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Cone-beam computed tomographic evaluation of dimensional hard tissue changes following alveolar ridge preservation techniques of different bone substitutes: a systematic review and meta-analysis

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ABSTRACT

Purpose: This study was conducted to evaluate and compare the effects of different graft materials used in alveolar ridge preservation on dimensional hard tissue changes of the alveolar ridge, assessed using cone-beam computed tomography (CBCT) scans.
Methods: A systematic electronic search of MEDLINE and the Cochrane Central Register of Controlled Trials and a manual search were conducted from November 2019 until January 2020. Randomized controlled trials were included if they assessed at least 1 variable related to vertical or horizontal hard tissue changes measured using CBCT scans. After a qualitative analysis of the included studies, subgroups were formed according to the graft material used, and a quantitative analysis was performed for 5 outcome variables: changes in vertical alveolar bone height at 2 points (midbuccal and midpalatal/midlingual) and changes in horizontal (buccolingual) alveolar bone width at 3 different levels from the initial crest height (1, 3, and 5 mm).
Results: The search resulted in 1,582 studies, and after an independent 3-stage screening, 16 studies were selected for qualitative analysis and 9 for quantitative analysis. The meta-analysis showed a significantly (P<0.05) lower reduction of alveolar ridge dimensions for the xenogenic subgroup than in the allogenic subgroup, both vertically at the midbuccal aspect (weighted mean difference [WMD]=−0.20; standard error [SE]=0.26 vs. WMD=−0.90; SE=0.22) as well as horizontally at 1 mm (WMD=−1.32; SE=0.07 vs. WMD=−2.99; SE=0.96) and 3 mm (WMD=−0.78; SE=0.11 vs. WMD=−1.63; SE=0.40) from the initial crest height. No statistical analysis could be performed for the autogenic subgroup because it was not reported in sufficient numbers.
Conclusions: Less vertical and horizontal bone reduction was observed when xenogenic graft materials were used than when allogenic graft materials were used; however, the loss of alveolar ridge dimensions could not be completely prevented by any graft material.

Keywords: Alveolar bone loss; Bone substitutes; Cone-beam computed tomography; Dental implants; Guided tissue regeneration; Tooth socket

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

INTRODUCTION

From 2018 to 2019, 2,958,000 tooth extractions were performed on adult patients in England [1]. Considering that partial or complete edentulism may not only lead to impaired oral function, but could also contribute to reduced self-confidence, dental implants have been regarded as a safe and reliable method to replace missing teeth [2,3]. Implant dentistry has evolved considerably in the last 2 decades from a bone-driven surgical approach to a biological and restoratively focused approach [4]. Consequently, researchers are increasing their focus on implant placement in the optimal prosthetically desired position. The presence of adequate alveolar ridge dimensions creates the foundation for optimal function, stability, and aesthetic outcomes, and therefore dictates the success of implant treatment. While tooth extraction might be required for various reasons, it is essential to understand the adaptive soft and hard tissue alterations that follow the loss of teeth, which have been studied in humans [5-7] as well as in different animal models [8-11]. Schropp et al. [12] observed that the buccal-lingual dimension of the edentulous ridge was reduced by at least 50% during the first year after tooth extraction, and that 30% of the initial ridge width was lost during the first 3 months. Several other authors have also reported a greater extent of resorption at the buccal plate than at the lingual/palatal plate [10,13,14].

In order to minimize the loss of ridge dimensions after tooth extraction and to avoid more demanding surgical bone augmentation procedures in the future [15], the placement of different bone graft materials into the post-extraction socket has been proposed and evaluated in several pre-clinical [16,17] and clinical studies [13,18-21]. The techniques for these alveolar ridge preservation procedures are diverse and include the use of different autogenic, allogenic, and xenogenic materials, without or in combination with the placement of different barrier membranes or autogenous soft tissue plugs. The graft material is meant to enhance bone formation, while the membrane should prevent the ingrowth of faster-proliferating soft tissues [22]. The dimensional and histological changes and characteristics of different alveolar ridge preservation techniques have been evaluated in various systematic reviews and meta-analyses [23-36]. These authors concluded that the loss of alveolar ridge dimensions could not be completely prevented by alveolar ridge preservation procedures, but those procedures resulted in less vertical (1.47 mm) and horizontal (1.83 mm) bone reduction than observed in unassisted socket healing [30]. Nevertheless, a consensus could not be reached on which technique would be the most suitable [30].

A recent quality assessment of systematic reviews on alveolar socket preservation found high methodological heterogeneity among systematic reviews despite the presence of very similar objectives [37]. Thus far, various methods of measurement to assess the dimensional changes of the alveolar ridge after tooth extraction have been reported using a variety of different reference points. Conventional methods of assessment include radiographic measurements on periapical and cephalometric radiographs, as well as direct measurements on study casts or at surgical re-entry with a periodontal probe or a caliper [13,18,38]. In addition to lacking accuracy and being difficult to reproduce, measurements on periapical and cephalometric radiographs or on study casts may also poorly reflect the 3-dimensional characteristics of the complex bone remodeling process. While direct measurements at surgical re-entry allow the most accurate measurements, it is often desirable to evaluate the alveolar ridge dimensions at the future implant site before flap elevation. New techniques from measurements using cone-beam computed tomography (CBCT) scans have been proposed and adopted by various studies in recent years [39-41]. Digital superpositioning of baseline and follow-up scans

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or the use of radiographic markers allows reproducible and accurate measurements of the complex dimensional changes of the alveolar process following tooth extraction and alveolar ridge preservation procedures, at relatively low radiation doses to patients [42].

Measurement methods have a considerable impact on the outcome data; therefore, heterogeneity should be minimized as much as possible in this regard. Ten Heggeler et al. [29] addressed this issue in their conclusion, suggesting that a study should be conducted to validate different evaluation methods. However, to the best of our knowledge, the literature only contains systematic reviews that combine results obtained using various conventional and radiographic methods of measurement. Therefore, this study aimed to systematically review the literature regarding data based only on CBCT radiographic evaluations of alveolar ridge preservation techniques after tooth extraction.

The specific objective was to compare the effects of different graft materials used in alveolar ridge preservation on dimensional changes of the alveolar ridge following atraumatic tooth extractions using CBCT scans.

MATERIALS AND METHODS

Protocol

This systematic review and meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) [43].

Eligibility criteria

According to the population, intervention, comparison, outcomes (PICO) design, the following focus question was developed (**Table 1**).

Primary focus question: *"What are the effects of different graft materials used in alveolar ridge preservation on dimensional changes of the alveolar ridge following atraumatic tooth extractions, as assessed using CBCT scans?"*

Inclusion criteria

The inclusion criteria were randomized controlled trials (RCTs) with healthy adult human subjects, articles published in the English language, and studies where at least 1 of the outcome variables was assessed radiologically with CBCT scans.

Table 1. PICO questions

Component	Description
Population (P)	Healthy patients without any contraindication to oral surgery who received any type of alveolar ridge preservation treatment following atraumatic permanent tooth extraction. Studies including subjects with a history of smoking were not excluded.
Intervention (I)	Alveolar ridge preservation procedures after atraumatic tooth extraction consisting of filling the alveolar socket with any of the following regenerative biomaterials: autogenic, allogenic, and xenogenic graft materials. Different barrier membranes or soft tissue grafts could be used to cover the sites.
Comparison (C)	Different graft materials in alveolar ridge preservation after atraumatic tooth extraction.
Outcome (O)	Radiological dimensional changes of the alveolar ridge measured with CBCT scans: 1. Mean linear changes in vertical midbuccal and vertical midpalatal height 2. Mean linear changes in horizontal (buccolingual) alveolar bone width at different levels from the initial vertical crest height

PICO: population, intervention, comparison, outcomes.

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Exclusion criteria

The exclusion criteria encompassed editorials, reviews, case reports, and case series, including subjects with any contraindication to oral surgery, studies not including a radiological evaluation with CBCT scans, studies not reporting relevant outcome data, studies that recorded data in a format that was incompatible with the outcome variables predetermined in the inclusion criteria, studies only evaluating third molar extraction sites, studies evaluating immediate implant placement for alveolar ridge preservation, studies that did not report follow-up data at or beyond 3 months, and studies reporting the same data or population as other included studies.

Search

A systematic electronic search was conducted in the MEDLINE databases and the Cochrane Central Register of Controlled Trials (CENTRAL) by applying the following combination of keywords and MeSH terms: (((((((((((((((("socket preservation") OR "ridge preservation") OR "ridge healing") OR "socket grafting") OR "ridge augmentation") OR "alveolar ridge preservation") OR "socket seal") OR "socket healing") OR "ridge change") AND "autogenous bone") OR allograft) OR xenograft) OR "bovine bone") AND radiological) OR “computer tomography”) OR radiographically) OR CBCT) AND "tooth extraction." The results were limited to human studies and dental journals.

A 3-stage screening process was performed independently by 2 investigators. In situations where disagreement over the application of the inclusion or exclusion criteria existed, differences were resolved by discussion. If no consensus could be reached, the decision of a third party (a senior reviewer) was adopted. In stage 1, the investigators independently screened all titles of the electronic search for relevance. In case of uncertainty, the articles in question were included for an additional evaluation during the following stages. In stage 2, the abstracts of all pre-selected articles were independently reviewed by the investigators to further exclude articles that did not meet the predetermined inclusion criteria. Stage 3 comprised full-text evaluation for eligibility after obtaining the full-text versions. Based on the references from the definitive list of included articles from stage 3, an additional manual search was performed.

Data collection

Qualitative and quantitative data were collected from the studies, including (1) general study characteristics and basic demographic data of subjects (author, year of publication, number of groups studied, number of subjects in each group, age and sex distribution of subjects, history of smoking habits), (2) surgical procedures (flap elevation, graft material, use of a barrier membrane, soft tissue closure, post-surgical pharmacological treatment), (3) outcome variables of interest (radiologically measured dimensional changes of the alveolar ridge, method of measurement, and reference points), (4) possible outcome-modifying clinical factors (location of extraction site, socket morphology, reason for extraction, presence of adequate oral hygiene, or presurgical basic periodontal treatment), and (5) qualitative data for the assessment of possible risk of bias.

Quality assessment

The assessment of possible risk of bias for all studies was performed according to the revised Cochrane Risk-of-Bias tool for randomized trials [44]. Therefore, the studies were evaluated for the following 5 categories, which were graded as low risk, some concerns, or high risk:

- Bias arising from the randomization process
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

Qualitative analysis

A descriptive synthesis was performed for all included articles. Only outcome variables assessing mean linear changes in vertical alveolar bone height as well as mean linear changes in horizontal (buccolingual) alveolar bone width at different levels from the initial vertical crest height were documented, as illustrated schematically in **Figure 1**. Other, only very sparely reported outcome variables, such as horizontal alveolar bone resorption at the buccal and palatal aspect at different levels from the initial crest, were not considered due to the substantial heterogeneity of measurements and for reasons of clarity and comprehensibility of the present review. To assess and compare the effects of the different alveolar ridge preservation materials, the test groups were further organized into 4 predetermined subgroups according to the graft material utilized: xenogenic, allogenic, autogenic, and control.

Quantitative analysis

Initially, for each outcome variable and each biomaterial subgroup, data from the selected studies were pooled to estimate the relative effect size for each subgroup, expressed as the weighted mean difference (WMD), standard error (SE), and 95% confidence interval (CI), using a random-effects model. To evaluate the heterogeneity of the effect size between studies, the Cochran Q test and the Higgin and Thompson I^2 index were used. Additionally, the Eggers test and funnel plot were used to evaluate for possible publication bias. Next, a meta-regression was performed for each outcome variable, estimating the β-coefficient and 95% CIs, to compare the estimated effect sizes between the different subgroups. In addition, the R^2 value for the meta-regression and its statistical significance were calculated. To test

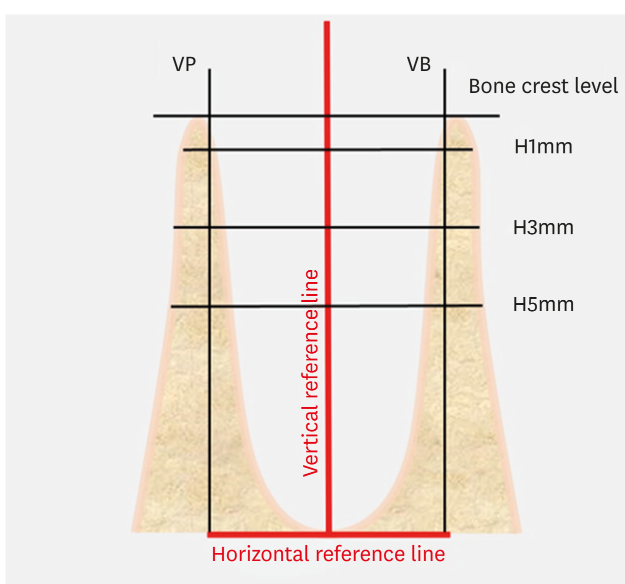

Figure 1. Schematic illustration of CBCT measurements.
CBCT: cone-beam computed tomography.

for statistical significance, the *P*-value threshold was set to 5% (*P*=0.05). The software used to perform all statistical analyses was R version 3.5.1 (R Core Team, 2018; R Foundation for Statistical Computing, Vienna, Austria) and SSPS version 24 (IBM Corp., Armonk, NY, USA).

RESULTS

Study selection

A total of 1,578 articles were identified through database searches and 4 additional articles were identified by manual searches. Following title and abstract screening, 1,552 records were excluded, and the remaining 30 were included for full-text assessment, which led to the exclusion of 14 additional articles, resulting in 16 studies retained for a descriptive synthesis. The list of articles excluded from this review is presented in **Table 2**. Eventually, data from 9 of these studies were included in the quantitative analysis. **Figure 2** shows a flow diagram of the search results.

Study characteristics

The detailed study and patient characteristics of the 16 included studies are presented in **Table 3** [39,41,45-58]. All studies reported outcomes in healthy patients who did not present any contraindications to oral surgery. Four RCTs were designed as split-mouth studies, while 12 had parallel arms. All studies were carried out in an academic setting. The length of the follow-up period ranged from 3 to 9 months, with an average of 4.53±1.63 months. The 16 RCTs included a total of 36 test arms, of which 11 represented xenogenic, 12 allogenic, and 3 autogenic graft materials, while 10 represented control groups that underwent unassisted socket healing. For each group, the specific graft materials, and barrier membranes, as well as all relevant outcome variables assessing dimensional changes of the alveolar ridge, are presented in **Table 4** [39,41,45-58].

Quality assessment

For the overall risk-of-bias judgment, 13 studies were assessed to be at low risk of bias, while 3 studies were judged to raise some concerns. The detailed evaluation of the possible risk of bias for all categories is summarized in **Table 5** [39,41,45-58].

Table 2. List of studies not included after full-text screening with reasons for exclusion

Study	Reason for exclusion
Farina et al. (2013)	Case series
Kotsakis et al. (2014)	No CBCT assessment of dimensional changes
Madan et al. (2014)	Multiple adjacent extraction sites
Festa et al. (2013)	No CBCT assessment of dimensional changes
Abdelhamid et al. (2016)	Volumetric assessment of dimensional changes
Barone et al. (2008)	No CBCT assessment of dimensional changes
Iasella et al. (2003)	No CBCT assessment of dimensional changes
Lambert et al. (2012)	Case series
Checchi et al. (2011)	No CBCT assessment of dimensional changes
Wallace et al. (2013)	No CBCT assessment of dimensional changes
Tomasi et al. (2018)	Soft tissue included in assessment of dimensional changes
Wallace et al. (2014)	Bone quality assessment only
Avila-Ortiz et al. (2014)	Method of measurement not described sufficiently
Sbordone et al. (2016)	Retrospective assessment

CBCT: cone-beam computed tomography.

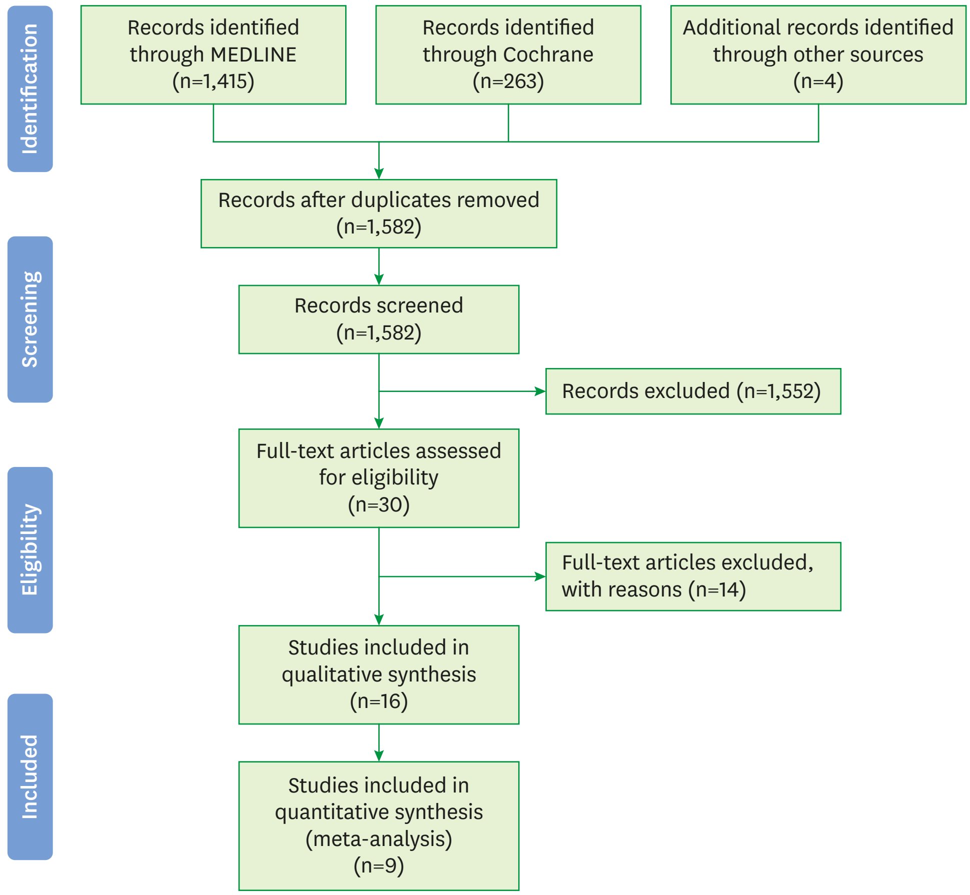

Figure 2. Flow diagram.

Statistical analysis

Due to the broad variety of outcome variables reported among the included studies, a quantitative synthesis could only be performed for vertical midbuccal (VB) bone height changes (7 studies), vertical midpalatal (VP) bone height changes (6 studies), and horizontal bone width changes at 1, 3, and 5 mm (H1mm, H3mm, and H3mm, respectively) from the initial crest height, which were analyzed in 6, 8, and 6 studies, respectively. No analysis could be performed for the autogenic and control subgroups since they were not reported in a sufficient number.

The meta-analysis performed in this study found that the use of xenogenic graft materials in alveolar ridge preservation procedures resulted in considerably less vertical reduction of the alveolar ridge height than when allogenic graft materials were used, both at the buccal (VB–xenogenic: WMD=−0.20, SE=0.26; VB–allogenic: WMD=−0.90, SE=0.22) and the palatal/lingual aspect of the alveolar ridge (VP–xenogenic: WMD=−0.31, SE=0.14; VP–allogenic: WMD=−0.71, SE=0.32). Additionally, xenogenic graft materials were found to preserve significantly more bone in horizontal dimensions at all analyzed levels than allogenic graft materials (H1mm–xenogenic: WMD=−1.32, SE=0.07; H1mm–allogenic: WMD=−2.99, SE=0.96; H3mm–xenogenic: WMD=−0.78, SE=0.11; H3mm–allogenic: WMD=−1.63, SE=0.40; H5mm–xenogenic: WMD=−0.41, SE=0.12; H5mm–allogenic: WMD=−1.84, SE=1.28). These differences between the 2 subgroups were found to be statistically significant for all outcome

Table 3. Study characteristics of general and patient-related, and surgical interventions

Author	Year	Study design	Setting	Follow-up (mo)	Method of evaluation	Groups	No. of sockets	Age (mean±SD)	Sex (male/female)	Maxilla/mandible	Socket location	Smoking habit			Adequate oral hygiene	Reason for extraction	Socket morphology	Flap elevation/primary closure	Adjunct pharmacological treatment			Complications
												Non-smokers	<10 cig/day	<20 cig/day					Antibiotics	NSAIDs	CHX	
Lim et al. [55]	2017	RCT	Academic	4	Superimposition	Test 1	12	53.83±16.22	5/7	NA	Non-molar	NA	NA	26	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Periodontal disease/endodontic reasons	NA	Yes/Yes	Yes	Yes	No	5 membrane exposures
						Test 2	14	48.14±16.11	11/3													8 membrane exposures
Nart et al. [53]	2016	RCT	Academic	5	Superimposition	Test 1	11	56.76	15/6	17/5	Non-molar	19	2	0	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Lack of tooth substance/caries	Intact	Yes/No	Yes	Yes	Yes	No complications
						Test 2	11															
Jung et al. [41]	2013	RCT	Academic	6	Superimposition	Control	10	48±15	6/4	10/0	Non-molar	30	0	10	Adequate oral hygiene (BOP <20%; PI <20%)	Caries, endodontic complications, periodontitis, orthodontic and prosthetic reasons	Intact	No/No	Yes	No	Yes	No complications
						Test 1	10	59±11	6/4	9/1												
						Test 2	10	65±13	4/7	7/4												
						Test 3	10	49±14	2/8	7/3												
Das et al. [51]	2016	RCT	Academic	6	Reference points	Test 1	15	30.25±8.65	13/13	NA	Non-molar	26	0	0	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Caries, endodontic complications, periodontitis, and prosthetic reasons	Intact	Yes/No	Yes	Yes	Yes	No complications
						Test 2	15	32.27±8.64														
Temmerman et al. [45]	2016	RCT split mouth	Academic	3	Superimposition	Test 1	22	54 (total)	15/7	18/4	Non-molar	22	0	0	NA	NA	Remaining ridge height 60%	No/No	No	Yes	Yes	No complications
						Control	22		15/7	18/4												2 altered healing
Kim et al. [57]	2014	RCT	Academic	3	Superimposition	Test 1	29	50.37±13.45	15/20	NA	Non-molar	NA			Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	NA	Intact	Yes/Yes	Yes	Yes	No	No complications
						Test 2	30	51.18±10.14	19/15													

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Table 3. (Continued) Study characteristics of general and patient-related, and surgical interventions

Author	Year	Study design	Setting	Follow-up (mo)	Method of evaluation	Groups	No. of sockets	Age (mean±SD)	Sex (male/female)	Maxilla/mandible	Socket location	Smoking habit			Adequate oral hygiene	Reason for extraction	Socket morphology	Flap elevation/primary closure	Adjunct pharmacological treatment			Complications
												Non-smokers	<10 cig/day	<20 cig/day					Antibiotics	NSAIDs	CHX	
Araújo et al. [46]	2014	RCT	Academic	4	Reference points	Test 1 Control	14 14	21–54	NA	28/0 (total)	Non-molar	NA			NA	Caries, root fracture	Intact	No/No	Yes	No	Yes	No complications
Karaca et al. [58]	2015	RCT split mouth	Academic	3	Reference points	Test 1 Control	10 10	46.7 46.7	5/5 5/5	10/0 10/0	Non-molar	NA			Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Periodontal disease and/or prosthetic reasons	NA	No/No	Yes	Yes	No	No complications
Hassan et al. [49]	2017	RCT split mouth	Academic	3 (3.5±0.5)	Stent	Test 1 Test 2	11 11	54.88 54.88	6/3 6/3	7/4 7/4	Non-molar	9	0	0	Adequate oral hygiene (BOP <20%; PI <20%)	NA	Intact	No/No	No	Yes	No	No complications
Brownfield et al. [39]	2012	RCT	Academic	3 (10–12 w)	Stent	Test 1 Control	10 10	25–69	5/12	16/4 (total)	Non-molar	20	0	0	Adequate oral hygiene (BOP <20%; PI <20%)	Non-restorable, or hopeless teeth	Intact	No/No	Yes	Yes	Yes	No complications
Natto et al. [54]	2017	RCT	Academic	4	Stent	Test 1 Test 2	14 14	55.6 55.1	7/7 10/4	23/5 (total)	Non-molar	NA	28	0	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Caries, endodontic complication, root fracture, or trauma	Intact	No/No	Yes	No	Yes	NA
Parashis et al. [47]	2016	RCT	Academic	4	Stent	Test 1 Test 2	11 12	52.2 54.8	4/7 8/4	9/2 12/0	Non-molar	NA	23	0	NA	Endodontic reasons, severe periodontitis, caries or trauma	NA	Yes/No	Yes	No	Yes	No complications
Cha et al. [56]	2019	RCT	Academic	6	Superimposition	Test 1 Control	20 19	54.85±8.37 51.89±12.08	14/6 12/7	20/0 19/0	Molar	NA	NA	39	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Periodontitis, fracture, endodontic failure	Remaining ridge height 4–8 mm	No/No	Yes	Yes	Yes	1 altered healing No complications

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Table 3. (Continued) Study characteristics of general and patient-related, and surgical interventions

Author	Year	Study design	Setting	Follow-up (mo)	Method of evaluation	Groups	No. of sockets	Age (mean±SD)	Sex (male/female)	Maxilla/mandible	Socket location	Smoking habit			Adequate oral hygiene	Reason for extraction	Socket morphology	Flap elevation/primary closure	Adjunct pharmacological treatment			Complications
												Non-smokers	<10 cig/day	<20 cig/day					Antibiotics	NSAIDs	CHX	
Walker et al. [52]	2016	RCT	Academic	3	Stent	Control Test 1	20 20	54 (total)	14/26	5/35 (total)	Molar	20	0	0	Basic periodontal treatment prior to surgery OR absence of untreated periodontal disease	Carious lesions, prosthetic failures, root fractures, or endodontic failures	Intact	Yes/No	NA			NA
Jung et al. [50]	2018	RCT split mouth	Academic	6	Superimposition	Test 1 Test 2 Control 1 Control 2	12 6 12 6	>18	NA	12/0 0/6 12/0 0/6	Mixed	NA	18	0	Adequate oral hygiene (BOP <20%; PI <20%)	NA	NA	No/No	No	No	Yes	No complications
Al Qabbani et al. [48]	2018	RCT	Academic	9	Reference points	Control Test 1	10 10	18–40 (total)	3/7 5/5	0/10 0/10	Non-molar	20	0	0	NA	Lack of tooth substance/caries	Intact	No/No	NA			No complications

RCT: randomized controlled trial, NA: not available; BOP: bleeding on probing; PI: plaque index, NSAID: nonsteroidal anti-inflammatory drug; CHX: chlorhexidine; NA: not available.

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Table 4. Subgroup distribution and variables for loss of alveolar ridge dimensions

Study	Group	Biomaterials		Vertical change		Horizontal change			Vertical change		
		Graft material	Membrane	VB	VP	H1mm	H3mm	H5mm	VC	VM	VD
Das et al. [51]	Test 1	PRF	-	−1.55	−1.26	NA	NA	NA	−0.35	NA	NA
Temmerman et al. [45]	Test 1	L-PRF	L-PRF	0.5±2.3	−0.4±1.1	−2.4±2.3	−0.6±0.7	−0.4±0.5	NA	NA	NA
Kim et al. [57]	Test 1	rhBMP-2/DBM	Porcine CM	NA	NA	−1.06±1.26	−0.43±0.71	−0.23±0.45	−1.17±0.82	NA	NA
	Test 2	DBM	Porcine CM	NA	NA	−1.21±1.31	−0.58±0.68	−0.37±0.61	−1.5±1.07	NA	NA
Hassan et al. [49]	Test 1	DFDBA+FDBA	-	NA	NA	−2.98±2.72	−1.33±0.72	NA	−0.24±0.91	−0.47±1.41	−0.64±1.1
	Test 2	DFDBA+FDBA	dPTFE	NA	NA	−3.8±2.64	−2.53±3.34	NA	1.18±2.22	2.06±1.99	1.31±2.58
Brownfield et al. [39]	Test 1	DBM	CM	NA	NA	NA	−1.6±0.8	NA	−0.8±1.2	NA	NA
Natto et al. [54]	Test 1	FDBA	CS	−0.79±3.07	−0.49±2.59	NA	NA	NA	NA	NA	NA
	Test 2	FDBA	Porcine CM	−0.3±1.09	−0.27±2.3	NA	NA	NA	NA	NA	NA
Parashis et al. [47]	Test 1	FDBA	CM	−0.7±1.1	−0.3±0.4	NA	NA	NA	NA	NA	NA
	Test 2	FDBA	ECM	−0.8±1.6	−0.5±2.5	NA	NA	NA	NA	NA	NA
Walker et al. [52]	Test 1	Mineralized cortical FDBA	dPTFE	−1.12±1.6	NA	NA	−2.48±2.86	−1.16±1.97	NA	−1.11±1.69	−1.01±1.85
Jung et al. [41]	Test 1	β-TCP	-	−2±2.4	−1.7±0.6	−6.1±2.5	−3.1±1.6	−5.7±3	NA	NA	
Das et al. [51]	Test 2	β-TCP-Cl	-	−0.99	−0.94	NA	NA	NA	−1.17	NA	
Lim et al. [55]	Test 1	DBBM	Porcine CM	−1.5±3	0.1±2.2	−1.2±0.5	−1.2±0.7	−0.97±0.7	NA	−1.3±1.4	2.6±−0.9
	Test 2	DBBM-C	Porcine CM	0.7±1.8	−0.2±1.7	−1.5±0.9	−1.2±0.7	−0.9±0.9	NA	−0.7±1.7	3.8±−0.6
Nart et al. [53]	Test 1	DBBM	Porcine CM	−0.61±0.77	−0.65±0.65	−0.91±1.35	−0.36±0.31	−0.065±0.172	NA	NA	NA
	Test 2	DBBM-C	Porcine CM	−0.98±1.28	−0.82±0.61	−1.53±1.53	−0.79±0.76	−0.16±0.76	NA	NA	NA
Jung et al. [41]	Test 2	DBBM-C	Porcine CM	0±1.2	−0.4±1.4	−1.2±0.8	−0.6±0.6	−0.1±0.2	NA	NA	NA
	Test 3	DBBM-C	Soft tissue punch graft	1.2±2.9	0.3±1.1	−1.4±1	−0.6±0.5	−0.6±0.9	NA	NA	NA
Araújo et al. [46]	Test 1	DBBM-C	Soft tissue punch graft	−40.6%±28.8%	−13.8%±22.5%	NA	NA	NA	NA	NA	NA
Cha et al. [56]	Test 1	DBBM-C	Porcine CM	NA	NA	NA	NA	NA	0.16 (−0.49/0.8)	NA	NA
Jung et al. [50]	Test 1	DBBM-C	Porcine CM	−0.32±0.68	−0.31±0.73	−1.18±1.5	−0.91±1.22	−0.43±0.63	NA	NA	NA
	Test 2	DBBM-C	Porcine CM	−0.12±0.21	−0.17±0.28	−1.6±0.92	−0.67±0.55	−0.21±0.21	NA	NA	NA
Al Qabbani et al. [48]	Test 1	Lyophilized freeze-dried bovine bone granules	Freeze-dried bovine pericardium	NA	NA	−0.77 (−1.92/−0.39)	−0.91 (−2.11/0.29)	0.05 (−1.08/1.18)	−1.75 (−3.41/−0.09)	NA	NA
Jung et al. [41]	Control	-	-	−0.5±0.9	−0.6±0.6	−3.3±2	−1.7±0.8	−0.8±0.5	NA	NA	NA
Temmerman et al. [45]	Control	-	-	−1.5±1.3	−0.7±0.8	−5.4±4.4	−1.2±1.1	−0.5±0.5	NA	NA	NA
Araújo et al. [46]	Control	-	-	−35.8%±26.6%	13.4%±24.4%	NA	NA	NA	NA	NA	NA
Karaca et al. [58]	Control	-	-	−1.03	−0.56	NA	NA	NA	NA	NA	NA
Brownfield et al. [39]	Control	-	CM	NA	NA	NA	−2.1±1.8	NA	−1.2±0.4	NA	NA
Cha et al. [56]	Control	-	-	NA	NA	NA	NA	NA	−3.14 (−4.11/−2.22)	NA	NA
Walker et al. [52]	Control	CS	-	−2.6±2.06	NA	NA	−3.11±3.83	−1.58±2.23	NA	−3.01±2.24	−2.33±1.72
Jung et al. [50]	Control 1	-	-	−0.84±0.67	−0.48±0.6	−2.17±1.8	−1.33±0.93	−1.18±0.85	NA	NA	NA
	Control 2	-	-	−1.94±1.26	−1.6±2.05	−3.82±3.1	−2.97±3.28	−1.24±1.55	NA	NA	NA
Al Qabbani A. [48]	Control	-	Freeze-dried bovine pericardium	NA	NA	−1.84 (−3.1/−0.57)	−1.7 (−3.12/−0.3)	−0.91 (−1.71/−0.12)	−1.91 (3.14/−0.64)	NA	NA
Karaca Ç. [58]	Test 1	-	Free gingiva graft	0.06	0.25	NA	NA	NA	NA	NA	NA

Data shown are mean±standard deviation not otherwise specified.

VB: midbuccal vertical change, VP: midpalatal/lingual vertical change, VC: vertical change at socket center, VM: vertical change at mesial aspect, VD: vertical change at distal aspect, HXmm: horizontal change at X mm from the initial crest height, β-TCP: β-tricalcium phosphate, CM: collagen membrane, CS: collagen sponge, DBM: demineralized bone matrix, DFDBA: demineralized freeze-dried bone allograft, dPTFE: high-density polytetrafluoroethylene, DBBM: deproteinized bovine bone mineral, DBBM-C: deproteinized bovine bone mineral + collagen, ECM: extracellular matrix, FDBA: freeze-dried bone allograft, rhBMP-2: recombinant human bone morphogenetic protein 2.

Table 5. Risk of bias assessment

Study	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of the outcome	Bias due to selection of the reported result
Lim et al. [55]	Low risk	Low risk	Low risk	Low risk	Low risk
Nart et al. [53]	Low risk	Low risk	Low risk	Low risk	Low risk
Jung et al. [41]	Low risk	Low risk	Low risk	Low risk	Low risk
Das et al. [51]	Some concerns	Low risk	Low risk	Low risk	Low risk
Temmerman et al. [45]	Low risk	Low risk	Low risk	Low risk	Low risk
Kim et al. [57]	Low risk	Low risk	Low risk	Low risk	Low risk
Araújo et al. [46]	Low risk	Low risk	Low risk	Low risk	Low risk
Karaca et al. [58]	Low risk	Low risk	Low risk	Low risk	Low risk
Hassan et al. [49]	Low risk	Low risk	Low risk	Low risk	Low risk
Brownfield et al. [39]	Low risk	Low risk	Low risk	Low risk	Low risk
Natto et al. [54]	Low risk	Low risk	Low risk	Low risk	Low risk
Parashis et al. [47]	Low risk	Low risk	Some concerns	Low risk	Low risk
Cha et al. [56]	Low risk	Low risk	Low risk	Low risk	Low risk
Walker et al. [52]	Low risk	Low risk	Low risk	Low risk	Low risk
Jung et al. [50]	Low risk	Low risk	Low risk	Low risk	Low risk
Al Qabbani et al. [48]	Some concerns	Low risk	Low risk	Low risk	Low risk

variables except VP and H5mm. A detailed description of the results of all meta-analysis and meta-regressions that were performed is given in **Tables 6-9** and **Figures 3-17**.

Table 6. Results of meta-analysis for changes in vertical alveolar bone height

Variable	Group	WMD	SE	95% CI	I^2	Q_H (*P* value)	Egger (*P* value)
VB	Allogenic	−0.90	0.22	−1.33 to −0.48	82.6%	0.003[a)]	0.390
	Xenogenic	−0.20	0.26	−0.70 to 0.30	95.0%	<0.001[b)]	0.944
VP	Allogenic	−0.71	0.32	−1.34 to −0.08	93.6%	<0.001	0.418
	Xenogenic	−0.31	0.14	−0.57 to −0.04	85.8%	<0.001	0.485

VB: midbuccal vertical change, VP: midpalatal/lingual vertical change, WMD: weighted mean difference, SE: standard error, CI: confidence interval, I^2: Higgin & Thompson index, Q: Cochran Q test.
a)*P*<0.01, b)*P*<0.001.

Table 7. Results of meta-regression for changes in vertical alveolar bone height

Variable	Group	β	SE	*P* value	95% CI for β	R^2
VB	Xenogenic	0.72	0.34	0.037[a)]	0.04 to 1.39	27.8%
VP	Xenogenic	0.45	0.31	0.144	−0.15 to 1.06	12.7%

SE: standard error, CI: confidence interval, VB: midbuccal vertical change, VP: midpalatal/lingual vertical change.
a)*P*<0.05.

Table 8. Results of the meta-analysis for changes in horizonal alveolar bone width

Variable	Group	WMD	SE	95% CI	I^2	Q_H (*P* value)	Egger (*P* value)
H1mm	Allogenic	−2.99	0.96	−4.89 to −1.11	97.0%	0.263	0.488
	Xenogenic	−1.32	0.07	−1.46 to −1.18	29.2%	0.205	0.978
H3mm	Allogenic	−1.63	0.40	−2.41 to −0.85	96.1%	<0.001[b)]	0.141
	Xenogenic	−0.78	0.11	−0.98 to −0.56	87.8%	<0.001[b)]	0.432
H5mm	Allogenic	−1.84	1.28	−4.34 to 0.67	99.6%	<0.001[b)]	0.001[a)]
	Xenogenic	−0.41	0.12	−0.65 to 0.17	96.9%	<0.001[b)]	0.004[a)]

HXmm: horizontal change at X mm from the initial crest height, WMD: weighted mean difference, SE: standard error, CI: confidence interval, I^2: Higgin & Thompson index, Q: Cochran Q test.
a)*P*<0.01, b)*P*<0.001.

Table 9. Results of meta-regression for changes in horizonal alveolar bone width

Variable	Group	β	SE	*P* value	95% CI for β	R^2
H1mm	Xenogenic	1.63	0.73	0.027[a)]	0.19 to 3.06	24.5%
H3mm	Xenogenic	0.78	0.37	0.032[a)]	0.07 to 1.50	18.9%
H5mm	Xenogenic	1.34	0.83	0.109	−0.30 to 2.98	11.7%

HXmm: horizontal change at X mm from the initial crest height, SE: standard error, CI: confidence interval.
a)*P*<0.05.

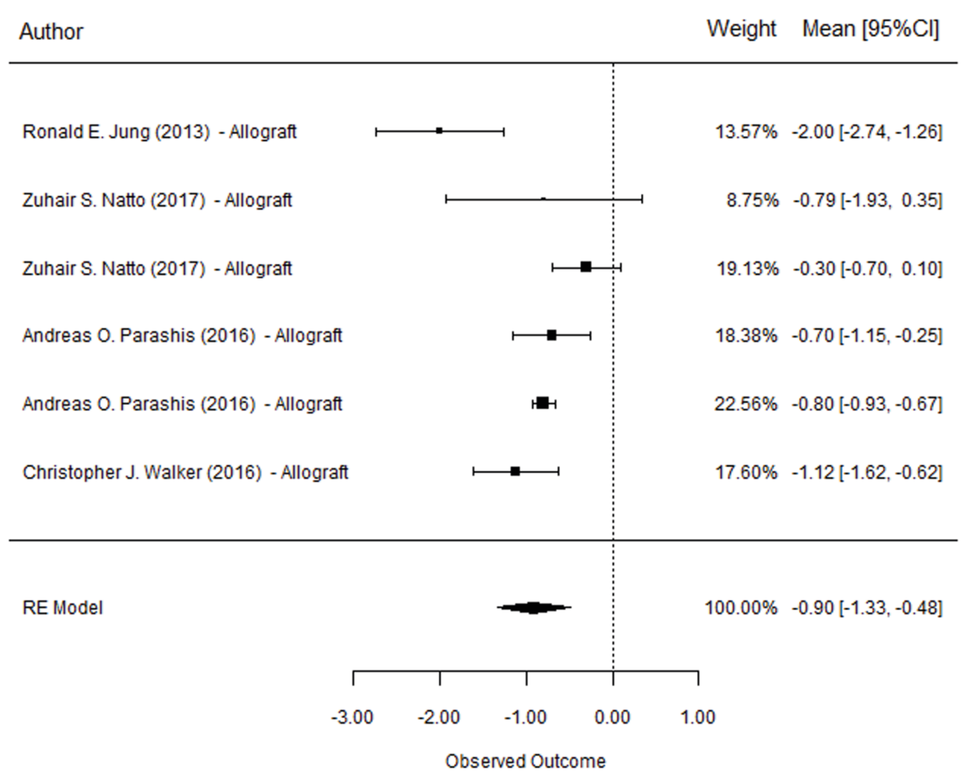

Figure 3. Results of meta-analysis: VB allogenic graft materials.
VB: midbuccal vertical change, CI: confidence interval.

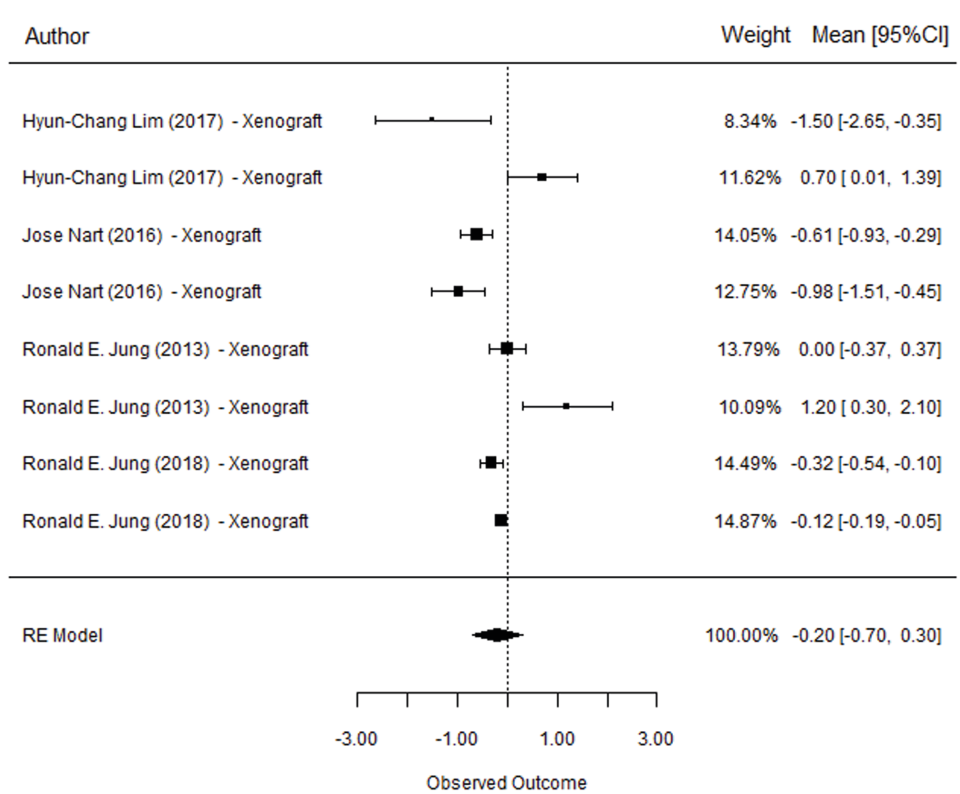

Figure 4. Results of meta-analysis: VB xenogenic graft materials.
VB: midbuccal vertical change, CI: confidence interval.

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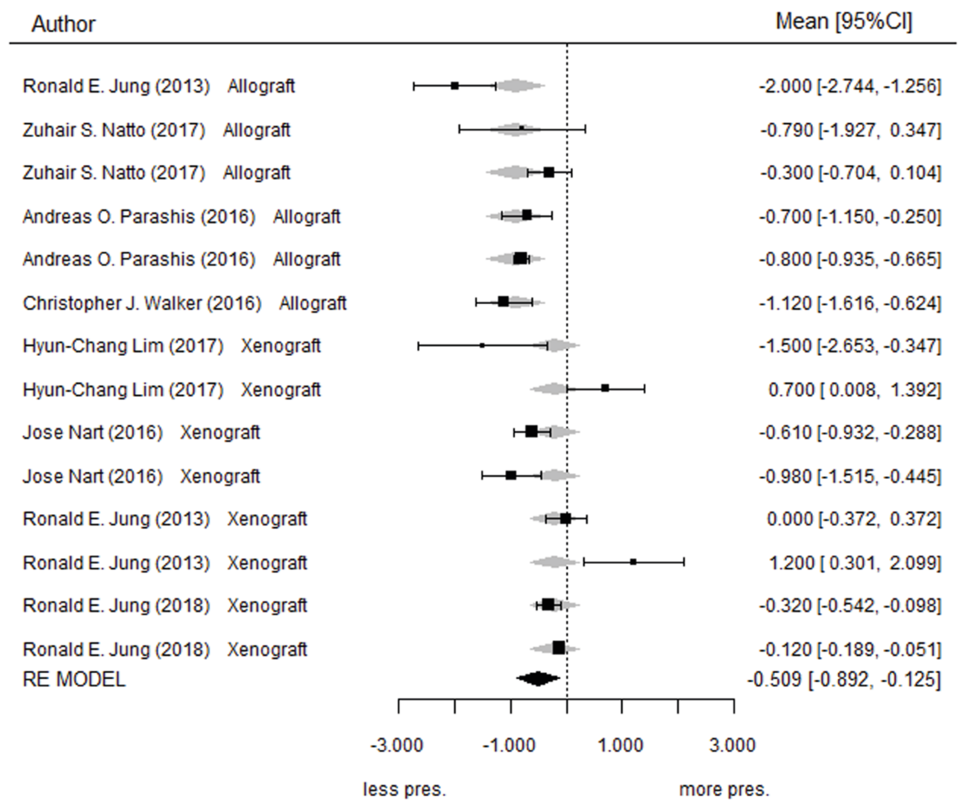

Figure 5. Results of meta-regression: VB.
VB: midbuccal vertical change, CI: confidence interval.

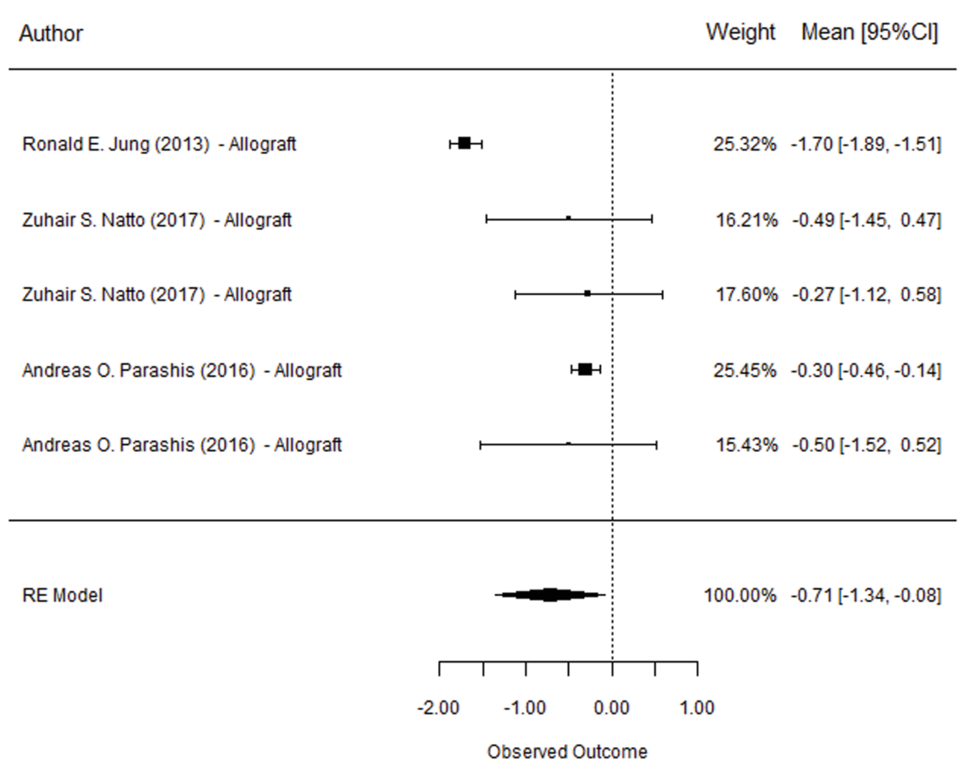

Figure 6. Results of meta-analysis: VP allogenic graft materials.
VP: midpalatal/lingual vertical change, CI: confidence interval.

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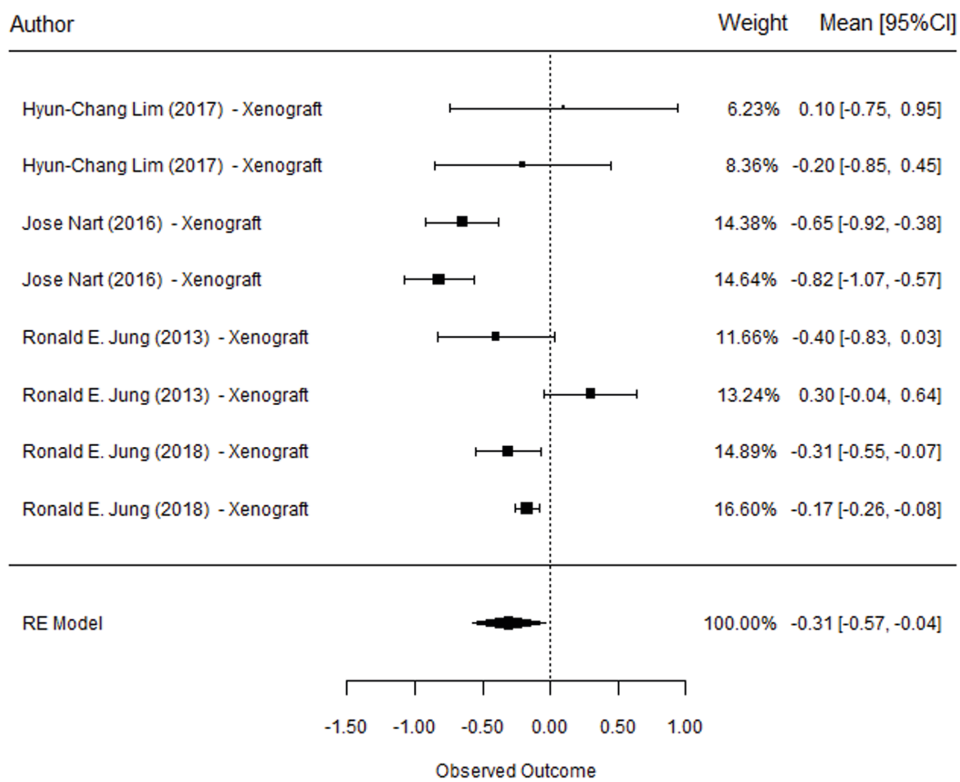

Figure 7. Results of meta-analysis: VP xenogenic graft materials.
VP: midpalatal/lingual vertical change, CI: confidence interval.

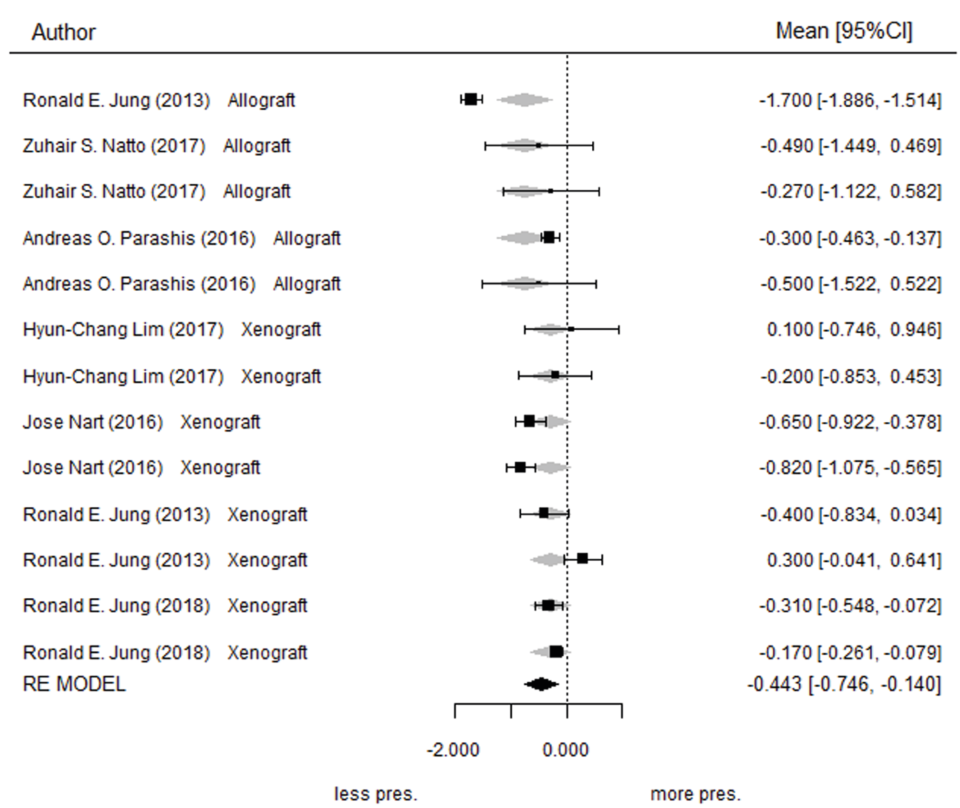

Figure 8. Results of meta-regression: VP.
VP: midpalatal/lingual vertical change, CI: confidence interval.

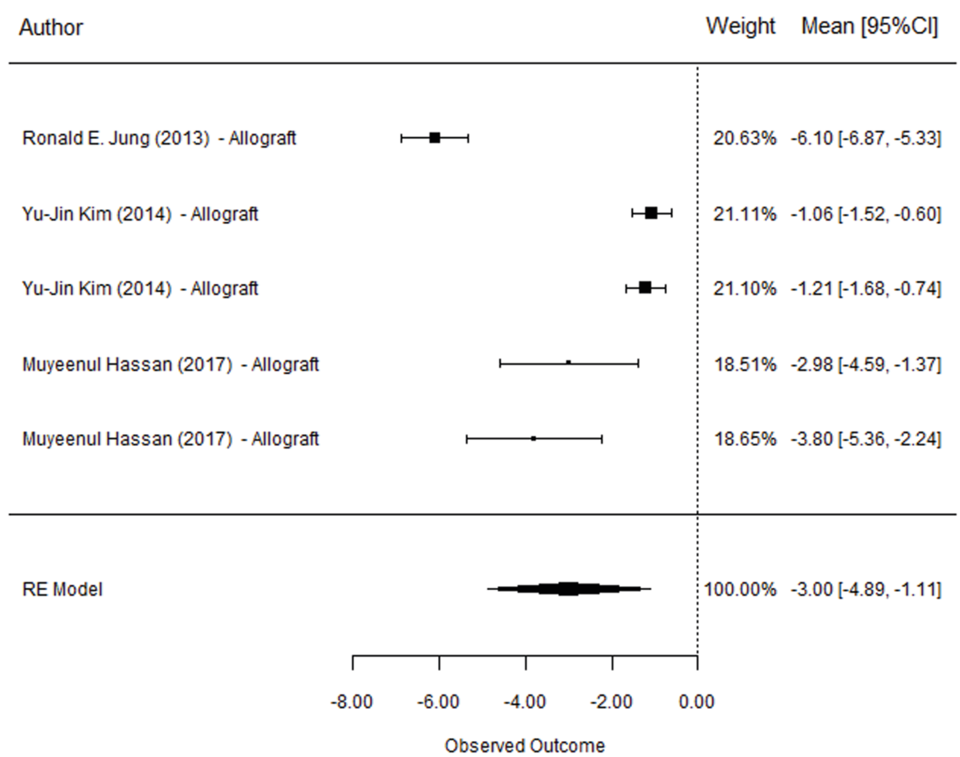

Figure 9. Results of meta-analysis: H1mm allogenic graft materials.
H1mm: height at 1 mm from the initial crest, CI: confidence interval.

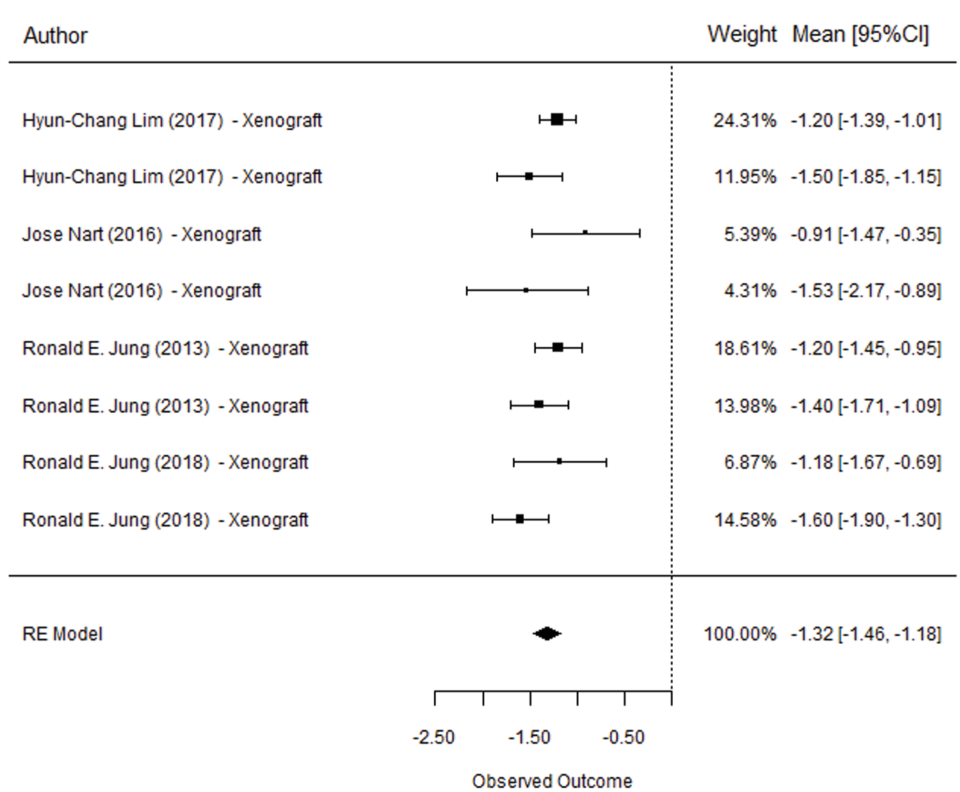

Figure 10. Results of meta-analysis: H1mm xenogenic graft materials.
H1mm: height at 1 mm from the initial crest, CI: confidence interval.

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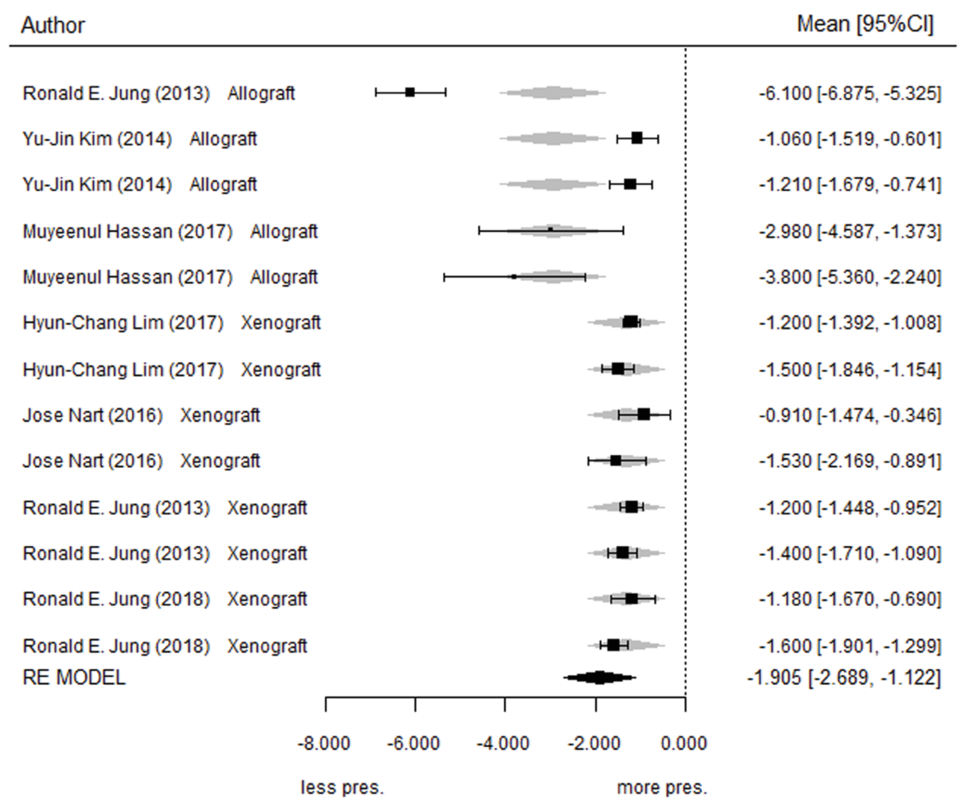

Figure 11. Results of meta-regression: H1mm.
H1mm: height at 1 mm from the initial crest, CI: confidence interval.

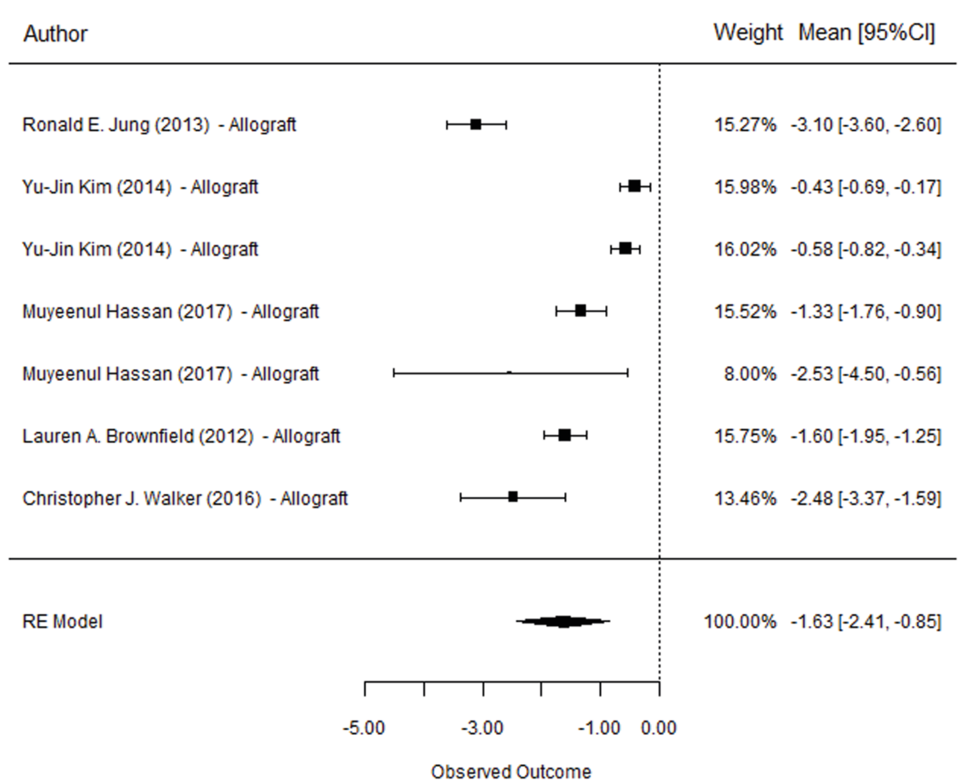

Figure 12. Results of meta-analysis: H3mm allogenic graft materials.
H3mm: height at 3 mm from the initial crest, CI: confidence interval.

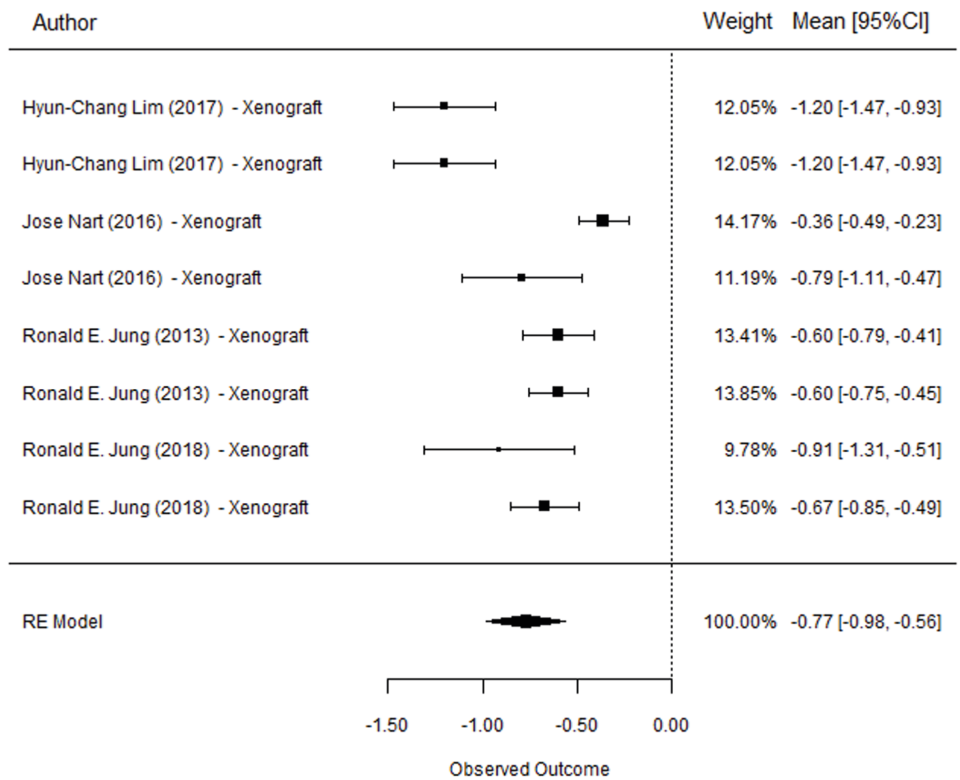

Figure 13. Results of meta-analysis: H3mm xenogenic graft materials.
H3mm: height at 3 mm from the initial crest, CI: confidence interval.

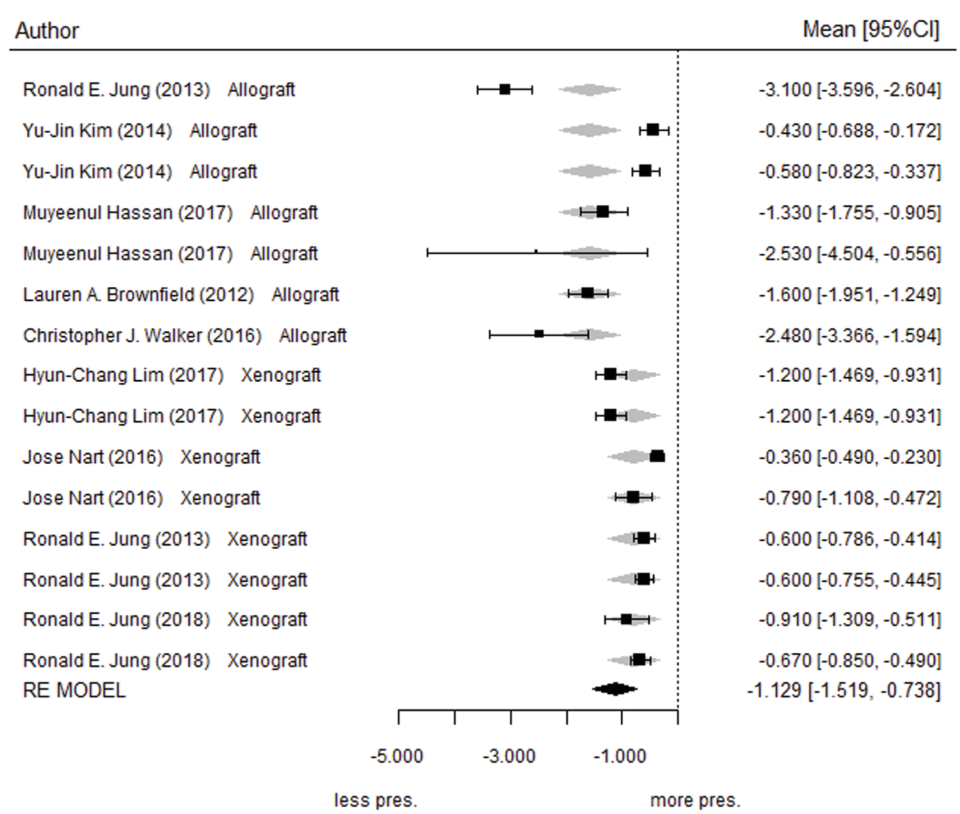

Figure 14. Results of meta-regression: H3mm.
H3mm: height at 3 mm from the initial crest, CI: confidence interval.

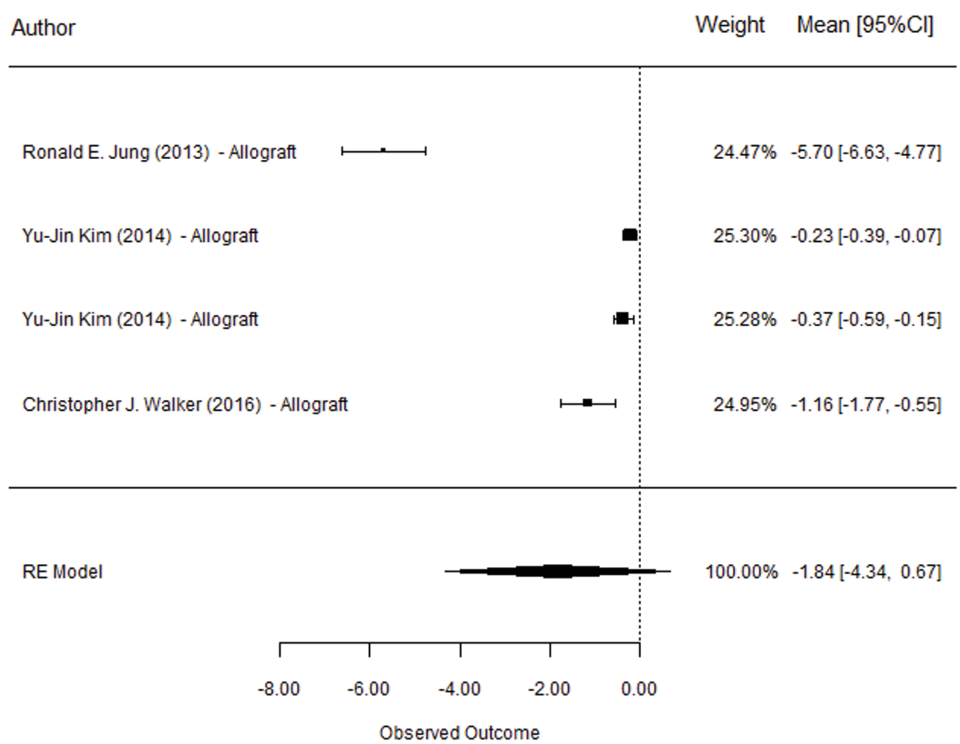

Figure 15. Results of meta-analysis: H5mm allogenic graft materials.
H5mm: height at 5 mm from the initial crest, CI: confidence interval.

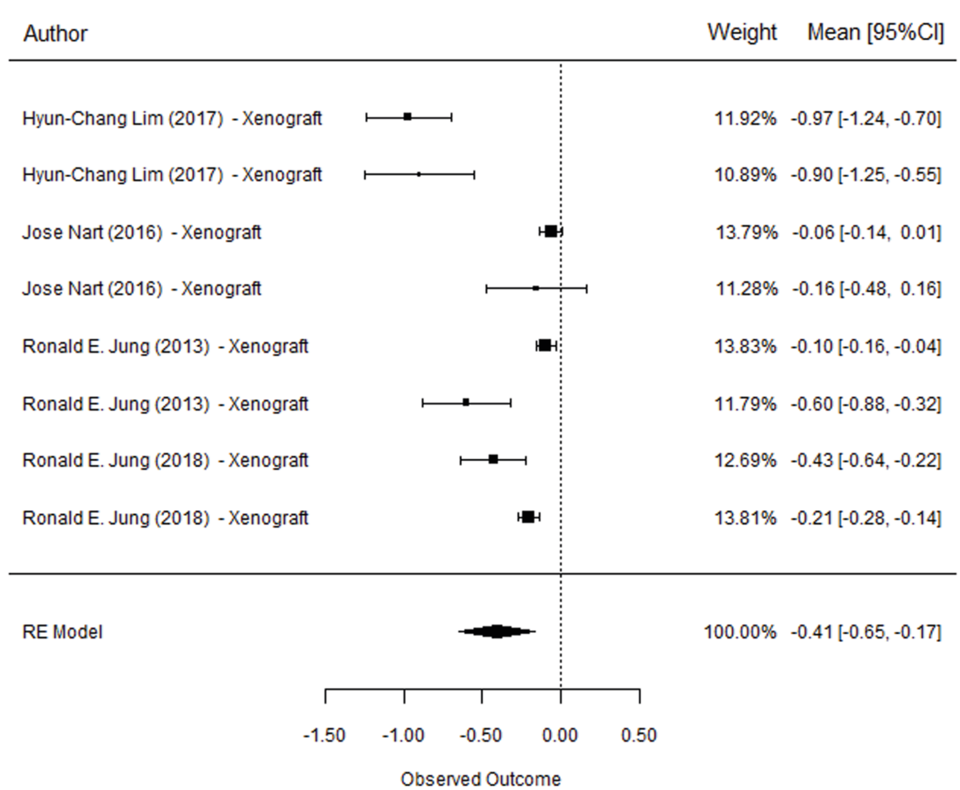

Figure 16. Results of meta-analysis: H5mm xenogenic graft materials.
H5mm: height at 5 mm from the initial crest, CI: confidence interval.

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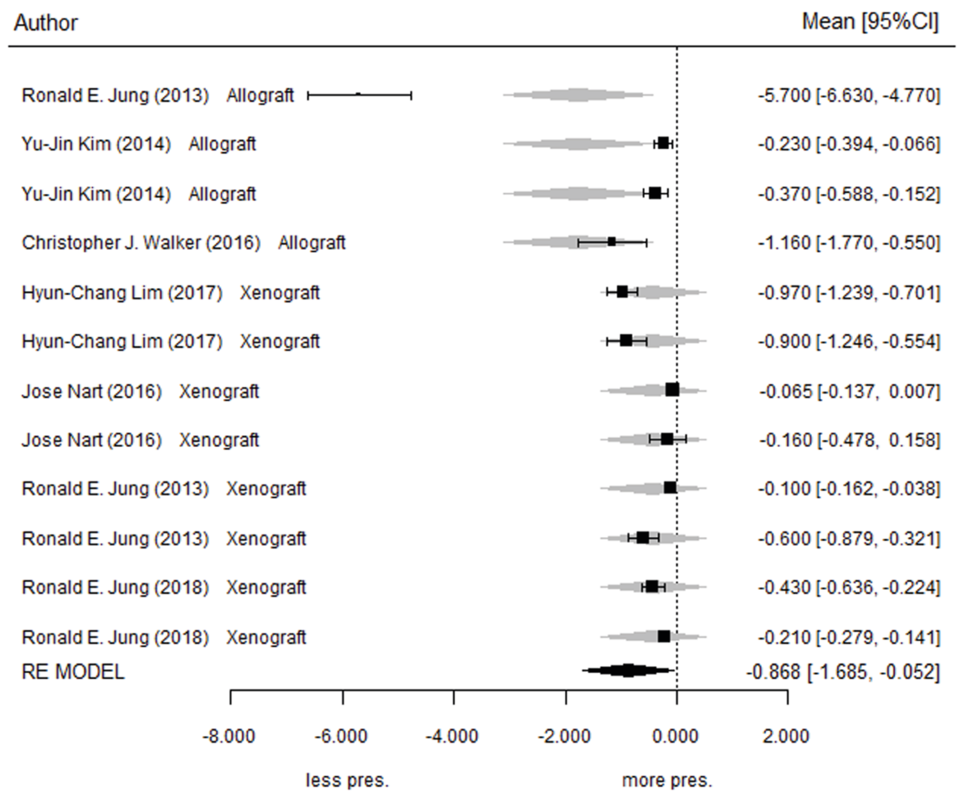

Figure 17. Results of meta-regression: H5mm.
H5mm: height at 5 mm from the initial crest, CI: confidence interval.

DISCUSSION

Previous meta-analyses have demonstrated that alveolar ridge preservation techniques may limit dimensional reduction of the alveolar ridge compared with unassisted socket healing; however, no consensus has been reached regarding the efficiency of the different procedures and biomaterials applied [26,27,30]. Therefore, the primary objective of this study was to compare the efficiency of different graft materials for alveolar ridge preservation and to determine which material resulted in the least amount of alveolar dimensional reduction. The meta-analysis performed in this study showed that the use of xenogenic graft materials in alveolar ridge preservation procedures resulted in considerably less vertical reduction of the alveolar ridge than the use of allogenic graft materials at the buccal and the palatal/lingual aspect of the alveolar ridge, as well as in horizontal dimensions at all analyzed levels.

In a recent meta-analysis that assessed the available histological and histomorphometric data on different alveolar ridge preservation techniques, the authors found that sites treated with allogenic graft materials showed the lowest percentage of residual graft materials at re-entry, while those grafted with xenogenic materials still presented over 35% of the residual graft materials at 7 months after the intervention [31]. Furthermore, their histological data showed that extraction sites treated with xenogenic graft materials showed the lowest percentage of new bone formation after 5 months [31]. These findings suggest a lower resorption rate of xenogenic grafts compared with allogenic graft materials, which could explain the greater radiologically measured dimensional stability of extraction sites treated with xenogenic graft materials found in the present review. These results are in accordance with an Osteology Consensus Report on the treatment of extraction sockets, which recommends the use of graft materials with a low resorption and replacement rate for alveolar ridge preservation techniques [59]. Several authors have demonstrated that the resorption process following tooth extraction was more pronounced at the buccal than at the palatal lingual aspect of the alveolar process [10,13,46]. Jung et al. [50] reported that horizontal bone loss due to the resorption process generally decreases with increasing distance to the alveolar crest. Therefore, it was suggested that horizontal changes at 1 mm below the crest and vertical changes at the buccal aspect would benefit the most from alveolar ridge preservation procedures because they suffer the greatest amount of resorption during the complex healing process [41]. Those findings are supported by the results of the present review. The benefit of using xenogenic graft materials regarding the dimensional stability of the extraction sites was more evident at the buccal aspect (VB: β=0.72) compared with the palatal aspect (VP: β=0.45), as well as at 1 mm from the initial crest height (H1mm: β=1.63) compared with the 3-mm level (H3mm: β=0.78). The difference between the subgroups at 5 mm was found to be considerable (H5mm: β=1.34), but did not reach statistical significance.

Limitations

It should be noted that the clinical outcome of alveolar ridge preservation techniques might also be affected by several other clinical and surgical parameters, such as flap elevation, wound closure, socket morphology, the use of a barrier membrane, the amount of graft material utilized, and the extraction site [28,35,60]. However, no further statistical subgroup analysis regarding these possible modifying factors could be performed in the present review.

Several systematic reviews and meta-analyses evaluating alveolar ridge preservation have been published in recent years, with objectives similar to those of the present study [26-28,30]. These meta-analyses combined and pooled different clinical and radiological data in the same analysis, while the present review solely focused on radiological data obtained by CBCT measurements. On the one hand, this can be considered as one of the strengths of the present meta-analysis, since most measurements of the included studies were performed in a similar and reproducible manner, allowing a fairly accurate 3-dimensional assessment of the complex remodeling and healing process following tooth extraction. On the other hand, a study evaluating the differences between direct intrasurgical and CBCT measurements of periodontal intrabony defects found that the radiological CBCT measurements underestimated the surgical measurements by 0.5±1.1 mm for re-entry and 0.9±0.8 mm for the initial measurements [61].

Solely focusing on radiological measurements of the outer dimensions of the alveolar process, without considering histological and histomorphological data, may not be enough evidence on its own to thoroughly assess different bone graft materials for alveolar ridge preservation. Furthermore, high heterogeneity concerning the graft materials was found across the studies included within the same subgroup, since some authors combined different materials or added bioactive substances, which could have affected and altered the remodeling process. Additionally, the variation of the follow-up periods between 3 and 9 months across the included studies may have further limited the validity of comparisons between subgroups. Consequently, these factors may limit the conclusions that can be drawn from the statistical outcomes in the present review. It should also be highlighted that the combination of keywords applied in the search strategy of the present review was very specific. The electronic search was also limited to 2 electronic databases and to articles

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published in English. This might have reduced the sensitivity of the search and should be noted as a limitation of the present review.

CONCLUSION

The following conclusion can be drawn within the limitations of this study:

1. The use of xenogenic graft materials in alveolar ridge preservation techniques following tooth extraction resulted in significantly less vertical dimensional changes at the midbuccal aspect and horizontal dimensional changes at 1 mm and 3 mm from the initial crest height, compared with the use of allogenic graft materials.
2. There is currently insufficient evidence to compare the effectiveness of autogenic graft materials in alveolar ridge preservation techniques based on radiological assessments using CBCT scans.
3. More homogeneous research protocols with standardized outcome variables and follow-up times are needed to thoroughly assess and compare the application of different graft materials in alveolar ridge preservation procedures.

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