Identification and Efficacy Ranking of Allograft and Xenograft for Extraction and Ridge Preservation Procedures

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The objective of this network meta-analysis was to identify and rank different ridge preservation procedures using allograft, xenograft, or extraction only by dimensional changes in ridge width and height after tooth extraction. Electronic and hand searches of several databases were performed in September 2016 to identify randomized controlled trials on extraction and ridge preservation with 3 to 7 months of follow-up. Eight studies were included in the network meta-analysis. The total number of teeth included in these trials was 466, which were randomly assigned to treatment groups. The effect sizes of ridge width ranged from −2.01 (credibility interval [CrI]: −2.92 to −1.04) for the least efficacious treatment (extraction only) to −0.21 (CrI: −2.09 to 1.67) for the most efficacious treatment (xenograft with barrier). For height, they ranged from −0.35 (CrI: −3.82 to 3.17) for the most efficacious treatment (freeze-dried bone allograft with barrier) to −1.11 (CrI: −6.21 to 3.88) for the least efficacious treatment (extraction).

No significant difference was detected between treatments nor inconsistency between the direct and indirect estimates. None of the selected interventions were statistically significant compared with any other treatment. All treatment options resulted in minimal bone loss in alveolar ridge width and height. Int J Periodontics Restorative Dent 2017;37:e253–e260. doi: 10.11607/prd.3323

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showed that grafted sockets had a smaller dimension loss compared to nongrafted sockets.\textsuperscript{2-4,6} Nongrafted sites lost 2 to 6 mm in alveolar ridge width, mainly in the buccal wall, and 1 mm of ridge height. On the other hand, grafted sites showed a width loss of < 2 mm and a height loss of < 0.5 mm.\textsuperscript{4}

Several biocompatible materials were tested for the ridge preservation procedures with membrane alone or membrane plus graft.\textsuperscript{1} These materials are best used immediately after extraction to preserve the alveolar bone and to ensure formation of alveolar bone in the extraction sites. Although autogenous bone has been used in the extraction socket to enable ideal implant placement,\textsuperscript{1} donor site morbidity and the amount of available bone are limitations of this graft type.\textsuperscript{3} Several alternative bone substitutes, such as allograft and xenograft, were developed to overcome the disadvantages associated with the autogenous bone grafts. The objective of this systematic review and network meta-analysis was to compare the use of allograft and xenograft for ridge preservation procedures, examining their effects on dimensional changes in width and height after tooth extraction.

Materials and Methods

Criteria for Study Inclusion

This study followed the PRISMA statement.\textsuperscript{8} Only randomized controlled trials (RCTs) that included reports of 3 to 7 months of follow-up were considered for inclusion. Articles meeting this criterion were then organized by the PICO method\textsuperscript{9} in the following manner:

- \textbf{(P) Participants:} Patients with a nonrestorable tooth who were surgically treated by extraction alone or in combination with ridge preservation procedure.
- \textbf{(I) Interventions:} The following surgical procedures were considered: xenograft with barrier, demineralized freeze-dried bone allograft (DFDBA) with barrier, freeze-dried bone allograft (FDBA) with barrier, and xenograft only. RCTs comparing ridge preservation materials (ie, alloplast, autogenous bone, or other materials such as gentamicin added to the xenograft/allograft) or RCTs explaining the comparison between the same bone grafts with different membranes or variations of materials not reported in mm were not included in this article due to the impossibility of direct comparison with other treatments or different measurement methods.
- \textbf{(C) Comparison:} All possible comparisons in the included surgical procedures with extraction only as a control were investigated.
- \textbf{(O) Outcome measures:} Alveolar width, the change at the most coronal width measurement (expressed in mm), and alveolar height, the change at the middle height measurement (expressed in mm), were considered.

Search Methods

The following four electronic databases were searched for articles published from their inception to September 2016: (1) the National Library of Medicine (MEDLINE via PubMed), (2) Web of Science Conference Proceedings, (3) Cochrane Central Register of Controlled Trials, and (4) Science Direct.

The following MeSH search terms were used: “tooth extraction” OR “tooth removal” OR “socket” AND (“preserv$” OR “reconstruct$” OR “augment$” OR “fill$” OR “graft$”) AND (“humans” AND (Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp])).


The search was limited to studies dealing with human subjects and written in the English language. Two reviewers (Z.N. and W.Y.) independently searched for articles. Inter-reviewer reliability was 0.87. Discrepancies were resolved by discussion between the reviewers.

Quality Assessment

The quality assessment of the included studies was performed by
two independent reviewers (Z.N. and W.Y.) (Table 1). Each article has been assigned a risk of bias (high, moderate, or low) based on the revised recommendations of the CONSORT statement.10

Bayesian Network Meta-analysis

A network meta-analysis is a statistical method that uses all available evidence for multiple comparisons within a framework and maintains the randomization within each trial.11–14 It is able to integrate any existing direct evidence with indirect evidence using a common reference.15 This method can provide an efficacy ranking among tested treatments with similar clinical status.16 It is rarely used in the dental field, specifically in periodontology.17 Therefore, it is considered a predictable and economic method for analyzing the performance of different alveolar ridge treatment options.

Statistical Analysis

The differences between the control and interventions were quantified using a network meta-analysis; all treatment options using allograft, xenograft, or extraction alone for width or height were analyzed12 (Fig 1). A multivariable Bayesian hierarchical random effects model for mixed multiple-treatment comparisons was used with noninformative prior distributions.13 Consistency between the direct and indirect estimates was assessed by using the node-splitting method.11 Results are presented as median effect size along with 95% central credibility intervals (CrIs). Several sensitivity analyses were performed to explore potential factors influencing the main effect. All analyses were performed using the Markov chain Monte Carlo simulation implemented through OpenBUGS software, version 3.2.2 (OpenBUGS Foundation). A previously published OpenBUGS code was adapted for this analysis.13

Results

Of the 821 articles identified, 675 were excluded based on the title or abstract during the first screening phase as they were not related to dentistry. An additional 117 articles were excluded on closer review. In the second phase, 8 full manuscripts of 29 were included for network meta-analysis. Figure 2 shows the network of studies that were chosen. Most of the studies contained
two experimental groups. However, three trials had three or more groups. The total number of teeth included in these trials was 466, and these were randomly assigned to a treatment group. Eight trials (267 teeth) contributed to the analyses of width-related outcomes, while six trials (199 teeth) were included in the analyses of height outcomes. The average age range of the participants was 20 to 78 years, and the percentage of women was 29.2% of the 68 total participants. The sample size ranged from 6 to 24 teeth (Table 2).

**Quality of Evidence**

The quality of included trials is summarized in Table 1. One study showed only a low risk of bias. The rest were high or moderate. The most frequently unsatisfied criteria were sample size calculation and masking.

**Width**

None of the selected interventions were found to be statistically significantly better than any other treatments (Table 3). All treatment options will result in loss in alveolar ridge width, with effect sizes ranging from \(-2.01\) (CrI: \(-2.92, -1.04\)) for the least efficacious treatment option (extraction only) to \(-0.21\) (CrI: \(-2.09, 1.67\)) for the most efficacious (xenograft with barrier). No significant inconsistency between direct and indirect estimates was detected.

**Height**

Although all treatment options were proven to reduce alveolar ridge height, FDBA with barrier was superior to all other treatments (Table 4), with effect sizes ranging...
from \(-0.35\) (CrI: \(-3.82, 3.17\)) for the most efficacious treatment option (FDBA with barrier) to \(-1.11\) (CrI: \(-6.21, 3.88\)) for the least efficacious (extraction only). No significant difference was detected between treatments, nor was any inconsistency seen between the direct and indirect estimates.

**Sensitivity Analysis**

The sensitivity analysis regarding measurement methods did not show any significant change.
Discussion

The present network meta-analysis compared the relative efficacy of several treatment options used for alveolar ridge preservation. In terms of width and height outcomes, all interventions were found to be similar (not statistically significant). This could be due to the limited number of trials investigating the possible options. However, all options were better than the control, treatment of extraction wound.

This study examines treatment options that have never been directly tested in RCTs. Direct comparisons were made in 6 out of 9 included studies for alveolar width and 3 out of 6 potential pairwise comparisons for height. This is important in clinical practice because indirect comparison of xenograft only with DFDBA and a barrier membrane showed that the first option was less effective in terms of width. This comparison has not yet been investigated in any RCTs.

Another important advantage of this analysis is the possibility of evaluating and ranking treatments. The probability that allograft was the best treatment was 40% in terms of height and 15% in terms of width (Figs 3 and 4). Extraction only (control) was considered the least effective treatment option in terms of alveolar ridge width and height. This could be because allografts and xenografts have been shown to stimulate bone growth through osteoconductive properties. However, some allografts may have bone growth factors and bone morphogenetic proteins, which are considered osteoinductive materials.5 In addition, barrier membranes are frequently used in ridge preservation procedures to guide bone healing by excluding the soft tissues from the extraction socket and maintaining space for bone regeneration.3 These graft materials should allow bone cells to grow around and inside the socket through porosity, which allows cell invasion and differentiation into active osteoblasts. The formed bone will be gradually replaced by native bone.3

In addition to the ranking and probabilities, the size of the relative effects should be carefully interpreted in clinical practice. For exam-

| Table 3 Effect Sizes (95% CrI) by Treatment for Bone Width at 3 to 7 Months* |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | DFDBA + barrier | FDBA + barrier | Xenograft       | Extraction      |
| Xenograft with barrier         | −0.21 (−2.09, 1.67) | −0.35 (−2.37, 1.72) | −0.88 (−2.87, 1.17) | −2.01 (−2.92, −1.04) |
| DFDBA with barrier             | −                  | −0.14 (−2.14, 1.83) | −0.68 (−3.42, 2.07) | −1.80 (−3.78, 0.25) |
| FDBA with barrier              | −                  | −                | −0.53 (−3.33, 2.24) | −1.66 (−3.68, 0.38) |
| Xenograft only                 | −                  | −                | −                | −1.14 (−3.13, 0.97) |
| Extraction only                | −                  | −                | −                | −                |

*Mean differences adjusted for small samples (Hedges g).
DFDBA = demineralized freeze-dried bone allograft; FDBA = freeze-dried bone allograft; CrI = credibility interval.

| Table 4 Effect Sizes (95% CrI) by Treatment for Bone Height at 3 to 7 Months* |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | DFDBA + barrier | Xenograft + barrier | Extraction |
| FDBA with barrier              | −0.35 (−3.82, 3.17) | −0.16 (−4.85, 4.63) | −1.11 (−6.21, 3.88) |
| DFDBA with barrier             | −0.19 (−3.13, 3.66) | −0.80 (−4.36, 2.93) |
| Xenograft with barrier         | −0.97 (−2.45, 0.54) |
| Extraction                     | −                |

*Mean differences adjusted for small samples (Hedges g).
P = .05.
DFDBA = demineralized freeze-dried bone allograft; FDBA = freeze-dried bone allograft; CrI = credibility interval.
Xenograft with barrier—which ranked first for width—had a difference of only 0.21 mm, with no clinical value, compared to DFDBA with a barrier membrane. However, both treatment options showed slight loss in bone width when the baseline measurements were compared with the last follow-up.

Most of the RCTs included in this review were classified as having a moderate to high bias (7 of 8) (Table 1). While this will most likely raise concerns about the validity of the study results, the limited inconsistency for width and height indicate good overall reliability of the results. Other considerations that may have had effects that should be considered in future analysis were type of extraction socket, single versus multicenters for presence of dehiscence or fenestration, clinical experience and who performed the surgical procedures, and variation in the included studies’ protocols.

Conclusions

Xenograft with a barrier membrane was potentially the most effective procedure for ridge width preservation, while FDBA with a barrier membrane was the most effective for ridge height preservation. However, none of the selected interventions were statistically significantly different. All treatment options resulted in some degree of bone loss.
Acknowledgments

The authors reported no conflicts of interest related to this study.

References


