Review

Graft-Free Maxillary Sinus Floor Elevation: A Systematic Review and Meta-Analysis

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Background: This systematic review and meta-analysis aims to investigate survival rates of dental implants placed simultaneously with graft-free maxillary sinus floor elevation (GFSFE). Factors influencing amount of vertical bone gain (VBG), protruded implant length (PIL) in sinus at follow-up (PILf), and peri-implant marginal bone loss (MBL) are also evaluated.

Methods: Electronic and manual searches for human clinical studies on simultaneous implant placement and GFSFE using the lateral window or transcrestal approach, published in the English language from January 1976 to March 2016, were conducted. The random-effects model and mixed-effect meta-regression were used to analyze weighted mean values of clinical parameters and evaluate factors that influenced amount of VBG.

Results: Of 740 studies, 22 clinical studies were included in this systematic review. A total of 864 implants were placed simultaneously with GFSFE at edentulous sites having mean residual bone height of 5.7 ± 1.7 mm. Mean implant survival rate (ISR) was $97.9\% \pm 0.02\%$ (range: 93.5% to 100%). Weighted mean MBL was 0.91 ± 0.11 mm, and it was significantly associated with the postoperative follow-up period (r = 0.02; $R^2 = 43.75\%$). Weighted mean VBG was $3.8 \pm$ 0.34 mm, and this parameter was affected significantly by surgical approach, implant length, and PIL immediately after surgery (PILi) (r = 2.82, 0.57, 0.80; $R^2 = 19.10\%$, 39.27%, 83.92%, respectively). Weighted mean PILf was $1.26 \pm$ 0.33 mm (range: 0.3 to 2.1 mm).

Conclusion: Within limitations of the present systematic review, GFSFE with simultaneous implant placement can achieve satisfactory mean ISR of 97.9% \pm 0.02%. *J Periodontol 2017;88:550-564.*

KEY WORDS

Alveolar bone loss; bone regeneration; bone substitutes; dental implants; sinus floor augmentation; systematic review.

he edentulous posterior maxilla is frequently a challenging site for dental implant rehabilitation because of inadequate alveolar ridge height and poor bone quality.^{1,2} As such, maxillary sinus augmentation techniques that use lateral window or transcrestal approaches³ have been proposed so that a dental implant of regular length (e.g., 10 mm) can be placed in a deficient posterior maxillary edentulous site. Numerous systematic reviews have documented that transcrestal or lateral window maxillary sinus augmentation can predictably increase vertical bone height using bone substitutes to fill the elevated space.⁴⁻⁷ Different types of bone substitutes have been used in sinus augmentation to maintain the space created after lifting the Schneiderian membrane off the bone surface.^{4,8-10} Autogenous bone is the gold standard bone graft because of its osteogenicity, osteoinductivity, and osteoconductivity.¹¹ However, it is not commonly used in maxillary sinus augmentation because of significant graft resorption over time and donor site morbidity.¹²⁻¹⁴ Other bone substitutes, such as human allograft, bovine xenograft, and synthetic alloplast, have been associated with disease transmission,^{15,16} low vital bone to biomaterial ratio, and low resorption rate.^{10,17} Also, they have been suggested to delay bone regeneration compared with autogenous bone or blood clot alone.^{12,18,19} Some studies even showed that sinuses grafted

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with bone substitutes demonstrated repneumatization^{20,21} and implants placed in grafted sinuses had higher peri-implant marginal bone loss (MBL) compared with native bone.^{22,23}

Therefore, some clinicians advocated use of blood clots in place of bone substitutes in sinus floor elevation (SFE).²⁴⁻²⁶ High implant survival rates (ISRs) were reported with graft-free maxillary SFE (GFSFE), in which implants acted as a tent against the elevated Schneiderian membrane.²⁴⁻²⁸ The purpose of this systematic review and meta-analysis is to evaluate effectiveness of GFSFE by assessing amount of vertical bone gain (VBG), protruded implant length (PIL) in sinus immediately after surgery (PILi) and at follow-up (PILf), MBL, and ISR. To the best of the authors' knowledge, this report is the first systematic review and meta-analysis of the value of GFSFE with simultaneous implant placement.

MATERIALS AND METHODS

Search Strategy

This systematic review was conducted at the University of Michigan, Ann Arbor, Michigan, from February to May 2016. A search of two electronic databases (PubMed/MEDLINE and Cochrane Central Register of Controlled Trials) for relevant studies published in the English language from January 1976 to March 2016 was performed. Search terms used were: ("sinus" OR "maxillary sinus") AND ("floor elevation" OR "lift" OR "augmentation" OR "elevation" OR "lateral approach" OR "Cosci" OR "crestal approach" OR "transcrestal approach" OR "BAOSFE" OR "OSFE" OR "Summers technique" OR "osteotome-mediated" OR "osteotome") AND (without graft [Title/Abstract] OR no graft [Title/ Abstract] OR graftless [Title/Abstract] OR graft free [Title/Abstract] OR nongraft [Title/Abstract] OR without bone graft [Title/Abstract] OR no bone graft [Title/Abstract] OR nongrafts [Title/ Abstract] OR grafts free [Title/Abstract]). Additionally, manual search of dental- and implantologyrelated journals, including Journal of Dental Research, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, International Journal of Oral & Maxillofacial Implants, Journal of Oral Implantology, and Journal of Oral and Maxillofacial Surgery from January 1976 to March 2016, was also performed to ensure a thorough screening process. Furthermore, a search in the references of included papers was conducted for publications that were not identified electronically. Two examiners (D-HD and WQ) performed the literature search independently. Any disagreement was resolved either through discussion or after consultation with a third examiner (JP). This systematic review was conducted based on PRISMA guidelines.

Eligibility Criteria

Articles were included in this systematic review if they fulfilled the following inclusion criteria: 1) human prospective or retrospective clinical studies, cohort studies, or case series; 2) simultaneous implant placement with GFSFE via lateral window or transcrestal approach; 3) sample size of ≥ 10 implants; and 4) reported information on ISR, VBG, PILi, PILf, or MBL. Systematic reviews, animal trials, and those studies using platelet-rich fibrin/plasma as graft material were excluded.

Data Extraction

Data were extracted from studies that met inclusion criteria. Parameters tabulated were: 1) demographics – patient sample size, number of augmented sinuses, number of implants placed, and implant system used; 2) independent variables – lateral or transcrestal approach, implant diameter, implant length, presence or absence of sinus window bone plate, percentage of membrane perforation, residual bone height (RBH), PILi (computed as the difference between implant length and RBH), and longest follow-up period after implant placement; and 3) dependent variables – VBG, PILf, MBL, and ISR.

Statistical Analyses

Extracted data were analyzed using statistical software.^{||} Study heterogeneity was assessed using DerSimonian and Laird Q test and I-square index. If significant heterogeneity was found, the random-effects model was chosen to minimize any bias caused by methodologic differences among studies. When heterogeneity values were high, meta-regression was carried out on dependent variables. Forest plots were generated to graphically represent the difference in outcomes for all included studies. *P* value of 0.05 was used as level of significance, and R^2 was used as proportion of variance explained by the regression model.

RESULTS

Literature Search

A total of 740 studies were found through electronic and manual searches. Of these, 80 studies were selected for full-text evaluation after screening titles and abstracts. After full-text evaluation, 58 studies were excluded (Table 1).^{6,8,24,25,28-81} There were 22 studies that fulfilled the inclusion and exclusion criteria (Table 2) and thus were selected for systematic review and meta-analysis.^{26,27,82-101} Interexaminer reliability was 0.87. There were three studies^{19,83,88} with two treatment arms, and results from both arms were combined in the analysis.^{27,87,92,97}

Comprehensive Meta-Analysis (version 2.2), Biostat, Englewood, NJ.

Summary of Excluded Studies

Authors/Year	Number of Studies	Reason for Exclusion
Chen et al. 2007; ²⁸ Altintas et al. 2013; ²⁹ Bassi et al. 2015; ³¹ Bruschi et al. 1998; ³⁵ Cricchio et al. 2011; ³⁷ Ellegaard et al. 1997; ³⁹ Gabbert et al. 2009; ⁴³ Hatano et al. 2007; ⁴⁵ Lai et al. 2008; ⁴⁹ Lundgren et al. 2004; ⁵⁰ Lundgren et al. 2008; ⁵¹ Markovic et al. 2016; ⁵² Pjetursson et al. 2009; ⁶³ Pjetursson et al. 2009; ⁶² Qian et al. 2016; ⁶⁴ Rammelsberg et al. 2015; ⁶⁵ Rasmusson et al. 2012; ⁶⁶ Schleier et al. 2008; ⁶⁸ Senyilmaz and Kasaboglu 2011; ⁶⁹ Smedberg et al. 2001; ⁷¹ Sohn et al. 2008; ⁷⁴ Sohn et al. 2010; ⁷⁵ Winter et al. 2002; ⁷⁹ Winter et al. 2003 ⁸⁰	24	Reported data were incomplete
Bruschi et al. 2012 ³⁴	I	Implants were not placed simultaneously with sinus augmentation
Atef et al. 2014; ³⁰ Kaneko et al. 2012; ⁴⁷ Munakata et al. 2016; ⁵⁴ Groeneveld et al. 1999; ⁴⁴ Felice et al. 2009; ⁴¹ Esposito et al. 2010; ⁴⁰ de Oliveira et al. 2013 ³⁸	7	Sinus was grafted with a space-maintaining device
Diss et al. 2008; ²⁴ Triplett et al. 2009; ⁷⁷ Boyne et al. 1997; ⁸ Boyne et al. 2005; ³³ Yamada et al. 2008; ⁸¹ Sohn et al. $2011;^{73}$ Simonpieri et al. $2011;^{70}$ Mazor et al. 2009; ⁵³ Kim et al. $2014;^{48}$ Kanayama et al. 2016^{46}	10	Sinus was grafted with platelet rich fibrin or bone morphogenetic proteins
van den Bergh et al. 2000; ⁷⁸ Nedir et al. 2009; ⁵⁹ Nedir et al. 2014; ⁵⁶ Chipaila et al. 2014; ³⁶ Biscaro et al. 2012 ³²	5	Ten or fewer implants were placed
Del Fabbro et al. 2012; ⁶ Riben and Thor 2012; ⁶⁷ Pinchasov and Juodzbalys 2014; ⁶¹ Taschieri et al. 2012; ⁷⁶ Sohn 2015; ⁷² Nedir et al. 2014 ⁵⁷	6	Systematic review
Nedir et al. 2006; ²⁵ Nedir et al. 2009; ⁵⁵ Nedir et al. 2010; ⁶⁰ Nedir et al. 2013; ⁵⁸ Fermergård and Astrand 2008 ⁴²	5	Sample population was reported in a subsequent study

Demographics

There were 864 implants placed simultaneously with GFSFE at edentulous sites with mean RBH of 5.7 ± 1.7 mm. Mean ISR was reported to be $97.9\% \pm 0.02\%$ (range: 93.5% to 100%) with 18 failed implants after mean follow-up duration of 26.6 \pm 24.3 months (range: 6 months to 10 years). Out of 18 failed implants, 14 reported time of failure, of which 10 implants (71.4%) failed before they were loaded.

Results of Peri-Implant MBL

Data on MBL were reported in 12 studies.^{82,84,85,88,90,93,94,96-98,100,101} Meta-analysis demonstrated that weighted mean MBL was 0.91 ± 0.11 mm after mean follow-up period of 41.5 ± 27.7 months (range: 9 months to 10 years) with a high degree of heterogeneity ($l^2 = 98.92\%$; P < 0.001) (Fig. 1A). To explore influence of postoperative follow-up on MBL, the mixed-effect model was used, and residual Q was reported to be 18.46 with P = 0.03. Therefore, one study⁹⁸ was excluded for its high heterogeneity despite its long follow-up period of 10 years. Regression analysis showed that MBL was significantly related to postoperative follow-up (r = 0.02; $R^2 = 43.75\%$) (Fig. 1B). The surgical approach, implant diameter, implant length, presence or absence of sinus window bone plate, percentage of membrane perforation, RBH, and PILi did not show any significant influence on MBL.

Results of PIL in Sinus at Follow-Up (PILf)

Data on PILf were reported in seven studies.^{82,84,89,91,97-99} Weighted mean PILf was 1.26 ± 0.33 mm (range: 0.3 to 5.5 mm) (Fig. 2) with a high degree of heterogeneity ($l^2 = 97.55\%$; P < 0.001) among selected studies. However, the surgical approach, implant diameter, implant length, presence or absence of sinus window bone plate, percentage of membrane perforation, RBH, and PILi did not show any significant influence on PILf.

Results of VBG

Data on VBG were reported in 18 studies.^{26,27,82-87,89,91,93,94,96-101} Meta-analysis showed that weighted mean VBG was 3.80 ± 0.35 mm (Fig. 3A)

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Characteristics of Included Studies

Authors/Year	No. Patient/ Sinus/Implant Placed	Implant Diameter (mm)	Implant Length (mm)	Surgical Approach	RBH (mm)	PIL at Baseline (mm)	PILf (mm)	Follow-Up (month)	Membrane Perforation (%)	Presence of Lateral Window Bone Plate*	ISR (%)	Peri-Implant MBL (mm)	VBG (mm)
Balleri et al. 2012 ⁸²	15/15/28	3.8	14.2	Lateral window	6.2 ± 1.6	8.2 ± 1.0	5.5 ± 1.6	81	37.5	Displaced	100.0	0.4 ± 0.2	5.5 ± 1.6
Borges et al. 2011 ⁸³	15/15/28	4.0	14.8	Lateral window	5.9 ± 2.9	9.0 ± 3.5	NR	9	6.7	Displaced	96.4	R	7.9 ± 3.6
Brizuela et al. 2014 ⁸⁴	36/36/36	4.0	9.8	Transcrestal	7.4 ± 0.4	NR	2.I ± 0.3	24	Ξ	AN	97.2	0.7 ± 0.1	I.8 ± 0.3
Cara-Fuentes et al. 2016 ⁸⁵	26/28/38	4 ± 0.4	Ξ	Lateral window	5.8 ± 0.9	щ	XX	38.7	Х Х	Replaced or Discarded	97.4	0.5 ± 0.5	2.7 ± 0.9 on distal 2.6 ± 0.9 on mesial
Crespi et al. 2010 ⁸⁶	20/NR/30	ы	12.3	Transcrestal	6.6 土 1.9	NR	NR	36	0.0	AN	100.0	NR	3.8 土 1.6
Crespi et al. 2012 ⁸⁷	80/NR/120 80/NR/120	4.8	12.3 12.1	Transcrestal Transcrestal	6.7 ± 1.6 6.5 ± 1.7	NR NR	NR NR	24 24	0.0	A A A	98.3 98.3	NR NR	4.2 ± 1.0 4.1 ± 1.0
Fermergård and Astrand 2012 ⁸⁸	36/NR/53	4.5	10.1	Transcrestal	6.3 ± 0.4	4.4 ± 0.3	NR	36	Х Х	A	94.0	0.5 ± 0.1	NR
Fornell et al. 2012 ⁸⁹	14/NR/21	4.1/4.8	0	Transcrestal	5.6 ± 2.1	4.4 ± 2.1	I.4 ± I.5	12	NR	AN	100.0	0.0	3.0 ± 2.1
Gu et al. 2016 ⁹⁰	25/NR/37	NR	NR	Transcrestal	2.8 ± 0.7	NR	NR	60	0.0	NA	94.6	1.5 ± 1.0	NR
He et al. 2013 ⁹¹	22/NR/27	4.7 ± 0.4	01	Transcrestal	6.7 ± 1.2	3.8 ± 1.8	1.3 ± 1.3	25	0.0	NA	100.0	NR	2.5 ± 1.5
Johansson et al. 2013 ⁹²	NR/10/NR NR/9/NR	E. E. E. E.	0 0	Lateral window Lateral	4.3 ± 1.3 3.5 ± 1.3	K K	AR NR	~ ~	N N N N	Displaced Discarded	100.0 90.0	NR NR	NR NR
				window									
Lai et al. 2010 ⁹³	25/NR/30	4.4	6	Transcrestal	5.0 ± 1.5	3.9 ± 1.1	NR	6	3.3	AA	100.0	1.2 ± 0.5	2.7 ± 0.9
Leblebicioglu et al. 2005 ²⁷	40/54/29 40/54/44	N N N	± .7 3.5 ± .1	Transcrestal Transcrestal	9.1 ± 2.0 9.1 ± 2.0	NR NR	NR NR	25 25	3.7 3.7	A A A A	97.3 97.3	NR NR	3.9 ± 1.9 2.9 ± 1.2
Lin et al. 2011 ⁹⁴	44/NR/80	NR	12.8	Lateral window	5.1 ± 1.5	7.8 ± 1.7	NR	60	NR	Replaced and Discarded	100.0	2.1 ± 0.5	7.4 ± 1.9
Moon et al. 2011 ⁹⁵	14/17/31	4.1	13	Lateral window	5.2 ± 1.6	NR	NR	24	8.11	Displaced	93.5	NR	NR

Authors/Year	No. Patient/ Sinus/Implant Placed	Implant Implant Surgical Diameter (mm) Length (mm) Approach	Implant Length (mm)	Surgical Approach	RBH (mm)	PIL at RBH (mm) Baseline (mm)	PILf (mm)	Follow-Up (month)	Follow-Up Membrane (month) Perforation (%)	Presence of Lateral Window Bone Plate*	ISR (%)	Peri-Implant ISR (%) MBL (mm) VBG (mm)	VBG (mm)
Nedir et al. 2009 ⁹⁷	32/NR/54	4.1/4.8	8.3	Transcrestal	3.8 ± 1.2	4.0 ± 1.7	1.8 ± 1.7	12	15.0	AN	100.0	0.2 ± 0.8	2.6 ± 1.7
Nedir et al. 2016 ⁹⁸	15/16/23	4.1/4.8	9.6	Transcrestal	5.4 ± 2.3	4.9 ± 2.1	1.9 ± 1.2	120	18.8	AN	100.0	1.0 ± 0.9	3.0 ± 1.4
Nedir et al. 2016 ⁹⁶	12/19/37	4.1/4.8	ω	Transcrestal	2.4 ± 0.9	NR	NR	36	0.0	NA	94.1	0.6 ± 1.1	4.1 ± 1.0
Schmidlin et al. 2008 ⁹⁹	24/24/24	4.4 ± 0.4	8.6	Transcrestal	5.0 ± 1.5	2.6 ± 1.8 on mesial 2.8 ± 1.7 on distal	0.3 ± 0.6 on mesial and distal	17.6 ± 8.4	8.3	₹Z	100.0	Х Х	2.2 ± 1.7 on mesial 2.5 ± 1.5 on distal
Si et al. 2013 ¹⁰⁰	20/20/20	4.5	8.7	Transcrestal	4.6 ± 1.5	3.9 ± 1.6	NR	36	0.0	AN	95.0	I.4 ± 0.2	3.1 ± 1.7
Thor et al. 2007 ²⁶	20/27/44	4.5/5.0/3.5	13.3	Lateral window	4.6	NR	NR	27.5	40.7	Displaced	97.6	NR	6.5 ± 2.5
Volpe et al. 2013 ¹⁰¹	20/NR/29	NR	NR	Transcrestal	7.2 ± 1.5	NR	NR	16.4	0.0	NA	0.001	0.7 ± 0.3	2.8 ± 1.1
NR = not reported; NA = not applicable.	; NA = not applic	cable.											

NR = not reported; NA = not applicable. * Displaced: Lateral window buccal bone plate displaced superiorly with SFE; Replaced: Lateral window buccal bone plate removed from the sinus membrane and replaced at its original spot after SFE; Discarded: Lateral window buccal bone plate removed from sinus membrane and discarded.

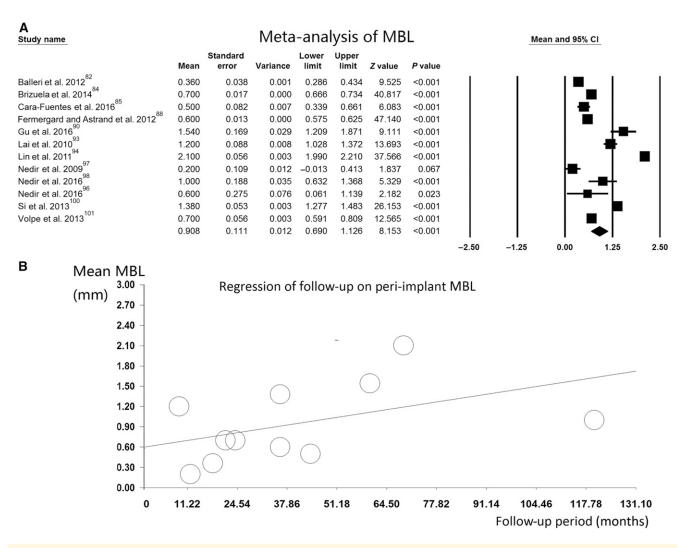


Figure 1.

A) Forest plot representing weighted mean MBL of 0.91 mm (95% confidence interval [CI] of 0.69 to 1.13 mm). **B)** Meta-regression graph illustrating effect of postoperative follow-up on mean MBL.

Study name			Meta	-anal	ysis c	of PILf	:
	Mean	Standard error	Variance	Lower limit	Upper limit	Z value	P value
Schmidlin et al. 2008 ⁹⁹	0.300	0.122	0.015	0.060	0.540	2.449	0.01
Johansson et al. 2013 ⁹²	0.600	0.200	0.040	0.208	0.992	3.000	0.003
Johansson et al. 2013 ⁹²	0.700	0.126	0.016	0.452	0.948	5.534	<0.001
He et al. 2013 ⁹¹	1.300	0.250	0.063	0.810	1.790	5.196	<0.001
Fornell et al. 2012 ⁸⁹	1.400	0.327	0.107	0.758	2.042	4.277	<0.001
Nedir et al. 2009 ⁹⁷	1.800	0.231	0.054	1.347	2.253	7.781	<0.001
Nedir et al. 2016 ⁹⁸	1.900	0.250	0.063	1.410	2.390	7.593	<0.001
Brizuela et al. 2014 ⁸⁴	2.100	0.051	0.003	1.999	2.201	40.817	<0.001
	1.257	0.331	0.110	0.608	1.907	3.794	<0.001

Mean and 95% CI

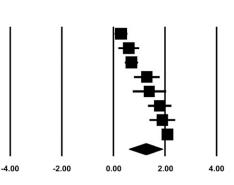


Figure 2. Forest plot representing weighted mean PILf of 1.26 mm (95% confidence interval [CI] of 0.61 to 1.91 mm).

Α												
Study name		M	leta-ar	nalysi	s of ۱	/BG			M	ean and 95%	, CI	
	Mean	Standard error	Variance	Lower limit	Upper limit		P value					
Balleri et al. 2012	5.500	0.302	0.091	4.907	6.093	18.190	<0.001	1	- T		-	- T
Borges et al. 2011	7.910	0.693	0.480	6.552	9.268	11.417	<0.001				- 1	╉-
Brizuela et al. 2014	1.800	0.051	0.003	1.699	1.901	34.986	<0.001					
Cara-Fuentes et al. 2016	2.700	0.148	0.022	2.410	2.990	18.248	<0.001					
Crespi et al. 2010	3.820	0.287	0.082	3.258	4.382	13.327	<0.001					
Crespi et al. 2012	4.170	0.130	0.017	3.915	4.425	32.030	< 0.001					
Crespi et al. 2012	4.070	0.134	0.018	3.807	4.333	30.352	<0.001					
Fornell et al. 2012	3.000	0.458	0.210	2.102	3.898	6.547	<0.001				╋	
He et al. 2013	2.500	0.289	0.083	1.934	3.066	8.660	<0.001					
Lai et al. 2010	2.660	0.159	0.025	2.349	2.971	16.746	< 0.001					
Leblebicioglu et al. 2005	3.900	0.353	0.124	3.208	4.592	11.054	<0.001					
Leblebicioglu et al. 2005	2.900	0.181	0.033	2.545	3.255	16.030	<0.001					
Lin et al. 2011	7.440	0.217	0.047	7.015	7.865	34.302	<0.001					
Nedir et al. 2009	2.600	0.231	0.054	2.147	3.053	11.239	<0.001					
Nedir et al. 2016	3.000	0.292	0.085	2.428	3.572	10.277	<0.001				-	
Nedir et al. 2016	4.100	0.250	0.063	3.610	4.590	16.400	<0.001					
Schmidlin et al. 2008	2.200	0.347	0.120	1.520	2.880	6.340	<0.001				F	
Si et al. 2013	3.070	0.385	0.149	2.315	3.825	7.965	<0.001				₩	
Thor et al. 2007	6.500	0.381	0.145	5.753	7.247	17.049	<0.001				_ ₩	
Volpe et al. 2013	2.800	0.204	0.042	2.400	3.200	13.708	<0.001					
	3.798	0.345	0.119	3.122	4.473	11.020	<0.001				•	
								-10.00	-5.00	0.00	5.00	10.00

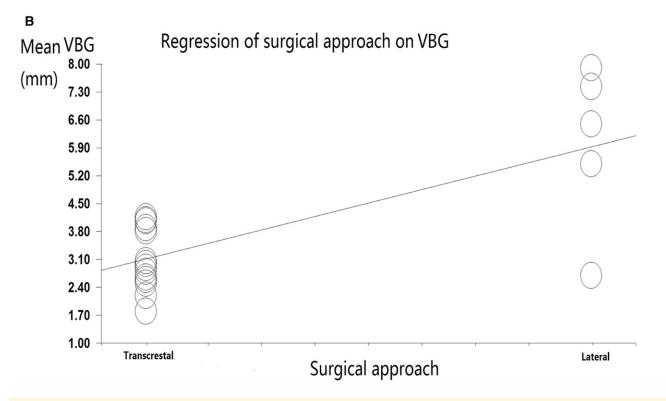
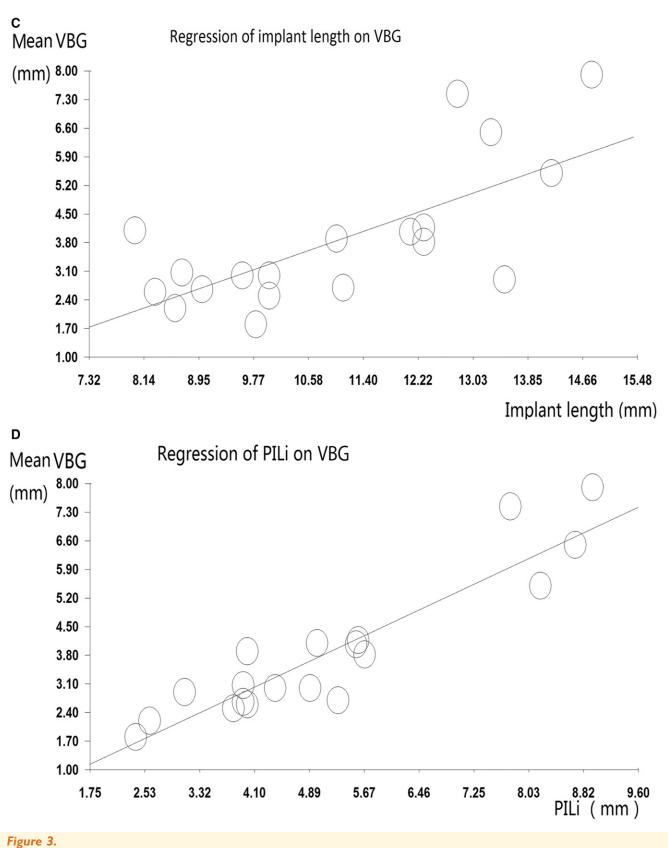


Figure 3.

A) Forest plot representing weighted mean VBG of 3.80 mm (95% Cl of 3.12 to 4.47 mm). **B)** Meta-regression graph illustrating effect of surgical approach (transcrestal versus lateral window) on mean VBG. **C)** Meta-regression graph illustrating effect of implant length on mean VBG. **D)** Meta-regression graph illustrating effect of PlLi on mean VBG.



Continued

with a high degree of heterogeneity (P = 98.56%; P < 0.001) among selected studies. VBG was found to be greater for the lateral window approach than for the transcrestal approach, and it increased with implant length and protrusion into the sinus cavity. Regression analysis demonstrated a statistically significant effect of the surgical approach, implant length, and PILi on VBG ($r = 2.82, 0.57, 0.80; R^2 = 19.10\%, 39.27\%, 83.92\%$, respectively) (Figs. 3B through 3D).

DISCUSSION

Cells, scaffolds, and signaling molecules are integral components in periodontal tissue engineering.¹⁰² The scaffold holds the space for cells and signaling molecules to act in a well-orchestrated symphony termed regeneration. In implant therapy, bone is the main structure that is regenerated. Numerous techniques, such as tenting titanium mesh,³⁰ long titanium screws,⁴⁷ or customized space-maintaining devices,⁵⁴ have been proposed to create and maintain space so that osteogenic cells can proliferate in a protected environment. Therefore, in GFSFE, the implant fixture acts as the tenting device for space creation and maintenance beneath the Schneiderian membrane. This allows formation of a stable blood clot that initiates the wound-healing cascade and promotes bone regeneration.^{103,104}

In line with the biologic concept of tissue regeneration, the present study shows that GFSFE appears to perform sufficiently well compared with the conventional approach of adding bone substitutes during augmentation. Meta-analysis highlighted weighted mean VBG of 3.80 ± 0.35 mm (range: 1.8 to 7.9 mm), which concurred with mean increase in bone height in the transcrestal approach and minimum VBG in the lateral window approach.^{3,104} Therefore, GFSFE was capable of regenerating bone vertically, and amount of VBG was determined by the vertical space generated by protruded implants.

Some studies have suggested a relationship between VBG and types of graft materials¹⁰⁵ and sinus width/size,¹⁰⁶⁻¹⁰⁸ but not with PILi¹⁰⁹ and RBH.¹¹⁰ Interestingly, the present study found that VBG was significantly related to PILi (r = 0.80; $R^2 = 83.92\%$; P < 0.001) but not to RBH (r = -0.19; P = 0.37). This finding can be explained by the PASS principle¹¹¹ of guided bone regeneration, which stands for primary wound closure, angiogenesis, space creation and maintenance, and wound stability. Healing in a graftfree augmented sinus is a temporal sequence of hemostasis, inflammation, proliferation, and maturation/ remodeling.¹⁹ Space and wound stability are crucial for undifferentiated mesenchymal stem cells or precursor cells within sinus to form bone.¹¹² Clinically, mechanical instability in the augmented sinus occurs mainly from air pressure within the sinus associated with respiration.^{113,114} When the Schneiderian membrane is tented by the protruded implant, space created beneath the membrane is relatively stable, thus favoring bone regeneration within the space.^{103,104,113} As such, the amount of VBG is determined by the amount of implant protruding into the sinus.

According to the Wolff law, ^{115,116} architecture and volume of regenerated bone within the sinus will change based on the functional load it bears. Maxillary sinuses augmented with bone substitutes, especially autogenous bone, generally undergo continuous bone resorption with a decreasing resorption rate over time.^{20,21,105,117} During the first 6 months of healing. rate of bone resorption was reported to be relatively high,^{20,21} and it gradually tapered down until 6 years after surgery.^{105,117} However, studies reported that GFSFE sites showed continuous but gradually decreasing bone formation. In initial stages of wound healing, VBG approached 2.5 mm at 6 months after surgery. This value gradually reduced to ≈ 1.5 mm at 24 months after surgery.^{86,87} Longitudinal studies reported that GFSFE had mean VBG of 2.5, 4.1, 3.2 to 3.8, and 3.0 mm at 1-, 3-, 5-, and 10-year follow-up periods, respectively,^{25,60,96-98,118} thereby indicating a plateauing effect on amount of VBG over time.

Faster bone formation was demonstrated in GFSFE compared with sinuses grafted with xenografts.¹⁹ In addition, graft-free sinuses had higher bone density than those grafted with allografts²⁹ and similar bone-to-implant contact (BIC) as autogenous bone grafted sinuses at 6 months after surgery.⁹² The present systematic review found that weighted mean PILf was 1.26 ± 0.33 mm, which was greatly reduced from mean PILi of 3.9 ± 1.1 mm, thus implying that bone regeneration occurred along the implant surface over time. A total of 97.9% of implants placed simultaneously with GFSFE survived after a mean follow-up period of 28.8 months. This high ISR was perhaps attributed to continuous formation of dense peri-implant bone leading to high BIC and thus functional stable implant restorations. Early implant failure rate of 71.4% was detected in this analysis, which concurred with implant failure rate of 85.7% in sinuses augmented with bone substitutes.¹¹⁹ Therefore, one can conclude that the early wound-healing phase is critical for osseointegration regardless of whether the sinus is augmented with bone substitutes or blood clot.

Peri-implant MBL is influenced by many biomechanical factors, for example, crown/implant ratio,¹²⁰ excessive cantilever length,¹²¹ and discrepancy in width of occlusal table and implant fixture diameter.¹²² Finite element analyses have suggested that load distribution and MBL of implants placed in grafted sinuses may be strongly related to characteristics of the grafting materials.¹²³⁻¹²⁵ It was observed that when native bone was stiffer than regenerated bone, functional loading increased concomitant stress at crestal bone level, 125 resulting in MBL around implants.¹²⁶ Clinical studies corroborated conclusions drawn from finite element analyses, in that MBL around implants in grafted sinuses was significantly greater than that in pristine bone within the first 12 months of functional loading.^{22,23} The present meta-analysis demonstrated that weighted mean MBL around implants placed at sites with GFSFE was 0.91 ± 0.11 mm after a follow-up period of 41.9 months. This figure was lower than MBL around implants placed in grafted sinuses^{23,127,128} and pristine maxillary posterior sites.¹²⁸ It could be speculated that the wound-healing cascade in a bonegrafted sinus occurred in an altered manner compared with that in a graft-free sinus, hence the difference in MBL over time. In addition, meta-regression of MBL on duration of postoperative follow-up showed that MBL in GFSFE was time dependent (r = 0.02; $R^2 = 43.75\%$), with a resorption rate of 0.2 mm per year. This value was similar to the proposed implant success criteria of MBL <0.2 mm per year from the second year of followup.^{129,130}

An area of concern with maxillary SFE is changes to the maxillary sinus cavity and quality of the sinus membrane. Previous animal and human studies found that penetration of dental implants through the Schneiderian membrane and into the sinus cavity had minimal effect on participants.¹³¹⁻¹³³ A canine model showed that there were no significant differences between untreated and membrane-lifted sinuses in terms of connective tissue and epithelium thickness, distribution and quantity of globet cells, and cilia orientation.¹³⁴ This implies that SFE did not affect ciliary function and sinus membrane quality and thus could be considered a safe procedure.

There are two limitations associated with this analysis. First, vertical bone dimension was measured on different radiographs; for example, dental panoramic tomograms, standardized or non-standardized periapical radiographs, spiral computed tomograms, and cone-beam computed tomography scans. Second, there was high heterogeneity among studies.

CONCLUSION

Within the limitations of this systematic review and meta-analysis, GFSFE using the lateral window or transcrestal approach with simultaneous implant placement appears to be a predictable treatment modality.

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