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Effect of Alveolar Ridge Preservation after Tooth Extraction: A Systematic Review and Meta-analysis

ABSTRACT

Alveolar ridge preservation strategies are indicated to minimize the loss of ridge volume that typically follows tooth extraction. The aim of this systematic review was to determine the effect that socket filling with a bone grafting material has on the prevention of postextraction alveolar ridge volume loss as compared with tooth extraction alone in nonmolar teeth. Five electronic databases were searched to identify randomized clinical trials that fulfilled the eligibility criteria. Literature screening and article selection were conducted by 3 independent reviewers, while data extraction was performed by 2 independent reviewers. Outcome measures were mean horizontal ridge changes (buccolingual) and vertical ridge changes (midbuccal, midlingual, mesial, and distal). The influence of several variables of interest (*i.e.*, flap elevation, membrane usage, and type of bone substitute employed) on the outcomes of ridge preservation therapy was explored via subgroup analyses. We found that alveolar ridge preservation is effective in limiting physiologic ridge reduction as compared with tooth extraction alone. The clinical magnitude of the effect was 1.89 mm (95% confidence interval [CI]: 1.41, 2.36; $p < .001$) in terms of buccolingual width, 2.07 mm (95% CI: 1.03, 3.12; $p < .001$) for midbuccal height, 1.18 mm (95% CI: 0.17, 2.19; $p = .022$) for midlingual height, 0.48 mm (95% CI: 0.18, 0.79; $p = .002$) for mesial height, and 0.24 mm (95% CI: –0.05, 0.53; $p = .102$) for distal height changes. Subgroup analyses revealed that flap elevation, the usage of a membrane, and the application of a xenograft or an allograft are associated with superior outcomes, particularly on midbuccal and midlingual height preservation.

KEY WORDS: alveolar bone loss, bone remodeling, alveolar bone grafting, evidence-based dentistry, alveolar bone atrophy, tooth loss.

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INTRODUCTION

Extraction is generally indicated when a tooth cannot be restored or maintained in acceptable conditions for long-term health, function, and/or esthetics. Tooth loss has a direct impact on quality of life by impairing the ability to masticate, speak, and, in some instances, socialize (Gerritsen *et al.*, 2010). Additionally, the absence of a tooth in its alveolus triggers a cascade of biological events that typically result in significant local anatomic changes (Van der Weijden *et al.*, 2009). Preclinical and clinical studies have demonstrated that alveolar ridge volume loss postextraction is an irreversible process that involves both horizontal and vertical reduction (Schropp *et al.*, 2003; Araujo and Lindhe, 2009). Alveolar ridge atrophy may have a considerable impact on tooth replacement therapy, particularly when implant-supported restorations are planned (Seibert and Salama, 1996). Therefore, alveolar ridge preservation (ARP) has become a key component of contemporary clinical dentistry.

Historically, the first therapeutic attempts to prevent alveolar ridge resorption were performed by root retention, with the primary goal of maximizing the stability of removable prostheses (Osburn, 1974). Nevertheless, root retention is not always feasible because of fracture, caries, and/or strategic reasons. ARP via "socket grafting" emerged in the mid-1980s as a therapeutic alternative to root submergence. Its use was rationalized on the notion that "filling" the space left by the extracted tooth with a biomaterial would emulate a "root retention effect" conducive to bone preservation (Figure 1), which would subsequently facilitate endosseous implant placement by reducing the need of ancillary grafting procedures (Artzi and Nemcovsky, 1998). This approach gained popularity over the years because of its conceptual attractiveness and technical simplicity (Christensen, 1996).

Over the past 2 decades, multiple studies evaluating the efficacy of different socket-filling approaches have been conducted. In these studies, a plethora of biomaterials has been employed, including autologous bone, bone substitutes (allografts, xenografts, and alloplasts), autologous blood-derived products, and bioactive agents, among others (Darby *et al.*, 2009). This body of knowledge contains a wealth of clinical, radiographic, and histologic outcomes. Unfortunately, the majority of studies available in the ARP literature are anecdotal case reports, case series, or inadequately powered clinical trials (Hammerle *et al.*, 2012). Surprisingly, many of them do not report on clinically relevant outcomes, such as linear or volumetric changes, and only a few include an adequate control (*i.e.*, undisturbed alveolus). These shortcomings are also reflected in the systematic reviews (Ten Heggeler *et al.*, 2011; Weng *et al.*, 2011; Horvath *et al.*, 2012; Morjaria *et al.*, 2014) and meta-analyses available on the topic (Vignoletti *et al.*, 2012; Vittorini Orgeas *et al.*, 2013), which present a major limitation: pooling of data from studies with marked methodological and clinical heterogeneity (*e.g.*, single- and multirooted teeth). This raises concerns about the possibility of generating inconsistent conclusions that over- or underestimated the therapeutic potential of specific ridge preservation strategies (De Buitrago *et al.*, 2013). Hence, there is a need for systematic reviews focused on this clinically important topic without the aforementioned limitations. The aim of this systematic review was to determine the effect of socket grafting to prevent postextraction ridge volume loss as compared to tooth extraction alone in nonmolar teeth.

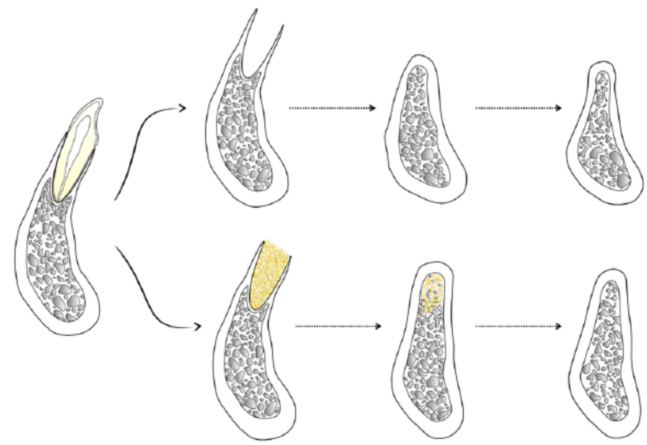

Figure 1. Illustration comparing expected alveolar bone changes after natural healing (upper row) as compared with alveolar ridge preservation via socket grafting (lower row) after tooth extraction.

MATERIALS & METHODS

This systematic review and subsequent meta-analysis follow the guidelines of PRISMA statement (*i.e.*, Preferred Reporting Items of Systematic Reviews and Meta-analyses; Moher *et al.*, 2009).

PICOT Question: Population, Intervention, Comparison, Outcomes, and Time

What is the effect of ARP via socket filling following nonmolar tooth extraction compared to extraction alone in preserving the alveolar ridge dimensions, after a minimum healing time of 12 wk reported in randomized clinical trials (RCTs) in adult human subjects?

Eligibility Criteria

Searches were limited to RCTs conducted in adult human subjects. Potential studies must have recruited patients older than 18 yr who had at least 1 nonmolar tooth extracted. Studies must have compared ARP postextraction via socket filling to untreated sockets (controls).

Additional inclusion criteria for study selection were as follows: The ridge preservation approach must have involved the utilization of a bone-grafting material (*i.e.*, autograft, xenograft, allograft, or alloplast), covered or not with a barrier/membrane, and had a minimum healing time of 12 wk; also, alveolar ridge dimensional changes (horizontal and/or vertical) must have been assessed clinically. Studies that involved the application of any additional therapy that could have affected healing outcomes (*e.g.*, immediate denture delivery, simultaneous soft tissue grafting, use of healing enhancers such as growth factors) were excluded. Finally, studies that used the same population as other included studies or that reviewed only the work of other investigators were excluded. The literature search and selection protocol are in the Appendix.

Outcome Measures

The outcome measures of interest in this systematic review were mean ridge dimensional changes—horizontal (buccolingual) and vertical (midbuccal, midlingual, mesial, distal)—from baseline (tooth extraction) to final assessment (minimum of 12 wk).

Data Extraction

Two reviewers (G.A.-O. and S.E.) independently extracted the data using an abstraction form. In the instance of inconsistencies in data extraction as observed by the arbiter (K.W.O.K.), specific items were referred back to the 2 reviewers for confirmation and reabstraction. Any unsettled discrepancies were resolved by consensus involving all the authors.

Data collected from each trial included (1) study and participant characteristics (year of publication, country where it was conducted, number of groups, number of subjects in each group, age of subjects), (2) clinical procedures (whether flap was elevated, number and condition of socket walls, grafting material used, application of a barrier/membrane, and follow-up time), and (3) outcomes of interest (changes in buccolingual width and midbuccal, midlingual, mesial, and distal height). Other variables recorded for subgroup analyses were flap elevation, whether a barrier was used in the experimental group, and type of grafting material applied. Corresponding authors of 5 studies were contacted for further information regarding study design or missing data to make a decision for inclusion and/or to utilize data specific to nonmolar teeth (Serino *et al.*, 2003; Kerr *et al.*, 2008; Azizi and Moghadam, 2009; Barone *et al.*, 2013; Cardaropoli *et al.*, 2012).

Data Analyses and Assessment of Heterogeneity and Bias

For the quantitative analyses, data from the selected studies were combined to estimate the effect size, defined as the difference in mean parameter change between the experimental and control groups. This was considered with respect to the 5 predetermined outcomes of interest: changes in buccolingual width and buccal, lingual, mesial, and distal height—all measured in millimeters. Random effects models were utilized throughout to estimate the effect sizes and provide 95% confidence intervals (CIs). The decision to use random effects modeling was supported not only by the clear diversity in details of the treatment protocols but by the evidence from formal statistical evaluation supporting significant heterogeneity in effect sizes (DerSimonian and Laird, 1986).

Heterogeneity of effect across the studies was formally assessed with the Cochran Q test (Cochran, 1954) and characterized with the I^2 statistic, which describes the proportion of total variation in the estimated effect sizes due to the heterogeneity among studies

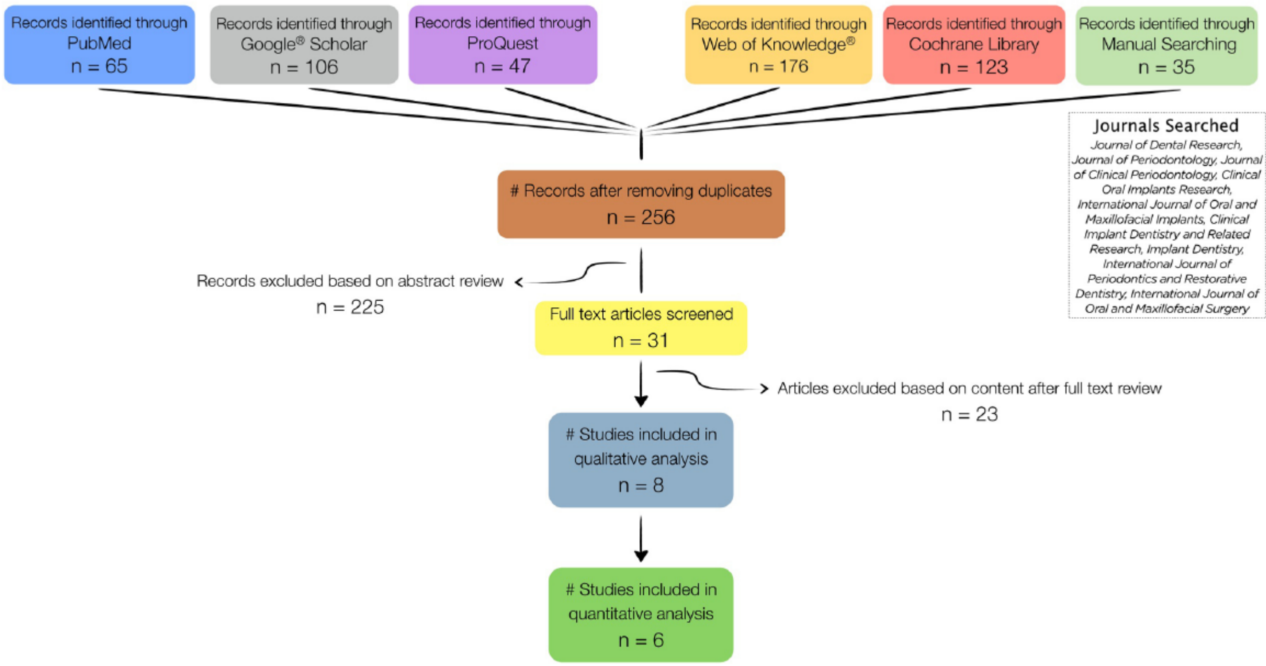

Figure 2. Flowchart depicting the search strategy and selection process.

(Higgins and Thompson, 2002). To further quantify the extent of heterogeneity among the studies, we estimated the between-studies variance (τ^2; Higgins *et al.*, 2003). Forest plots were used to depict individual effect sizes as well as combined effects.

Evaluations of subgroup effects based on aspects of the experimental protocol were also undertaken to explore the potential impact of protocol variation. Three factors were considered for the subgroup analyses: whether the flap was elevated as part of the intervention, whether a barrier membrane was used, and what type of bone graft was used (xenograft, alloplast, or allograft). If status for a particular factor was not reported, a "not reported" category was used in the subgroup analysis. Differences in effect size associated with subgroups were formally assessed with respect to each of the 5 ridge measurements of interest (Borenstein *et al.*, 2009). Estimated effect sizes and 95% CIs based on individual studies and combined analyses were displayed with forest plots. Risk of bias of the included RCTs was assessed according to Higgins *et al.* (2011). Potential publication bias for the studies included in the quantitative analyses was assessed via the funnel plot approach. Statistical analyses and funnel plots were performed with statistical software (Comprehensive Meta-Analysis Version 2; Biostat Inc., Englewood, NJ, USA), and forest plots were constructed with another software package (Stata Statistical Software Release 12; StataCorp LP, College Station, TX, USA).

RESULTS

Study Selection

The initial search in 5 databases yielded a total 552 records. After duplicates and nonpertinent articles were eliminated, a total of 31 articles were left for full-text assessment. Based on the predetermined eligibility criteria, a final selection of 8 RCTs for qualitative analysis was made (Camargo *et al.*, 2000; Iasella *et al.*, 2003; Barone *et al.*, 2008, 2013; Aimetti *et al.*, 2009; Azizi and Moghadam, 2009; Festa *et al.*, 2011; Cardaropoli *et al.*, 2012). Several studies were excluded for more than one reason. Reasons for exclusion were as follows: control group did not meet the inclusion criteria (Mardas *et al.*, 2010; Oghli and Steveling, 2010; Mardas *et al.*, 2011); molar teeth were included (Kerr *et al.*, 2008; Casado *et al.*, 2010); no bone graft was used in the experimental group (Lekovic *et al.*, 1997, 1998; Yilmaz *et al.*, 1998; Serino *et al.*, 2003; Bianchi *et al.*, 2004; Fiorellini *et al.*, 2005; Kerr *et al.*, 2008; Oghli and Steveling, 2010; Pelegrine *et al.*, 2010); soft tissue grafting was performed simultaneously (Hu *et al.*, 2009); immediate denture was delivered postextraction (Quinn *et al.*, 1985; Kwon *et al.*, 1986; Hoad-Reddick *et al.*, 1994; Bolouri *et al.*, 2001); outcomes of interest were not reported (Hoad-Reddick *et al.*, 1994; Bolouri *et al.*, 2001; Nevins *et al.*, 2006; Crespi *et al.*, 2009; Barone *et al.*, 2012; Brownfield and Weltman, 2012; Heinemann *et al.*, 2012); follow-up time was <12 wk (Nevins *et al.*, 2006; Heinemann *et al.*, 2012); and study was not on the topic of ridge preservation postextraction (Sisti *et al.*, 2012). Two selected RCTs had a split-mouth design, which made pooled meta-analysis with parallel arms studies not feasible; hence, they were excluded from the quantitative analysis (Camargo *et al.*, 2000; Festa *et al.*, 2011). The search and selection flowchart is displayed in Figure 2. Characteristics and risk of bias assessment of the selected studies are in Appendix Tables 1 and 2, respectively.

Synthesis of Results from Meta-analyses

Data from the 6 studies eligible for quantitative analysis (Table 1) were combined to estimate the effect size of all the parameters of interest (Iasella *et al.*, 2003; Aimetti *et al.*, 2009; Azizi and

Table 1. Outcomes of Interest Reported in the Included Studies: Mean Change

	Control Group					Experimental Group				
		Vertical					Vertical			
Author Year	Horizontal[a]	MB	ML	Mesial	Distal	Horizontal[a]	MB	ML	Mesial	Distal
Aimetti 2009	–3.2 ± 1.8	–1.2 ± 0.6	–0.9 ± 1.1	–0.5 ± 0.9	–0.5 ± 1.1	–2.0 ± 1.1	–0.5 ± 1.1	–0.7 ± 0.6	–0.2 ± 0.6	–0.4 ± 0.9
Azizi 2010	–4.1 ± 0.6	–4.2 ± 1.5	–2.8 ± 1.4	–0.3 ± 1.1	–0.4 ± 1.0	–2.6 ± 1.2	–0.9 ± 1.4	–0.3 ± 1.1	–0.1 ± 0.7	–0.3 ± 0.8
Barone 2008	–4.5 ± 0.8	–3.6 ± 1.5	–3.0 ± 1.6	–0.4 ± 1.2	–0.5 ± 1.0	–2.5 ± 1.2	–0.7 ± 1.4	–0.4 ± 1.3	–0.2 ± 0.8	–0.4 ± 0.8
Barone 2012	–3.1 ± 0.4	–2.3 ± 0.5	–2.1 ± 0.8	–1.5 ± 0.8	–1.1 ± 0.8	–1.3 ± 0.5	–1.6 ± 0.9	–1.8 ± 0.5	–0.6 ± 0.5	–1.0 ± 0.9
Camargo 2000	–3.0 ± 2.4	–1 ± 2.25	NR*	NR*	NR*	–3.48 ± 2.68	–0.38 ± 3.18	NR*	NR*	NR*
Cardaropoli 2012	–4.4 ± 0.7	–1.8 ± 0.3	NR*	NR*	NR*	–1.1 ± 1.1	1.1 ± 0.8	NR*	NR*	NR*
Festa 2011	–3.7 ± 1.2	–3.1 ± 1.3	–2.4 ± 1.6	–0.4 ± 1.2	–0.5 ± 1	–1.8 ± 1.3	–0.6 ± 1.4	–0.5 ± 1.3	–0.3 ± 0.8	–0.4 ± 0.8
Iasella 2003	–2.6 ± 2.3	–0.9 ± 1.6	–0.4 ± 1.0	–1.0 ± 0.8	–0.8 ± 0.8	–1.2 ± 0.9	1.3 ± 2.0	0.0 ± 1.3	–0.1 ± 0.7	–0.1 ± 0.7

All values are expressed in millimeters, mean ± SD.
MB, midbuccal; ML, midlingual; NR, not reported.
[a]Buccolingual.

Table 2. Results of Meta-analysis Assessing the Effect of Experimental Treatment *vs.* Control Based on the Mean Difference in Change on Alveolar Bone Measurements and Utilizing a Random Effects Model

		Treatment Effect Test	Heterogeneity Test			
Outcome	Mean Difference[a]	*p* Value[b]	*Q* Value[c] (*df*)	*p* Value[d]	I^2, %[e]	Tau[f]
Buccolingual	1.89 (1.41, 2.36)	< .001	12.28 (5)	.031	59.3	0.44
Midbuccal	2.07 (1.03, 3.12)	< .001	48.83 (5)	<.001	89.8	1.22
Midlingual	1.18 (0.17, 2.19)	.022	35.77 (4)	<.001	88.8	1.08
Mesial	0.48 (0.18, 0.79)	.002	5.33 (4)	.26	24.9	0.17
Distal	0.24 (–0.05, 0.53)	.102	2.92 (4)	.57	0.0	0.0

[a]The effect size estimated is the difference (treatment – control) in mean change in the specified alveolar bone measurement and represents the gain associated with treatment. Values in millimeters, mean (95% confidence interval).
[b]Significance probability associated with the test of a significant treatment effect.
[c]Test statistic and degrees of freedom associated with the Cochran *Q* test of heterogeneity of treatment effect among studies.
[d]Significance probability associated with the Cochran *Q* test of heterogeneity of treatment effect among studies.
[e]Estimated proportion of total variation across studies that is due to heterogeneity.
[f]Estimate of the standard deviation of underlying effects across studies, reflecting variability among effect sizes.

Moghadam, 2009; Barone *et al.*, 2008, 2013; Cardaropoli *et al.*, 2012). Results of the meta-analysis are displayed in Table 2.

Buccolingual Width Changes

Quantitative analyses revealed a strong positive ridge preservation effect in favor of the experimental group (ARP via socket grafting) of 1.89 mm (95% CI: 1.41, 2.36; *p* for test of treatment effect < .001; heterogeneity: I^2 = 59.3%; τ = 0.44) as illustrated in Figure 3A.

Midbuccal Height Changes

Quantitative analyses revealed a strong positive ridge preservation effect in favor of the experimental group (ARP via socket grafting) of 2.07 mm (95% CI: 1.03, 3.12; *p* for test of treatment effect < .001; heterogeneity: I^2 = 89.8%; τ = 1.22) as illustrated in Figure 3B.

Midlingual Height Changes

Quantitative analyses revealed a positive ridge preservation effect in favor of the experimental group (ARP via socket grafting) of 1.18 mm (95% CI: 0.17, 2.19; *p* for test of treatment effect = .022; heterogeneity: I^2 = 88.8%; τ = 1.08), as illustrated in Figure 3C.

Mesial Height Changes

Quantitative analyses revealed a positive ridge preservation effect in favor of the experimental group (ARP via socket grafting) of 0.48 mm (95% CI: 0.18, 0.79; *p* for test of treatment effect = .002; heterogeneity: I^2 = 24.9%; τ = 0.17), as illustrated in Figure 3D.

Distal Height Changes

Quantitative analyses revealed a positive ridge preservation effect in favor of the experimental group (ARP via socket grafting) of 0.24 mm (95% CI: –0.05, 0.53; *p* for test of treatment effect = .102; heterogeneity: I^2 = 0%; τ = 0) but did not achieve statistical significance, as illustrated in Figure 3E.

Subgroup Analyses

Table 3 displays results of subgroup analyses exploring possible differences in treatment effect based on variations in the experimental treatment protocol (*i.e.*, whether flap elevation was

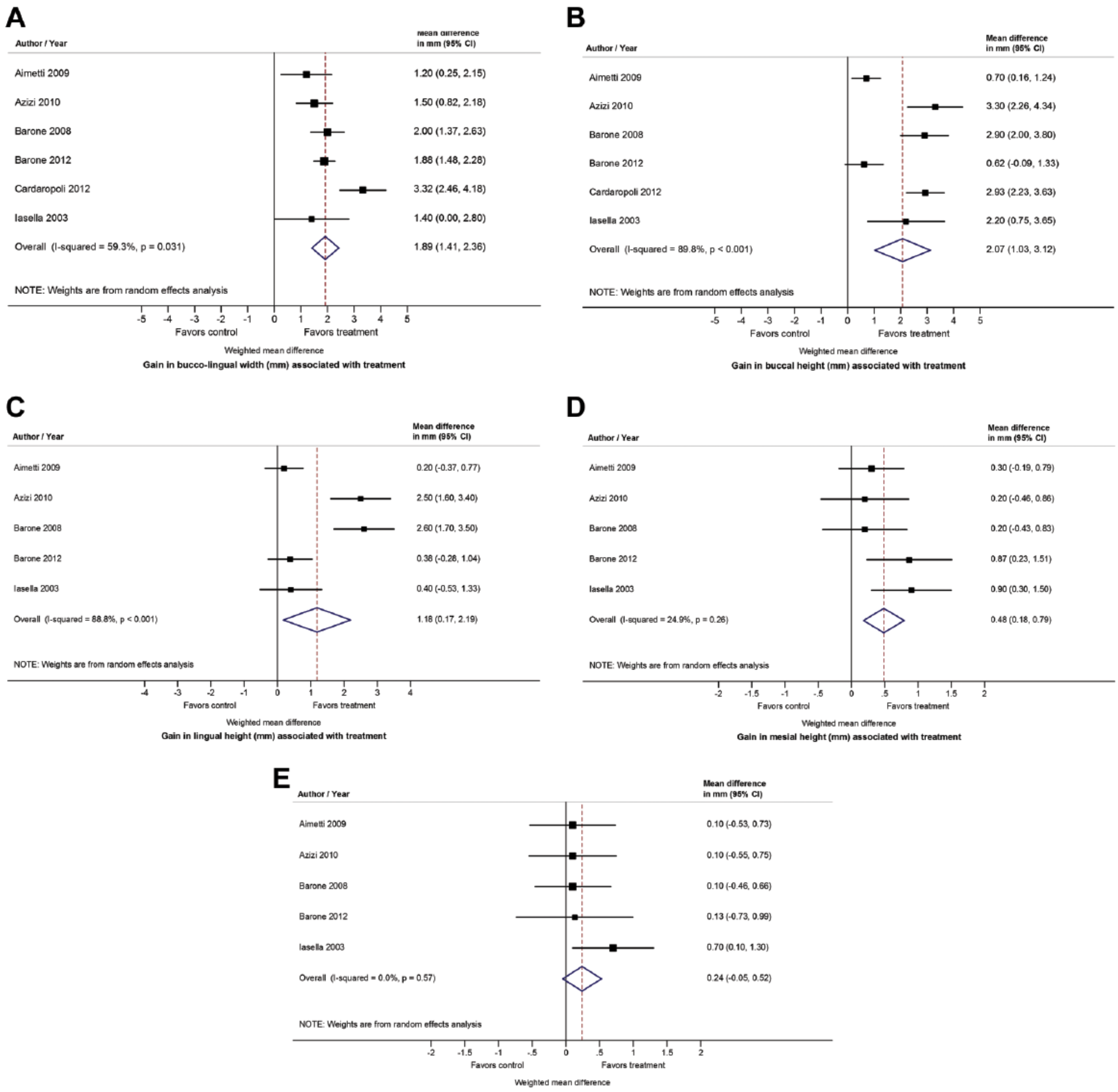

Figure 3. Forest plots showing differences in buccolingual width (**A**), midbuccal height (**B**), midlingual height (**C**), mesial height (**D**), and distal height (**E**) changes between groups.

performed, integrity of extraction socket, whether a barrier membrane was used, and type of bone grafting material employed). Of the 15 assessments, 3 were significant at the nominal .05 level, while 2 suggested a correlation (.05 < p < .10). Details for all significant and suggestive results are presented below.

Flap Elevation

Metaregression analyses revealed that flap elevation could have a beneficial effect on preservation of midbuccal (p = .059) and midlingual (p = .035) alveolar bone height. Corresponding forest plots are in Appendix Figures 1 and 2.

Use of a Barrier/Membrane

Among the experimental sites, the use of a membrane had a strong beneficial effect on preservation of midbuccal (p = .008) and midlingual (p = .067) alveolar bone height. Corresponding forest plots are in Appendix Figures 3 and 4.

Type of Bone-Grafting Material

Subgroup analyses revealed that the use of a xenograft or an allograft had a beneficial effect in midbuccal alveolar bone height preservation as compared to alloplastic materials (p = .017). Forest plot is in Appendix Figure 5.

Table 3. Results of Subgroup Analyses Exploring Possible Differences in Treatment Effect Based on Treatment Protocol Variations: Horizontal and Vertical Change, *p* Values

	Test of Subgroup Heterogeneity[b] for 5 Outcomes of Interest				
Factor[a]	Buccolingual Horizontal	Midbuccal Vertical	Midlingual Vertical	Distal Vertical	Mesial Vertical
Flap elevation	.505	.059[c]	.035[d]	.56	.797
Use of a barrier membrane	.131	.008[d]	.067[c]	.621	.415
Type of bone graft used	.235	.017[d]	.159	.232	.286

[a]Factor upon which subgroup analysis was based.
[b]Significance probability associated with the test of the null hypothesis that subgroups defined by the specified moderating factor did not differ in treatment effect.
[c].05 < *p* < .10; possible suggestive result.
[d]*p* ≤ .05; however, result did not remain significant after adjustment for multiple comparisons.

DISCUSSION

As dentistry evolves into a modern era, research aimed at further understanding the biological processes underlying alveolar bone healing, osseointegration, and tissue augmentation procedures is critical to develop predictable and successful dental implant therapy protocols with the ultimate goal of providing high-quality patient care (Berglundh and Giannobile, 2013). Over the past 2 decades, numerous tissue augmentation techniques (hard and soft) have been proposed to re-create missing structures that would facilitate implant placement, as well as ridge preservation approaches to minimize bone loss after tooth extraction (McAllister and Haghighat, 2007). However, the indication of specific approaches to achieve a predictable and satisfactory outcome in a given scenario remains a significant challenge in clinical practice. In our systematic review, we made a purposeful attempt to maximize the clinical relevance of the reported results by selecting only studies with a well-defined clinical protocol (ARP via socket grafting with or without a barrier) in a particular scenario (single-tooth extraction of nonmolar teeth) that likely represents the most commonly indicated approach for ARP in contemporary dental practice (Horowitz *et al.*, 2012).

Interestingly, several split-mouth RCTs have reported information demonstrating that the magnitude of ridge alterations after tooth extraction varies not only between but also within subjects (Camargo *et al.*, 2000; Serino *et al.*, 2003; Crespi *et al.*, 2009; Festa *et al.*, 2011). This is suggestive of the role that individual systemic and local characteristics may play on the rate, extent, and timing of ridge resorption. A plethora of factors may influence ridge resorption patterns—such as the number of neighboring teeth to be extracted, socket morphology (*i.e.*, single- *vs.* multirooted teeth and socket integrity), periodontal biotype (*i.e.*, bony buccal plate and soft tissue thickness), grafting material, smoking status, systemic factors (*e.g.*, uncontrolled diabetes, bone metabolic disorders), and patient compliance. Therefore, eligibility criteria were carefully established to avoid the influence of some of these factors in study outcomes. For example, molars were excluded since the size and morphology of the sockets are quite different from those of single-rooted teeth and, therefore, the healing processes are not comparable.

Main Findings

We found that ARP is effective in limiting physiologic ridge reduction as compared with tooth extraction alone. The clinical magnitude of the effect was 1.89 mm (95% CI: 1.41, 2.36; $p < .001$) in terms of buccolingual width, 2.07 mm (95% CI: 1.03, 3.12; $p < .001$) for midbuccal height, 1.18 mm (95% CI: 0.17, 2.19; $p = .022$) for midlingual height, 0.48 mm (95% CI: 0.18, 0.79; $p = .002$) for mesial height, and 0.24 mm (95% CI: –0.05, 0.53; $p = .102$) for distal height changes. Hence, strong evidence for a significant treatment effect was found for changes in buccolingual width, midbuccal height, and midlingual height. There was also evidence of a beneficial effect for mesial height, but it was not as pronounced. There was no evidence of a significant treatment effect for distal height. Interestingly, I^2 values demonstrate a strong evidence for heterogeneity of effect size for buccolingual width, midbuccal height, and midlingual height but not for distal height or mesial height (Table 2). In relation to this, it is important to remark that in one of the studies included in the quantitative analysis, a net increase of approximately 1.1 mm in midbuccal height was observed in the experimental group (Cardaropoli *et al.*, 2012). This can be considered an unusual outcome, possibly explained by measurement errors owing to the absence of examiner calibration and the fact that it was the only included study that assessed therapy outcomes based on stone cast measurements, which may have errors due to the inclusion of the soft tissue in the dimensional measurements.

Our buccolingual width findings are in agreement with other meta-analyses of similar design on this topic. Vignoletti *et al.* (2012) reported a significant reduction of bone width when ARP was performed: 1.83 mm (95% CI: –2.947, –0.79; $p < .001$). However, it should be mentioned that the results from 10 studies that followed diverse clinical protocols in noncomparable clinical scenarios were pooled, which may have had a significant influence in the results. Vittorini Orgeas *et al.* (2013) performed a meta-analysis distinguishing among multiple clinical ridge preservation approaches. They found that in sites that received bone grafting and a barrier—which represents the protocol followed in the majority of the studies included in our quantitative analysis (5 of 6)—the weighed benefit of ARP was 1.99 mm

(95% CI: –0.086, 2.485; p = .06). In terms of height changes, Vignoletti *et al.* observed a beneficial effect of 1.47 mm (95% CI: –1.982, –0.953; p < .001) when ARP was performed as compared to a control. Vittorini Orgeas *et al.* found a nonsignificant difference of 0.96 mm (95% CI: –1.177, 3.101; p = .37) in terms of height change differences between ARP via bone grafting and a membrane as compared with controls, in favor of the former. This observation may be explained on the basis that only 3 studies, which reported quite divergent findings, were considered in this category (Camargo *et al.*, 2000; Iasella *et al.*, 2003; Barone *et al.*, 2008). However, a comparison of these height changes with those reported in this review does not appear to be reasonable, since a specific distinction among midbuccal, midlingual, mesial, and distal height changes was not made in previous systematic reviews. As mentioned in previous systematic reviews (Ten Heggeler *et al.*, 2011; Vignoletti *et al.*, 2012; Morjaria *et al.*, 2014), although a benefit was observed in association with ARP, some degree of horizontal and vertical bone loss should still be generally expected (Table 1).

Subgroup Analyses

Subgroup analyses were conducted to assess the influence of flap elevation, usage of a membrane to cover the socket, and type of bone graft on the observed effect sizes for each clinical outcome. Of the 15 assessments, 3 were significant ($p \leq .05$), while 2 of them were suggestive ($.05 < p < .10$). Buccolingual width and mesial and distal height changes were not influenced by variations on flap elevation, membrane usage, and type of bone graft. Sites that underwent flap elevation exhibited less average midbuccal (p = .059) and midlingual (p = .035) height loss (Appendix Figures 1 and 2). There were 3 studies on each subgroup: flap elevation (Iasella *et al.*, 2003; Barone *et al.*, 2008; Azizi and Moghadam, 2009) and no flap elevation (Aimetti *et al.*, 2009; Barone *et al.*, 2013; Cardaropoli *et al.*, 2012). This is an interesting result: although it is generally acknowledged that flap elevation has a detrimental impact in bone remodeling because of the interruption of the periosteal vascular supply and an increase in postsurgical local inflammation, recent preclinical evidence indicates that flap elevation does not promote alveolar bone loss (Araujo and Lindhe, 2009; Fickl *et al.*, 2011). The usage of a membrane was strongly associated with less average midbuccal height loss (p = .008) and midlingual height loss (p = .067; Appendix Figures 3 and 4). There were 5 studies in the membrane subgroup (Iasella *et al.*, 2003; Barone *et al.*, 2008, 2013; Azizi and Moghadam, 2009; Cardaropoli *et al.*, 2012), and only 1 did not report the use of a membrane (Aimetti *et al.*, 2009), which may have had an influence in the observed results; however, these findings are aligned with current evidence. Interestingly, sites grafted with a xenograft (Barone *et al.*, 2008, 2013; Azizi and Moghadam, 2009; Cardaropoli *et al.*, 2012) or an allograft (Iasella *et al.*, 2003) exhibited less midbuccal height loss (p = .017) as compared with sites that received an alloplast (Aimetti *et al.*, 2009), as shown in Appendix Figure 5. To our knowledge, this is the first study that reports a subanalysis to determine the effect of the biomaterial used on clinical outcomes of interest.

Limitations

Although we utilized a comprehensive search strategy to identify articles in the gray literature, it is possible that some gray literature was not included, because only 1 database containing this type of information was searched. Although the total number of subjects enrolled in the selected studies can be considered sufficient for the assessment of effect size differences between groups for the main outcomes of interest, it is important to remark that the reported subgroup analysis results should be taken with caution, given the limited number of studies (n = 6) that were eligible for the quantitative analysis. Also, the assessment method used in all the included studies (*i.e.*, nonstandardized linear measurements) does not necessarily provide critical information on bone availability for implant placement planning. This stresses the importance of developing and applying research protocols that would allow a precise and objective quantification of the total tridimensional changes after tooth extraction (Chappuis *et al.*, 2013) in future clinical trials.

CONCLUSIONS

The results of this systematic review and subsequent meta-analysis showed that ARP via socket filling with a bone graft can be an effective therapy to prevent physiologic bone loss after extraction of nonmolar teeth, in both the horizontal and the vertical dimension. Subgroup analyses showed that flap elevation, the usage of a membrane, and the application of a xenograft or an allograft may contribute to enhance the outcomes, particularly on midbuccal and midlingual height preservation.

Nevertheless, a certain degree of ridge volume loss should be expected even if ARP is applied. Hence, ARP may significantly prevent alveolar bone remodeling postextraction, but this effect is variable, likely due to the influence of local and systemic factors that are not fully understood yet. While in certain cases ARP could result in the maintenance of sufficient bone volume to place an implant in an ideal restorative position without the need of ancillary implant site development procedures, it may not be sufficient in other clinical instances. This information is expected to be of use not only to clinicians and patients but also to policy makers, given the apparently robust beneficial effect that ARP may provide in the specific scenario addressed in this review.

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