The Fate of Lateral Ridge Augmentation: A Systematic Review and Meta-Analysis

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Purpose: *Owing to volumetric changes after tooth extraction, lateral ridge augmentation has become a common procedure prior or simultaneous to implant placement. Nonetheless, little is known with regard to the dimensional remodeling after healing of these lateral ridge augmentation procedures. Hence, the purpose of this systematic review was to assess the stability of bone grafting material between augmentation procedures and final healing, in terms of resorption rate.* ***Materials and Methods:*** *An electronic and hand literature search was conducted in several databases, such as the Cochrane Oral Health Group Trials Register, Embase, and Cochrane Central Register of Controlled Trials, up until February 2017. Only randomized controlled trials (RCTs) with a mean follow-up of at least 6 months after implant placement aiming to evaluate the stability of grafting material for lateral ridge augmentation were included and quantitatively analyzed.* ***Results:*** *A total of 35 articles were evaluated; however, only 17 RCTs met the inclusion criteria. A total of 15 studies reported information on bone resorption, leading to a total sample of 304 implants. The estimated overall mean horizontal bone gain at the time of regeneration was 3.71 ± 0.24 mm, with 4.18 ± 0.56 mm for the block graft technique and 3.61 ± 0.27 mm for guided bone regeneration (GBR). The estimated overall net bone gain at final re-evaluation (11.9 ± 7.8) was 2.86 ± 0.23 mm. The estimated mean (± SD) resorption after 6 months was 1.13 ± 0.25 mm, with 0.75 ± 0.59 mm for the block graft technique and 1.22 ± 0.28 mm for GBR. The implant survival rate was 97% to 100%.* ***Conclusion:*** *Regardless of the material used for regeneration, different degrees of graft resorption should be expected. Given the sample of investigations analyzed in this review, block grafts seemed to maintain the volume of the initial augmentation site more than GBR techniques. During the initial stages of healing, the GBR technique experienced more changes compared with block grafts. The resorption of the xenograft group was inferior compared with the combination of xenograft and autologous bone groups. Consequently, overcorrection of the horizontal defects should be performed to compensate for the resorption of the grafting materials.* Int J Oral Maxillofac Implants 2018;33:xxx–xxx. doi: 10.11607/jomi.6290

Keywords: *alveolar bone atrophy, bone regeneration, dental implant, evidence-based dentistry*

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Bone regenerative procedures can be performed using a wide variety of techniques and grafting materials. Due to their high predictability,[1] these operations are employed in a multitude of different clinical scenarios. As widely described in the literature, extractions lead to dimensional changes in bone architecture,[2,3] occurring mostly within the first 12 months.[2–6] Overall, the crestal width reduction can be greater than 50%, with two-thirds of this horizontal resorption occurring during the first 3 months after extraction.[2,4–6] Due to these volumetric changes, different approaches have been proposed, including but not limited to: guided bone regeneration (GBR),[7] block grafting techniques,[8] ridge split,[9] and also the use of narrow-diameter implants.[10] Nevertheless, to achieve an adequate tridimensional position of standard-diameter implants,[10] these horizontally compromised ridges require bone augmentation procedures.

As a result, different classification systems have been developed proposing several horizontal augmentation techniques based on the remaining alveolar process.[8] Nonetheless, predictable regenerative procedures can often be successfully accomplished by a variety of different approaches depending mostly on operator skills and flap management rather than the specific technique utilized. Similarly, several bone grafting materials have been described based on their origin; namely, autografts (AGs) derive from the individual's own body, allografts (ALLs) derive from another individual of the same species, xenografts (XEs) derive from a different species, and alloplasts (ALPs) derive from synthetic materials.

In the case of bone dehiscence and/or fenestrations during implant insertion, the success of deproteinized bovine bone mineral (DBBM) or AG particulate in conjunction with membranes has been widely reported. On the other hand, in the case of horizontal augmentation, autologous bone blocks have been claimed to offer the best results.[7] In a systematic review, Milinkovic and Cordaro described a 3.31-mm gain when using GBR versus a 4.3-mm gain when using bone blocks for horizontal defects.[8] On the other hand, more recent investigations have proven GBR techniques to be the most reliable in terms of bone gain and absence of complications. As such, Urban and colleagues demonstrated vertical bone gain of 5.1 ± 1.8 mm and horizontal bone gain of 7.0 ± 1.5 mm by means of combination of XE and AG with barrier membranes.[11–13]

While bone regeneration has been widely proved to be a predictable procedure,[14,15] its short- and long-term volumetric stability remains to be further investigated. Prosthetically driven implant positioning is of paramount importance for optimal treatment outcomes[16]; however, the peripheral bone stability over time also represents a key factor for long-term success.[17] Despite the vast amount of literature reporting data on horizontal bone gain,[1,7,8] the stability of bone regenerative procedures over time remains poorly studied. Hence, it is the objective of the present review to report the current evidence on horizontal grafting technique stability over time.

MATERIALS AND METHODS

Information Sources

An electronic literature search was conducted by two independent reviewers (B.E. and C.P.) in several databases, including MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and the Cochrane Oral Health Group Trials Register databases, covering articles written in English up until February 2017. The study focused on the following PICO (problem, intervention, comparison, outcome) question: What is the mean resorption rate of horizontal bone grafts?

- P: Partially edentulous patients with moderate/severe horizontal alveolar atrophy
- I: Regenerative approaches for horizontal bone augmentation
- C: Different regenerative approaches, such as GBR and autogenous block grafts, calculating the weighted mean of the included studies
- O: Total bone gain, bone resorption, and implant survival

Screening Process

In the PubMed library, combinations of controlled terms (MeSH and EMTREE) and keywords were used whenever possible, with "[mh]" representing the MeSH terms. In addition, other terms not indexed as MeSH and filters were applied. The key terms used were the following: ((((((((((((((((((jaw, edentulous, partially[MeSH Terms]) OR mouth, edentulous[MeSH Terms]) OR alveolar bone loss[MeSH Terms]) OR alveolar bone atrophy[MeSH Terms]) AND alveolar ridge augmentation[MeSH Terms]) OR augmentations, maxillary ridge[MeSH Terms]) OR augmentation, mandibular ridge[MeSH Terms]) OR bone regenerations[MeSH Terms]) OR bone grafting[MeSH Terms]) AND dental implants[MeSH Terms]) OR dental implantation, endosseous[MeSH Terms]) OR dental implantation[MeSH Terms]) AND resorption) OR bone resorption) AND English[Language]) NOT animals[MeSH Terms]) NOT letter[MeSH Terms]) NOT editorial[MeSH Terms]) NOT comment[MeSH Terms]. In addition, a manual search was also performed in several journals including: the *International Journal of Oral & Maxillofacial Implants*, *Journal of Dental Research*, *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *Implant Dentistry*, *Journal of Clinical Periodontology*, and the *International Journal of Periodontics & Restorative Dentistry*, covering the period from September 2015 to February 2017.

Eligibility Criteria

Articles that met the following inclusion criteria were included in this systematic review: prospective randomized trials involving human subjects that analyzed clinical outcomes of horizontal bone augmentation. Accordingly, several factors such as study design, number of patients included in the last follow-up assessment, number of defect sites, smoking or other systemic conditions that might alter the outcome, and type of procedure (including whether bone grafting material or barrier membranes were used) were extracted from the selected studies and analyzed (Table 1). On the other hand, nonrandomized studies, retrospective and in vitro investigations, studies failing to report horizontal bone augmentation, case reports or case series with less than

Table 1 Characteristics of the Included Investigations

RCT studies (year)	Groups	No. of patients	No. of sites grafted	Location of grafted sites	Bone augmentation	Origin of bone graft	Type of bone graft	Fixed (Y/N)	Membrane (Y/N)	Fixed (Y/N)	Additional grafting material/ growth factor	Bone augmentation achieved at baseline Width (mm/cm^3)
Abrahamsson et al[20] (2012)	Test	10	10	A	OE+GBR	AG	AG particulate	N	TM+RCM	Y	N	4.5 ± 3 mm
	Control	10	10	A	Block	AG	AG	Y	N	N	N	3.8 ± 0.8 mm
Annen et al[22] (2011)	Test	9	9	NR	GBR	XE	BBM	N	CLM	N	N	3.4 ± 1.1 mm
	Control		9	NR	GBR	XE	BBM	N	RCM	N	N	3.4 ± 1.0 mm
Amorfini et al[21] (2014)	Test	16	16	P	Block	ALLO	ALL	Y	RCM	N	rhPDGF-BB SS	0.16 cm^3 0.20 cm^3
	Control		16		GBR	XE	BBM+G	Y	RCM	N	rhPDGF-BB SS	0.15 cm^3 0.20 cm^3
Van Assche et al[23] (2013)	Test	14	14	A/P	GBR	AG+SBS	AG+SBS	N	RCM	N	N	NR
	Control		14	A/P	GBR	AG+XE	AG+BBM	N	RCM	N	N	NR
Becker et al[24] (2009)	Test	23	23	NR	GBR	XE	BBM	N	CLM	N	N	NR
	Control	26	26	NR	GBR	XE	BBM	N	RCM	N	N	NR
Beitlitum et al[25] (2010)	Test	27	12	NR	GBR	ALLO	FDBA	N	CLM	N	N	NR
	Control	23	15	NR	GBR	ALLO+AG	FDBA+AG	N	CLM	N	N	NR
Carpio et al[26] (2000)	Test	23	23	NR	GBR	AG+XE	AG+BBM	N	ePTFE	Y	N	NR
	Control	25	26	NR	GBR	AG+XE	AG+BBM	N	RCM	Y	N	NR
Castagna et al [27] (2013)	Test	12	12	A/P	Block	AG	ICBG	Y	N	N	N	NR
	Control	4	4	A/P	Block	AG	ICBG	Y	N	N	N	NR
Cordaro et al[28] (2011)	Test	11	11	NR	Block	AG	AG	Y	RCM	N	N	4.18 ± 1.17 mm
	Control	11	11	NR	Block	AG+XE	AG+BBM	Y	RCM	N	N	4.56 ± 1.38 mm
Eskan et al[29] 2014	Test	14	14	A/P	GBR	ALLO	CAN	N	PRM	N	PRP	3.4 ± 1.0 mm
	Control	14	14	A/P	GBR	ALLO	CAN	N	PRM	N	N	3.5 ± 1.1 mm
de Freitas et al[30] (2013)	Test	12	12	A	GBR	N	N	N	TM	Y	rhBMP-2/ ACS	2.1 ± 0.8 mm
	Control	12	12	A	GBR	AG	AG particulate	N	TM	Y	N	3.1 ± 0.7 mm
Fu et al[33] (2014)	Test	13	13	A	GBR	ALLO	CAN+CORT	N	BOPM	N	N	3.04 ± 0.22 mm
	Control	13	13	A	GBR	ALLO	CAN+CORT	N	N	N	N	3.83 ± 0.54 mm
Lumetti et al[31](2014)	Test	12	12	NR	Block	ALLO	FFB	Y	RCM	N	N	1.5 ± 0.91 mm
	Control	12	12	NR	Block	AG	AG	Y	RCM	N	N	0.44 ± 1.04 mm
Merli et al[34] (2015)	Test	25	25	A/P	GBR	SBS+AG	SBS+AG	N	POPM	Y	N	NR
	Control	25	25	A/P	GBR	AG+XE	BBM+AG	N	RCM	Y	N	NR
Mordendfeld et al[35](2014)	Test	13	14	A/P	GBR	AG+XE	BBM+AG 60:40	N	RCM	N	FG	5.6 ± 1.1 mm
	Control		14	A/P	GBR	AG+XE	BBM+AG 90:10	N	RCM	N	FG	5.7 ± 1.3 mm
Park et al[36] (2008)	Test	22	9	NR	GBR	ALLO	CAN+CORT	N	CLM	N	N	3
	Test		9	NR	GBR	ALLO	CAN+CORT	N	ADM	N	N	3
	Control		9	NR	GBR	ALLO	CAN+CORT	N	N	N	N	3
Pinho et al[37] (2006)	Test	10	10	A	GBR	AG	AG	N	TMB	Y	N	NR
	Control		10	A	GBR	N	N	N	TMB	Y	N	NR

A = anterior; P = posterior; OE = osmotic expander; GBR = guided bone regeneration; AG = autogenous; TM = titanium mesh; RCM = resorbable collagen membrane; Y = yes; N = no; NR = not reported; CBCT = cone beam computed tomography; BBM = bovine bone mineral; CLM = cross linked membrane.

five subjects, systematic reviews, preclinical animal studies, and human trials not studying any of the aforementioned regenerative therapies were excluded. Human trials with missing information were also excluded.

Risk of Bias

Two reviewers (B.E. and C.P.) designed and assessed the proposal for the present project to make sure that the STROBE statement and PRISMA guidelines were followed. STROBE stands for an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers, and journal editors involved

Immediate loading	Measurement	Healing period (mo)	Resorption	Final bone gain (mm/cm³)	No. of implants placed	Implant protocol (mo)	Follow-up of implants (mo)	Implant survival %	Implant success %	Failed technique (%)		
										Failed (%)	Timing (mo)	Cause
N	Probe	6	14%	3.9 ± 1.4 mm	10	3	NR	100	NR	0	0	0
N		6	28%	2.7 ± 0.8 mm	13	3	NR	100	NR	0	0	0
N	Probe	6	56%	1.0 ± 1.7 mm	9	6	NR	100	NR	33	1	Exposition/ infection
N		6	22%	1.7 ± 1.9 mm	9	6	NR	100	NR	0	0	0
N	CBCT	6	0 cm³	0.16 cm³	25	6	12	100	NR	0	0	0
N		6	0.01 cm³ –0.03 cm³	0.16 cm³ 0.19 cm³	25	6	12	100	NR	0	0	0
N	Probe	6.5	NR	2.5 ± 0.8 mm	14	6.5	12	100	NR	0	0	0
N		6.5	NR	2.5 ± 0.8 mm	14	6.5	12	100	NR	0	0	0
N	Probe	4	NR	3.17 ± 0.61 mm	41	4	NR	100	NR	13	NR	Wound infection
N		4	NR	2.63 ± 0.48 mm	37	4	NR	100	NR	38	NR	Wound infection
N	CBCT	5–7	NR	5 ± 1.28 mm	106	5–7	NR	100	NR	0	0	0
N		5–7	NR	3.6 ± 1.72 mm		5–7	NR	100	NR	0	0	0
N	Probe	6	NR	1.71 ± 0.16 mm	NR	6	NR	83.3	NR	NR	NR	NR
N		6	NR	1.41 ± 0.32 mm	NR	6	NR	78.3	NR	NR	NR	NR
PI	Probe	6	NR	4.9 ± 2.84 mm	96	NR	NR	98.96	NR	NR	NR	NR
N		6	NR	5.08 ± 2.19 mm	24	NR	NR	100	NR	NR	NR	NR
N	Probe	4	0.25 ± 1.03 mm	3.93 ± 1.36 mm	28	3	24	100	100%	0	0	0
N		4	0.89 ± 1.5 mm	3.67 ± 1.1 mm	27	3	24	100	100%	0	0	0
N	Caliper	4	28% ± 17%	2.9 ± 1.0 mm	14	NR	NR	NR	NR	0	0	0
N		4	34% ± 17%	2.0 ± 1.2 mm	14	NR	NR	NR	NR	0	0	0
N	CBCT	6	NR	3.2 ± 0.9 mm	32	NR	6	100	NR	0	0	0
N		6	NR	3.7 ± 1.4 mm	30	NR	6	100	NR	0	0	0
N	CBCT	6	NR	1.09 ± 0.05 mm	NR	6	12	100	NR	0	0	0
N		6	NR	0.65 ± 0.32 mm	NR	6	12	100	NR	0	0	0
N	CBCT	6	–52% ± 25.87%	0.79 ± 0.62 mm	NR	NR	NR	NR	NR	NR	NR	NR
N		6	–25% ± 12.73%	0.67 ± 0.68 mm	NR	NR	NR	NR	NR	NR	NR	NR
N	Probe	6	NR	3.5 ± 1.7 mm	29	6	6	100	NR	0	0	0
N		6	NR	3.1 ± 1.2 mm	32	6	6	100	NR	0	0	0
N	CBCT	8	2.0 ± 1.3 mm	3.5 ± 1.3 mm	71	NR	NR	97	NR	NR	NR	NR
N		8	2.7 ± 1.6 mm	2.9 ± 1.3 mm		NR	NR		NR	NR	NR	NR
N	Probe	6	1.43 ± 0.76 mm	1.57 ± 0.76 mm	9	6	NR	100	NR	0	0	0
N		6	1.26 ± 0.38 mm	1.74 ± 0.38 mm	9	6	NR	100	NR	0	0	0
N		6	1.98 ± 0.47 mm	1.02 ± 0.47 mm	9	6	NR	100	NR	0	0	0
N	Probe	6	1.40 ± 0.98 mm	NR	NR	NR	NR	NR	NR	0	0	0
N		6	1.40 ± 1.97 mm	NR	NR	NR	NR	NR	NR	0	0	0

in the conduction and dissemination of observational studies, and consists of a 22-item checklist to be fulfilled in a systematic review.

Qualitative Assessment

The quality of the selected randomized controlled trials (RCTs) was established from the randomized clinical trial checklist of the Cochrane Center and CONSORT (Consolidated Standards of Reporting Trials) statement, which provided guidelines for the following parameters: *(1)* sequence generation; *(2)* allocation concealment method; *(3)* masking of the examiner; *(4)* address of incomplete outcome data; and *(5)* free of selective outcome reporting (Moher et al, 2010; Schulz et al, 2010).[18,19]

Statistical Analysis

The R 3.0.2 software package was used to perform the meta-analysis. The primary variables were: initial bone gain (mm), final bone gain (mm), and resorption (mm). The secondary variable was implant survival. The analysis was performed using the methodology described below. When bone change values were missing relative standard deviation, an estimate was made from the linear correlation between the initial and final bone gain. Graft resorption data showed high heterogeneity, due to the variability in the measurement units (mm versus %). Mean millimeter values were selected for analysis.

Bone gain and resorption were analyzed as subject units, while implant survival rates were analyzed as implant units. Furthermore, meta-regression models with the moderator variable being the technique used (block or GBR) and type of biomaterial (ALL, AG, ALP) were estimated likewise under the random effects approach. This analysis would afford an aggregate estimate of major responses and conclude whether there were differences in the moderator variable. Calculations were based on the inverse variance method of DerSimonian and Laird. Resorption value units differed among authors. The absolute value was recorded in mm, cm^3, and as percentages. Volumetric and percentage values were discarded, the latter being computed as absolute values directly from the difference between the baseline and final bone gain. The meta-analysis consisted of an estimation of total graft resorption upon healing and, hence, final regenerated bone gain as well as survival for all the studies based on the mean value based on a random effects model.

Study of Heterogeneity

Heterogeneity was assessed based on calculation of the I^2 statistic (percentage variability of estimated effect that can be attributed to the heterogeneity of the effects) and the null statistic test. Galbraith graphs displayed the degree of heterogeneity. In studies where great heterogeneity was detected, a sensitivity analysis was performed to determine its source. Funnel plots and the Egger test were used to assess risk of bias; the accepted statistical significance level was 5% ($P = .05$).

RESULTS

Study Screening

The initial manual and electronic search resulted in a total of 2,879 publications, 750 of which were selected after evaluation of titles and abstracts. Thirty-five full-text investigations were further evaluated. Of these, 17 fulfilled the inclusion criteria[20–31,33–37] (Fig 1). Details of the excluded articles are provided in Table 2.

Study Quality

All the articles selected were RCTs. The randomized clinical trial checklist of the Cochrane Center and CONSORT (Consolidated Standards of Reporting Trials) statement was used to score study quality. The degree of bias was categorized as low risk if all the criteria were met, moderate risk when only one criterion was missing, and high risk if two or more criteria were missing.[18,19] Low (45%) to moderate (65%) estimated potential risk of bias was found from the studies included in the qualitative appraisal.

Intergroup Meta-analysis

A thorough literature review was made, leading to a final selection of 17 studies, all of which were RCTs. Therefore, the design allowed the comparison of results between a test group and a control group. Fifteen of these articles provided information on number of implants employed.[1,20-30,34–37] Three studies[26,31,32] did not mention the number of implants, and therefore had to be excluded from the numerical analysis. The 15 eligible articles were divided into 31 independent studies (separating test and control groups), with a total of 772 implants. The mean follow-up for implants was 11.9 ± 7.8 months.

Initial Bone Gain

A total of eight studies[20,22,28–30,33,35,36] reported information on initial bone gain, which led to a total sample of 310 implants. The measures of mean gain given by the different studies ranged from 2.10 mm in the GBR group as reported by de Freitas et al[30] to 4.56 mm in the bone block group in the study by Cordaro et al.[28] For all techniques combined, the estimated mean (± SD) initial bone gain was 3.71 ± 0.24 mm (Fig 2a). The 95% confidence interval (95% CI) for this mean gain was [3.24 to 4.19]. The above measures and their graphic synthesis also revealed important heterogeneity: $I^2 = 0.959$ (95.9% of total variability). The Cochran heterogeneity test confirmed statistical significance ($P < .001$). Discrepancy was noted among some studies in terms of bone volume gain measurement.

Final Bone Gain

A total of 13 studies[20,22–25,27–30,33–36] reported information on final bone gain after 4 to 8 months. With regard to the implants, there was a mean time for re-evaluation of 6 months with a range of 11.9 ± 7.8 months. These investigations led to a total sample of 703 implants. The measures of mean gain given by the different studies ranged from 0.65 mm (Annen et al[22])

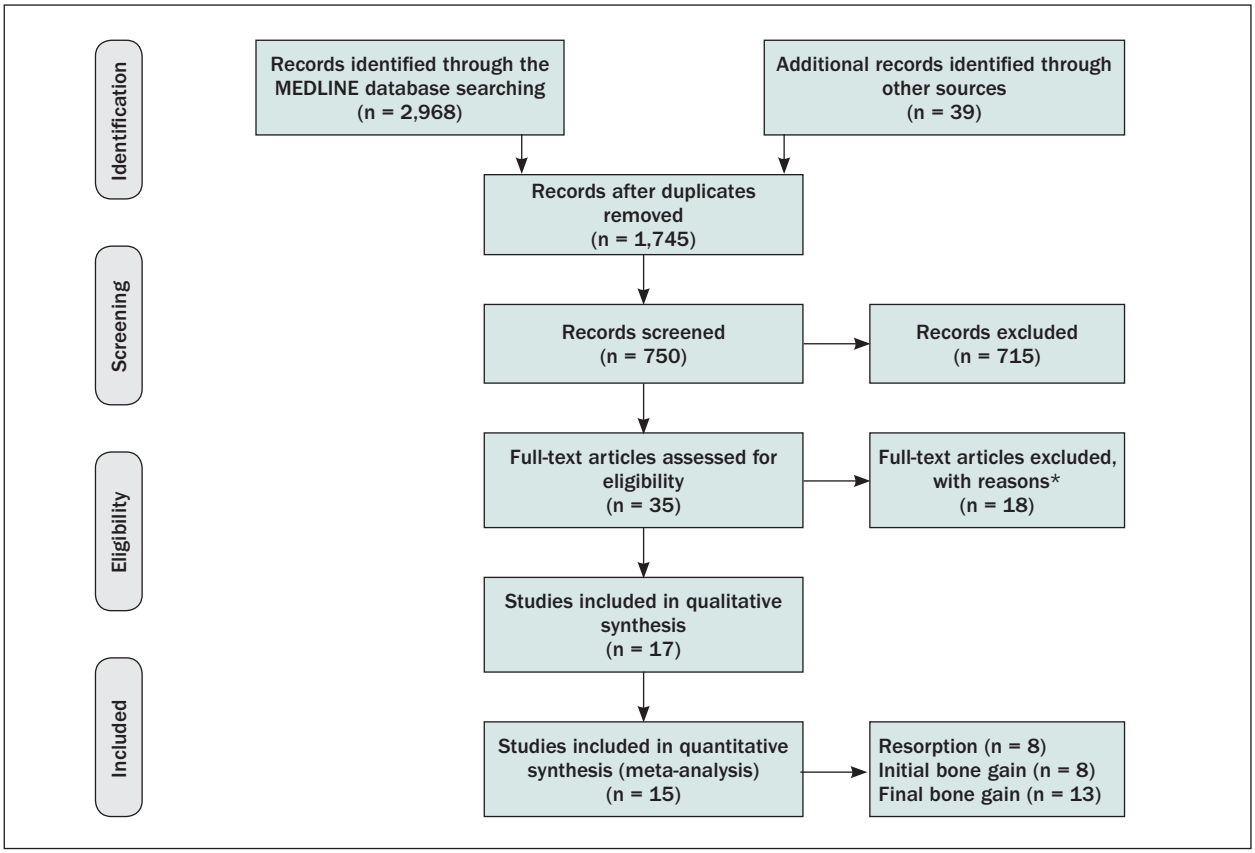


Fig 1 PRISMA flowchart of the screening process.

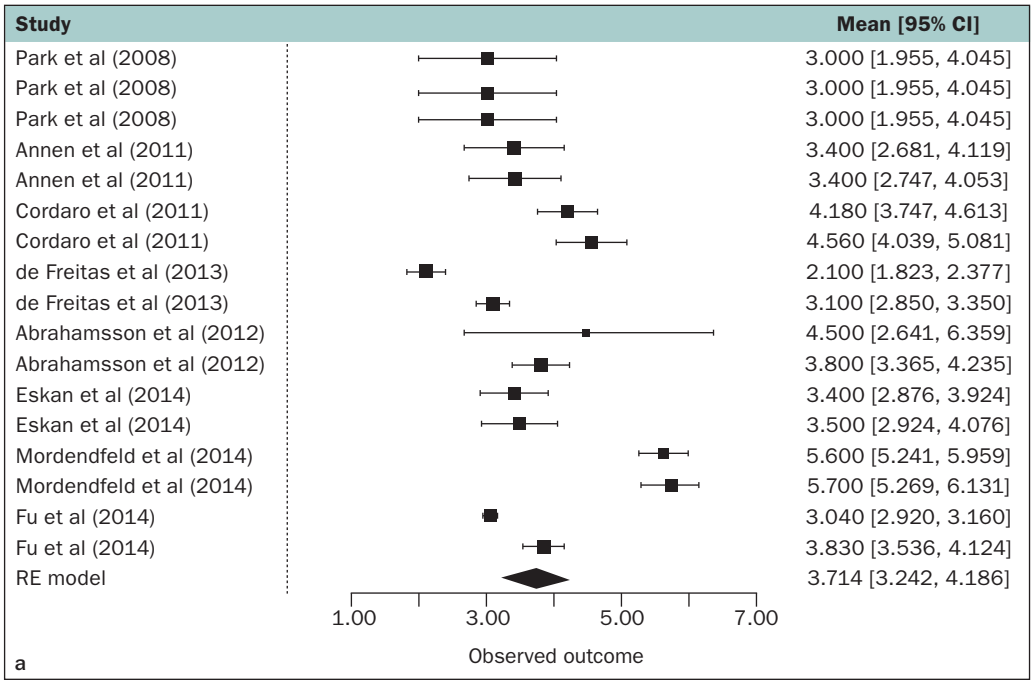
to 5.08 mm (Castagna et al[27]). It should be noted that all studies except the one from Annen et al[22] concluded with non-null final bone gain. The estimated final mean gain (± SD) was 2.86 ± 0.23 mm (Fig 2b). The 95% confidence interval (CI) for this mean gain was [2.40 to 3.32]. This was interpreted in the usual way; ie, with a 95% confidence interval, the true mean value of the final gain in the sample would be between these two values. The final gain for blocks was 4.03 ± 0.49 mm, CI [3.06, 5.00]; while the final bone gain for GBR was 2.59 ± 0.23 mm, CI [2.13, 3.06]. There was not a significant difference with regard to different techniques and resorption rates ($P = .412$). However, with block grafting procedures, the resorption can be considered almost null ($P = .193$); while with GBR it was significantly non-null ($P < .001$). Therefore, a non-null gain was concluded ($P < .001$). The Egger test accepted symmetry ($P = .423$). In other words, studies with low relative weight (due to small sample size or high variability), resulted in dispersed gain values.

Biomaterial Effect

The mean bone gain of the 13 studies[20,22–25,27–30,33–36] using different biomaterials was compared: AG, AG+XE, ALP, and XE (group N of de Freitas et al[30] was excluded). The estimated measures when comparing

Table 2 Articles Excluded and Reasons for Exclusion

Reason for exclusion	Investigations
Study design (No RCT)	Cordaro et al (2002) Cordaro et al (2010) Hof et al (2011)
No horizontal regeneration	Grandi et al (2011)
Different grafting technique	Jung et al (2013) Jung et al (2015) Mardas et al (2010)
Not enough information	Shibly et al (2013) Sisti et al (2011) Lumetti et al (2014) Zuffetti et al (2013) Jung et al (2009) Meijndert et al (2008) Ramel et al (2012) Urban et al (2012) Friedman et al (2002) Merli et al (2015)
Prior to year 2000	Zitzmann et al (1997)



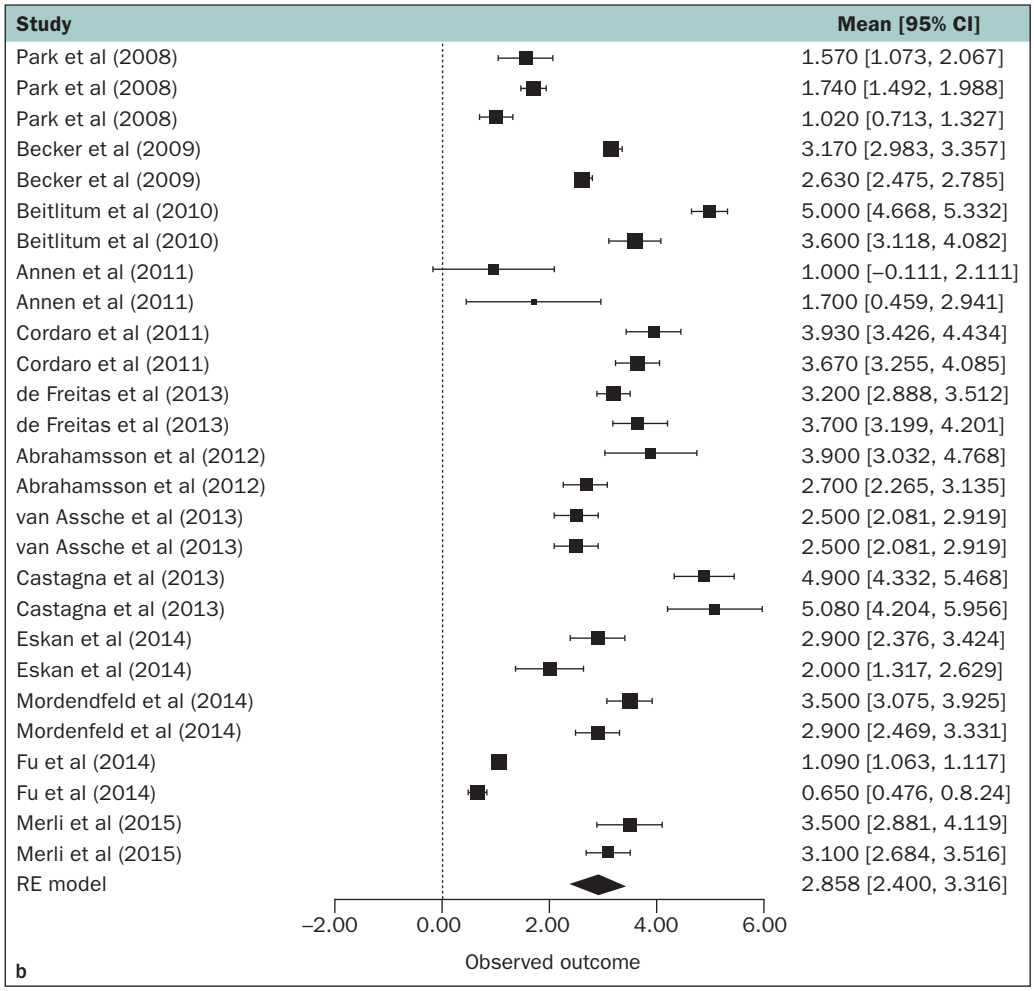
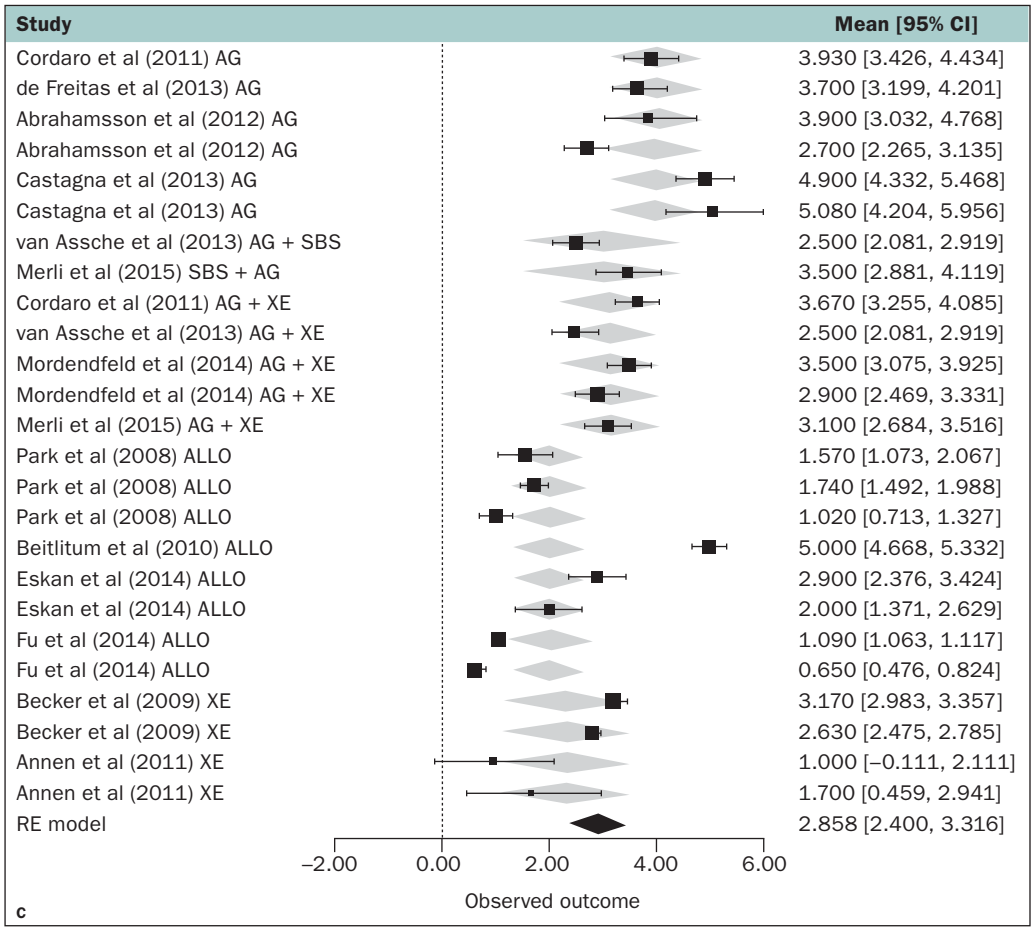
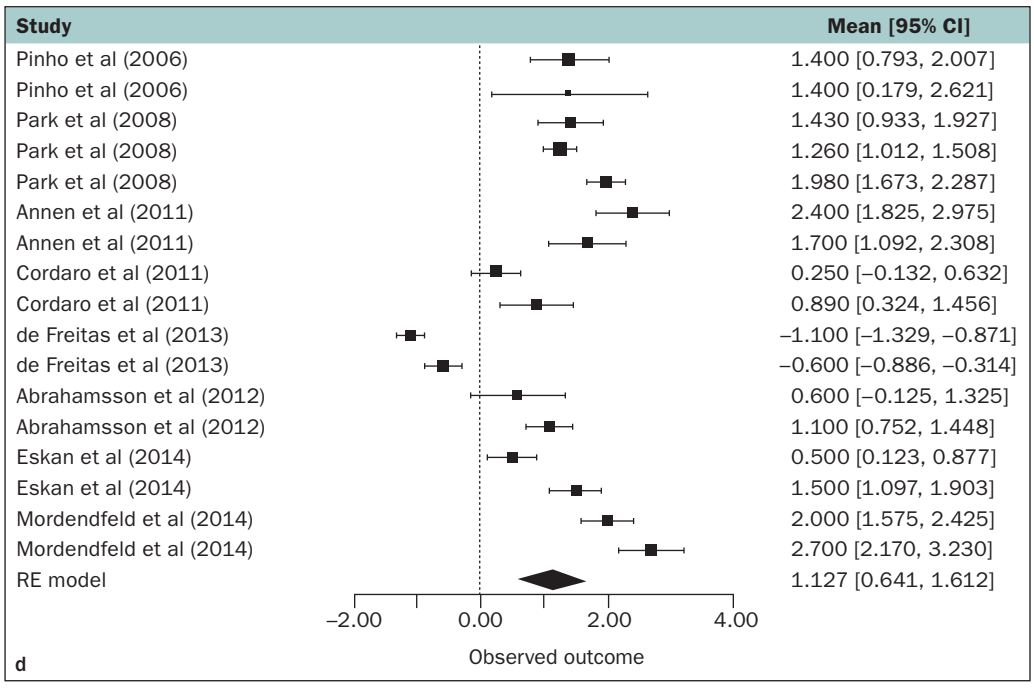
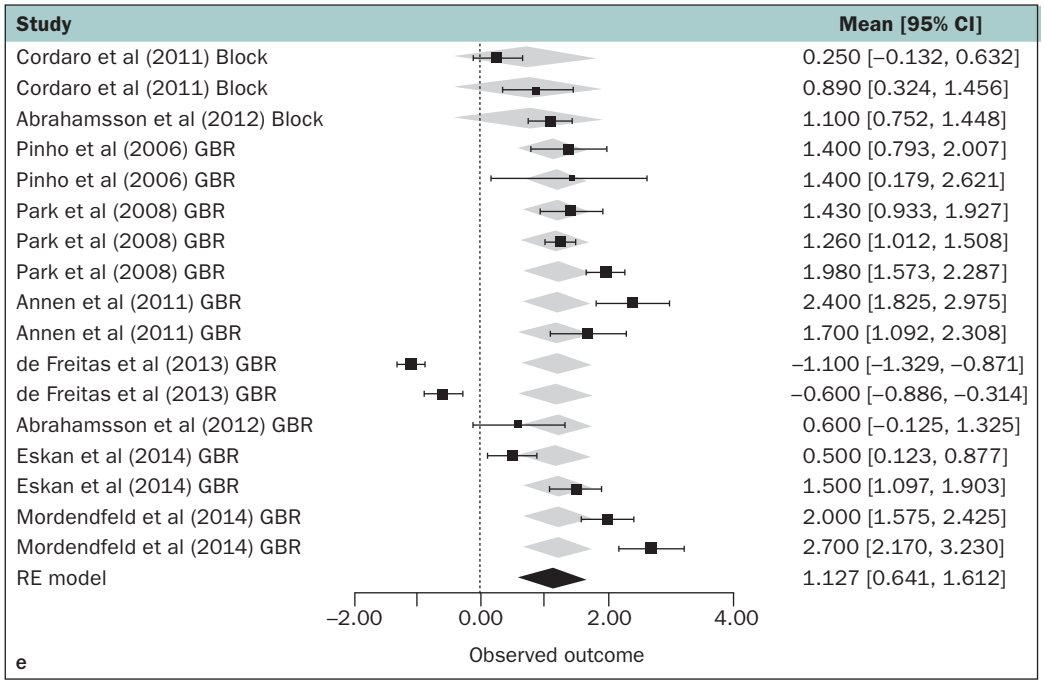


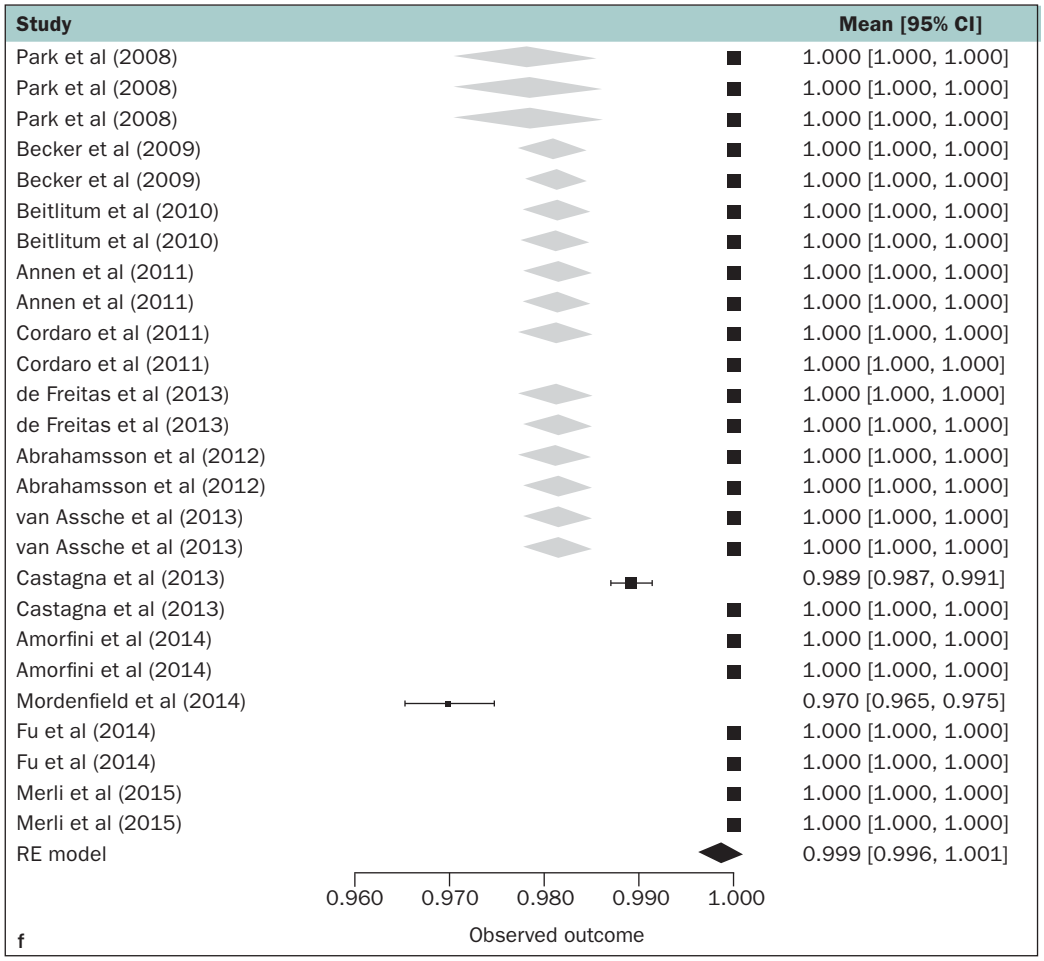
Fig 2 Statistical analysis for different variables. (a) Initial bone gain. *(b)* Final bone gain. *(c, facing page)* Biomaterial effect. *(d, facing page)* Resorption. *(e, back of facing page)* Technique effect. *(f, back of facing page)* Survival.


Study
Mean [95% CI]
Cordaro et al (2011) AG
3.930 [3.426, 4.434]
de Freitas et al (2013) AG
3.700 [3.199, 4.201]
Abrahamsson et al (2012) AG
3.900 [3.032, 4.768]
Abrahamsson et al (2012) AG
2.700 [2.265, 3.135]
Castagna et al (2013) AG
4.900 [4.332, 5.468]
Castagna et al (2013) AG
5.080 [4.204, 5.956]
van Assche et al (2013) AG + SBS
2.500 [2.081, 2.919]
Merli et al (2015) SBS + AG
3.500 [2.881, 4.119]
Cordaro et al (2011) AG + XE
3.670 [3.255, 4.085]
van Assche et al (2013) AG + XE
2.500 [2.081, 2.919]
Mordendfeld et al (2014) AG + XE
3.500 [3.075, 3.925]
Mordendfeld et al (2014) AG + XE
2.900 [2.469, 3.331]
Merli et al (2015) AG + XE
3.100 [2.684, 3.516]
Park et al (2008) ALLO
1.570 [1.073, 2.067]
Park et al (2008) ALLO
1.740 [1.492, 1.988]
Park et al (2008) ALLO
1.020 [0.713, 1.327]
Beitlitum et al (2010) ALLO
5.000 [4.668, 5.332]
Eskan et al (2014) ALLO
2.900 [2.376, 3.424]
Eskan et al (2014) ALLO
2.000 [1.371, 2.629]
Fu et al (2014) ALLO
1.090 [1.063, 1.117]
Fu et al (2014) ALLO
0.650 [0.476, 0.824]
Becker et al (2009) XE
3.170 [2.983, 3.357]
Becker et al (2009) XE
2.630 [2.475, 2.785]
Annen et al (2011) XE
1.000 [−0.111, 2.111]
Annen et al (2011) XE
1.700 [0.459, 2.941]
RE model
2.858 [2.400, 3.316]
−2.00
0.00
2.00
4.00
6.00
Observed outcome
c


Study
Mean [95% CI]
Pinho et al (2006)
1.400 [0.793, 2.007]
Pinho et al (2006)
1.400 [0.179, 2.621]
Park et al (2008)
1.430 [0.933, 1.927]
Park et al (2008)
1.260 [1.012, 1.508]
Park et al (2008)
1.980 [1.673, 2.287]
Annen et al (2011)
2.400 [1.825, 2.975]
Annen et al (2011)
1.700 [1.092, 2.308]
Cordaro et al (2011)
0.250 [−0.132, 0.632]
Cordaro et al (2011)
0.890 [0.324, 1.456]
de Freitas et al (2013)
−1.100 [−1.329, −0.871]
de Freitas et al (2013)
−0.600 [−0.886, −0.314]
Abrahamsson et al (2012)
0.600 [−0.125, 1.325]
Abrahamsson et al (2012)
1.100 [0.752, 1.448]
Eskan et al (2014)
0.500 [0.123, 0.877]
Eskan et al (2014)
1.500 [1.097, 1.903]
Mordendfeld et al (2014)
2.000 [1.575, 2.425]
Mordendfeld et al (2014)
2.700 [2.170, 3.230]
RE model
1.127 [0.641, 1.612]
−2.00
0.00
2.00
4.00
Observed outcome
d


Study
Mean [95% CI]
Cordaro et al (2011) Block
0.250 [–0.132, 0.632]
Cordaro et al (2011) Block
0.890 [0.324, 1.456]
Abrahamsson et al (2012) Block
1.100 [0.752, 1.448]
Pinho et al (2006) GBR
1.400 [0.793, 2.007]
Pinho et al (2006) GBR
1.400 [0.179, 2.621]
Park et al (2008) GBR
1.430 [0.933, 1.927]
Park et al (2008) GBR
1.260 [1.012, 1.508]
Park et al (2008) GBR
1.980 [1.573, 2.287]
Annen et al (2011) GBR
2.400 [1.825, 2.975]
Annen et al (2011) GBR
1.700 [1.092, 2.308]
de Freitas et al (2013) GBR
–1.100 [–1.329, –0.871]
de Freitas et al (2013) GBR
–0.600 [–0.886, –0.314]
Abrahamsson et al (2012) GBR
0.600 [–0.125, 1.325]
Eskan et al (2014) GBR
0.500 [0.123, 0.877]
Eskan et al (2014) GBR
1.500 [1.097, 1.903]
Mordendfeld et al (2014) GBR
2.000 [1.575, 2.425]
Mordendfeld et al (2014) GBR
2.700 [2.170, 3.230]
RE model
1.127 [0.641, 1.612]
–2.00
0.00
2.00
4.00
Observed outcome

e


Study
Mean [95% CI]
Park et al (2008)
1.000 [1.000, 1.000]
Park et al (2008)
1.000 [1.000, 1.000]
Park et al (2008)
1.000 [1.000, 1.000]
Becker et al (2009)
1.000 [1.000, 1.000]
Becker et al (2009)
1.000 [1.000, 1.000]
Beitlitum et al (2010)
1.000 [1.000, 1.000]
Beitlitum et al (2010)
1.000 [1.000, 1.000]
Annen et al (2011)
1.000 [1.000, 1.000]
Annen et al (2011)
1.000 [1.000, 1.000]
Cordaro et al (2011)
1.000 [1.000, 1.000]
Cordaro et al (2011)
1.000 [1.000, 1.000]
de Freitas et al (2013)
1.000 [1.000, 1.000]
de Freitas et al (2013)
1.000 [1.000, 1.000]
Abrahamsson et al (2012)
1.000 [1.000, 1.000]
Abrahamsson et al (2012)
1.000 [1.000, 1.000]
van Assche et al (2013)
1.000 [1.000, 1.000]
van Assche et al (2013)
1.000 [1.000, 1.000]
Castagna et al (2013)
0.989 [0.987, 0.991]
Castagna et al (2013)
1.000 [1.000, 1.000]
Amorfini et al (2014)
1.000 [1.000, 1.000]
Amorfini et al (2014)
1.000 [1.000, 1.000]
Mordenfield et al (2014)
0.970 [0.965, 0.975]
Fu et al (2014)
1.000 [1.000, 1.000]
Fu et al (2014)
1.000 [1.000, 1.000]
Merli et al (2015)
1.000 [1.000, 1.000]
Merli et al (2015)
1.000 [1.000, 1.000]
RE model
0.999 [0.996, 1.001]
0.960
0.970
0.980
0.990
1.000
Observed outcome

f

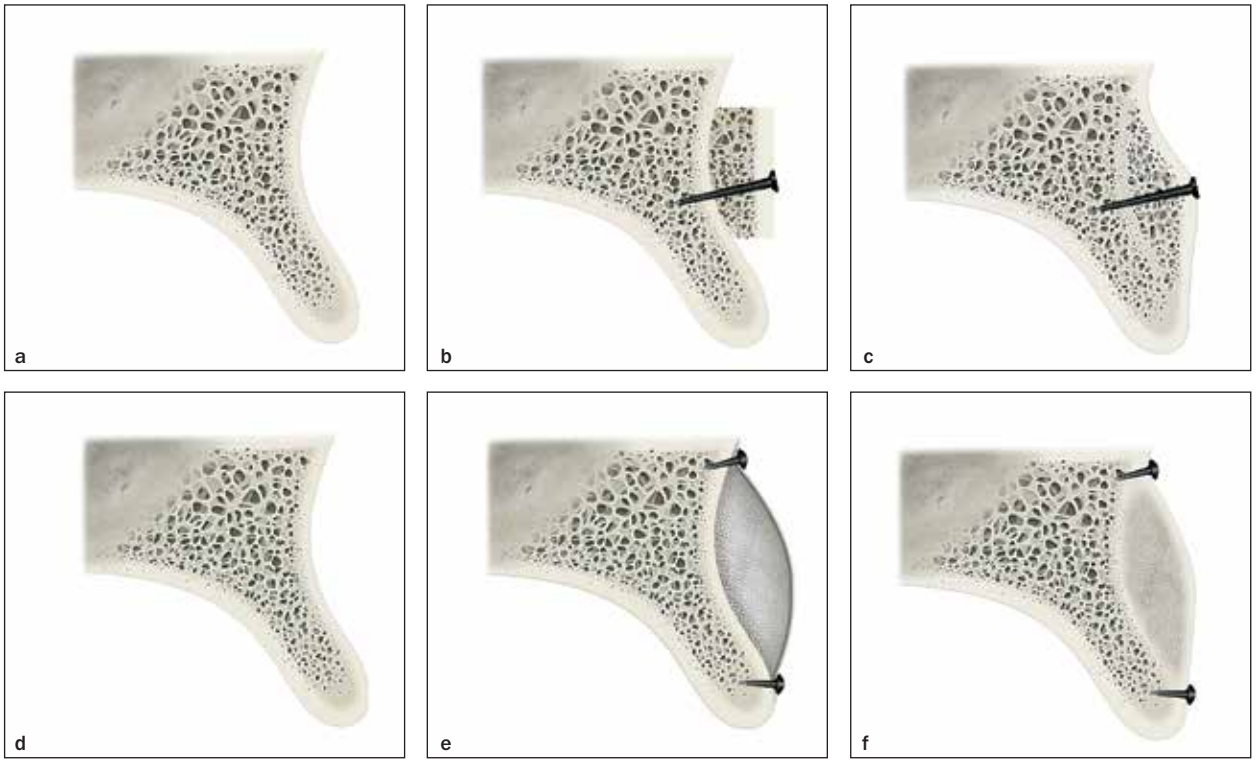


Fig 3 Graphic representation of block graft and GBR techniques for baseline, initial bone gain, and final bone gain. *(a)* Baseline prior block graft. *(b)* Initial bone gain after block graft (4.18 ± 0.56 mm). *(c)* Final bone gain after block graft (4.03 ± 0.49 mm). *(d)* Baseline prior GBR. *(e)* Initial bone gain after GBR (3.61 ± 0.27 mm). *(f)* Final bone gain after GBR (2.59 ± 0.23 mm). Total bone gain: initial, 4.18 ± 0.56 mm; final: 2.86 ± 0.23 mm. Resorption: Block, 0.75 ± 0.57 mm; GBR, 1.26 ± 0.25 mm; Total: 1.17 ± 0.23 mm.

bone gain depending on the material and regardless of the technique employed were: AG: 4.01 ± 0.44 mm, CI [3.15 to 4.87], $P < .001$; AG+ALP: 2.99 ± 0.75 mm, CI [1.52 to 4.45], $P < .001$; AG+XE: 3.13 ± 0.47 mm, CI [2.13 to 4.05], $P < .001$; ALL: 1.99 ± 0.37 mm, CI [1.27 to 2.71], $P < .001$; XE: 2.23 ± 0.55 mm, CI [1.16 to 3.31], $P < .001$ (Fig 2c).

For the mean initial bone gain in eight studies,[20,22,28–30,33,35–36] six studies using GBR[20,22,30,33,35,36] were compared with two studies using the block graft technique.[28,29] The estimated measures were: 4.03 ± 0.49 mm, CI [3.06 to 5.00] ($P < .001$) for block grafting and 2.59 ± 0.23 mm, CI [2.13 to 3.06] ($P < .001$) for GBR. The final mean gain in all the groups proved positive (significantly non-null) for GBR. There were statistically significant differences in the bone gain achieved with one technique or the other ($P = .009$). This observation was taken to indicate that the block technique is superior to the GBR technique.

Resorption

Resorption was defined as the difference between the initial postsurgical site increase and the residual gain after healing 4 to 8 months later. This parameter was regarded as the main outcome of the investigation. A total of nine studies reported information on resorption,[22,23,28–30,33,35–37] which led to a total sample of 304 implants. The estimated mean resorption (± SD) was 1.17 ± 0.23 mm (Fig 2d). The 95% confidence interval for this measure was [0.73 to 1.62]. This was interpreted in the usual way; ie, with a 95% confidence interval, the true mean value of resorption in the sample would be between 0.73 and 1.62 mm. Hence, it could be admitted that there is non-null resorption ($P < .001$). It can be visually observed that for the final estimation (RE random effects model), the confidence interval excludes zero. The heterogeneity between studies was 95.4% of the total variability (between studies + within studies), implying $I^2 = 0.954$. The result of the Cochran heterogeneity test confirmed the importance of this value ($P < .001$). The shape of the funnel plot is slightly different than usual. For example, in the middle right part of the cone, some studies show a small sample and/or high standard deviation (high standard error). These studies report high positive resorption. The Egger test reflected this general asymmetry ($P = .136$) without reaching statistical significance.

Technique Effect

Resorption values, deriving from eight studies using the GBR technique,[22,23,29,30,33,35–37] were compared with those reported in two studies[20,28] using the block

technique. The estimated measures were: 0.75 ± 0.59 mm, CI [–0.42 to 1.91] (P = .209) for block grafting and 1.22 ± 0.28 mm, CI [0.66 to 1.76] (P < .001) for GBR (Fig 2e). The differences in resorption were not statistically significant between techniques (P = .412). However, an important observation is that with the block graft technique, resorption can be considered almost zero (the interval includes zero; P = .193), while resorption with the GBR technique is significantly non-null (P < .001).

Survival

A total of 13 studies[20–30,33–37] reported information on final bone gain, which led to a total sample of 725 implants. The rates among different investigations were practically invariable: all reported a survival rate of 100%, except for the study performed by Castagna and colleagues, in which bone blocks were performed along with immediate implant placement and loading,[27] where the survival rate was 98.9%. Also, the study published by Mordenfeld et al[35] reported a survival rate of 97%. The weighted survival rate was 99.9%, with a 95% confidence interval of [99.6 to 100] (Fig 2f).

DISCUSSION

Since the early 1980s, when Dahlin et al[14] applied the principles of cellular exclusion with bone regeneration for augmentation of the bone crest, many studies have reported success with the regeneration of horizontal defects.[38–41] The initial bone gain found in this systematic review was 3.71 ± 0.24 mm, with an estimated final gain of 2.86 ± 0.23 mm after 1 year. These findings are consistent with the results of previous studies in which a gain of 3.31 mm was reported.[10] Sanz-Sánchez et al[42] found that for the staged approach, the combination of bone blocks, particulated grafts, and barrier membranes provided the best outcomes, despite the potential morbidity and advent of postoperative complications. The maximum bone width gain was reported for the combination of particulate xenograft + autologous bone + absorbable membrane (weighted mean difference [WMD] = 5.68 mm; 95% CI: 5.00, 6.35; P < .001), whereas the minimum was for the combination of particulate synthetic graft + nonabsorbable membrane (WMD = 1.10 mm; 95% CI: –0.33, 2.53; P = .131). The lateral bone augmentation procedure using an autologous bone block alone was the most frequently used, demonstrating a significant width gain (WMD = 4.25 mm; 95% CI: 4.04, 4.47; P < .001).[42]

The comparison between GBR and block graft techniques showed a mean greater initial bone gain after the second procedure (4.03 ± 0.49 mm).[20,21,27,28,31] This difference may have been influenced by the technique itself, since placing a xenograft and a membrane over the block graft could minimize bone resorption.[28] When the GBR technique was used, the mean bone gain was found to be 2.59 ± 0.23 mm[1,22–26,29,33–37] (Fig 3). In this group, the use of a titanium mesh showed the greatest gain[20,30] among other membranes.

The comparison of final bone gain based on the biomaterial used demonstrated the autologous bone as the one providing the greatest gain (4.01 ± 0.44 mm). Autologous bone has been considered the gold standard due to its osteoinductive, osteogenic, and osteoconductive capacity.[43] However, its resorption is substantial during the first periods of integration, especially if the bone is of endochondral origin.[44] Hence, depending on the origin, the graft will exhibit a different remodeling pattern. On the other hand, allografts yielded a comparatively lesser bone gain of 1.99 ± 0.37 mm. These findings are consistent with those of other studies[45] where greater peri-implant resorption was observed in those regenerations performed with mineralized freeze-dried bone allograft compared with pristine bone. Two different types of allografts are used in this review: demineralized freeze-dried bone allograft (DFDBA) and mineralized freeze-dried bone allograft (FDBA). However, no significant differences were observed in relation to the bone regeneration achieved.[46]

With regard to resorption rates, not only the material used for regeneration but also the type of defect (self-contained or not) must be considered. Along with site morphology, the behavior of graft during the different healing phases could be of clinical interest. In fact, the estimated mean graft resorption after healing in this systematic review was 1.13 ± 0.25 mm after 6 months. Regardless of the technique or the material used, resorption will occur, and thus, it should be anticipated by overcorrecting the defect. Finally, the weighted survival rate was 99.9%, which is similar to the survival rate of implants placed in pristine bone.[47–50] In a clinical study with a split-mouth design, a survival rate of 100% was reported for implants placed simultaneously with GBR at 5 years of follow-up.[51] Similarly, a systematic review of augmentation procedures reported a survival rate ranging from 93% to 100% after 12 to 60 months of follow-up.[7] No significant differences were found in survival rates between implants placed in regenerated bone or in pristine bone. However, more long-term studies are needed to establish the resorption behavior of regeneration around implants over time.

When analyzing the present results, it is important to bear in mind that the majority of the studies reporting on the utilization of GBR needed minimal bone augmentation for dehiscence or fenestrations, while the studies reporting on the use of block grafts needed more significant bone augmentation for implant

placement. Hence, the results from the present investigation, when comparing both techniques, are to be interpreted cautiously since the defects and amount of grafting materials employed differed between them. Also, while the employment of block grafting techniques is usually performed prior to implant placement, GBR procedures are very commonly employed at the time of implant placement. These variables could also play a role in the reported outcomes. On the other hand, collagen barrier membranes could collapse more compared with block grafts due to the lack of rigidity. Also, this could have played a role in the reported outcomes.

While the present report may seem contradictory to the widely reported resorption rate of block grafts and the slow resorption rate of xenografts, several theories could be hypothesized. First, the follow-up periods evaluated are rather short, and more collapse of the block grafts could be expected with longer healing times. As previously mentioned, the characteristics of the defects also influence the outcomes. Also, of paramount importance due to its influence on the reported outcomes is the utilization of xenograft particulate material as well as barrier membranes over the block grafting sites, which could significantly minimize the resorption rate. Similarly, the lack of proper stabilization of the barrier membranes employed for the GBR investigations may have limited the regeneration potential, allowing for mobilization of the site and further graft volume loss.

Horizontal bone regeneration has proven to be a highly predictable technique. Accordingly, studies establishing the type of material offering the best results not only referring to bone quantity but also to bone quality are required. All factors influencing bone remodeling, such as the type of graft and the type of membrane, should also be defined in the future so that clinicians can predict the quantity of biomaterial required for performing bone regeneration. Tissue engineering could also define new materials, avoiding the need for a secondary donor site and offering the same qualitative properties as autologous bone.

Several limitations could be described for the present review. First, the type of defect could prejudge the final outcome, and not all horizontal defects have the same regenerative potential. As has been noted before, the heterogeneity of the defect may influence the final results obtained. The type of defect varies among articles, and the potential for regeneration of a bone defect depends not only on the type of biomaterial and surgical technique, but also on its extent and morphology[52]; therefore, variability of the analyzed defects is an important factor to be taken into account in relation to the results of this study. On the other hand, there are differences between the membranes used, and this might also influence the final outcome. Similarly, consideration is also required on how the measures were made, since in some investigations the measures were taken directly from the bone crest,[22–26,28–30,33–37] while in other articles they were taken from the cone beam computed tomography images.[1,20,21,27,31,32,35] Also, the number of articles evaluated greatly differ in between procedures, with 16 investigations included for GBR[20–37] and only 3 for block grafts.[20,27,28] This difference might have also influenced the final result. Lastly, only two articles reported on complications,[22,24] with most of them being wound infections and membrane exposure. Nonetheless, block grafting procedures are always at higher risk due to the secondary surgical site needed and present with significantly more patient morbidity.

CONCLUSIONS

Within the limitations of this investigation, it can be concluded that no differences in mean bone gain were found among the regenerative techniques analyzed in this review. Block grafts seemed to maintain the volume of the initial augmentation site more than GBR techniques; on the other hand, AG, ALL, and XE were associated with inferior bone gain compared with AG + XE. Regardless of the material used for bone regeneration, graft resorption will occur; consequently, overcorrection of the defect should be performed to compensate for this resorption. Nonetheless, owing to the heterogeneity of the studies, the results presented should be used with caution. In addition, a high survival rate was observed regardless of the biomaterials used for bone augmentation. Long-term results with more than 12 months of follow-up are needed.

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REFERENCES

1. Mardas N, Chadha V, Donos N. Alveolar ridge preservation with guided bone regeneration and a synthetic bone substitute or a bovine-derived xenograft: A randomized, controlled clinical trial. Clin Oral Implants Res 2010;21:688–698.

2. Pietrokovski J, Massler M. Residual ridge remodeling after tooth extraction in monkeys. J Prosthet Dent 1971;26:119–129.
3. Pietrokovski J, Massler M. Ridge remodeling after tooth extraction in rats. J Dent Res 1967;46:222–231.
4. Schropp L, Wenzel A, Kostopoulos L, Karring T. 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.
5. Tan WL, Wong TL, Wong MC, Lang NP. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clin Oral Implants Res 2012;23(suppl):s1–s21.
6. Johnson K. A study of the dimensional changes occurring in the maxilla following closed face immediate denture treatment. Aust Dent J 1969;14:370–376.
7. Jensen SS, Terheyden H. Bone augmentation procedures in localized defects in the alveolar ridge: Clinical results with different bone grafts and bone-substitute materials. Int J Oral Maxillofac Implants 2009;24(suppl):s218–s236.
8. Milinkovic I, Cordaro L. Are there specific indications for the different alveolar bone augmentation procedures for implant placement? A systematic review. Int J Oral Maxillofac Surg 2014;43:606–625.
9. Elnayef B, Monje A, Lin GH, et al. Alveolar ridge split on horizontal bone augmentation: A systematic review. Int J Oral Maxillofac Implants 2015;30:596–606.
10. Ortega-Oller I, Suárez F, Galindo-Moreno P, et al. The influence of implant diameter on its survival: A meta-analysis based on prospective clinical trials. J Periodontol 2014;85:569–580.
11. Urban IA, Lozada JL, Jovanovic SA, Nagursky H, Nagy K. Vertical ridge augmentation with titanium-reinforced, dense-PTFE membranes and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: A prospective case series in 19 patients. Int J Oral Maxillofac Implants 2014;29:185–193.
12. Urban I, Jovanovic SA, Buser D, Bornstein MM. Partial lateralization of the nasopalatine nerve at the incisive foramen for ridge augmentation in the anterior maxilla prior to placement of dental implants: A retrospective case series evaluating self-reported data and neurosensory testing. Int J Periodontics Restorative Dent 2015;35:169–177.
13. Urban IA, Monje A, Lozada JL, Wang HL. Long-term evaluation of peri-implant bone level after reconstruction of severely atrophic edentulous maxilla via vertical and horizontal guided bone regeneration in combination with sinus augmentation: A case series with 1 to 15 years of loading. Clin Implant Dent Relat Res 2017;19:46–55.
14. Dahlin C, Simion M, Hatano N. Long-term follow-up on soft and hard tissue levels following guided bone regeneration treatment in combination with a xenogeneic filling material: A 5-year prospective clinical study. Clin Implant Dent Relat Res 2010;12:263–270.
15. Blanco J, Alonso A, Sanz M. Long-term results and survival rate of implants treated with guided bone regeneration: A 5-year case series prospective study. Clin Oral Implants Res 2005;16:294–301.
16. Belser UC, Schmid B, Higginbottom F, Buser D. Outcome analysis of implant restorations located in the anterior maxilla: A review of the recent literature. Int J Oral Maxillofac Implants 2004;19(suppl):s30–s42.
17. Hämmerle CH, Lang NP. Single stage surgery combining transmucosal implant placement with guided bone regeneration and bioresorbable materials. Clin Oral Implants Res 2001;12:9–18.
18. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol 2010;63:e1–e37.
19. Schulz KF, Altman DG, Moher D, Fergusson D. CONSORT 2010 changes and testing blindness in RCTs. Lancet 2010;375:1144–1146.
20. Abrahamsson P, Wälivaara DÅ, Isaksson S, Andersson G. Periosteal expansion before local bone reconstruction using a new technique for measuring soft tissue profile stability: A clinical study. J Oral Maxillofac Surg 2012;70:e521–e530.
21. Amorfini L, Migliorati M, Signori A, Silvestrini-Biavati A, Benedicenti S. Block allograft technique versus standard guided bone regeneration: A randomized clinical trial. Clin Implant Dent Relat Res 2014;16:655–667.
22. Annen BM, Ramel CF, Hämmerle CH, Jung RE. Use of a new cross-linked collagen membrane for the treatment of peri-implant dehiscence defects: A randomised controlled double-blinded clinical trial. Eur J Oral Implantol 2011;4:87–100.
23. Van Assche N, Michels S, Naert I, Quirynen M. Randomized controlled trial to compare two bone substitutes in the treatment of bony dehiscences. Clin Implant Dent Relat Res 2013;15:558–568.
24. Becker J, Al-Nawas B, Klein MO, Schliephake H, Terheyden H, Schwarz F. Use of a new cross-linked collagen membrane for the treatment of dehiscence-type defects at titanium implants: A prospective, randomized-controlled double-blinded clinical multicenter study. Clin Oral Implants Res 2009;20:742–749.
25. Beitlitum I, Artzi Z, Nemcovsky CE. Clinical evaluation of particulate allogeneic with and without autogenous bone grafts and resorbable collagen membranes for bone augmentation of atrophic alveolar ridges. Clin Oral Implants Res 2010;21:1242–1250.
26. Carpio L, Loza J, Lynch S, Genco R. Guided bone regeneration around endosseous implants with anorganic bovine bone mineral. A randomized controlled trial comparing bioabsorbable versus non-resorbable barriers. J Periodontol 2000;71:1743–1749.
27. Castagna L, Polido WD, Soares LG, Tinoco EM. Tomographic evaluation of iliac crest bone grafting and the use of immediate temporary implants to the atrophic maxilla. Int J Oral Maxillofac Surg 2013;42:1067–1072.
28. Cordaro L, Torsello F, Morcavallo S, di Torresanto VM. Effect of bovine bone and collagen membranes on healing of mandibular bone blocks: A prospective randomized controlled study. Clin Oral Implants Res 2011;22:1145–1150.
29. Eskan MA, Greenwell H, Hill M, et al. Platelet-rich plasma-assisted guided bone regeneration for ridge augmentation: A randomized, controlled clinical trial. J Periodontol 2014;85:661–668.
30. de Freitas RM, Susin C, Spin-Neto R, et al. Horizontal ridge augmentation of the atrophic anterior maxilla using rhBMP-2/ACS or autogenous bone grafts: A proof-of-concept randomized clinical trial. J Clin Periodontol 2013;40:968–975.
31. Lumetti S, Consolo U, Galli C, et al. Fresh-frozen bone blocks for horizontal ridge augmentation in the upper maxilla: 6-month outcomes of a randomized controlled trial. Clin Implant Dent Relat Res 2014;16:116–123.
32. Lumetti S, Galli C, Manfredi E, et al. Correlation between density and resorption of fresh-frozen and autogenous bone grafts. Biomed Res Int 2014;2014:508328.
33. Fu JH, Oh T, Benavides E, Rudek I, Wang HL. A randomized clinical trial evaluating the efficacy of the sandwich bone augmentation technique in increasing buccal bone thickness during implant placement surgery. I. Clinical and radiographic parameters. Clin Oral Implants Res 2014;25:458–467.
34. Merli M, Moscatelli M, Mariotti G, et al. Membranes and bone substitutes in a one-stage procedure for horizontal bone augmentation: A histologic double-blind parallel randomized controlled trial. Int J Periodontics Restorative Dent 2015;35:463–471.
35. Mordenfeld A, Johansson CB, Albrektsson T, Hallman M. A randomized and controlled clinical trial of two different compositions of deproteinized bovine bone and autogenous bone used for lateral ridge augmentation. Clin Oral Implants Res 2014;25:310–320.
36. Park SH, Lee KW, Oh TJ, Misch CE, Shotwell J, Wang HL. Effect of absorbable membranes on sandwich bone augmentation. Clin Oral Implants Res 2008;19:32–41.
37. Pinho MN, Roriz VL, Novaes AB Jr, et al. Titanium membranes in prevention of alveolar collapse after tooth extraction. Implant Dent 2006;15:53–61.
38. Buser D, Brägger U, Lang NP, Nyman S. Regeneration and enlargement of jaw bone using guided tissue regeneration. Clin Oral Implants Res 1990;1:22–32.
39. Buser D, Dula K, Lang NP, Nyman S. Long-term stability of osseointegrated implants in bone regenerated with the membrane technique. 5-year results of a prospective study with 12 implants. Clin Oral Implants Res 1996;7:175–183.
40. Fugazzotto PA, Shanaman R, Manos T, Shectman R. Guided bone regeneration around titanium implants: Report of the treatment of 1,503 sites with clinical reentries. Int J Periodontics Restorative Dent 1997;17:292, 293–299.

41. Hämmerle CH, Jung RE, Feloutzis A. A systematic review of the survival of implants in bone sites augmented with barrier membranes (guided bone regeneration) in partially edentulous patients. J Clin Periodontol 2002;29(suppl):s226–s231; discussion 232–233.
42. Sanz-Sánchez I, Ortiz-Vigón A, Sanz-Martín I, Figuero E, Sanz M. Effectiveness of lateral bone augmentation on the alveolar crest dimension: A systematic review and meta-analysis. J Dent Res 2015;94(suppl):s128–s142.
43. Sajid MA, Warraich RA, Abid H, Ehsan-ul-Haq M, Shah KL, Khan Z. Reconstruction of mandibular defects with autogenous bone grafts: A review of 30 cases. J Ayub Med Coll Abbottabad 2011;23:82–85.
44. Burchardt H. The biology of bone graft repair. Clin Orthop Relat Res 1983;(174):28–42.
45. Huang HY, Ogata Y, Hanley J, Finkelman M, Hur Y. Crestal bone resorption in augmented bone using mineralized freeze-dried bone allograft or pristine bone during submerged implant healing: A prospective study in humans. Clin Oral Implants Res 2016;27:e25–e30.
46. Cammack GV 2nd, Nevins M, Clem DS 3rd, Hatch JP, Mellonig JT. Histologic evaluation of mineralized and demineralized freeze-dried bone allograft for ridge and sinus augmentations. Int J Periodontics Restorative Dent 2005;25:231–237.
47. Arvidson K. A subsequent two-stage dental implant system and its clinical application. Periodontol 2000 1998;17:96–105.
48. Tsai ES, Crohin CC, Weber HP. A five-year evaluation of implants placed in extraction sockets. J West Soc Periodontol Periodontal Abstr 2000;48:37–47.
49. Leonhardt A, Gröndahl K, Bergström C, Lekholm U. Long-term follow-up of osseointegrated titanium implants using clinical, radiographic and microbiological parameters. Clin Oral Implants Res 2002;13:127–132.
50. Jung RE, Pjetursson BE, Glauser R, Zembic A, Zwahlen M, Lang NP. A systematic review of the 5-year survival and complication rates of implant-supported single crowns. Clin Oral Implants Res 2008;19:119–130.
51. Benić GI, Jung RE, Siegenthaler DW, Hämmerle CH. Clinical and radiographic comparison of implants in regenerated or native bone: 5-year results. Clin Oral Implants Res 2009;20:507–513.
52. Garaicoa C, Suarez F, Fu JH, et al. Using cone beam computed tomography angle for predicting the outcome of horizontal bone augmentation. Clin Implant Dent Relat Res 2015;17:717–723.