outcome?* *Int J Oral Maxillofac Implants*, 2007. **22 Suppl**: p. 203-23.
66. Chen, S.T., et al., *Consensus statements and recommended clinical procedures regarding surgical techniques*. *Int J Oral Maxillofac Implants*, 2009. **24 Suppl**: p. 272-8.
67. Bornstein, M.M., et al., *Consensus statements and recommended clinical procedures regarding contemporary surgical and radiographic techniques in implant dentistry*. *Int J Oral Maxillofac Implants*, 2014. **29 Suppl**: p. 78-82.
68. Esposito, M., et al., *Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment*. *Cochrane Database Syst Rev*, 2008(3): p. Cd003607.
69. Esposito, M., et al., *The efficacy of horizontal and vertical bone augmentation procedures for dental implants - a Cochrane systematic review*. *Eur J Oral Implantol*, 2009. **2**(3): p. 167-84.
70. Chen, S.T., T.G. Wilson, Jr., and C.H. Hämmerle, *Immediate or early placement of implants following tooth extraction: review of biologic basis, clinical procedures, and outcomes*. *Int J Oral Maxillofac Implants*, 2004. **19 Suppl**: p. 12-25.