Vertical Ridge Augmentation in the Atrophic Mandible: A Systematic Review and Meta-Analysis

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Purpose: *To systematically appraise the effectiveness/reliability of vertical ridge augmentation (VRA) in the atrophic mandible. Articles that addressed any one of the following four areas were included in this study: amount of VRA, implant survival (ISR) and success rates (SSR) in the area of newly regenerated bone, complication rate during the bone augmentation procedure, and bone resorption.* ***Materials and Methods:*** *An electronic literature search was conducted by two independent reviewers in several databases, including MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Cochrane Oral Health Group Trials Register databases for articles reporting VRA in the atrophic mandible via distraction osteogenesis (DO), inlay block grafting (IBG), onlay block grafting (OBG), and guided bone regeneration (GBR). For meta-analysis, two primary (VRA and ISR [%]) and two secondary outcomes were studied (SSR [%] and vertical bone resorption [VBR] [%]). Additionally, for qualitative assessment, complications (ie, causes of failure) were further extracted and comprehensively described.* ***Results:*** *Overall, 73 full-text papers were evaluated. Of these, 52 articles fulfilled the inclusion criteria. The weight mean (WM) of VRA (± SD) was 4.49 ± 0.33 mm (95% CI: 3.85 to 5.14 mm). It was most notable that DO involved greater VRA than IBG, and thus, significantly higher than GBR and OBG. The technique significantly influenced the mean VRA obtained (P < .001). Nonetheless, no technique showed superiority in terms of ISR or SSR. VBR and complications were shown to be minimized for GBR.* ***Conclusion:*** *If ≈ 4 mm of VRA is needed, any technique in optimum local and systemic conditions should be equally reliable in the atrophic mandible. However, when greater VRA is needed, DO and IBG have demonstrated accuracy. By means of complication and VBR rates, GBR was shown to have the lowest. For ISR and SSR, no statistical differences existed among all techniques. Controlled studies are needed to examine the long-term peri-implant bone fate and the frequency of biologic complications in each technique applied for the vertical augmentation of the atrophied mandible.* Int J Oral Maxillofac Implants 2017;32:xxx–xxx. doi: 10.11607/jomi.4861

Keywords: *alveolar bone, bone, dental implant, endosseous implant, evidence-based dentistry, trabecular*

In the era of modern implantology, the advancement of techniques and biomaterials as well as implant micro-/macrodesigns allows clinicians to confront challenging scenarios with high predictability. For instance, short[1] and narrow[2] implants in the edentulous ridges permit oral rehabilitation in the areas of limited bone height and width. For example, short dental implants have shown not only to be effective in restoring function,[1,3] but also for having acceptable long-term outcomes in the presence of an incommensurable crown-to-implant ratio.[4] However, in cases of severe ridge atrophy, the aforementioned alternatives might not be feasible. As such, bone regenerative procedures are needed. It has been shown that in areas of slight vertical atrophy (≤ 3 mm), more conservative approaches are often recommended (ie, orthodontic extrusion); however, for medium (4 to 6 mm) or large (> 7 mm) defects, guided bone regeneration (GBR) or onlay bone graft (OBG) might be preferred.[5] Furthermore, not only the size of the defect but also the defect location might play a role in deciding what procedure to choose. In the posterior atrophic maxilla, sinus floor augmentation has shown high reliability in achieving mechanical and biologic stability.[6] On the contrary, in the resorbed mandible,

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GBR,[7,8] distraction osteogenesis (DO),[9] or block grafting[10] have been advocated with the understanding of less predictable outcomes. This may be attributed to the mandibular bone density/composition (dense trabecular bone with a thick cortical layer)[11] when compared with the maxilla. For instance, bone microarchitecture (namely, bone density or quality) is determined by the combination of factors associated with trabecular morphology and porosity.[12] Indeed, the maxilla is poorer in bone density compared with the mandible, where a thicker cortical bone layer and higher presence of lamellar bone are determinants in implant primary stability.[13,14] Nevertheless, these properties may negatively impact blood supply, and thus, its regenerative potential.[15] Consequently, to overcome atrophy, strategies should be systematically studied.

Some reviews have addressed the predictability and potential of the different regenerative approaches by means of bone gain and implant survival rate (ISR).[16,17] In terms of technique, GBR reported a vertical increase of 2 to 8 mm, with ISR ranging from 92.1% to 100%[16,17]; for DO, the vertical dimension achieved ranged from 5 to 15 mm and an ISR of 90% to 100%; for OBG, depending on the source of the graft, it was 4.22 to 4.6 mm when extra- or intraoral grafts were used, with the ISR ranging from 76% to 100%.[16,17] Nevertheless, to the best of the authors' knowledge, there is no study investigating meta-analytically the success of all the procedures framing all the determinants that might lead to better clinical and histologic outcomes. Therefore, the aim of the present systematic review was to appraise the effectiveness/reliability of vertical ridge augmentation (VRA) procedures in the atrophic mandible by means of amount of vertical bone gain, implant survival/success rate, complication rate, and resorption.

MATERIALS AND METHODS

Information Sources

An electronic literature search was conducted by two independent reviewers (B.E. and A.M.) in several databases, including MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Cochrane Oral Health Group Trials Register databases for articles written in English up to January 2015.

The focused PICO question was as follows:

- P: Completely or partially edentulous healthy patients with severe/moderate vertical with/without horizontal atrophy in the edentulous mandible
- I: Regenerative approaches for vertical with/without horizontal bone augmentation to achieve implant stability at the same/second stage:
- distraction osteogenesis (DO),
- guided bone regeneration (GBR),
- onlay block bone grafting (OBG),
- inlay block bone grafting (IBG)
- C: Other regenerative approach calculating the weight mean of the included studies
- O: Quantitative: Total bone gain, implant survival and success rates; Qualitative: Causes of failure and histologic/morphologic findings

Screening Process

For the PubMed library, combinations of controlled terms (MeSH and EMTREE) and keywords were used whenever possible. The search terms were used, where "[mh]" represented the MeSH terms and "[tiab]" represented title and/or abstract. In addition, other terms not indexed as MeSH and filters were applied. As such, the key terms used were as follows:

PubMed Library:

- DO: (distraction osteogeneses [MeSH Terms]) OR distraction osteogenesis) OR osteogenesis, distraction [MeSH Terms]) AND mandible [MeSH Terms]) AND dimension, vertical [MeSH Terms]) OR alveolar bone atrophy [MeSH Terms]
- GBR: (bone regeneration [MeSH Terms]) OR material, bone replacement [MeSH Terms]) AND dimension, vertical [MeSH Terms]) OR alveolar bone atrophy [MeSH Terms]) OR alveolar bone loss [MeSH Terms]
- OBG: (onlay [MeSH Terms]) AND bone regeneration [MeSH Terms]) AND dimension, vertical [MeSH Terms]) OR alveolar bone atrophy [MeSH Terms]) OR alveolar bone loss [MeSH Terms]
- IBG: (inlay [MeSH Terms]) AND bone regeneration [MeSH Terms]) AND dimension, vertical [MeSH Terms]) OR alveolar bone atrophy [MeSH Terms]) OR alveolar bone loss [MeSH Terms]

Embase Library and Cochrane Library (Title, Abstract, Keywords):

- DO: distraction osteogenesis AND bone augmentation AND vertical OR distraction osteogenesis AND bone loss OR atrophic AND vertical AND 'clinical trials' AND 'humans'
- GBR: guided bone regeneration AND bone augmentation AND vertical OR guided bone regeneration AND bone loss OR atrophic AND vertical AND 'clinical trials' AND 'humans'
- OBG: onlay block graft AND bone augmentation AND vertical OR onlay graft AND bone loss OR atrophic AND vertical AND 'clinical trials' AND 'humans'
- IBG: inlay block graft AND bone augmentation AND vertical OR inlay graft AND bone loss OR atrophic AND vertical AND 'clinical trials' AND 'humans'

Additionally, a manual search of periodontics and implantology-related journals, including *Journal of Dental Research*, *Journal of Clinical Periodontology*, *Journal of Periodontology,* and *The International Journal of Periodontics & Restorative Dentistry*, from January 2014 up to February 2015, was also performed to ensure a thorough screening process. Furthermore, references of included articles were screened to check all available articles.

Eligibility Criteria

Articles were included in this systematic review if they met the following inclusion criteria: prospective or retrospective, randomized or not; cohort or case series involving human subjects in which clinical outcomes of vertical bone augmentation for the atrophic mandible utilized regenerative approaches. Accordingly, several factors such as study design, number of patients included at 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 membrane were used) were extracted from the selected studies and analyzed. Moreover, in order to address more comprehensively the aim of this study, parameters such as bone gain, bone resorption, graft survival, implant survival and success rates, and surgical complications were extracted (Tables 1 and 2). On the contrary, case reports or case series with fewer than five subjects, systematic reviews, preclinical animal studies, and human trials not studying the utilization of any of the aforementioned regenerative therapies were excluded. Moreover, human trials with missing information were further excluded (Table 3).

Risk of Bias

Two reviewers (B.E. and A.M.) designed and assessed the proposal for the present project to make sure the PRISMA and STROBE guidelines were followed to avoid risk of bias and provide a high level of evidence. STROBE stands for an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers, and journal editors involved in the conduct and dissemination of observational studies. It consists of a checklist of 22 items that should be fulfilled in a systematic review. PRISMA consists of a 27-item checklist and a four-phase flow diagram.

Qualitative Assessment

The criteria used to evaluate the quality of the selected randomized controlled trials (RCTs) were modified from the randomized clinical trial checklist of the Cochrane Center and the 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. 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] Two independent reviewers (B.E. and A.M.) evaluated all the included articles. On the other hand, for nonrandomized clinical trials, the New Castle Ottawa Scale (NOS) was used to rank risk of bias of included studies.

Statistical Analysis

The software R 3.0.2 was utilized for the meta-analysis. For the meta-analysis, two primary (total bone gain [mm] and implant survival [%]) and two secondary outcomes were studied (implant success [%] and vertical bone resorption [VBR] [mm]). Additionally, for qualitative assessment, complications (ie, causes of failure) and histologic findings were further extracted and comprehensively described. Since not all the studies provided all these data, the follow methodology for the analysis was conducted:

- For studies that reported two groups (test and control) and only one represented the regenerative approach, such information was retrieved to be included in the analysis.
- Implant survival and success rates were extracted independently, when possible.
- For bone gain, only studies reporting mean value ± standard deviation were included in the analysis.
- High heterogeneity was preliminarily found for VBR due to the variability in the measurement units (mm vs %). Therefore, it was opted to analyze the mean for both values but without performing a meta-analysis.
- Bone gain was analyzed as the subject unit, and ISR and SSR were analyzed as the implant unit.
- Within each group (approach), the meta-analysis consisted of an estimation of ISR and SSR and total bone gain based on the mean value through a random effect model.
- To study the primary outcome, a meta-regression with the variable that represented the approach and under the random effect approach was carried out. This analysis provides global estimations to figure out whether any approach has statistical superiority compared with the others. It is based upon the inverse variances model of DerSimonian and Laird.

Study of Heterogeneity

It was carried out through the statistical calculation of I^2 (percentage of variability of estimated effect that can be attributed to the heterogeneity of the effects) and

Table 1a Characteristics for Included Studies in DO

Author (year)	Study design	Groups	No. of patients	No. of distractors	Location of augmented sites	Type of distractor	Distractor system	Additional grafting material/growth factor	Bone augmentation achieved at baseline (mm)	Healing period (mo)	Resorption
Amir et al[50] (2006)	PS	NCG	16	16	NC	(Groningen distractor, KLS Martin) (KLS Martin and Mondeal Medical System)	I/E	N	4.74 ± 2.08	1–5	NR
Bianchi et al[20] (2008)	PS	IL	6	7	P	–	–	N	5.91 ± 0.76	3–4	14.2%
		DO	5	5	P	KLS Martin	E	N	10.36 ± 2.95	3–4	14.0 %
Chiapasco et al[60] (2004)	PS	GBR	6	6	P/A	–	–	MR/CH	4.9 ± 1.52	6–7	NC
		DO	9	9	P/A	Gebrüder Martin	I	N	6.5 ± 1.43	2–3	NC
Chiapasco et al[51] (2006)	PS	NCG	7	7	A/P	Track 1,5 Gebrüder Martin	E	N	6.857 ± 1.34	3	2.40 mm
Chiapasco et al[35] (2007)	PRD	OL	8	-	P	–	–	AG particled MR	4.6	4–5	1.1 mm
		DO	9	9	P	Gebrüder Martin	E	N	5.3	2–3	1.3 mm
Ettl et al[52] (2010)	RS	NCG	NR	25	A/P	Track Distractor 1.0 or 1.5 mm, Martin	E	N	8.2	4.5	1.9 mm
Faysal et al[53] (2013)	PS	Test	9	9	A	Modus; Medartis	E	N	6.968 ± 0.917	6	(11.82%) / 6 months (19.66%) / 1 year (22.52%)
		Control	9	9	A	Modus; Medartis	E	N	7.031 ± 0.900	6	(10.34%)/ 6 months (15.60%) /1 year (19.99%)
Gaggl et al[49] (2000)	CS	NCG	17	34	A/P	SIS Trade Systems	I	N	5.29 ± 0.77	1.5	NR
Günbay et al[54] (2008)	CS	NCG	6	6	A/P	Lead System distractors (Modus Ars 1.5; Medartis)	I	N	7.835 ± 1.94	2	NR
Klug et al[55] (2001)	CS	NCG	10	13	A/P	Track 1.0 distractor, Gebrüder Martin	E (4 cases with titanium membranes)	N	7.5 ± 1.26	2.5	NR
Perdijk et al[56] (2007)	RS	Test	45	45	A	Mondeal Vertical Distraction device, Mondeal	I	N	6.0 ± 1.7	3	NR
		Control	43	43	A	Endo-Distraction Krenkel, Mondeal	I	N	9.2 ± 4.13	3	NR
Raghoebar et al[57] (2002)	CS	NCG	10	10	A	The Groningen Distraction Device (GDD, Martin Medizin Technik)	I	N	6.8 ± 0.78	2	NR
Robiony et al[9] (2008)	CS	NCG	12	N/R	A/P	Track 1.5 mm, Gebrüder Martin or a bidirectional device (FAD, Cizeta Surgical)	I	ILC, with autologous platelet concentrate	7.4 ± 2.45	2.5	2.3% (3 mo) 18.7% after 5 years
Schortinghuis et al[58] (2005)	RCT	Test	4	4	A	The Groningen Distraction Device (GDD, Martin Medizin Technik)	I	Active Sonic Accelerated Fracture Healing System devices were used for ultrasound treatment (SAFHS model 20001, Smith & Nephew, Memphis, TN, USA)	6.6 ± 1.1	31 ± 3.8 days	NR
		Control	4	4	A	The Groningen Distraction Device (GDD, Martin Medizin Technik)	I	N			
Türker et al[59] (2007)	CS	NCG	10	10	A	LEAD System (Leibinger)	I	N	9.6 ± 1.77	3	NR

NR = not reported; NCG = no control group; NC = unclear; CS = case series; PS = prospective; PRD = prospective randomized; RS= retrospective; RCT = randomized clinical trial; A = anterior; P = posterior; I =intraosseous; E = extraosseous; N = No; CH = chin; MR = mandibular ramus; NDF = no distractor failed; NFB = no failed block; ILC = illiac crest; AG = autogenous graft; IL = inlay; OL = onlay; DO = distraction osteogenesis; GBR = guided bone regeneration.

Final bone gain (mm)	No. of implants placed	Implant loading protocol (mo)	Follow-up of implants (mo)	Implant survival (%)	Implant success (%)	Failed DO			Histologic findings			
						Failed DO (%)	Timing (mo)	Cause	Timepoint (mo)	Connective tissue (%)	Remaining particles (%)	Newly formed bone (%)
NC	NR	NR	NR	NR	NR	NR	NR	NR	3	55.2 ± 6.6	NR	NR
5.02 ± 0.57	21	3/4	22.5	100	95	NFB	NFB	NFB	NR	NR	NR	NR
8.38 ± 1.74	16	4	30	100	93.7	NDF	NDF	NDF				
NC	15	Immediate/ 6	24–36	100	NC	33.33	3 to 10 wk	Exposure	NR	NR	NR	NR
NC	30	3	24–36	100	NC	NDF	NDF	NDF				
NR	20	3	18	100	95	NDF	NDF	NDF	3	61.5 ± 11.70	NR	38.5 ± 11.70
NR	19	NR	38	100	89.5	12.5	2	Partial exposure	NR	NR	NR	NR
NR	21	NR	41.3	100	94.7	11.11	NR	Impossibility of the distracted segment,incorrect design of the vertical osteotomic lines				
6.4	NC	NC	45.8	NC	NR	8	4	Device breakage/ mandibular fracture	NR	NR	NR	NR
5.35 ± 0.68	18	2	12	94	94.4	NDF	NDF	NDF	NR	NR	NR	NR
5.59 ± 0.60	18	2	12	94	94.4	NDF	NDF	NDF				
NR	34	4/6	9	97.06	NR	NDF	NDF	NDF	NR	NR	NR	NR
NR	14	3/4	50	NR	NR	16.6	NR	Lack of device activation	NR	NR	NR	NR
NR	NR	NR	10	NR	NR	10	NR	Fracture of the microplate distractor	NR	NR	NR	NR
NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	20	3	11.2 ± 4.3	95	NR	NDF	NDF	NDF	2	NR	NR	NR
11 (7.6 ± 0.78) 12 (7.12 ± 2.3)	47	6	60	97.9	91.5	8.33	NR	Secondary to scar retraction of the mobilized segment	NR	NR	NR	NR
NR	16	NR	30.1 ± 4.1	NR	NR	NDF	NDF	NDF	1	NR	NR	NR
NR	NR	NR	NR	NR	NR	10	3	The transported segment was resorbed at the consolidation period	3/12	NR	NR	NR

Table 1b Characteristics for Included Studies in OBG

Author (year)	Study design	Groups	No. of patients	No. of sites grafted	Location of grafted sites	Bone augmentation (onlay/inlay)	Type of bone block graft	Fixed (Y/N)	Membrane (Y/N)	Additional grafting material/ growth factor	Bone augmentation achieved at baseline (mm/cm^3)	Healing period (mo)
Amorfini et al[8] (2014)	RCT	Test	8	16	P	OL	ALG	Y	Y	Particled ALG/ rhPDGF-BB	0.19 cm^3	6
		Control	8	16	P	GBR	ABBM + AG (MR) particled	Y	Y	N /rhPDGF-BB	0.19 cm^3	6
Chiapasco et al[35] (2007)	PRD	Test	8	8	P	OL	MR	Y	N	AG particled MR	4.6 mm	4–5
		Control	9	9	P	DO	–	Y	N	N	5.3 mm	2–3
Cordaro et al[36] (2002)	CS	NCG	5	8	P	OL	MR/CH	Y	N	AG bone chip MR/CH	2.4 ± 0.2 mm	5
Dias et al[37] (2014)	PS	NCG	12	16	P	OL	HFF ALG	Y	Y	XG	4.8 ± 1.6 mm	6
Felice et al[24] (2009)	CCT	Test	10	10	P	IL	ILC	Y	Y	ILC particulated	4.9 mm	4
		Control	10	10	P	OL	ILC	Y	Y	N	6.5 mm	
Khojasteh et al[34] (2012)	R	NCG	NC	24	P	OL	AG (MR/ CH)	Y	N	ALG/XG/Mono-phasic synthetic/ biphasic synthetic: (mixed with PRGF)	2.25 ± 1.05 mm	5
Nissan et al[38] (2011)	PS	NCG	21	11	P	OL	HFF ALG	Y	Y	HFF ALG DBBM	4.3 ± 1.6 mm	6
Peñarrocha-Oltra et al[39] (2014)	RS	Test	20	26	P	OL	MR/CH	Y	Y	Particled AG + ß-TCP	NR	6
		Control	17	–	P	SI	–	–	–	–	–	2
Pistilli et al[40] (2014)	RCT	Test	20	7	P	OL	XG	Y	Y	XG particled	NC	7
		Control	20	5	P	OL	MR/ILC	Y	Y	AG (MR/ILC) particled	NC	4
Proussaefs and Lozada[41] (2005)	PS	NCG	12	10	P	OL	MR/CH	Y	N	AG (MR/CH) and DBBM	5.7 ± 1.05 mm	6
Roccuzzo et al[42] (2004)	PS	NCG	9	9	P	OL	MR/CH	Y	TM	AG (MR/CH) particled	NR	4.5
Roccuzzo et al[43] (2007)	CCT	Test	4	4	P	OL	MR	Y	TM	AG (MR) particled	4	4
		Control	8	9		OL	MR	Y	N	AG (MR) particled	5.4 ± 1.01 mm	
Rochietta et al[48] (2015)	PS	Test	10	11	P	GBR	–	Y	Y	AG particulate	5.4 mm (3–6 mm)	6–10
	PS	Control		11	P	OL	Intra oral	Y	Y	Intra oral	3.18 mm (2–5 mm)	6–10
Sbordone et al[44] (2012)	RS	NCG	13	13	NC	OL	ILC	Y	N	AG (ILC) particled	1.25 cm^3	3–5
Smolka et al[45] (2006)	PS	NCG	10	10	A	OL	CA	Y	N	N	11.8 ± 2.48 mm	6
van der Meij et al[46] (2005)	RS	NCG	17	17	P	OL	ILC	N	N	ILC particled	8.5 mm	3
Verhoeven et al[47] (2006)	PS	NCG	13 (–2)	13	A	OL	ILC	Y	N	N	8.9 mm	3

RCT = randomized clinical trial; R = retrospective; CS = case series; NCG = no control group; PRD = prospective randomized; CCT = controlled clinical trial; OL = onlay; DO = osteo distractor; G = group; AG = autogenous; XG = xenograft; P = posterior; A = anterior; GBR = guided bone regeneration; ALG = allograft; ALP = alloplastic; ILC = iliac crest; Y = yes; N = no; SI = short implants; TM = titanium mesh; rhPDGF-BB = platelet-derived growth factor-BB; PRGF= plasma rich in growth factors; ß-TCP = ß-tricalcium phosphate; HFF = human fresh-frozen; MR = mandibular ramus; CH = chin; CA = calvaria; PS = prospective; NC = unclear; IL = inlay; NR = not reported; ABBM = anorganic bovine bone mineral; NFB = no failed blocks; DBBM = deproteinized bovine bone mineral.

Resorption	Final bone gain	No. of implants placed	Implant loading protocol	Follow-up of implants (mo)	Implant survival (%)	Implant success (%)	Failed blocks (%)			Histologic findings			
							Failed blocks (%)	Timing (mo)	Cause	Timepoint (mo)	Connective tissue (%)	Remaining particles (%)	Newly formed bone (%)
3.3%	0.16 cm^3	25	6	12	100	NR	NFB	NFB	NFB	NR	NR	NR	NR
3.8%	0.18 cm^3	25	6	12	100	NR	NR	NR	NR				
1.1 ± 0.5 mm	NR	19	NR	38	100	89.5	12.5	2	Partial exposure	NR	NR	NR	NR
1.3 ± 0.4 mm	NR	21		41.3	100	94.7	11.11	NR	Impossibility of the distracted segment, incorrect design of the vertical osteotomic lines	NR	NR	NR	NR
43.5 %	1.4 ± 0.2 mm	10	6	12	100	100	NFB	NFB	NFB	NR	NR	NR	NR
45%	2.6 ± 2 mm	30	6	26 ± 4.1	96.66	NR	NFB	NFB	NFB	6	48.6 ± 14.9	32.5 ± 14.8	18.9 ± 8.1
							NFB	NFB	NFB				
0.5 mm	4.1 mm	20	4	18	100	90	1	2 weeks	Buccal dehiscence	NR	NR	NR	NR
2.7 mm	4 mm	20			100	86.9	1	2 weeks	Dehiscence				
NR	3.6 ± 1.7 mm	NA	Conventional	20.3 ± 10.9	NR	NR	NC	NC	NC	NR	NR	NR	NR
0.5 ± 0.2 mm	NR	NC	3	37 ± 17	NC	NC	20.7	NR	NR	NR	NR	NR	NR
NR	NR	45	2	12	95.6	91.1	NFB	NFB	NFB	NR	NR	NR	NR
0.6 ± 0.3 mm	–	35	2	12	97.1	97.1	-	-	-				
NR	NR	NA	4	4	0	0	100	1	Dehiscence	NR	NR	NR	NR
NR	NR	NA	4	4	100	NR	NFB	NFB	NFB				
NR	4 ± 1.05 mm	NA	NC	NC	NR	NR	20	6	Block mobile	4-8	41 ± 12.05	24 ± 10.23	34.85 ± 9.97
NR	4.7 ± 0.94 mm	21	4–6	NC	100	100	NFB	NFB	NFB	NR	NR	NR	NR
0.5 mm	4 mm	NR	4–6	NC	NR	NR	16.6	1	Estensive mesh exposure	NR	NR	NR	NR
1.75 ± 1.28	5.2 ± 1.12 mm						33.3	4	Incomplete integration of graft, block mobile	NR	NR	NR	NR
0.09	2.91 mm	NR	3	NR	NR	NR	10	4	Abscess	6–10	NR	NR	26.62 ± 14.4
0.27	4.0 mm	NR			NR	NR	10	4	NR	6–10	NR	NR	42.34 ± 17.05
87%	NR	36	NR	72	100	NR	NR	NR	NR	NR	NR	NR	NR
0.68 mm (4.1%)	NR	20	3	30.3	95	NR	NFB	NFB	NFB	6	NR	NR	NR
15%	NC	34	3	48	NR	88.2	5.88	NR	Major dehiscences, partially loss of the grafted bone	NR	NR	NR	NR
49%	NR	24	3	96	100	NR	NFB	NFB	NFB	NR	NR	NR	NR

Table 1c Characteristics for Included Studies in IBG

Author (year)	Study design	Groups	No. of patients	No. of sites grafted	Location of grafted sites	Bone augmentation (onlay/inlay)	Type of bone block graft	Fixed (Y/N)	Membrane (Y/N)	Additional grafting material/ growth factor	Bone augmentation achieved at baseline (mm)	Healing period (mo)
Bianchi et al[20] (2008)	PS	DO	5	5	P	DO			N	N	10.36 ± 2.95	3–4
		IL	6	7	P	IL	ILC	Y	N	N	5.91 ± 0.76	3–4
Bormann et al[21] (2011)	RS	NCG	27	40	P / A	IL	MR	Y	Y	N	NR	3
											NR	
Brandtner et al[22] (2014)	RS	NCG	18	26	P	IL	CA / ILC /MR	N	N	XG and AG (NC)	6.5 ± 1.3	4
Dottore et al[23] (2012)	PS	Test	11	11	P	IL	NcHA	Y	N	NcHA	7.0 ± 2.6	6
		Control		11	P		AG(MR)	U	N	AG(MR) particulate	6.5 ± 1.6	
Felice et al[24] (2009)	CCT	Test	10	10	P	IL	ILC	Y	Y	ILC particulated	4.9	4
		Control	10	10	P	OL	ILC	Y	Y	N	6.5	
Felice et al[25] (2009)	RCT	Test	10	5	P	IL	ILC	Y	Y	ILC particled	–	4
		Control		5			ABBM	Y	Y	XG particled	NR	4
Felice et al[26] (2010)	RCT	Test (short implants)	60	–	P	–	–	–	–	N	–	4
		Control		30	P	IL	ABBM	Y	Y	XG particled	NR	4
Hölzle et al[27] (2011)	CS	NCG	10	10	A	IL	PCCP (ALP)	Y	N	N	NR	3
Kawakami et al[28] (2013)	PS	Test	11	11	P	IL	NcHA	Y	N	N	NR	6
		Control		11			MR	Y	N	N	NR	6
Laino et al[29] (2014)	RCS	Test	12		P	IL	CH	Y	Y	N	NR	6
		Control			P	IL	ALG	Y	Y	N	NR	6
Laviv et al[30] (2014)	PS	NCG	5	5	P / A	IL	XG particulate	Y	N	N	6.2	5
López-Cedrún[31] (2011)	RS	NCG	23	30	P	IL	6 ILC/24 ALG	Y	N	NR	NR	6
Marchetti et al[32] (2007)	RS	NCG	6	7	P	IL	ILC	Y	N	N	NR	3–4
Pelo et al[10] (2010)	CS	NCG	19	19	A	IL	ILC	Y	N	N	11 ± 1	6
					A						9.6 ± 0.2	6
					8 mm P						8.3 ± 0.1	6
					16 mm P						7.3	6
Scarano et al[33] (2011)	CS	NCG	9		P	IL	XG equine block	N	Y	XG porcine bone	14.5 ± 1.9 premolar 13.8 ± 0.5 molars	4

PS = prospective; RS = retrospective; CCT = control clinical trial; RCT= randomized clinical trial; RCS = randomized case series; DO = distractor osteogenesis; NCG = no control group; ABBM = anorganic bobine bone mineral; P = posterior; A = anterior; IL = inlay; OL =onlay; ILC = iliac crest; AG = autograft; NcHA = resorbable nonceramic hydroxyapatite; PCCP = particulate carbonated calcium phosphate bone cement; ALP = alloplastic; ALG = allograft; XG = xenograft; NR = no reported; NC = unclear; NFB = no failed blocks; CH = chin; MR = mandibular ramus; CA = calvarial; Y = yes; N = no; CS = case series; DBBM = deproteinized bovine bone mineral.

							Failed blocks			Histologic findings			
Resorption	Final bone gain (mm)	No. of implant placed	Implant loading protocol (mo)	Follow-up of implants (mo)	Implant survival (%)	Implant success (%)	Failed blocks (%)	Timing	Cause	Timepoint (mo)	Connective tissue (%)	Remaining particles (%)	Newly formed bone (%)
14.0% (1.4 mm)	8.38 ± 1.74	16	4	30	100	93.7	NR	NR	NR	NR	NR	NR	NR
14.2% (0.9 mm)	5.02 ± 0.57	21	3	22.5	100	95	NFB	NFB	NFB				
NR	Posterior = 3.14 ± 1.93	88	NR	17.55	100	NR	NFB	NFB	NFB	NR	NR	NR	NR
	Anterior = 6.28 ± 2.43						NFB	NFB	NFB				
2.3 mm	4.2 ± 1.4	53	4	31	100	NR	NFB	NFB	NFB	NR	NR	NR	NR
0.78 ± 0.82 mm	NA	22	6	12	95.45	90.9	NFB	NFB	NFB	NR	NR	NR	NR
1.02 ± 0.93 mm	NA	22											
0.5 mm	4.1	20	4	18	100	90	1	2 wk	Buccal dehiscence	NR	NR	NR	NR
2.7 mm	4	20			100	86.9	1	2 wk	Dehiscence	NR	NR	NR	NR
0.82 ± 0.59 mm	NR	10	4	16	90	NR	1	12 mo		4	46.7 ± 11.4	22.1 ± 9.5	31.2 ± 6.9
0.59 ± 0.4 mm	NR	10	4	16	90	NR	NFB	NFB	NFB	4	41.0 ± 7.7	32.0 ± 4.7	27.3 ± 7
–	–	60	4	12	98.4	NR	–	–	–	NR	NR	NR	NR
NR	NR	61	4	12	95.1	NR	2	4 mo	NR				
NR	NR	40	3	60	98	NR	NFB	NFB	NFB	NR	NR	NR	NR
NR	7.0 ± 1.76	22	6	6	90.91	NR	1	6 mo	Reabsorption	NR	NR	NR	NR
NR	6.5 ± 2.4	22	6	6	NC	NR	NFB	NFB	NFB				
NR	NC	72	NR	NR	NR	NR	NFB	NFB	NFB	6	NR	28.9 ± 5.05	30.6 ± 3.72
NR	NC									6	NR	19.56 ± 4.17	31.47 ± 2.26
NC	NC	NR	5	NC	NR	NR	NFB	NFB	NFB	NR	NR	NR	NR
NC	5.3	65	3	46.5	100	90.8	NFB	NFB	NFB	NR	NR	NR	NR
NA	6.5	21	3	15	100	NR	NFB	NFB	NFB	NR	NR	NR	NR
27%	8	73 A / 68 P	4	48	96 anterior	NR	NR	NR	NR	NR	NR	NR	NR
41.1%	5.6						NR	NR	NR				
43%	4.7				91 posterior	NR	NR	NR	NR				
46%	3.9						NR	NR	NR				
2.26 ± 0.3 mm at premolar 2.7 ± 0.3 mm in molars	NA	18	4	NC	100	NR	NFB	NFB	NFB	4	NR	33 ± 2.4	44 ± 2.1

Table 1d Characteristics for Included Studies in GBR

Author (year)	Study design	Groups	No. of patients	No. of sites grafted	Location of grafted sites	Bone augmentation GBR	Type of bone graft	Fixed (Y/N)	Membrane	Additional grafting material/ growth factor	Bone augmentation achieved at baseline height (mm/cm^3)	Healing period (mo)	Resorption
Amorfini et al[8] (2014)	RCT	Test	8	16	P	OL	ALG	Y	RCB	Particled ALG/ rhPDGF-BB	0.19 (0.14 to 0.25) cm^3	6	3.3%
		Control	8	16	P	GBR	ABBM + AG (MR) particled	Y	RCB	N /rhPDGF-BB	0.19 (0.14 to 0.25) cm^3	6	3.8%
Anitua et al[61] (2013)	RS	NCG	72	70%	P	GBR	ABBM + AG (from drilling); AG (from drilling) + PRGF-Endoret	N	PRGF	N	1 to 3 mm	4	1 mm
Artzi et al[62] (2003)	PS CS	NCG	7	7	P	GBR	DBBM	Y	TM	N	6.85 ± 1.06 mm	9	NR
Chiapasco et al[60] (2004)	PS	Test	6	6	P/A	GBR	MR/CH	Y	e-PTFE	N	4.9 ± 1.52 mm	6–7	NC
		Control	9	9	P/A	DO			N	N	6.5 ± 1.43 mm	2–3	NC
Fontana et al[63] (2008)	PS RCT	Test	5	5	P	GBR	ALG	Y	e-PTFE	N	5.15 ± 0.34 mm	6	0.45 ± 0.37 mm
		Control		5	P		AG (MR)	Y	e-PTFE	N	4.90 ± 0.93 mm		0.80 ± 1.08 mm
Llambés et al[7] (2007)	CS	NCG	11	14	P	GBR	AG (from drilling) + ABBM	N	e-PTFE	N	3.5 mm	4	0.5 mm
Merli et al[64] (2007)	RCT	Test	11	NR	P/A	GBR	MR/CH/TB	Y	RCB	N	2.93 ± 0.86 mm	6	0.77 ± 1.25 mm
		Control	11	NR	P/A	GBR			e-PTFE		2.73 ± 0.79 mm		0.25 ± 0.62 mm
Rocchietta et al[48] (2015)	PS CS	Test	10	11	P	GBR	AG particulate	Y	e-PTFE	N	5.45 mm (3–6 mm)	6–10	0.09
		Control		11	P	OL	Intraoral block graft	Y	e-PTFE	N	3.18 mm (2–5 mm)	6 –10	0.27
Ronda and Stacchi[65] (2011)	PS CS	NCG	52	69	P	GBR	ALG + AG (MR)	Y	e-PTFE	N	5.2 ± 1.8 mm	6	NR
Simion et al[66] (2007)	PS	NCG	7	10	P	GBR	DBBM (Bio-Oss) + AG (MR)	Y	e-PTFE	N	AG and DBBM 3.29 ± 1.17 mm	7	0.15 ± 0.73 mm
							AG (MR)				AG 3.85 ± 1.23 mm		
Todisco[67] (2010)	PS cohort	NCG	19	24	P/A	GBR	DBBM	Y	e-PTFE	N	5.25 ± 1.56 mm	12	1 mm

PS = prospective; RCT = randomized clinical trial; RS = retrospective; CS = case series; DO = osseous distractor; AG = autogenous; MR = mandibular ramus; CH = chin; TB = tuberosity; P = posterior; A = anterior; GBR = guided bone regeneration; ALG = allograft; Y = yes; N = no; TM = titanium mesh; ePTFE = expanded polytetrafluoroethylene; RCB = reabsorbable collagen barriers; PRGF = plasma rich in growth factors; OL = onlay; NR = not reported; NFB = no failed blocks; NC = unclear; NCG = no control group; NDF = no distractor failed; ABBM = anorganic bovine bone mineral; DBBM = deproteinized bovine bone mineral.

						Failed GBR			Histologic findings			
Final bone gain	No. of implants placed	Implant protocol (mo)	Follow-up of implants (mo)	Implant survival (%)	Implant success (%)	Failed GBR (%)	Timing (mo)	Cause	Timepoint (mo)	Connective tissue (%)	Remaining particles (%)	Newly formed bone (%)
0.16 cm^3	25	6	12	100	NR	NFB	NFB	NFB	NR	NR	NR	NR
0.18 cm^3	25	6	12	100	NR	NR	NR	NR	NR	NR	NR	NR
NR	43	Immediate	26; 12–24	98.2	NR	NFB	NFB	NFB	NR	NR	NR	NR
5.57 ± 0.53 mm	NC	9	24	100	NR	28.5	9	Exposure	9	NR	NR	NR
NC	15	Immediate/ 6	24–36	100	NC	33.33	1–2.5	Exposure	NR	NR	NR	NR
NC	30	3	24–36	100	NC	NDF	NDF	NDF	NR	NR	NR	NR
4.70 ± 048 mm	13	Immediate	12–36	100	NR	NFB	NFB	NFB	6	5.21 ± 7.43	3.20 ± 1.48	32.98 ± 8.27
4.10 ± 0.88 mm	12					NFB	NFB	NFB	6	16.40 ± 11.28	9.35 ± 2.55	34.13 ± 11.55
3 mm	32	Immediate/ 6	12	96.8	100	9.09	1	Exposure	6	NR	NR	NR
2.16 ± 1.51 mm	10	Immediate	6	100	NR	18	NR	Abscesses	NR	NR	NR	NR
2.48 ± 1.13 mm	11					9.09	1	Dehiscence/ infection	NR	NR	NR	NR
4.36 mm	NC	3	NR	NR	NR	10	4	Abscesses	6 –10	NR	NR	26.62 ± 14.4
2.91 mm	NC	3	NR	NR	NR	10	4	NR	6–10	NR	NR	42.34 ± 17.05
NR	187	Immediate	NR	NR	NR	5.8	1	Infection	NR	NR	NR	NR
3.15 ± 1.12 mm	27	Immediate	6	100	NR	10	3	Exposure	6	8.8 ± 13.51	8.63 ± 10.8	35.56 ± 11.68
		6–9.5								0	0	18.28 ± 9.47
NR	63	Delayed	12	100	NR	8.3	1	Exposure	12	NR	16.304 ± 16.7	38.56 ± 10.95

Table 2 Types of Complications and Their Frequency (%) for All the Techniques Studied

Technique	Complications	Average (%)	Evidence
IBG	Sensory disorder	3.8– 50	Brandtner et al (2014); Bormann et al (2011); Hölzle et al (2010); Laino et al (2014); Kawakami et al (2013); López-Cedrún (2011); Pelo et al (2010).
	Infection	10–20	Felice et al (2009); Laviv et al (2014)
	Excessive bone resorption	3.3–41	Brandtner et al (2014); Felice et al (2009); Hölzle et al (2010); López-Cedrún (2011); Pelo et al (2010)
	Prosthetic	2.5–10	Dottore et al (2012); Felice et al (2010); Laviv et al (2014)
	Dehiscence	8–30	Bormann et al (2011); Bianchi et al (2008); Felice et al (2009); Felice et al (2009); Felice et al (2010); Hölzle et al (2010); Laino et al (2014); Laviv et al (2014)
OBG	Sensory disorder	3.8–83	Chiapasco et al (2007); Cordaro et al (2002); Khojasteh et al (2012); Peñarrocha et al (2014); Roccuzzo et al (2004); Roccuzzo et al (2007); van der Meij et al (2005)
	Infection	10–16.6	Khojasteh et al (2012); Smolka et al (2006)
	Excessive bone resorption	4.1–49	Roccuzzo et al (2007); Sbordone et al (2012); Smolka et al (2006); van der Meij et al (2004); Verhoeven et al (2006)
	Dehiscence	3.8–45.8	Amforini et al (2013); Chiapasco et al (2007); Dias et al (2014); Khojasteh et al (2012); Peñarrocha et al (2014); Proussaefs et al (2005); Roccuzzo et al (2004); Roccuzzo et al (2007); Smolka et al (2006); van der Meij et al (2004); Verhoeven et al (2006)
	Prosthetic	5	Pistilli et al (2014)
	Graft failure	10–100	Amforini et al (2013); Chiapasco et al (2007); Nissan et al (2011); Pistilli et al (2014); Smolka et al (2006)
DO	Sensory disorder	8.3–57.14	Faysal et al (2013); Gaggl et al (2000); Günbay et al (2008); Perdijk et al (2007); Robiony et al (2008)
	Bone fracture	16.6–21	Perdijk et al (2007); Robiony et al (2008)
	Excessive bone resorption	10–21.6	Ettl et al (2010); Faysal et al (2013); Robiony et al (2007); Türker et al (2007)
	Prosthetic	6.8	Gaggl et al (2000)
	Dehiscence	8.3–20	Ettl et al (2010); Günbay et al(2008); Klug et al (2001); Raghoebar et al (2002); Robiony et al (2008)
	Lingual inclination vector	10–41.7	Chiapasco et al (2006); Ettl et al (2010); Günbay et al (2008); Perdijk et al (2007); Robiony et al (2008); Türker et al (2007)
	Removal/loose of the distraction	6.8–18.8	Ettl et al (2010); Gaggl et al (2000); Klug et al (2001);
GBR	Sensory disorder	18.8–20	Chiapasco et al (2004); Fontana et al (2008)
	Infection	5.8–31.8	Chiapasco et al (2004); Merli et al (2007); Rocchietta et al (2015); Ronda and Stacchi (2011)
	Dehiscence	8–27.27	Artzi et al (2003); Chiapasco et al (2004); Llambés (2007); Merli et al (2007); Simion et al (2007); Todisco (2010)

Table 3 Articles Excluded and Their Reasons for Exclusion

Case report: < 5 patients	Hwang et al (2004); Raghoebar et al (2000); Uckan et al (2002); Block et al (2009); Polini et al (2009); Cornelini et al (2000); Peñarrocha et al (2012); Urban et al (2014)
Studies in maxilla	Gaggl et al (2002); Gaggl et al (2005); Jensen et al (2002); Kim et al (2005)
Patients with medical history of oral tumor	Klesper et al (2002); Cheung et al (2013); Shen et al (2012)
Not separated information of mandible/maxilla	Froum et al (2008); Lizio et al (2009); Mazzonetto et al (2005); McAllister et al (2001); Schleier et al (2007); Rachmiel et al (2001); Watzak et al (2006); Chiapasco et al (2011); Chiapasco et al (2013); Kaner et al (2011); Kim (2013); Scavone Macedo et al (2011); Mertens et al (2012); Uckan et al (2008); Beitlitum et al (2010); Friedman et al (2011); Jung et al (2008); Urban et al (2009)
Not enough information	Feichtinger et al (2003); Enislidis (2005); Garcia Garcia et al (2002); Garcia Garcia et al (2003); Pérez-Sayáns et al (2013); Smolka et al (2006); Verhoeven et al (2010); Verhoeven et al (2013); Bell et al (2002); Funato et al (2013); Juodzbalys et al (2007); Pieri et al (2008); Miyamoto et al (2012); Simion et al (2001); Merli et al (2006)
Risk of sample recurrence	Bormann (2011); Esposito et al (2011); Felice et al (2008); Shon et al (2010); Proussaefs et al (2002); Sbordone (2009); Merli et al (2010)
Duplicate articles	Kawakami et al (2013); Bormann et al (2010); Pelo et al (2010)
Technical note	McAllister et al (2003); Louis (2010)
Prior to year 2000	Lekholm et al (1998); Lekholm et al (1999); Parma-Bentenati et al (1999); Peleg et al (1999)
Systematic review	Saulacic et al (2008); Maestre-Ferrín et al (2009); Esposito et al (2009); Milinkovic et al (2014); Rocchietta et al (2008)

the null statistic test. Galbraith graphs displayed the degree of heterogeneity. In studies where high heterogeneity was detected, a sensitivity analysis was conducted to study its source. For the risk of bias, Funnel graphs and the Egger test were conducted. The level of significance was 5% ($P = .05$).

RESULTS

Study Selection

An electronic and manual literature search resulted in a total of 4,705 publications for all the techniques studied, of which 1,183 were selected after evaluation of their abstracts. Seventy-five full-text papers were evaluated. Of these, 52 articles fulfilled the inclusion criteria (IBG [15],[10,20–33] OBG [17],[8,24,34–48] DO [15],[9,20,35,49–60] and GBR [11].[7,8,48,60–67] Six of these studies reported results for two different approaches, and thus, each approach was grouped with their corresponding one. Accordingly, they were analyzed for each group. For quantitative synthesis, 21 were meta-analyzed for VRA, 37 for ISR, and 13 for SSR (Fig 1). Excluded articles and their reasons are summarized in Table 3.

Qualitative Assessment

Nine out of the 52 included studies in the qualitative and quantitative analyses were RCTs. The randomized clinical trial checklist of the Cochrane Center and the CONSORT (Consolidated Standards of Reporting Trials) statement was used to score the quality of the studies. Low (55.5%) to moderate (44.5%) estimated potential risk of bias was found from the studies included in the qualitative appraisal. On the other hand, for nonrandomized clinical trials, the Newcastle Ottawa Scale (NOS) was applied to rank the study quality. The mean (± SD) NOS for the studies included in the present systematic review was 6.13 ± 1.87, failing generally in the "selection" section. This indicated "acceptable" quality of the nonrandomized clinical trials. It was not found to be superior by means of quality for any of the techniques assessed.

Intergroup Meta-Analysis

VRA. A total of 24 studies with 346 patients were analyzed. The WM of VRA (± SD) was 4.49 ± 0.33 mm (95% CI [3.85 to 5.14 mm]). The VRA was considered significantly not null ($P < .001$). It was most notable that DO involved higher VRA than IBG, and thus, higher than GBR and OBG. The technique significantly influenced the mean VRA obtained ($P < .001$). The results showed the large difference in VRA with respect to DO compared with OBG and GBR ($P < .001$ for both). Moreover, the difference was also significant with respect to IBG ($P = .011$). More VRA was achieved with IBG than with OBG ($P = .015$) and with GBR, although the difference was not statistically significant ($P = .084$) (Figs 2a to 2e).

The test of the residual heterogeneity ($P < .001$) suggests that, apart from the technique, there can be some other factors not contemplated in the design that might influence VRA. The Egger test concludes that a lack of publication bias can be stated ($P = .230$).

ISR. Overall, 1,353 implants provided data for the implant survival rate extracted from 40 included studies. The WM of ISR was 98.4% (95% CI: 97.6% to 99.2%). There is not enough statistical evidence to conclude that the technique affects ISR ($P = .245$). The high ISR achieved by GBR was at the limit of significance compared with IBG ($P = .054$) (Figs 3a to 3e).

SSR. There were 16 studies that provided SSR data, which involved 471 implants. The estimation of global SSR was 93.4% (95% CI: [91.3% to 95.4%]). The GBR group reported the highest SSR (100%). However, the other techniques had comparable results. Thus, there was not enough statistical evidence to conclude that the technique had any effect on SSR ($P = .307$) (Figs 4a to 4d).

VBR. It was not possible to perform a meta-analysis on this variable, given the heterogeneity and the lack of information of some studies. Qualitative analysis showed that the highest means occurred in IBG (1.60 mm), DO (1.47 mm), OBG (1.21 mm), and GBR (0.90 mm).

IBG

VRA. Six studies provided information on the final VRA, representing a sample of 95 patients. The result of the meta-analysis provided a mean gain (± SD) of 4.92 ± 0.34 mm (95% CI [4.26 to 5.58 mm]). The VRA was considered significantly not null ($P < .001$). Specifically, the heterogeneity between studies supposed 79.8% of the total variability ($I^2 = 0.798$). The result of the test of heterogeneity of DerSimonian and Laird) confirms its importance ($P = .001$). In other words, the individually estimated mean differed much compared with the intrastudies variability. A sensitivity analysis was performed to ensure homogeneity of the included studies. Excluding Kawakami et al's study,[28] the final mean bone gain was 4.66 ± 0.23 mm (95% CI [4.21 to 5.10 mm]). By applying this, the degree of heterogeneity was reduced to acceptable levels ($I^2 = 54.4\%$, $P = .064$). Kawakami et al provided a significantly higher VRA compared with the other studies.

ISR. Of the included studies, 13 with 614 implants provided ISR data and could be meta-analyzed. The WM of ISR was 97.3% (95% CI: 95.4% to 99.2%). Due to the existent studies with null variability, it is not possible to estimate the value I^2, but descriptively, the ISR analysis showed that two studies seemed quite heterogeneous in their conclusions with regard to the rest.[25,28]

SSR. Four studies provided information on the SSR, which supposed a global sample of 150 implants. The

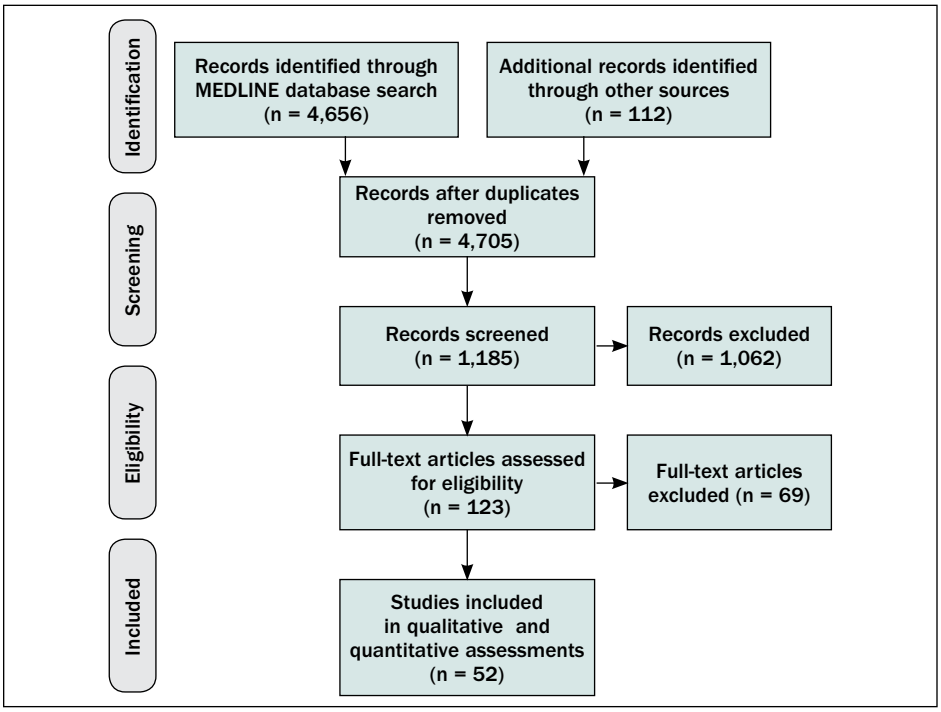
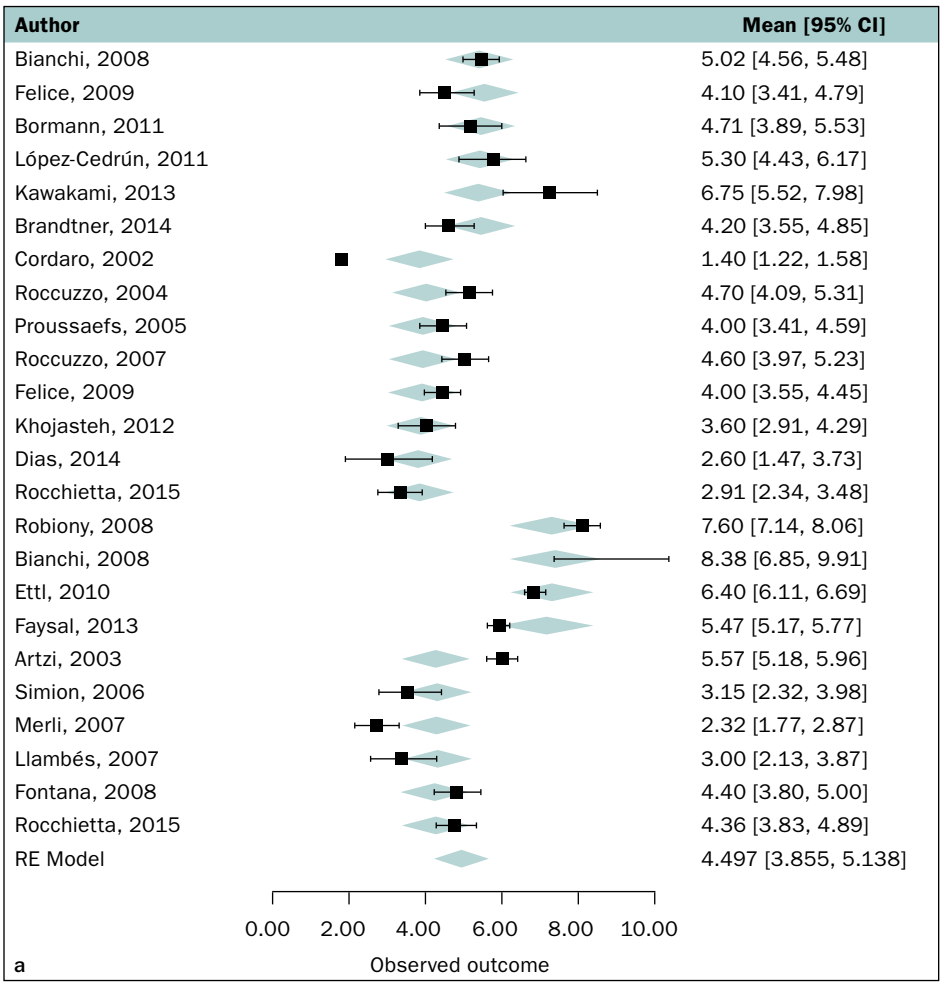


Fig 1 PRISMA flowchart of the screening process.



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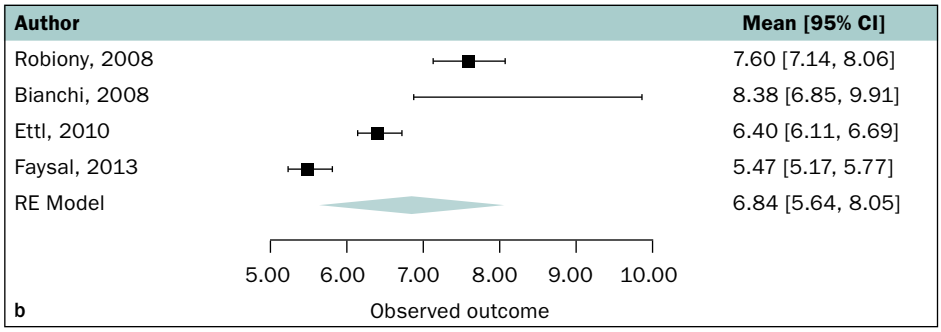
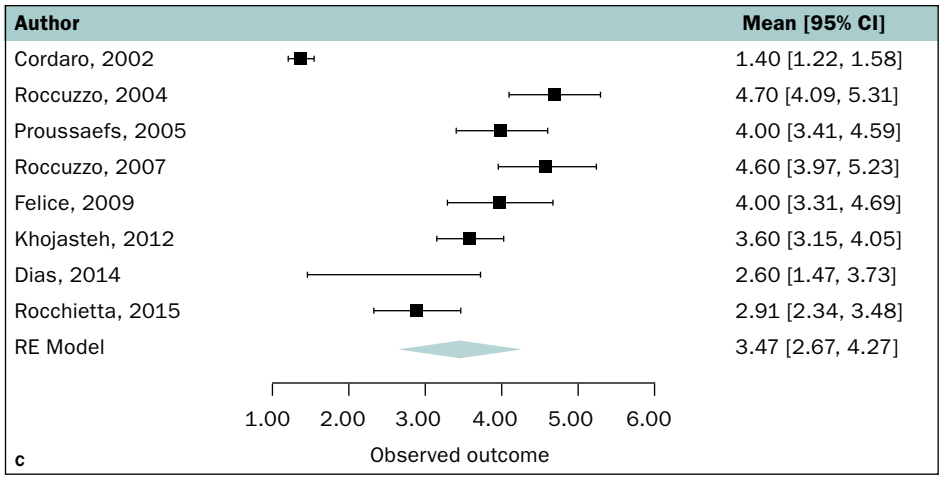
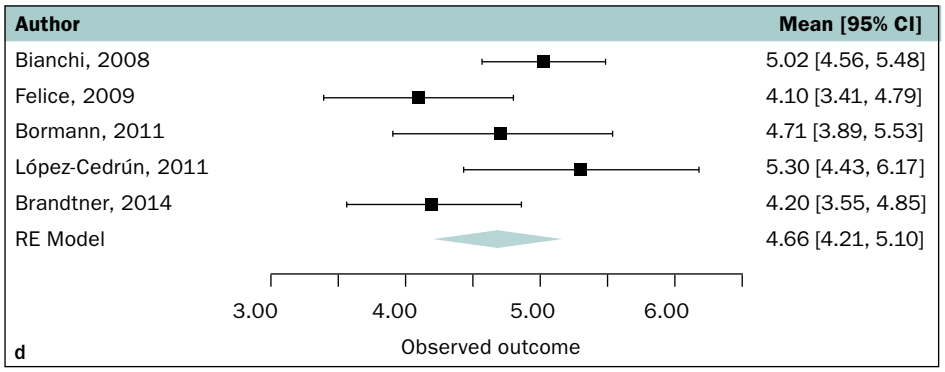






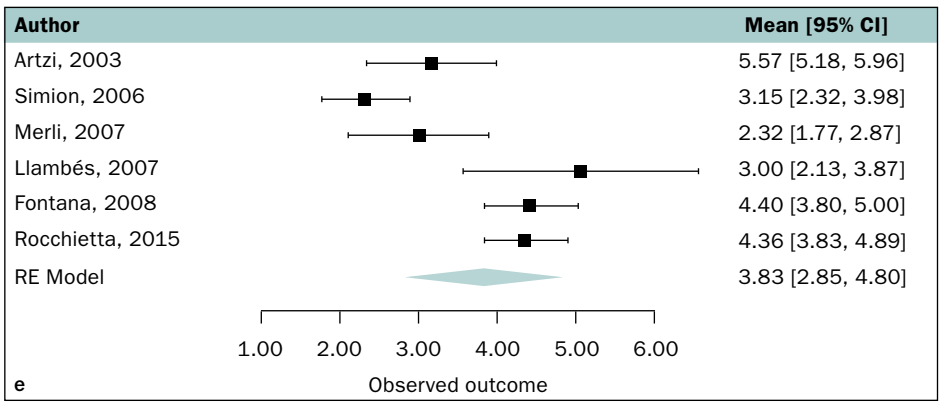
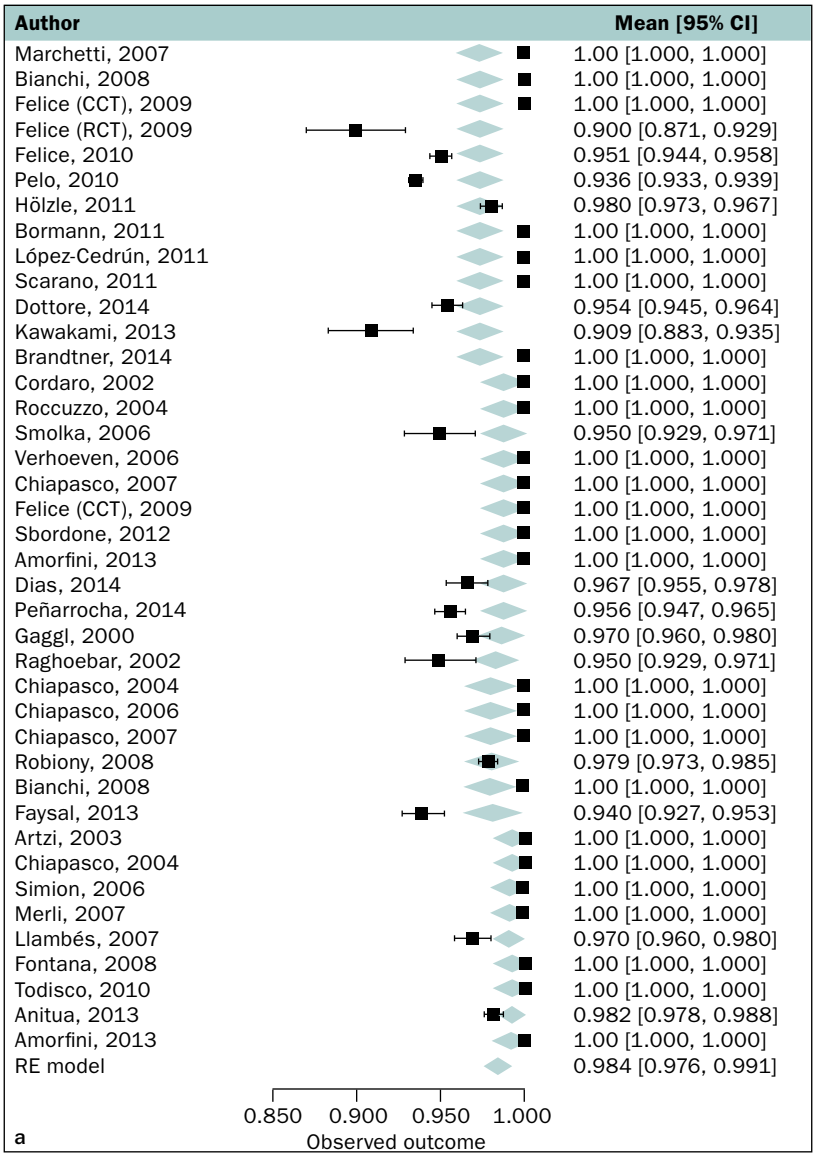


Fig 2 Funnel plots for the primary outcome vertical ridge augmentation (mean [95% CI]): *(a, facing page)* global, *(b)* DO, *(c)* OBG, *(d)* IBG, and *(e)* GBR.



WM SSR was 91.7% (95% CI [89.6 to 93.8 mm]). The heterogeneity test confirmed that for any study, it is questionable how the SSR compared with the rest (I^2 = 86.3%, P = .001). Bianchi et al[20] showed a statistically higher SSR compared with the other studies, even though the Galbraith test showed that homogeneity had to be considered.

OBG

VRA. Eight studies contributed with information about the final VRA, with a global sample size of 125 patients. The result of the meta-analysis provided a mean gain of 3.47 ± 0.41 mm (95% CI [2.67 to 4.27 mm]). The VRA was statistically significant (P < .001). Cordaro et al provided a medium gain markedly lower than the other works, which represented the cause of the high heterogeneity (I^2 = 95.2%, P < .001).[36] Egger's test concluded that there was insufficient statistical evidence to suspect the existence of bias (z = 0.83, P = .406).

ISR. Ten studies provided information on the ISR, representing a global sample size of 250 implants. Pistilli et al[40] was excluded from this analysis, because it provided a statistically lower ISR (46.9%), showing the heterogeneity compared with other studies when the sensitivity was applied. Thus, the WM ISR was 98.9% (95% CI [97.7% to 100%]). Additionally, ISR was not found to be associated with the loading or placement protocol. The Galbraith test suggested acceptance of the global homogeneity of the rest of the studies.

SSR. Five studies provided information on the SSR, representing a global sample of 129 implants. Again, Pistilli et al[40] was excluded due to statistically lower SSR (0%) compared with other studies. Hence, the WM SSR was 93.9% (95% CI [88.8% to 99%]). The Galbraith test did not show a significant grade of heterogeneity.

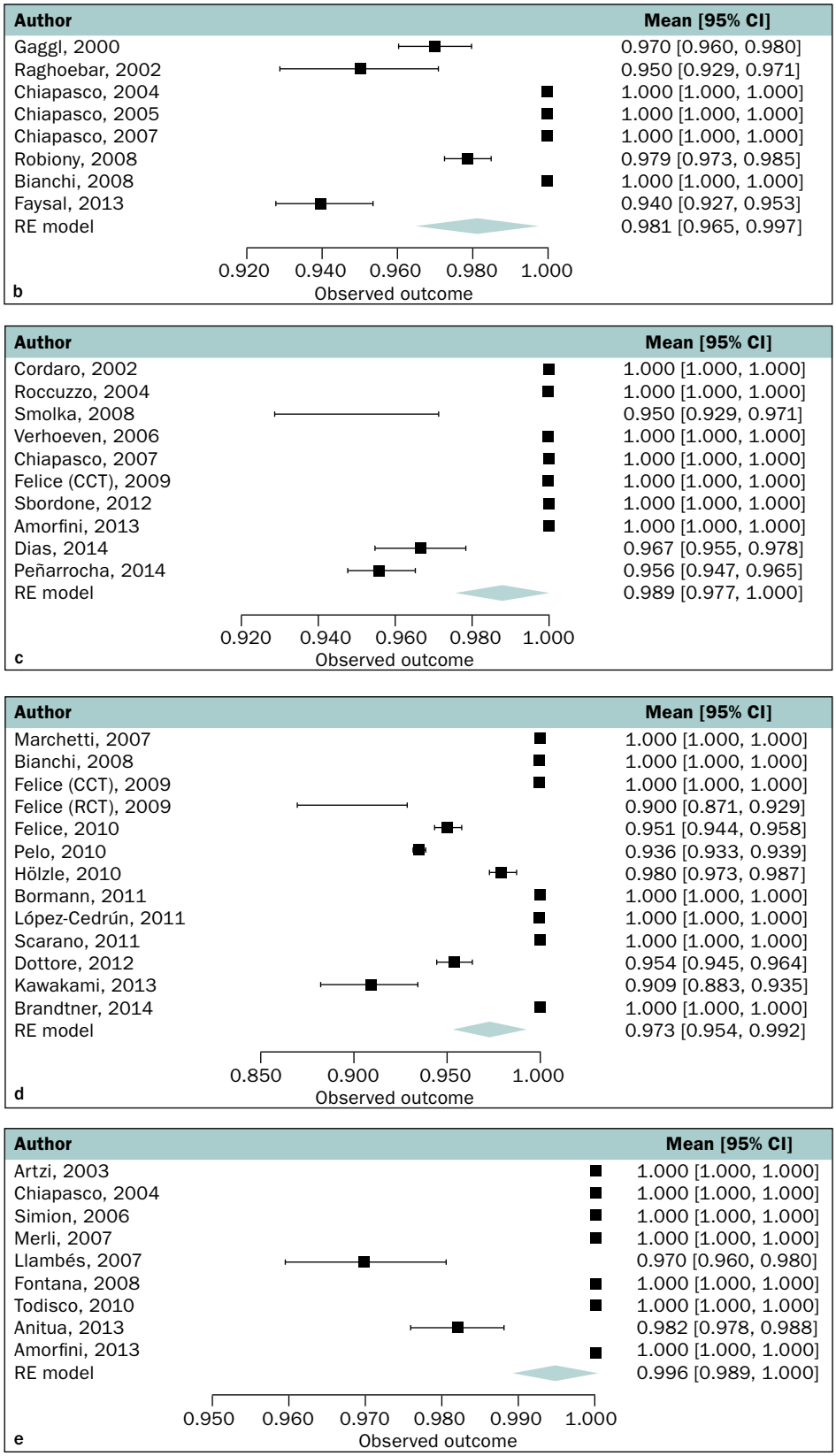


Fig 3 Funnel plot for the primary outcome implant survival rate (mean [95% CI]) *(a, facing page)* global, *(b)* DO, *(c)* OBG, *(d)* IBG, and *(e)* GBR.

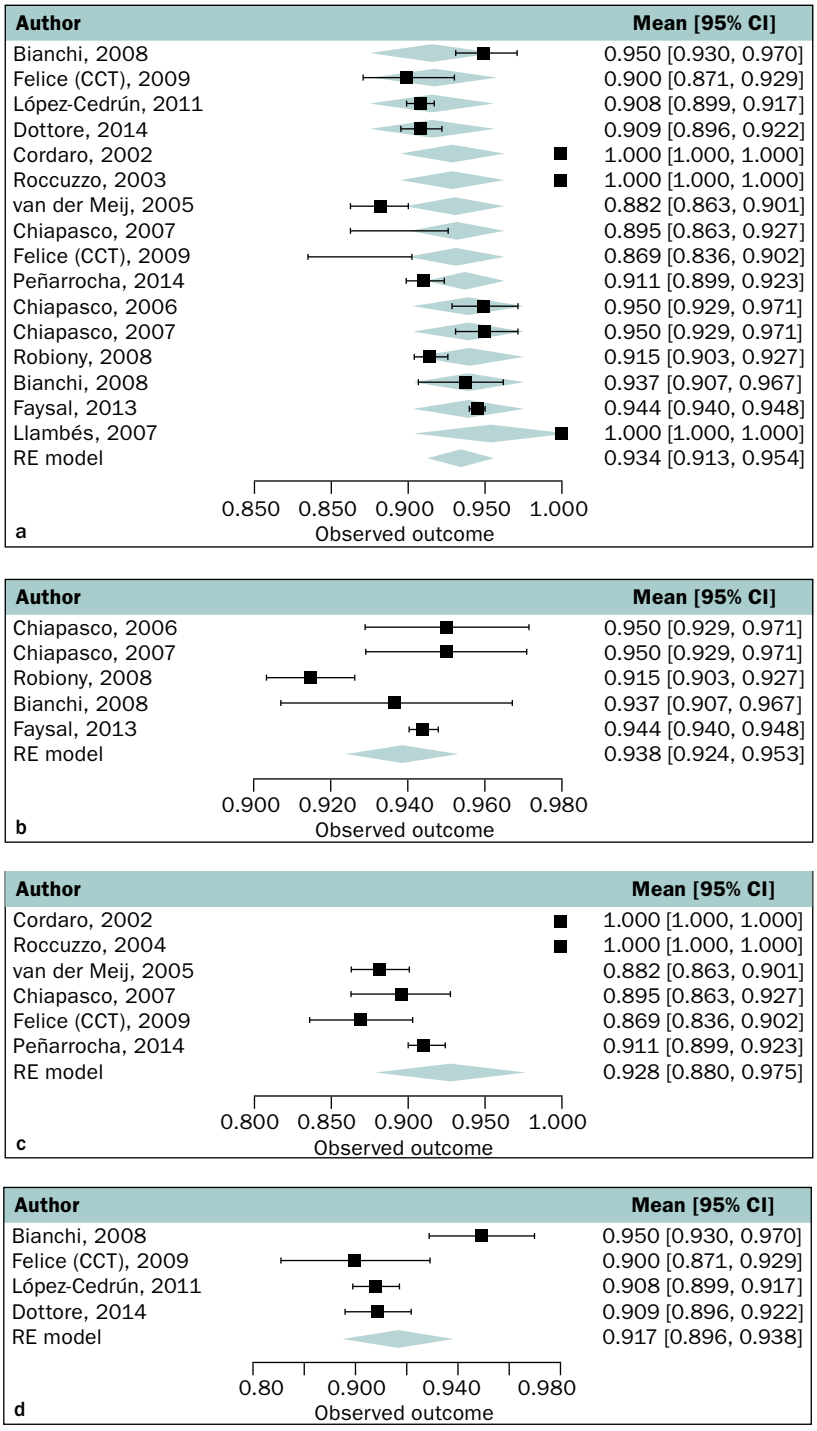


Fig 4 Funnel plots for the primary outcome implant success rate (mean [95% CI]): *(a)* global, *(b)* DO, *(c)* OBG, and *(d)* IBG. Mean implant success rate for GBR was only provided by one study, and hence, it was not plotted.

DO

VRA. Four studies provided information on VRA, representing a sample size of 64 patients. The result of the meta-analysis showed a mean gain of 6.84 ± 0.61 mm (95% CI [5.64 to 8.05 mm]). The gain was considered significantly not null ($P < .001$). The heterogeneity was shown to be high ($I^2 = 96.9\%$, $P < .001$). With only four studies, the Egger's test was underpowered, but the result may be considered as indicative ($P = .093$). There was also a remarkable lack of symmetry in the studies with greater sample sizes.

ISR. Eight studies provided information on the ISR, representing a global sample size of 224 implants. The WM ISR was 98.1% (95% CI [96.5% to 99.8%]). Despite the apparent heterogeneity shown, it was only due to the amplification of the scale (92% to 100%). As such, the Galbraith test demonstrated the homogeneity.

SSR. Five studies provided information on the SSR, representing a global sample of 140 implants. The WM SSR was 93.8% (95% CI [92.4% to 95.3%]). Moderate heterogeneity was detected, triggered by the lower SSR noted in one study ($I^2 = 80.7\%$, $P < .001$).

GBR

VRA. Six studies provided information on the VRA, representing a sample size of 62 patients. The result of the meta-analysis provided a mean gain of 3.83 ± 0.49 mm (95% CI [2.85 to 4.80 mm]). The gain was considered significantly not null ($P < .001$). Different studies provided estimates of quite divergent VRA, leading to a high heterogeneity ($I^2 = 93.9\%$, $P < .001$). Moreover, according to the Egger test, publication bias was not found ($P = .102$).

ISR. Nine studies provided information on the ISR, representing a global sample size of 265 implants. The WM ISR was 99.6% (95% CI [98.9% to 100%]). The Galbraith test placed the study of Llambés et al[7] in the limit of what is permissible in terms of heterogeneity.

SSR. Based only upon one study, Llambés et al,[7] the SSR was 100%.

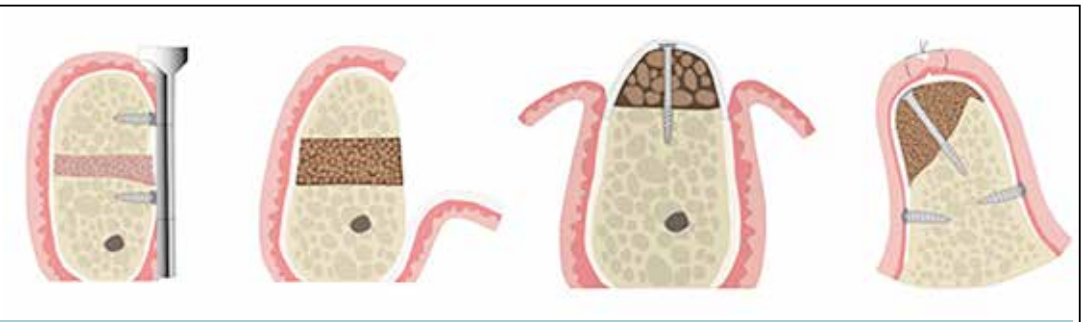
DISCUSSION

Rehabilitation of the atrophic mandible is one of the challenging clinical scenarios in implant dentistry due to three major factors: *(1)* bone morphology (often uneven, impairing the stability of the clot and the graft); *(2)* bone composition (small marrow content with limited blood supply); and *(3)* it is difficult to achieve primary soft tissue coverage (attachment from the mylohyoid muscle or shallow vestibule may restrict tension-free coverage). Although minimally invasive approaches, namely, short or tilted implants,[1,68] have been used in these challenging clinical conditions, their prosthetic long-term results remain to be determined. Hence, VRA using different techniques and biomaterials has been attempted. The present systematic review supports the idea that the technique used actually influences the amount of VRA; DO had the highest amount of VRA (mean: 6.84 mm), with OBG being the lowest (mean: 3.47 mm). These results are in partial accordance with previous systematic assessments.[16,17] The minor disagreements observed are attributable to the combination of maxillary and mandibular ridges in these two studies, and this systematic review only focused on the atrophic mandible. Among all techniques, IBG and GBR demonstrated acceptable VRA of ≈ 4 mm. This implies that, if a standard-length implant (≥ 10 mm) is planned, for any ridge of less than 8 mm, VRA will be needed to avoid sensory disturbances, and since GBR was shown to be the most reliable approach to achieve VRA with minor resorption and complications, it should be the advocated technique.[69]

Nonetheless, these regenerative therapies might encounter some biologic complications. For instance, OBG and IBG had higher sensory disorders, followed by DO, with the GBR being the least. Also, OBG and IBG might encompass more wound opening, which might potentially compromise the VRA.[70] On the other hand, DO holds the majority of complications, such as lingual vector inclination and loosening of the distractor. Thus, although only based upon descriptive analysis and within the limitations, it is possible to conclude that GBR entails fewer complications compared with the other studied techniques. Again, as long as the local and external factors are controlled, operator sensitivity will be the determinant to achieve flap-free tension, which remains the key for successful GBR.

In this sense, it is also important to remark that VRA should be consistent throughout the time required to ensure the achievement of implant success. Although a narrow range was found pooling all the approaches together, it is noteworthy that IBG almost doubled VBR obtained by GBR (1.60 mm vs 0.90 mm). In other words, regardless of the regenerative approach, a particular graft is often needed at the time of implant placement to seal any potential gap/space. Hence, the graft type/origin/preservation process can be other factors that influence the outcome of vertical bone augmentation procedures. Xenogeneic grafts have been regarded as one of the good space holders. On the other hand, autogenous grafts might resorb too quickly and lose their osteoconductive capacity.[71] Likewise, bone histologic behavior is directly related to the biomaterials and their properties as bone inductors/conductors.

Last but not least is the examination of ISR and SSR. It was demonstrated that regardless of what



	DO	IBG	OBG	GBR
VRA (mm)	6.84 ± 0.61	4.92 ± 0.34	3.47 ± 0.41	3.83 ± 0.49
VBR (mm)	1.47	1.60	1.21	0.90
ISR (%)	98.1	97.3	98.9	99.6
SSR (%)	93.8	91.7	92.8	100

Fig 5 Representative depictions and findings of the parameters studied in each technique. VRA = vertical bone augmentation; VBR = vertical bone resorption; ISR = implant survival rate; SSR = implant success rate.

VRA technique was applied, the ISR and SSR in the short term remained high (mean = 98.4% and 93.4%, respectively). This represents similar ISR and SSR rates to those implants placed in pristine bone,[72] into fresh extraction sockets,[73] or into augmented maxillary sinuses.[74] However, studies are needed to analyze the real fate of these techniques on implant long-term outcomes.

Limitations and Recommendations for Future Research

Although a comprehensive and strict screening was performed for the present systematic review, some limitations might bias the outcomes. First, it is known that bone grafting materials in any sort of regenerative therapy may have a potential influence upon the final clinical and histologic outcome. Nonetheless, due to the heterogeneity, it was not possible to discriminate these for a more individualized analysis. Second, the authors opted to also include nonrandomized studies. Although "acceptable" quality was obtained according to the standards of quality assessment, risk of bias might be elicited from their design. Lastly, these results cannot be extrapolated to long-term clinical outcomes due to the lack of investigations on this matter.

In the accomplishment of adequate soft tissue management, GBR has demonstrated achievement of acceptable outcomes by means of VRA, ISR, SSR, and low resorption with minor complications. Hence, it is considered that investigations should keep exploring this technique to obtain higher predictability through the utilization of biologic agents (ie, platelet-derived growth factor BB or bone morphogenetic protein) to more rapid and anticipated angiogenesis. Furthermore, the continuous testing of new membrane designs must be further analyzed to achieve better long-term space maintenance and graft stability. Lastly, although very premature, in vitro and ex vivo results in tissue engineering via customized scaffold designs are showing very promising results in regeneration of injured and lost tissues.[75]

CONCLUSIONS

Within the displayed limitations, the following conclusions can be made (Fig 5).

- Regardless of the technique/approach applied, implant survival and success rates in the augmented mandible are high in the short-term evaluation. Long-term results remain to be determined.
- While the greatest vertical bone augmentation can be obtained utilizing distraction osteogenesis and inlay block grafting, these techniques are also identified as having higher complication rates.
- Guided bone regeneration is the most reliable technique in terms of bone stability (minor resorption and low complication rate and morbidity).
- More studies are needed comparing these techniques under equal local and systemic conditions to explore the real impact of the approach upon final clinical outcomes.

ACKNOWLEDGMENTS

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper. This study was partially supported by the University of Michigan Periodontal Graduate Student Research Fund and by the Department of Oral Surgery and Implantology of the International University of Catalonia (Barcelona, Spain). Dr Basel Elnayef wants to express his special acknowledgment to Dr Hatchem Elnayef for the scientific support. In addition, the authors want to thank Mr Juan Luis Gómez Martínez for the support in the statistical analysis.

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