ACTA ODONTOLOGICA SCANDINAVICA
2019, VOL. 77, NO. 2, 99–106
https://doi.org/10.1080/00016357.2018.1508743

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Validity of a regenerative procedure for a minor bone defect with immediate implant placement: a systematic review and meta-analysis

Jungwon Lee, Dueun Park, Ki-Tae Koo, Yang-Jo Seol and Yong-Moo Lee

Department of Periodontology and Dental Research Institute, School of Dentistry, Seoul National University, Seoul, Republic of Korea

ABSTRACT

Objective: This systematic review evaluates implant survival and the change in the width of the horizontal ridge following immediate implant placement with or without a regenerative procedure.

Materials and methods: An electronic search of MEDLINE, EMBASE, and the LILACS database of the Cochrane Central Register of controlled trials was performed, along with a manual search, up to April 2018. Randomized controlled trials (RCTs) and quasi-randomized controlled clinical trials (CCTs) with >10 subjects were eligible for this systematic review. A meta-analysis of the risk difference in implant failure between the regenerative and non-regenerative procedure groups was performed using a fixed-effect model. In addition, a meta-analysis of the change in alveolar bone width was conducted using a fixed-effect model.

Results: Seven studies (six RCTs and one CCT) were included. A meta-analysis of three studies found no statistically significant risk difference in implant failure between the regenerative procedure and non-regenerative procedure groups. A meta-analysis of four studies showed that horizontal shrinkage of the alveolar ridge in the site of immediate implant placement was statistically significantly lower with the regenerative procedure than without it (<1 year follow up studies: weighted mean difference (WMD) 0.75 mm, 95% confidence interval 0.41–1.09, $p < .00001$; ≥1 year follow up study: WMD 1.22, 95% confidence interval 0.52–1.91, $p = .00006$; total: WMD 0.84 mm, 95% confidence interval 0.53–1.14, $p < .00001$).

Conclusion: Within the study limitations, immediate implant placement with a regenerative procedure showed similar implant survival and less shrinkage of the ridge width than immediate implant placement without a regenerative procedure. Due to the high risk of bias and small sample sizes of the included studies, further clinical studies are warranted to draw definitive conclusions.

ARTICLE HISTORY
Received 1 February 2018
Revised 21 June 2018
Accepted 27 July 2018

KEYWORDS
Guided bone regeneration; bone graft; implant survival; immediate implant

Introduction

For well-selected cases of tooth extraction, immediate implant placement is an acceptable treatment option that can reduce the treatment time, number of surgical interventions, and the healing period by several months [1]. Planning for immediate implant placement should carefully consider preoperative conditions that could lead to complications. In particular, inadequate bone width or height could jeopardize the success of the implant. In this situation, alveolar bone reconstruction should be performed to improve function and esthetics.

In many clinical situations, minor bone defects that cause a disparity of dimension between the implant and the extraction socket, such as a marginal gap or dehiscence, can be encountered when performing immediate implant placement. To manage such bone defects for predictable results from the implant restoration, a regenerative procedure was proposed [2] and showed favorable results [3,4].

However, despite accumulating positive results from immediate implant placement with a regenerative procedure, considerable controversy remains regarding the necessity for bone augmentation procedures. Some authors have demonstrated that immediate implant placement without bone grafting could be performed successfully with adequate esthetic and functional outcomes [5,6]. These contradictory results can be explained by the low-level evidence of those publications. Two previous systematic reviews [7,8] have considered immediate implant placement with a regenerative procedure. However, no meta-analysis has directly compared regenerative and non-regenerative groups who received immediate implant placement.

This systematic review assesses the results of immediate implant placement with and without a regenerative procedure and measures the clinical outcomes with respect to implant failure and changes in the alveolar bone width.

Materials and methods

The protocol of this systematic review was registered with PROSPERO (2016: CRD42017067859) and developed and reported according to the PRISMA guidelines.

Focus question (PICO)

For the systematic review, the detailed protocol in the Preferred Reporting Items for Systematic Review and Meta-Analyses statement was followed [9]. The PICO (Population, Intervention,

CONTACT Yong-Moo Lee ymlee@snu.ac.kr Department of Periodontology and Dental Research Institute, School of Dentistry, Seoul National Universitym, 101, Daehak-ro, Seoul 110-749, Korea

Supplemental data for this article can be accessed here.

Comparison and Outcome) criteria were used to focus the review: Patients with a minor bone defect, such as buccal bone dehiscence or a marginal gap, were investigated following immediate implant placement with or without a regenerative procedure, and outcomes such as implant failure and width changes in the alveolar ridge around the implant were compared.

Search strategy

An electronic search of MEDLINE, EMBASE, and the LILACS database of the Cochrane Central Register of controlled trials were performed, along with a manual search, up to April 2018. The electronic search used combinations of MeSH terms and text words (Appendix S1). The manual search was conducted within the bibliographies of the retrieved articles and related reviews. The following journals were screened from 2001 to April 2018: *Clinical Oral Implants Research; Clinical Implant Dentistry and Related Research; European Journal of Oral Implantology; Implant Dentistry; International Journal of Oral and Maxillofacial Implants; International Journal of Periodontics and Restorative Dentistry; Journal of Clinical Periodontology; Journal of Dental Research; Journal of Investigative and Clinical Dentistry; Journal of Oral Implantology; Journal of Oral and Maxillofacial Surgery; Journal of Periodontology; Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics;* and *Journal of Periodontal & Implant Science*.

Articles were screened without any language restriction, nor were unpublished data or studies excluded from the search process. Two reviewers (JL and DP) independently performed the database and manual searches. In cases of inconsistencies, consensus was achieved in discussion with a third reviewer (YML). To reduce bias and errors, a calibration test was performed with the first 1000 searched studies, which resulted in a 98.6% concurrence. The Cohen's kappa coefficient was calculated to evaluate the agreement level between the two reviewers.

Study selection

The inclusion criteria were as follows:

- human studies,
- randomized controlled trials (RCTs) or quasi-randomized controlled clinical trials (CCTs) conducted with and without a regenerative procedure for immediate implant placement and
- clinical, radiographic, or histological evaluations of hard or soft tissues at least 3 months after surgery, with at least 10 subjects per group.

The exclusion criteria were as follows:

- studies that did not satisfy all the inclusion criteria;
- studies that included medically compromised patients, such as those with cancer, osteonecrosis, osteomyelitis, or uncontrolled diabetes mellitus and irradiated patients;
- preclinical studies, case reports, case series, narrative reviews and systematic reviews.

When different publications reported more than one set of data about a single set of participants, only the most recent data were considered in this review.

Assessment of heterogeneity

To evaluate the statistical heterogeneity of the included studies, Chi^2 was calculated using RevMan software (version 5.3, The Cochrane Collaboration).

Assessment of risk of bias

The quality of the included studies was independently assessed by two reviewers (JL and DP). The risk of bias of RCTs was ranked as low, unclear, or high according to the Cochrane tool for evaluating the risk of bias [10] and the following evaluation items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data. The assessment for CCTs was performed using the checklist by Downs and Black [11]. That checklist includes 27 criteria that cover reporting quality, external and internal validity, and power.

Quantitative analysis

The meta-analyses were performed using RevMan software (version 5.3, The Cochrane Collaboration). A dichotomous outcome (implant failure) was analyzed, and the 95% confidence interval (CI) was calculated. The weighted mean difference (WMD) was estimated for the continuous variable (change in alveolar bone width). Because the included studies were considered to be homogeneous, fixed effect models were used for the meta-analyses.

Results

Study selection

The initial electronic search resulted in 2497 records, and the subsequent manual search yielded five articles. Eighty-eight duplicates were excluded, and the titles and abstracts of 2414 articles were then assessed (Figure 1). After the title and abstract evaluation, 19 articles were included in the full-text evaluation. Of the 19 articles, 12 did not meet the inclusion criteria: seven had no control group (without a regenerative procedure) [12–18], two had control groups with no pre-existing bone defects [19,20], two did not describe the immediate implant placement protocol [21,22], and one used platelet-rich fibrin (PRF) instead of bone graft materials [23]. The Cohen's kappa coefficient was 0.80, indicating a reliable level of agreement between the two reviewers.

Study characteristics

The characteristics of the included studies are given in Table 1. One study was a quasi-randomized CCT, and six were RCTs. The mean age of the patients ranged from 34 to 48.5 years,

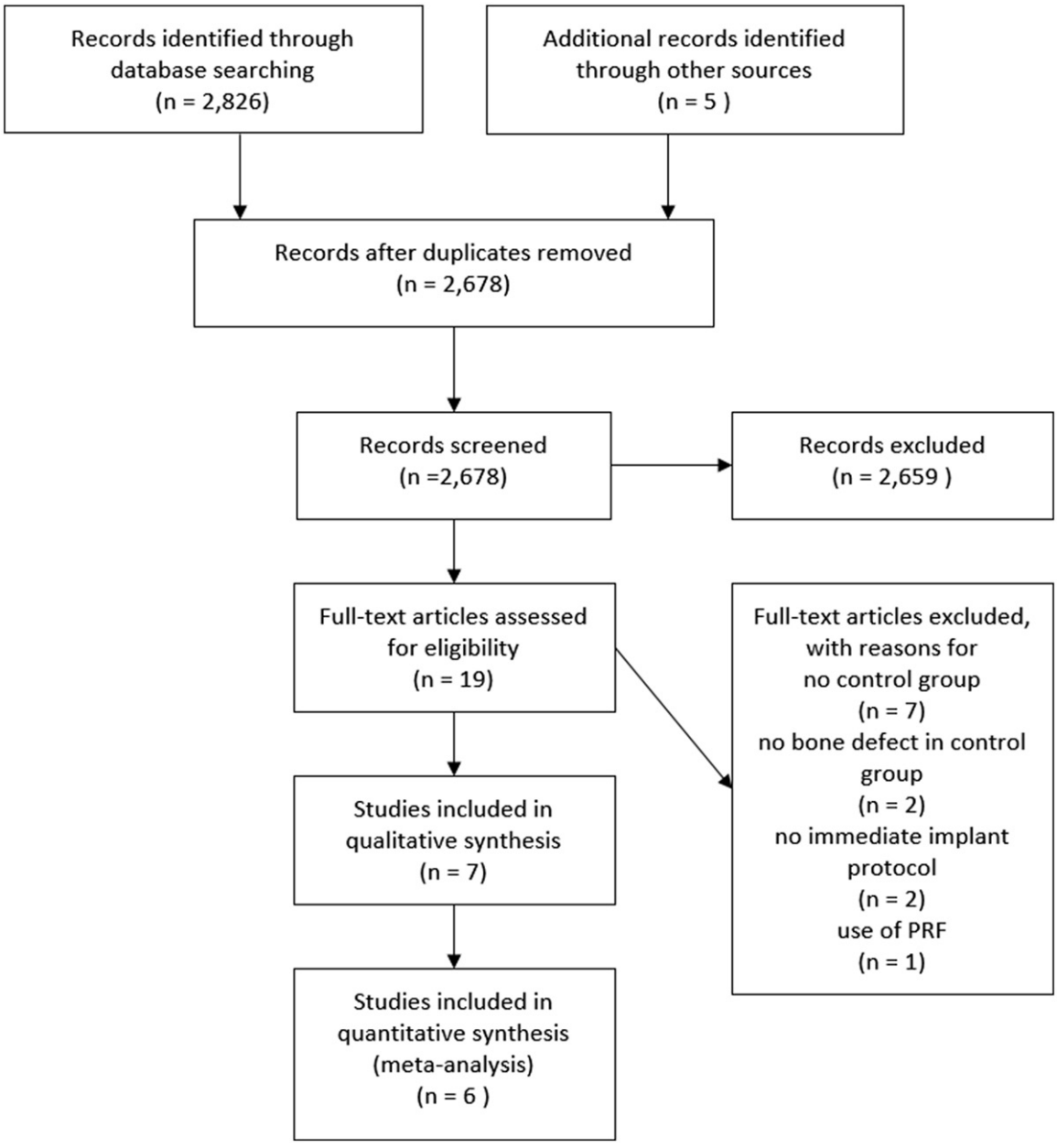

Figure 1. Flow diagram of study selection.

and the mean patient age was not mentioned in one study [24]. The reasons for extraction were failure of endodontic treatment, localized periodontitis, trauma and advanced dental caries, although two studies did not address the reason for extraction [24,25]. In all studies, the defect existed between the buccal bone wall and implant fixture, and the defect type was a marginal gap or dehiscence. The defect size was described in four studies [24–27]. The horizontal defect size ranged from 1.57 to 2.25 mm, with no statistical differences between the control and test groups.

Various graft materials were used in the included studies. An allograft was used in two studies [26,28], a xenograft in three [24,27,29], and an autograft in one [30]. Three types of bone graft materials (autograft, allograft and xenograft) were used to repair the defects in one study [25].

A membrane was used in the regenerative procedure in two studies [27,30]. Expanded polytetrafluoroethylene and bioresorbable polyglycolic and polylactic acid copolymer membranes were used in one study [30], and bioresorbable collagen membranes were used in another study [27]. Instead of a barrier membrane, a collagen sponge was used in one study [29].

All but two studies used the internal connection type implant. One study used an external connection type implant [30], and another used an internal, non-submerged type implant [27]. The implant diameter ranged from 3.5 to 4.7 mm, and the implant size was not mentioned in two studies [27,30].

Immediate implant placement was performed after atraumatic tooth extraction for all included studies. A flap was raised after tooth extraction for the implant placement in three studies [24,27,30], and no flap elevation was performed in four studies [25,26,28,29].

Of the seven included studies, 311 dental implants were immediately placed in the extracted sites with or without a

Table 1. Characteristics of the included studies.

Study (year)	Study design	Age (mean), years	Subjects (*n*): intervention	Implant position	Defect type	Defect size (horizontal)	Bone graft material	Membrane type	Diameter of implant (mm)	Implant type	Flap management	Implant failure	Follow-up period (months)	Assessment modality
Assaf et al. (2013)	CCT	48.5	T (11): bone graft C (9): no graft	Maxillary incisors and premolars	Marginal gap	T: 2.12 (0.4) C: 1.96 (0.3)	BCP	None	4.1	Internal	Flapless	T: 0 C: 0	6	CT: Buccolingual width of ridge, bone wall thickness
Bottini et al. (2012)	RCT	45	T (20): bone graft C (20): no graft	Mandibular	Marginal gap	NM	Porcine bone	Collagen sponge	3.75, 4.2, 5	Internal	Flapless	T: 0 C: 0	6	Probe, caliper: Buccolingual width of ridge
Chen et al. (2005)	RCT	41.8	T1 (12): ePTFE membrane only T2 (11): resorbable membrane only T3 (13): resorbable membrane + bone graft T4 (14): bone graft only C: no graft (12)		Dehiscence, Marginal gap	NM	Autograft	e-PTFE, resorbable membrane	NM	External	Flapped	T1: 0 T2: 0 T3: 1 T4: 1 C: 0	24	Re-entry: Bone defect size (vertical, horizontal)
Chen et al. (2007)	RCT	45.2	T1 (10): bone graft only T2 (10): resorbable membrane + bone graft C (10): no bone graft		Marginal gap, dehiscence	T1: 1.9 (0.9) T2: 1.8 (0.9) C: 1.9 (0.5)	DBBM	T2: resorbable collagen membrane	NM	Internal	Flapped	T1: 0 T2: 0 C: 0	36	Re-entry: Horizontal and vertical dimension Clinical, periapical radiograph: mPI, mBI, probing pocket depth, crestal bone level
Daif (2013)	RCT	34	T (14): bone graft C (14): no graft		Marginal gap	NM	Beta-TCP	None	3.75 or 4	Internal	Flapless	T: 0 C: 0	6	CT: Bone density
Sanz (2017)	RCT	NM	T (43): bone graft C (43): no graft		Marginal gap	T: 1.57 (1.27) C: 2.23 (1.22)	DBBM-C	None	3.5 or 4.0	Internal	Flapped	T: 1 C: 0	4	Re-entry: Buccolingual width of ridge Vertical bone height (buccal, palatal)
Spinato et al. (2012)	RCT	42.5	T (22): bone graft C (23): no graft		Marginal gap	T: 2.25 (0.55) C: 2.03 (0.74)	Autograft, allograft, xenograft	None	3.7 or 4.7	Internal	Flapless	T: 0 C: 0	32	Clinical, periapical radiograph: Papilla index score, Peri-implant bone loss, Probing depth

CCT: quasi-randomized controlled clinical trial; RCT: randomized controlled trial; T: test group; C: control group; NM: not mentioned; BCP: biphasic calcium phosphate; beta-TCP: beta-tricalcium phosphate; DBBM-C: deproteinized bovine bone mineral with 10% collagen.

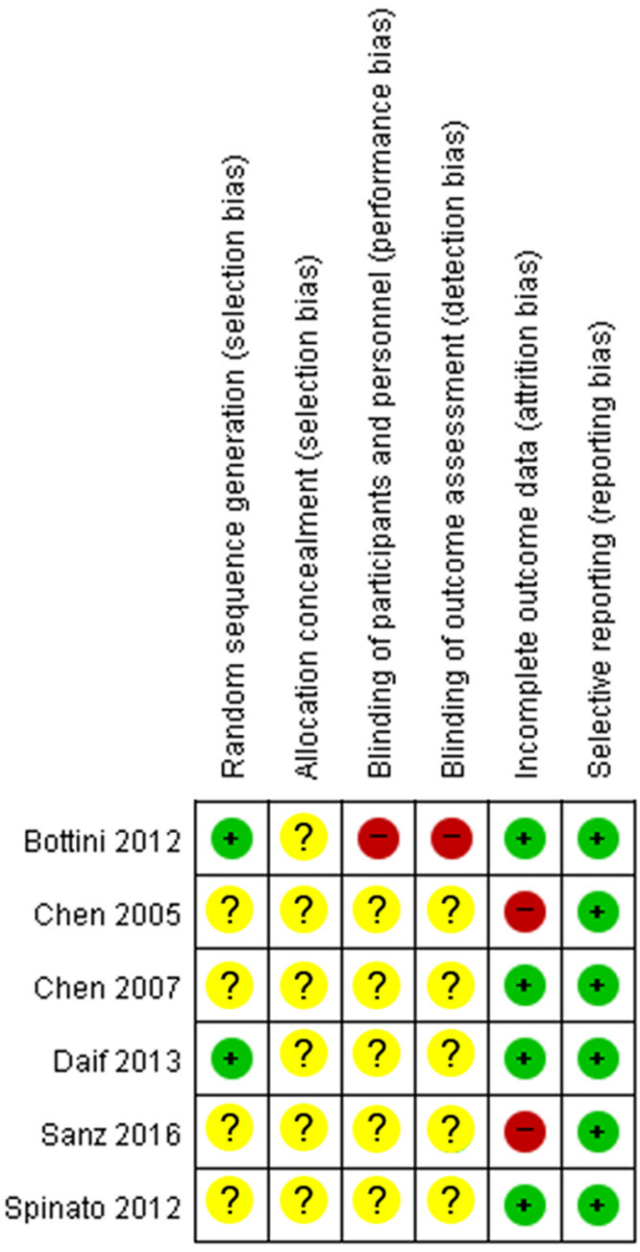

Figure 2. Risk of bias summary: each risk of bias item for each included study.

regenerative procedure. In five studies [25–29], the healing process was uneventful for all patients, and no implant was lost in either the test or control group. The remaining two studies [24,30] included three implant failures in the test group. The follow-up period after the surgical intervention ranged from 4 to 32 months.

Evaluation parameters and methods

Four of the included studies provided data about changes in the alveolar ridge thickness after immediate implant placement [24,26,27,29]. Measurements were performed using computed tomography (CT) in one study [26], and they were performed during surgery and re-entry with a probe or caliper in three studies [24,27,29].

Only one study reported peri-implant bone loss on the mesial or distal side and soft tissue dimensions [25]. One study used multi-slice helical CT to measure the change in bone density in Hounsfield units (HUs) between baseline and 4 months after immediate implant placement with or without a regenerative procedure [28].

Assessment of risk of bias

The risk of bias assessment for the included RCTs is shown in Figure 2. None of the included studies had a low risk of bias for all evaluated items. Most of the included studies were deemed to have an unclear to high risk of bias for the following four evaluation items: random sequence generation, allocation concealment, blinding of participants and blinding of outcome assessment. Random sequence generation was deemed to have a low risk of bias in two studies [28,29], which used a computer-generated random number. Blinding of the outcome assessment (detection bias) was considered to have a low risk of bias in two studies [24,26]. All but two of the included studies were considered to have a low risk of bias for incomplete outcome data [24,30]. All of the included studies had a low risk of bias in selective reporting. A funnel plot asymmetry test to identify publication bias was not performed because <10 studies were included in the analysis [31]. The quality assessment of the included CCT is shown in Table 2. The included study showed a high risk of bias, with a total quality assessment score of less than 20 (Table 2). Although a clear aim and intervention were reported, the study lacked a power analysis and a description of the principal confounders.

Meta-analysis

In this systematic review, quantitative analyses were performed of the data in the included studies. The categories of the meta-analyses were implant failure and changes in the crestal bone width after immediate implant placement with or without a regenerative procedure. The results are shown in Figures 3 and 4. There was no significant difference in the risk of implant failure from immediate implant placement with or without a regenerative procedure (risk difference, 0.01; 95% CI: -0.03 to 0.05; $p = .54$). The WMD of the change in alveolar bone width after immediate implant placement was lower in the regenerative procedure group than in the non-regenerative procedure group (<1 year follow up studies: WMD 0.75 mm, 95% CI: 0.41–1.09, $p < .00001$; ≥ 1 year follow up study: WMD 1.22 mm, 95% CI: 0.52–1.91, $p = .00006$; total: WMD 0.84 mm, 95% CI: 0.53–1.14, $p < .00001$).

Discussion

The necessity of a regenerative procedure for immediate implant placement remains controversial. In a previous study, implants that were immediately placed in a fresh extraction socket with a marginal gap and without a primary flap closure, graft, or membrane showed intimate bone contact to the first thread of the implant and reestablishment of the implant biologic width coronal to the bone contact with the connective tissue and junctional epithelium 10 months after implant placement [32]. In contrast, immediate implant

Table 2. Quality assessment of the CCT based on checklist of Downs and Black [11]. Reporting: 1, yes; 0, no.

Contents	Study
Reporting	Assaf (2013)
Q1. Hypothesis/aim/objective clearly described	1
Q2. Main outcomes in introduction or methods	1
Q3. Patient characteristics clearly described	1
Q4. Interventions of interest clearly described	1
Q5. Principal confounders clearly described	0
Q6. Main findings clearly described	1
Q7. Estimates of random variability provided for main outcomes	0
Q8. All adverse events of intervention reported	0
Q9. Characteristics of patients lost to follow-up described	1
Q10. Probability values reported for main outcomes	1
EXTERNAL VALIDITY	
Q11. Subjects asked to participate were representative of source population	0
Q12. Subjects prepared to participate were representative of source population	0
Q13. Location and delivery of study treatment was representative of source population	0
INTERNAL VALIDITY – BIAS & CONFOUNDING	
Q14. Study participants blinded to treatment	0
Q15. Blinded outcome assessment	1
Q16. Any data dredging clearly described	0
Q17. Analyses adjust for differing lengths of follow-up	1
Q18. Appropriate statistical tests performed	1
Q19. Compliance with interventions was reliable	1
Q20. Outcome measures were reliable and valid	1
Q21. All participants recruited from the same source population	1
Q22. All participants recruited over the same time period	1
Q23. Participants randomized to treatment(s)	0
Q24. Allocation of treatment concealed from investigators and participants	0
Q25. Adequate adjustment for confounding	0
Q26. Losses to follow-up taken into account	0
POWER	
Q27. Sufficient power to detect treatment effect at significance level of 0.05	0
TOTAL	14

placement was not found to counteract the shrinkage of the alveolar ridge after tooth extraction [33,34]. To rehabilitate the architecture of the hard and soft tissues, a regenerative procedure was suggested for immediate implant placements [35]. The overall loss of hard and soft tissue volume took place during the first 3 months following tooth extraction [36], and therefore, 3 months was set as the minimal follow-up period for inclusion in this review.

Immediate implant placement with a regenerative procedure does not appear to obstruct the healing of the peri-implant bone or the survival of the implant. A previous study reported that implant placement with simultaneous guided-bone regeneration in the healed ridges showed good osseointegration and bone regeneration [37,38]. However, the immediate insertion of bone graft material in an extraction socket might retard the healing of the extraction wound [39]. In other words, immediate implant placement with a regenerative procedure might interfere with the healing of the bone around the implant and jeopardize osseointegration. To investigate the safety of performing a regenerative procedure with immediate implant placement, a meta-analysis was performed to determine whether there is a risk difference for implant failure between the regenerative procedure and non-regenerative procedure groups. The results reveal that a regenerative procedure performed with immediate implant placement did not adversely affect the survival of the implant. Therefore, a suitable protocol for immediate implant placement should enable adequate healing before functional loading.

A preclinical study demonstrated that prominent shrinkage of the buccal contour could be prevented by using a regenerative procedure with immediate implant placement

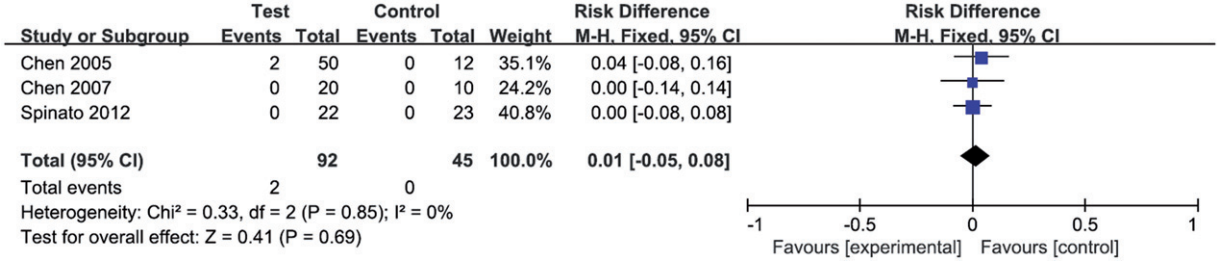

Figure 3. Forest plot of the risk difference between the regenerative procedure group (test) and the non-regenerative procedure group (control).

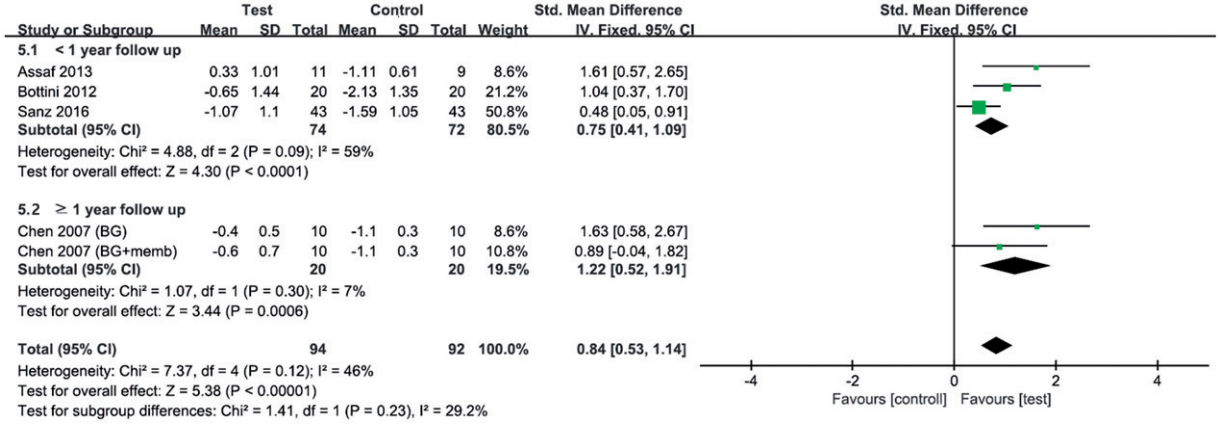

Figure 4. Forest plot of changes in the ridge width between baseline and follow-up.

[35]. To test that finding, a meta-analysis was performed for changes in the buccolingual ridge width from baseline to follow-up. The results show that the reduction was significantly lower in the regenerative procedure group than in the non-regenerative procedure group after more than and less than 1 year of follow up (Figure 4). On the basis of this finding, a regenerative procedure is recommended for immediate implant placement to reduce complications around the implants.

However, care should be taken in generalizing these results; the regenerative procedure in all studies included here was performed for a minor bone defect. Teeth with severe bone defects were excluded. The defect size was ~2 mm (three studies did not present the exact defect size), and the type of defect was a marginal gap or dehiscence. Chen et al. [27,30] demonstrated that immediate implant placement in an extraction socket with a damaged labial plate showed significant labial bone resorption irrespective of the performance of a regenerative procedure. Foreseeing esthetic complications caused by hard tissue deficiency, overcorrecting the regenerative procedure with bone graft material and an additional soft tissue graft seems to be needed [40].

CT findings revealed that the bone density improved when bone graft material was inserted in the marginal gap around the immediately placed dental implant [28]. HUs at 6 months were significantly greater in the regenerative procedure group than in the non-regenerative procedure group (1490 ± 358 vs. 1245 ± 165). However, further studies are required to investigate the clinical relevance of CT bone density findings. A previous study demonstrated that bone density findings using HUs did not reflect bone quality, with the exception of type 4 bone [41]. The mean HUs of types 1, 2, 3 and 4 bone were 612 ± 332, 519 ± 374, 546 ± 403 and 171 ± 541, respectively, suggesting that further studies are warranted to determine whether enhanced bone density, as monitored using CT, indicates improved bone quality of the peri-implant hard tissue.

This study had some limitations that should be addressed. Most of the included studies had small sample sizes and short follow-up periods. Four studies [24,26,28,29] included less than 1 year of follow up. Given that most studies did not have a low risk of bias, further studies with a larger number of patients and longer follow-up periods are warranted. Moreover, further studies are required to determine the effect of bone grafting on the success and survival of implants and to evaluate dimensional changes in soft and hard tissue over long periods. Another issue is the heterogeneity of bone graft materials and barrier membranes used in the included studies. To obtain clear conclusions, studies using more homogeneous bone graft materials and barrier membranes should be conducted and included in future systematic reviews.

Conclusions

Within the limitations of this meta-analysis, the following conclusions are drawn:

1. No evidence suggests that immediately placed implants with regenerative procedure in small bone defects face impaired survival compared with those that are allowed to heal spontaneously.
2. The use of a regenerative procedure improved the preservation of alveolar bone width around immediately placed implants. A regenerative procedure for immediate implant placement is therefore recommended in esthetic areas to improve the architecture of hard tissues.
3. Overall, previously published studies in this area showed a high risk of bias. High-quality RCTs with homogeneous bone graft material and barrier membrane are needed.

Acknowledgements

The authors hereby acknowledge the diligent support provided by the Dental Research Institute, Seoul National University, in the management of this study. The authors also thank eWorldEditing for technical support.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Hammerle CH, Chen ST, Wilson TG. Jr. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. Int J Oral Maxillofac Implants. 2004;19(Suppl):26–28.
[2] Fugazzotto PA. Immediate implant placement and GBR in humans: a case report and histologic evaluation. Int J Periodontics Restorative Dent. 1999;19:457–463.
[3] Park JB. Restoration of the maxillary anterior tooth using immediate implantation with simultaneous ridge augmentation. Indian J Dent Res. 2010;21:454–456.
[4] Sarnachiaro GO, Chu SJ, Sarnachiaro E, et al. Immediate implant placement into extraction sockets with labial plate dehiscence defects: a clinical case series. Clin Implant Dent R. 2016;18:821–829.
[5] Atalay B, Oncu B, Emes Y, et al. Immediate implant placement without bone grafting: a retrospective study of 110 cases with 5 years of follow-up. Implant Dent. 2013;22:360–365.
[6] Bersani E, Coppede AR, de Paula Pinto Prata HH. Immediate loading of implants placed in fresh extraction sockets in the molar area with flapless and graftless procedures: a case series. Int J Periodontics Restorative Dent. 2010;30:291–299.
[7] Clementini M, Tiravia L, De Risi V, et al. Dimensional changes after immediate implant placement with or without simultaneous regenerative procedures: a systematic review and meta-analysis. J Clin Periodontol. 2015;42:666–677.
[8] AlKudmani H, Al Jasser R, Andreana S. Is bone graft or guided bone regeneration needed when placing immediate dental implants? A systematic review. Implant Dent. 2017;26:936–944.
[9] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Bmj. 2009;339:b2535.
[10] Higgins JP, Altman DG, Gotzsche PC, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. Bmj. 2011;343:d5928.
[11] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Commun Health. 1998;52:377–384.
[12] Acocella A, Bertolai R, Sacco R. Modified insertion technique for immediate implant placement into fresh extraction socket in the

first maxillary molar sites: a 3-year prospective study. Implant Dent. 2010;19:220–228.
[13] Cornelini R, Cangini F, Martuscelli G, et al. Deproteinized bovine bone and biodegradable barrier membranes to support healing following immediate placement of transmucosal implants: a short-term controlled clinical trial. Int J Periodontics Restorative Dent. 2004;24:555–563.
[14] De Rouck T, Collys K, Cosyn J. Immediate single-tooth implants in the anterior maxilla: a 1-year case cohort study on hard and soft tissue response. J Clin Periodontol. 2008;35:649–657.
[15] De Angelis N, Felice P, et al. Guided bone regeneration with and without a bone substitute at single post-extractive implants: 1-year post-loading results from a pragmatic multicentre randomised controlled trial. Eur J Oral Implantol. 2011;4:313–325.
[16] Benic GI, Mokti M, Chen CJ, et al. Dimensions of buccal bone and mucosa at immediately placed implants after 7 years: a clinical and cone beam computed tomography study. Clin Oral Impl Res. 2012;23:560–566.
[17] Gher ME, Quintero G, Assad D, et al. Bone grafting and guided bone regeneration for immediate dental implants in humans. J Periodontol. 1994;65:881–891.
[18] Gher ME, Quintero G, Sandifer JB, et al. Combined dental implant and guided tissue regeneration therapy in humans. Int J Periodontics Restorative Dent. 1994;14:332–347.
[19] Covani U, Crespi R, Cornelini R, et al. Immediate implants supporting single crown restoration: a 4-year prospective study. J Periodontol. 2004;75:982–988.
[20] Covani U, Chiappe G, Bosco M, et al. A 10-year evaluation of implants placed in fresh extraction sockets: a prospective cohort study. J Periodontol. 2012;83:1226–1234.
[21] Benic GI, Ge Y, Gallucci GO, et al. Guided bone regeneration and abutment connection augment the buccal soft tissue contour: 3-year results of a prospective comparative clinical study. Clin Oral Impl Res. 2017;28:219–225.
[22] Jung RE, Herzog M, Wolleb K, et al. A randomized controlled clinical trial comparing small buccal dehiscence defects around dental implants treated with guided bone regeneration or left for spontaneous healing. Clin Oral Impl Res. 2017;28:348–354.
[23] Al Nashar A, Yakoob H. Evaluation of the use of plasma rich in growth factors with immediate implant placement in periodontally compromised extraction sites: a controlled prospective study. Int J Oral Maxill Surg. 2015;44:507–512.
[24] Sanz M, Lindhe J, Alcaraz J, et al. The effect of placing a bone replacement graft in the gap at immediately placed implants: a randomized clinical trial. Clin Oral Impl Res. 2017;28:902–910.
[25] Spinato S, Agnini A, Chiesi M, et al. Comparison between graft and no-graft in an immediate placed and immediate nonfunctional loaded implant. Implant Dent. 2012;21:97–103.
[26] Assaf JH, Zanatta FB, de Brito RB Jr, et al. Computed tomographic evaluation of alterations of the buccolingual width of the alveolar ridge after immediate implant placement associated with the use of a synthetic bone substitute. Int J Oral Maxillofac Implants. 2013;28:757–763.
[27] Chen ST, Darby IB, Reynolds EC. A prospective clinical study of non-submerged immediate implants: clinical outcomes and esthetic results. Clin Oral Implants Res. 2007;18:552–562.
[28] Daif ET. Effect of a multiporous beta-tricalicum phosphate on bone density around dental implants inserted into fresh extraction sockets. J Oral Implantol. 2013;39:339–344.
[29] Bottini LP, Ricci L, Piattelli A, et al. Bucco-lingual crestal bone changes around implants immediately placed in fresh extraction sockets in association or not with porcine bone: a non-blinded randomized controlled trial in humans. J Periodontol. 2012;1. doi: 10.1902/jop.2012.120396.
[30] Chen ST, Darby IB, Adams GG, et al. A prospective clinical study of bone augmentation techniques at immediate implants. Clin Oral Implants Res. 2005;16:176–184.
[31] Sterne JA, Sutton AJ, Ioannidis JP, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. Bmj. 2011;343:d4002.
[32] Tarnow DP, Chu SJ. Human histologic verification of osseointegration of an immediate implant placed into a fresh extraction socket with excessive gap distance without primary flap closure, graft, or membrane: a case report. Int J Periodontics Restorative Dent. 2011;31:515–521.
[33] Botticelli D, Berglundh T, Lindhe J. Hard-tissue alterations following immediate implant placement in extraction sites. J Clin Periodontol. 2004;31:820–828.
[34] Matarasso S, Salvi GE, Iorio Siciliano V, et al. Dimensional ridge alterations following immediate implant placement in molar extraction sites: a six-month prospective cohort study with surgical re-entry. Clin Oral Implants Res. 2009;20:1092–1098.
[35] Araujo MG, Linder E, Lindhe J. Bio-Oss collagen in the buccal gap at immediate implants: a 6-month study in the dog. Clin Oral Implants Res. 2011;22:1–8.
[36] Schropp L, Wenzel A, Kostopoulos L, et al. Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study. Int J Periodontics Restorative Dent. 2003;23:313–323.
[37] Benic GI, Bernasconi M, Jung RE, et al. Clinical and radiographic intra-subject comparison of implants placed with or without guided bone regeneration: 15-year results. J Clin Periodontol. 2017;44:315–325.
[38] Konstantinidis I, Kumar T, Kher U, et al. Clinical results of implant placement in resorbed ridges using simultaneous guided bone regeneration: a multicenter case series. Clin Oral Invest. 2015;19:553–559.
[39] Araujo M, Linder E, Lindhe J. Effect of a xenograft on early bone formation in extraction sockets: an experimental study in dog. Clin Oral Implants Res. 2009;20:1–6.
[40] Lee YM, Kim DY, Kim JY, et al. Peri-implant soft tissue level secondary to a connective tissue graft in conjunction with immediate implant placement: a 2-year follow-up report of 11 consecutive cases. Int J Periodontics Restorative Dent. 2012;32:213–222.
[41] Shapurian T, Damoulis PD, Reiser GM, et al. Quantitative evaluation of bone density using the Hounsfield index. Int J Oral Maxill Implants. 2006;21:290–297.