# Xenogeneic Bone Block in Lateral Ridge Augmentation: Where Are We Now? A Systematic Review and Meta-analysis

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Purpose: To investigate the clinical outcomes of xenogeneic bone blocks (XBBs) used for lateral ridge augmentation, specifically focusing on bone gain, graft survival, and implant survival. Materials and Methods: Data searches were conducted in PubMed, Embase, and ClinicalTrials.gov for randomized controlled trials (RCTs) and prospective cohort studies up to March 1, 2024. Horizontal bone gain (HBG), horizontal bone resorption (HBR), graft survival rates, and implant survival rates were analyzed. The Cochrane Risk of Bias Tool 2 (RoB2) and Newcastle-Ottawa Scale (NOS) were applied to assess the quality and risks of the included studies. Results: Four RCTs and five prospective cohort studies comprised a total of 120 bone graft sites and 141 implants that were included in the meta-analysis. A noncomparative analysis resulted in a weighted mean HBG of 4.38 mm and HBR of 0.85 mm. Comparative analysis with data from four RCTs compared XBBs with autogenous bone blocks (ABBs). The analysis resulted in a statistically significant greater HBG in XBBs, with a mean difference of 0.72 mm (95% CI = 0.067 to 1.382, P = .031,  $I^2 = 28.2\%$ ). The weighted graft survival rate for XBBs was 91.3% (95% CI = 76.6% to 97.1%,  $I^2$  = 58.0%), and the weighted implant survival rate was 84.3% (95% CI = 72.6% to 91.6%,  $l^2 = 31.6$  %). Histologically, the mean percentage of mineralized vital bone in XBBs ranged from 11.6% to 29.8%, and the resorption rate ranged from 7.3% to 21%. Conclusions: The use of XBBs for lateral ridge augmentation demonstrates an acceptable survival rate and yields an adequate bone volume for subsequent implant therapy. However, the survival rate of implants placed in ridges augmented with XBBs is less favorable when compared to those augmented with ABB grafts. Int J Oral Maxillofac Implants 2025;40:151–161. doi: 10.11607/jomi.11048

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ollowing the extraction of a tooth, the alveolar ridge often undergoes a significant process of bone resorption, which affects both its horizontal and vertical dimensions. Studies have indicated a significant reduction of the alveolar ridge volume by approximately 25%, with the width experiencing a reduction of 40% to 60% within the first 3 years postextraction.<sup>1-3</sup> Despite attempts to preserve the alveolar ridge through various employed techniques and materials, none have fully arrested the decline of the ridge width, which continues to exhibit an average reduction ranging from 1.47 to 2.31 mm.<sup>4</sup> Recent studies have also highlighted the significance of maintaining a minimum of 2 mm of peri-implant bone thickness to mitigate the risk of vertical bone loss, mucosal recession, and potentially implant failure. Therefore, attempts to obtain the

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Submitted May 25, 2024; accepted August 19, 2024. ©2025 by Quintessence Publishing Co Inc. proper diameter for implant placement is still challenging when the ridge width is 2 mm.<sup>5</sup>

A variety of bone grafting materials have been employed in the practice of horizontal bone augmentation, such as autografts (autologous bone), allografts (allogeneic bone), xenografts (xenogeneic bone), and alloplastic materials, all of which are available in both particulate and block configurations. Additionally, clinicians often incorporate barriers such as absorbable or nonresorbable membranes and bovine bone grafts during the procedure to maintain space and minimize bone resorption.<sup>6</sup>

For extensive or severely atrophic ridges, bone block grafting emerged as a highly advocated and predictable approach, primarily due to its exceptional biologic properties and space-maintaining effect.<sup>7,8</sup> While autogenous bone is still the gold standard for bone reconstruction, it is not without its disadvantages, including high resorption rates, limited harvest sites, and potential patient morbidity.<sup>9</sup> Given these concerns, clinicians have considered alternative solutions in the form of employing allogeneic bone blocks (ALBs) or xenogeneic bone blocks (XBBs) for severe ridge atrophy cases in the hopes that they can provide results comparable to those achieved with autogenous bone block (ABB) grafts.

The effectiveness of ALBs has been documented in several systematic reviews<sup>10-13</sup> that demonstrated

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significant horizontal bone gain (HBG). This has been further corroborated by histologic evidence illustrating the formation of new bone and blood vessels during the bone-healing process. However, concerns regarding the potential elicitation of human leukocyte antigen (HLA) responses have prompted many surgeons to opt for XBBs.

The first use of XBBs in horizontal bone augmentation—particularly within the maxillary region—was initially reported in a human case that broadened the scope of available biomaterials for surgical application.<sup>14</sup> Further advancements include the design of an equine-derived collagenated xenogeneic cancellous bone block (CXCBB), which was enhanced with naturally occurring type 1 and type 3 collagens. This biomaterial has been specifically tailored for staged lateral grafting in severely atrophic ridges. Histologic animal studies have underscored its osteoconductive properties, such as its remodeling and superior integration capabilities in comparison to other xenogeneic blocks.<sup>15</sup>

Like ABBs, bone substitute blocks need stability and intimate contact with the recipient bed to foster neo-vascularization, thus necessitating contouring and adaptation to maximize the contact surface.<sup>16,17</sup> At times, this process can be time-consuming.

The recent adoption of CAD/CAM technology has significantly advanced the field of bone grafting. This approach involves digitally customizing bone block designs that are precisely milled from allograft or xenograft sources, ensuring an optimal fit with the recipient site. This process not only allows for a more precise adaptation but also reduces the duration of surgical procedures. Studies by Chiapasco et al<sup>18</sup> and Cucchi et al<sup>19</sup> have demonstrated that CAD/CAM technology has accelerated the development of these custom-tailored materials.

Vertical bone augmentation is an another frequently encountered clinical scenario in the field of implant dentistry. This procedure, known for its technical sensitivity, presents significant challenges in bone regeneration when using bone block materials because of its high complication rate.<sup>20</sup> In contrast to lateral bone augmentation, vertical augmentation offers more reliable alternatives such as the use of short implants and sinus elevation, which are selected based on the specific implantation site.<sup>21,22</sup> Consequently, this study is focused exclusively on lateral ridge augmentation because of its broader applicability in clinical practice. The objective of this systematic review and meta-analysis is to evaluate and provide updated insights into the clinical outcomes of XBBs. The key outcomes of interest include the extent of HBG and the incidence of associated complications. Through this analysis, we aim to synthesize existing evidence and contribute to the optimization of bone regeneration strategies.

# MATERIALS AND METHODS

## **General Guidelines**

This meta-analysis study adhered to the PRISMA 2020 guidelines (Appendix Table 1; all appendix tables and figures are available in the online version of this article). Registration was made in INPLASY under the number INPLASY202450010. Due to the nature of this study, there was no need to obtain ethical approval.

# Database Searches and Identification of Eligible Manuscripts

Independent electronic searches in PubMed and Embase databases were conducted by two authors (H.P.L. and E.K.) using the following keywords: ('xenogeneic' OR 'xenograft' OR 'heterograft' OR 'bovine' OR 'porcine' OR 'equine') AND ('block') AND ('bone') AND ('reconstruction' OR 'augmentation' OR 'grafting'). The search included data up to March 1, 2024. There were no language restrictions applied to this search. Additionally, to include data that has not been published yet, we performed electronic searches on ClinicalTrials.gov using the same keywords and search strategy (Appendix Table 2).

The same two authors (H.P.L. and E.K.) were responsible for conducting a screening of the titles and abstracts from the identified articles and had to reach a consensus. A manual search was also carried out by examining the references of essential articles. In situations where the two authors (H.P.L. and E.K.) could not reach a consensus, a third reviewer (H.L.W.) was consulted.

# Inclusion and Exclusion Criteria

The present systematic review included both one-arm and two-arm clinical studies that evaluated the outcomes of XBBs in lateral ridge augmentation with or without a comparison to ABBs. The PICO framework (population, intervention, comparison, and outcome) for this study includes:

- P (population): human adult participants (≥ 18 years old) who received alveolar ridge augmentation
- I (intervention): horizontal ridge augmentation with XBBs
- C (comparison): horizontal ridge augmentation with ABBs
- O (outcome): changes in horizontal bone thickness

For studies that did not have a control group, the focus question was adapted to a PIO question because the C (comparison) was not applicable.

The inclusion criteria were as follows: (1) randomized controlled trials (RCTs) and prospective cohort studies with a sample size greater than five, (2) studies investigating the quantitative evaluation of changes in



horizontal bone thickness, and (3) follow-up time greater than or equal to 3 months. The exclusion criteria were as follows: (1) studies lacking bone block information, (2) studies enrolling participants that overlapped with a previously published trial, and (3) studies that involved vertical bone augmentation.

# Methodologic Quality Appraisal

To evaluate the methodologic integrity of the included studies, a structured approach was taken using the Cochrane risk of bias tool for randomized trials version 2 (RoB2) (Fig 1). For nonrandomized trials, the Newcastle-Ottawa Scale (NOS) was applied to assess the quality and risks of the included studies. The overall NOS RoB was categorized as "high" ( $\geq$  7 stars), "moderate" (4–6 stars), or "low" (< 4 stars). This approach ensured a systematic evaluation of the study's quality and potential biases across the included studies.

## **Primary and Secondary Outcomes**

The primary outcome evaluated in this study was changes in horizontal bone thickness after bone grafting surgeries with XBBs. In studies featuring two comparative arms, the comparison of HBG was made between XBBs and ABBs.

The secondary outcomes evaluated in this investigation were horizontal bone resorption (HBR), bone graft and implant survival rates, and soft tissue dehiscence rates.

# **Data Extraction and Management**

The data extraction phase of the reviewed studies was jointly conducted by two authors (H.P.L. and E.K.). This procedure entailed gathering demographic parameters, identifying distinct clinical characteristics of each participant group, as well as obtaining information for the primary and secondary outcomes. In instances where requisite data were not explicitly presented or were missing from the published reports, concerted efforts were made to reach out to the corresponding authors with requests for data.

## **Statistical Analyses**

This study opted to perform the analysis with a randomeffects model implemented using Comprehensive Meta-Analysis software version 3 (Biostat). A two-tailed *P* value of < .05 was considered statistically significant. In this study, the mean differences were used to quantify the primary and secondary study outcomes. I<sup>2</sup> and Cochran's Q statistics were also examined to evaluate the degree of heterogeneity across studies. I<sup>2</sup> values of 25%, 50%, and 75% were considered low, moderate, and high heterogeneity, respectively.<sup>23</sup>

To enhance the reliability and robustness of this meta-analysis, the sensitivity analyses employed the one-study removal method. This systematic approach involved sequentially excluding individual trials from the analysis to evaluate whether the removal of a specific study led to a statistically significant alteration in the summary effect size.<sup>24</sup>

# RESULTS

#### Study Identification and Selection

The literature search process, as illustrated in Fig 2 with the PRISMA flowchart, involved the elimination of duplicate articles and exclusion of nonrelevant ones through title and abstract review. Ultimately, our analysis included nine articles, of which four were RCTs<sup>25–28</sup> and five were prospective cohort studies.<sup>29–33</sup>

Excluded articles are systematically documented in Appendix Table 3.<sup>34–43</sup>

The aggregate of trials that satisfied the inclusion criteria comprised 120 bone graft sites and 141 implants in total. Details of the collected trials are summarized in

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#### Table 1 Summary of the Enrolled Participants in the Retrieved Randomized Controlled Trials

First author, year	Country	Participants (F/M)	Age*	Study design	Test group graft N (implant N)	Control group graft N (implant N)	Allocation concealment	Randomization	Funding/ grants/ support
Lima, 2018 <sup>25</sup>	Brazil	Total: 8 (5/3)	53.3 ± 9.5	RCT, split- mouth	8 (8)	8 (8)	Independent investigator	Computer- generated	N/A
Thoma, 2019 <sup>28</sup>	Switzerland	Test: 12 Control: 12	Test: 56.17 ± 12.64 Control: 47.50 ± 17.73	RCT	12 (20)	12 (20)	Sealed envelope	Computer- generated	<ul> <li>Geistlich</li> <li>Pharma</li> <li>Dentsply-</li> <li>Sirona</li> </ul>
Romito, 2022 <sup>27</sup>	Brazil	Test: 32 (22/10) Control: 32 (20/12)	Test: 45.3 ± 10.1 Control: 43.6 ± 9.7	RCT, open- label	30 (30)	30 (30)	N/A	Not mentioned	<ul> <li>Geistlich</li> <li>Pharma</li> <li>Osteology</li> <li>Foundation</li> </ul>
Marques, 2023 <sup>26</sup>	Brazil	Test: 5 Control: 5	Not mentioned	RCT, split- mouth	5 (5)	5 (5)	Not mentioned	Online service	N/A

F = female; M = male; N = number; RCT = randomized controlled trial; N/A = not applied.

\*Age is presented as mean  $\pm$  standard deviation or as median (range).

Tables 1 and 2, while specific intervention particulars, target outcomes, and complications are outlined in Table 3.

#### Primary Outcome HBG

Four studies measured alveolar ridge thickness via CBCT scan,<sup>25–28</sup> and five studies measured alveolar ridge thickness via calipers at reentry.<sup>29–33</sup> A weighted mean of 4.38 mm (95% CI = 3.63 to 5.13, I<sup>2</sup> = 92.5 %) of

HBG was computed from 120 grafted sites in 9 studies, which had a follow-up period of 4 to 10 months (Fig 3); note that high heterogeneity was found among these studies. However, in the combined data from four trials<sup>25–28</sup> that specifically compared XBBs with ABBs (Fig 4), the XBBs group exhibited a mean difference of 0.72 mm (95% CI = 0.067 to 1.382, P = .031,  $I^2 = 28.2$  %), which was statistically significant greater than ABBs. In addition, low heterogeneity was observed in each analysis (Appendix Fig 1).

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Table 2 Summa	ry of the l	Enrolled Part	icipants in	the Retrieved Pro	spective Tria	ls
First author, year	Country	Participants (F/M)	Age*	Study design	Graft site N (implant N)	Funding/grants/support
Schwarz, 2017 <sup>33</sup>	Germany	5/4	49.4 (36–72)	Prospective single- arm cohort	10 (8)	Geistlich Pharma
Ortiz-Vigón, 2018 <sup>30</sup>	Spain	12/3	54.5 (8.34)	Prospective single- arm cohort	15 (24)	N/A
Qiu, 2018 <sup>32</sup>	China	14	29.3	Prospective single- arm cohort	14 (21)	Program for New Clinical Techniques and Therapies of Peking University School and Hospital of Stomatology
Angermair, 2020 <sup>29</sup>	Germany	3/2	51.6 (22–66)	Prospective single- arm cohort	10 (9)	Geistlich Pharma
Parvini, 2021 <sup>31</sup>	Germany	12/4	46.0 ± 14.0	Prospective single- arm cohort	16 (16)	Geistlich Pharma

F = female; M = male; N = number; N/A = not applied.

\*Age is presented as mean ± standard deviation or as median (range).

# Secondary Outcomes

#### HBR

Four studies showed the HBR data of XBBs.<sup>25,26,28,32</sup> Computed from 39 grafted sites with a follow-up period of 4 to 8 months, a weighted mean resorption of horizontal bone thickness was 0.85 mm (95% CI = -1.221 to -0.474,  $I^2$  = 41.0 %) (Fig 5).

In three out of the four studies that directly compared XBBs with ABBs on HBR,<sup>25,26,28</sup> there was no statistically significant difference between them (mean difference = -0.056, 95% CI = -0.667 to 0.555, P = 0.857,  $I^2 = 0\%$ ) (Fig 6).

#### Graft survival rates

A total of 120 graft sites of XBB had follow-up periods of 4 months to 6 years postoperatively, of which 9 failed and were removed before implant placement. The weighted graft survival rate of XBB was 91.3% (95% CI = 76.6% to 97.1%, I<sup>2</sup> = 58.0%) (Fig 7).

#### Implant survival rates

A total of 141 implants were placed in 111 patients who received XBBs. The follow-up period ranged from 4 months to 6 years. The weighted implant-based implant survival rate was 84.3% (95% CI = 72.6% to 91.6%,  $I^2 = 31.6$ %) (Fig 8).

#### Soft tissue dehiscence rates

The weighted soft tissue dehiscence rate was 18.8% (95% CI = 8.4% to 36.9%,  $I^2 = 61.5\%$ ) (Fig 9).

#### Histologic analysis

Four studies<sup>26,29,35,39</sup> had descriptive or analytical histologic findings. Three studies<sup>29,35,39</sup> revealed mean percentages of mineralized vital bone in XBBs that ranged from 11.6% to 29.8%, as well as mean percentages of residual graft materials that ranged from 9.6% to 22.2%. Two out of the four studies<sup>26,39</sup> had control groups that were ABB grafts harvested from the mandibular ramus or chin. The percentages of mineralized tissue of these control groups ranged from 53.5% to 75%.

#### Sensitivity Test

When comparing XBBs with ABBs, the direction of association between the use of XBBs and HBG was consistent, and it was not altered when any of the included studies were removed from the analysis (Appendix Fig 2). However, for graft survival rates and implant survival rates, the data from Angermair et al<sup>29</sup> appeared to be lower than other studies. After conducting the onestudy removal test (removing Angermair et al<sup>29</sup>), the graft survival rate was increased to 94.0% and the implant survival rate was increased to 86.9 (Appendix Figs 3 and 4).

#### Methodologic Quality of the Included Studies

Regarding the overall methodologic quality of the randomized studies included in our analysis, our assessment using RoB2 revealed that 50% of the assessed studies had a "low" RoB, while the remaining 50% had "some" RoB. None of the studies were found to have a "high" RoB (see Fig 1). Upon conducting a detailed assessment, two studies<sup>26,28</sup> were rated as having "some" RoB in the randomization process due to the absence of allocation concealment details. The details of the RoB2 assessment are summarized in Table 4. Nonrandomized prospective cohort studies enrolled in the present study were evaluated with the NOS, and the scores ranged from 6 to 7 (Table 5).

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Table 3 Details	of Data Extra	action from Included Trials		
First author, year	Materials	Method, analysis	Clinical and histologic outcome	Complications
Schwarz, 2017 <sup>33</sup>	CXBB + DBBM + CM	<ul> <li>Reentry, 6 months postgrafting: measuring with caliper, 2 mm below crest</li> <li>100% follow-up at 2.5 years</li> </ul>	• Baseline width: 4.18 ± 0.92 mm • Reentry width: 7.18 ± 2.64 mm	<ul> <li>Graft loss: 0/10 site-based</li> <li>Implant loss: 0/8 implant, patient-based</li> <li>Soft tissue dehiscence: Early: 7/10 Late: 4/7</li> </ul>
Ortiz-Vigón, 2018 <sup>30</sup>	CXBB + DBBM + CM	<ul> <li>Reentry, 26 weeks postgrafting: measuring with caliper, 2 mm below crest, and vertical bone biopsy</li> <li>Up to 50 weeks follow-up after grafting</li> </ul>	<ul> <li>Baseline width: 2.78 ± 0.57 mm</li> <li>Reentry width: 6.90 ± 1.22 mm</li> <li>Mineralized vital bone (MVB): 26.90% ± 12.21%</li> <li>Residual CXBB: 20.89% ± 7.35%</li> <li>Marrow: 26.24% ± 16.43%</li> <li>Connective: 25.05% ± 22.07%</li> </ul>	<ul> <li>Graft loss: 2/15 site, patient- based</li> <li>Implant loss: 7/24 (without graft failure) implant-based, 4/13 patient-based</li> <li>1 maxilla, 6 mandible; 4 before loading, 3 after loading</li> <li>Soft tissue dehiscence: Early: 5/15 site-based</li> </ul>
Qiu, 2018 <sup>32</sup>	Graft: 1 mm ramus cortical plate + CXBB + DBBM + CM	<ul> <li>Anterior maxilla only</li> <li>Reentry, 6 months postgrafting: measuring with caliper, 1 mm below crest</li> <li>6-year follow-up</li> </ul>	<ul> <li>Baseline width: 3.36 ± 0.69 mm</li> <li>Immediate postgrafting width: 9.39 ± 0.71 mm</li> <li>Reentry width: 8.73 ± 0.82 mm</li> <li>Resorption rate: 7.03%</li> <li>All implants had torque &gt; 35 Ncm</li> </ul>	<ul> <li>Graft loss: 0/14 site-based, patient-based</li> <li>Implant loss: 0/21 implant- based, 0/14 patient-based</li> <li>Soft tissue dehiscence: Early: 0/14 site-based, Late: (4/14) site-based, with isolated graft</li> </ul>
Angermair, 2020 <sup>29</sup>	CXBB + DBBM + CM	<ul> <li>Reentry, 6.9 months postgrafting: measuring with caliper and horizontal bone biopsy</li> <li>Mean follow-up time: 28.9 months</li> </ul>	<ul> <li>Baseline width: 3.5 ± 0.7 mm</li> <li>Reentry width: 7.1 ± 0.9 mm</li> <li>3-month mean new bone formation: 8.6% (4%–13%)</li> <li>6-month mean new bone formation: 11.6% (1.6%–22%)</li> <li>Residual graft: 22.2%</li> </ul>	<ul> <li>Graft loss: 6/10 site-based, 4/5 patient-based</li> <li>Implant loss: 3/9 implant-based (combined with graft failure), 2/5 patient-based 3 after loading (1 maxilla, 2 mandible)</li> <li>Soft tissue dehiscence: 3/10 sites, 2 related to graft loss</li> </ul>
Parvini, 2021 <sup>31</sup>	CXBB + DBBM + CM	<ul> <li>13 posterior mandible, 3 anterior maxilla</li> <li>Reentry, 26 weeks postgrafting: measuring with caliper, 2 mm below crest</li> </ul>	• Horizontal bone gain: 5.09 ± 1.07 mm	<ul> <li>Graft loss: 0/16 site, patient- based</li> <li>Implant loss: 0/16 implant, patient-based</li> <li>Soft tissue dehiscence: Early 1/16 site-based</li> </ul>
Lima, 2018 <sup>25</sup>	Test: CXBB + CM Control: Ramus block + CM	<ul> <li>24 weeks postgrafting: CBCT and caliper, measured adjacent to screw hole</li> <li>Up to 6 months follow-up</li> </ul>	<ul> <li>Test: Horizontal bone thickness Baseline width: 3.6 ± 1.4 mm Reentry width: 9.3 ± 1.6 mm</li> <li>Control: Horizontal bone thickness Baseline width: 3.7 ± 1.6 mm Reentry width: 7.8 ± 1.8 mm</li> </ul>	No postoperative complications
Thoma, 2018, <sup>39</sup> 2019 <sup>28</sup>	Test: CXBB + rhBMP-2 + DBBM + CM Control: Ramus block + DBBM + CM	• 4 months postgrafting: Reentry, CBCT measured at prospect implant shoulder, and vertical bone biopsy	<ul> <li>Test: Horizontal bone thickness Baseline width: 3.6 ± 1.4 mm Reentry width: 9.3 ± 1.6 mm</li> <li>Control: Horizontal bone thickness Baseline width: 3.7 ± 1.6 mm Reentry width: 7.8 ± 1.8 mm</li> <li>Histologic outcome: Test: bone 29.8%, graft 9.6%, soft tissue 31.53% Control: bone 75.8%, graft 0%, soft tissue 7.8%</li> </ul>	1 ABB graft failed (1/12) site- based, patient-based - No implant loss - No soft tissue dehiscence

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Table 3 (cont) D	<b>Details of Dat</b>	a Extraction from Included	Trials	
First author, year	Materials	Method, analysis	Clinical and histologic outcome	Complications
Romito, 2022 <sup>27</sup>	Test: CXBB + DBBM + CM Control: Ramus block + DBBM + CM	<ul> <li>30 weeks postgrafting: CBCT measured at 2 mm below crest</li> <li>Up to 10 months follow-up</li> </ul>	• Horizontal bone gain: Test: 3.69 ± 1.50 mm Control: 3.51 ± 1.23 mm	<ul> <li>Graft loss: Test: 1/30 site, patient-based Control: 0</li> <li>Implant loss (all after loading) Test: 6/30 implant, patient- based (4 maxilla, 2 mandible) Control: 3/10 implant, patient- based (1 maxilla, 2 mandible)</li> <li>Soft tissue dehiscence: Test: 1/32 (related to graft loss) Control: 13/32</li> </ul>
Marques, 2023 <sup>26</sup>	Test: CXBB + DBBM + CM Control: Chin block	<ul> <li>All anterior maxilla</li> <li>8 months postgrafting: Reentry, CBCT measured at 5 mm away from screw, bone biopsy</li> </ul>	<ul> <li>Test: 4.25 ± 0.78 mm</li> <li>Control: 3.08 ± 0.8 mm</li> <li>Histology: Test: 48.10% ± 2.88% mineralized tissue Control: 53.53% ± 1.05% mineralized tissue</li> </ul>	<ul> <li>Graft loss: Test: 0/5 site-based Control: 0/5 site-based</li> <li>Implant loss Test 1/5 implant, patient-based (maxilla, early)</li> <li>No soft tissue dehiscence</li> </ul>

CXBB = collagenated xenogeneic bone block; DBBM = deproteinized bovine bone mineral; CM = collagen membrane; rhBMP-2 = recombinant human bone morphogenetic protein-2.

Fig 3 Forest plot showing that the weighted HBG of XBBs was 4.38 mm (95% Cl = 3.63 to 5.13,  $l^2 = 92.5$ %).

Study name	Stat	istics for	each stud	у	Diff	erence in	means a	nd 95% (	21	
	Difference in means	Lower limit	Upper limit	P value						Relative weight
Qiu 2018	6.030	5.663	6.397	0.000						12.36
Ortiz-Vigon 2018	4.150	3.546	4.754	0.000						11.77
Lima 2018	5.700	4.654	6.746	0.000				-		10.22
Thoma 2019	3.460	2.322	4.598	0.000						9.86
Angermair 2020	3.600	3.093	4.107	0.000						12.04
Schwarz 2021	3.000	1.392	4.608	0.000			-   -	-		8.05
Parvini 2021	5.090	4.566	5.614	0.000						11.99
Romito 2022	3.690	3.240	4.140	0.000						12.18
Marques 2023	4.250	3.566	4.934	0.000				-		11.52
Pooled	4.382	3.630	5.134	0.000				•		
					-8.00	-4.00	0.00	4.00	8.00	

**Fig 4** Forest plot of studies comparing the effect of XBBs and ABBs on HBG. The XBB group showed a mean difference of 0.72 mm (95% Cl = 0.067 to  $1.382, P = .031, l^2 = 28.2 \%$ ), which was statistically significant.

Study name	Sta	tistics for e	each study		Di	fference	in means	and 95%	% Cl	
	Difference in means	Lower limit	Upper limit	P value						Relative weight
Lima 2018	1.600	0.020	3.180	0.047					-	14.44
Thoma 2019	0.540	-1.174	2.254	0.537		-				12.59
Romito 2022	0.180	-0.528	0.888	0.618						43.28
Marques 2023	1.170	0.191	2.149	0.019			- F-1	<b></b>		29.68
Pooled	0.724	0.067	1.382	0.031				•		
					-4.00	-2.00	0.00	2.00	4.00	
						XBB		ABB		

**Fig 5** Forest plot showing the weighted HBR of XBBs as -0.85 mm (negative value means resorption) (95% Cl = -1.221 to -0.474,  $l^2 = 41.0\%$ ).

Study name	Sta	tistics for e	each study		Di	fference i	n means	and 959	% Cl	
	Difference in means	Lower limit	Upper limit	P value						Relative weight
Qiu 2018	-0.660	-1.064	-0.256	0.001		- I -I	-			36.85
Lima 2018	-0.200	-1.199	0.799	0.695				-		11.48
Thoma 2019	-1.580	-2.686	-0.474	0.005	- I -		-			9.69
Marques 2023	-1.020	-1.362	-0.678	0.000		-	-			41.98
Pooled	-0.847	-1.221	-0.474	0.000		_ ₹	▶			
					-3.00	-1.50	0.00	1.50	3.00	

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#### Liu et al



#### ing the effect of XBBs and ABBs on HBR. The mean difference of XBBs compared to ABBs was -0.056 mm (95% CI = -0.667 to $0.555, P = 0.857, I^2 = 0\%$ ).

Fig 7 Forest plot showing that the weighted graft survival rate of XBB was 91.3% (95% CI = 76.6% to

Fig 8 Forest plot showing that the weighted implant survival of XBB was 84.3% (95% CI = 72.6% to

ing that the weighted soft tissue dehiscence rate of XBB was 18.8% (95% CI = 8.4% to 36.9%, l<sup>2</sup> = 61.5%).

# DISCUSSION

Based on the present study, the use of XBBs for lateral ridge augmentation resulted in a weighted mean HBG of 4.38 mm with a HBR of 0.85 mm. This is comparable to the findings of a recent systematic review by Sanz-Sánchez et al,<sup>10</sup> which reported an HBG of 4.25 mm for

ABBs and 4.79 mm for ALB. However, the present study further revealed that XBBs resulted in 0.72 mm greater bone thickness compared to ABBs, as determined by a meta-analysis of four RCTs. This indicated that XBBs still offered greater HBG compared to ABBs in staged lateral ridge augmentation procedures. This may have been attributed to the resorption-resistant properties of XBBs.

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Table 4 Detailed Qu	ality Assessment	of Included St	udies Using Co	chrane RoB 2 T	ool	
First author, year	Randomization process	Intervention adherence	Missing outcome data	Outcome measurement	Selective reporting	Overall RoB
Lima, 2018	L	L	L	L	L	L
Thoma, 2019	L	L	L	L	L	L
Romito, 2022	S*	L	L	L	L	S
Marques, 2023	S*	L	L	L	L	S

H = high risk of bias; L = low risk of bias; S = risk of bias.

\*The studies didn't provide allocation concealment details.

# Table 5 Detailed Quality Assessment of Included Studies Using NOS

		Se	ection		Comparability	Outcome	
First author, year	Representative of patients	Selection of control	Ascertainment of measurement	Demonstration of outcome of interest	Comparability of cohorts on basis of design or analysis	Assessment of outcome	Total point
Schwarz, 2017 <sup>33</sup>	*	-	*	*	*	**	6
Ortiz-Vigón, 2018 <sup>30</sup>	*	-	*	*	*	**	6
Qiu, 2018 <sup>32</sup>	*	-	*	*	*	***	7
Angermair, 2020 <sup>29</sup>	*	-	*	*	*	**	6
Parvini, 2021 <sup>31</sup>	*	-	*	*	*	**	6

Star = one point.

Overall, the results suggested that the use of XBBs for lateral ridge augmentation yields clinically acceptable outcomes, particularly in terms of bone thickness.

According to the present study, the weighted mean graft survival rate for XBBs was 91.2% at the site-based level, and the implant-based implant survival rate was 84.3% in up to a 6-year follow-up period. Comparatively, ABBs are considered the gold standard for block bone grafting material and can achieve close to a 100% survival rate, provided that clinicians follow the proper protocols. Similarly, various data have reported ALB block survival rates ranging from 94.7% to 100%.<sup>11</sup>

Several studies have reported high implant survival rates for ABBs ranging from 96.9% to 100%.<sup>10,44</sup> Similarly, two retrospective studies with sample sizes exceeding 100 implants and with up to 4 years of follow-up reported implant survival rates with the use of ALBs ranging from 91.0% to 99.2%.<sup>12,13</sup> In comparison, the implant survival rate of XBBs was 84.3% in the present study, which was less than the lower range of ALBs and was noticeably inferior to ABBs.

The occurrence of soft tissue dehiscence following horizontal alveolar ridge augmentation procedures can range from 0% to 70%, as reported by Sanz-Sánchez et al.<sup>45</sup> In the present study, the overall weighted rate of soft tissue dehiscence was found to be 18.8%. However, it is important to note that only 3 out of 21 cases of soft tissue dehiscence were reported to be related to graft loss.<sup>28,29</sup> When compared to guided bone regeneration, where achieving primary wound closure is a

crucial surgical principle,<sup>46</sup> the minor dehiscence that is often observed in bone block grafting cases seemed to cause fewer complications. Nevertheless, whether or not these instances of dehiscence are associated with subsequent implant failure remains inconclusive.

Among the nine articles included in this study, four of them were able to calculate the rate of HBR based on the provided data.<sup>25,26,28,32</sup> In these studies, XBBs demonstrated resorption rates ranging from 7.3% to 21%, which were relatively lower than the reported rates of up to 60% for ABBs in previous evidence.<sup>47</sup> This discrepancy may help explain the greater HBG observed with XBBs in lateral ridge augmentation procedures. However, histologic analysis revealed that XBBs had a lower percentage of vital bone (ranging from 11.6% to 29.8%) than ABB, which showed percentages of vital bone ranging from 53.5% to 75%. According to Araujo and Lindhe,<sup>48</sup> the mineralized bone-to-implant contact (BIC) with the intrabony portion of the successful implant was reported to be approximately 60%. In addition, one study found no significant differences in terms of BIC between implants placed in ALBs and ABBs, with BIC percentages of 38.1% and 47.1%, respectively.<sup>49</sup> As a result of comparing with ALBs and ABBs, clinicians may still have concerns regarding the primary stability of implant placement and the ability of osseointegration in XBB graft sites. While there is a lack of human studies specifically investigating BIC on XBBs, one study has reported adequate primary torgue values of more than 35 Ncm during implant placement.<sup>32</sup> However, Lima et al<sup>25</sup> compared autogenous and xenogeneic bone groups and found that the torque value in the xenogeneic group was significantly lower than in the autogenous group ( $32 \pm 22$  Ncm vs  $18 \pm 9$  Ncm, respectively). Overall, both studies found no implant loss, and the difference in torque values could potentially be attributed to the original base bone volume of the host.

It is concerning that a study highlighted the possibility of implant loss even in the absence of complications during bone graft healing<sup>27</sup>; note that grafts had higher survival rates than implants in cases receiving XBB grafting (91.2% to 84.3%). Additionally, based on cumulative data from the present study involving 141 implants, 17 implant losses were observed, 4 of which were classified as early losses occurring before loading. Early implant loss, which can be attributed to failed osseointegration, is directly influenced by the altered primary healing process of the bone replacement graft and its integration with native bone and bone marrow to provide a biologic foundation for dental implant osseointegration. Biopsy samples from sites experiencing later implant failure have shown significantly lower amounts of vital bone (P = .01) and higher amounts of connective tissue (P = .02) compared to sites with successful implants.<sup>35</sup> Nonetheless, the precise mechanisms behind implant loss after loading remain unclear. This highlights the need for further research to better understand and prevent such occurrences.

The present study had several limitations. Firstly, the literature review yielded only four RCTs available, while the other included studies were one-arm prospective cohort studies lacking control groups. Furthermore, randomization was challenging to achieve with the limited evidence currently available to support the use of XBBs in lateral ridge augmentation. Moreover, the longest follow-up period among the included studies was 6 years,<sup>32</sup> which encompassed a sample of just 14 patients. Another study reported a 5-year follow-up period and yet it suffered from a substantial follow-up loss of 77.8%.<sup>37</sup>

To enhance the outcomes associated with the use of XBBs in lateral ridge augmentation, future research should focus on two avenues. First, the use of biologic agents, coupled with the implementation of less invasive surgical techniques, has been posited to enhance clinical outcomes in bone reconstruction procedures. Specifically, the application of recombinant human platelet-derived growth factor-BB (rhPDGF-BB) has shown promise in revitalizing xenografts, potentially rendering bone formation processes more reliable. An illustrative animal study by Nevins et al<sup>50</sup> reported that an equine bone block infused with rhPDGF-BB successfully facilitated vertical ridge augmentation. Nonetheless, corroborative clinical research in human subjects remains sparse, and the results thus far have been inconclusive. The second avenue should be conducting RCTs or prospective cohort studies with extended follow-up periods. This would be helpful to more accurately assess the long-term efficacy and reliability of XBBs for this indication.

# CONCLUSIONS

The use of XBBs in lateral alveolar ridge augmentations demonstrates an acceptable survival rate and yields an adequate bone volume for subsequent implant therapy. Nonetheless, the survival rate of implants placed in laterally augmented ridges with XBBs was less favorable compared to those augmented with ABB grafts.

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The authors declare no conflicts of interest.

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# **APPENDIX**



Appendix Fig 1 The funnel plot of four enrolled RCTs on HBG. The funnel plot of the four included trials showed obvious asymmetry in effect size distributions.

Appendix Fig 2 The direction of association between the use of XBB and HBG was consistent during the onestudy removal test.

Study name	Sta	atistics with stud	ly removed	i	Differe	nce in r stud	neans y remo	(95% C ved	) with
	Point	Lower limit	Upper limit	P value					
Lima 2018	0.522	-0.022	1.066	0.060				·	
Thoma 2019	0.646	0.106	1.185	0.019				F I I	
Romita 2022	1.146	0.398	1.895	0.003			ΗŦ		
Marques 2023	0.433	-0.172	1.037	0.161				-	
Pooled	0.636	0.122	1.151	0.015			- 🖣	•	
					-4.00	-2.00	0.00	2.00	4.00
						XBB		ABB	

Appendix Fig 3 Onestudy removal test of the weighted graft survival of XBB. The data from Angermair et al<sup>29</sup> appeared to be lower than the findings of other studies. With the removal of Angermair's study, the survival rate was 94.0%.

oint Lo		Upper				
	werlimit	limit				
.910	0.742	0.973				
.923	0.748	0.980				
.905	0.734	0.970				
.906	0.736	0.971				
.940	0.872	0.973				
.908	0.739	0.972				- +
.903	0.732	0.970				+
.900	0.722	0.969				
.914	0.750	0.974				
.913	0.766	0.971				
	923 905 906 940 908 903 900 914 913	910         0.742           923         0.748           905         0.734           906         0.736           940         0.872           908         0.739           903         0.732           900         0.722           914         0.750           913         0.766	910         0.742         0.973           923         0.748         0.980           905         0.734         0.970           906         0.736         0.971           940         0.872         0.973           908         0.739         0.972           903         0.732         0.970           900         0.722         0.969           914         0.750         0.974           913         0.766         0.971	910         0.742         0.973           923         0.748         0.980           905         0.734         0.970           906         0.736         0.971           940         0.872         0.973           908         0.739         0.972           903         0.732         0.970           900         0.722         0.969           914         0.750         0.971           913         0.766         0.971	910         0.742         0.973           923         0.748         0.980           905         0.734         0.970           906         0.736         0.971           940         0.872         0.973           908         0.739         0.972           903         0.732         0.970           900         0.722         0.969           914         0.750         0.971	910     0.742     0.573       923     0.748     0.980       905     0.734     0.970       906     0.736     0.971       940     0.872     0.973       908     0.739     0.972       903     0.732     0.970       900     0.722     0.969       914     0.750     0.971

Study name				Difference in means (95% CI) w study removed
	Point	Lower limit	Upper limit	
Qiu 2018	0.816	0.698	0.895	
Ortiz-Vigon 2018	0.875	0.755	0.941	
Lima 2018	0.836	0.709	0.914	
Thoma 2019	0.817	0.698	0.896	
Angermair 2020	0.869	0.750	0.936	
Schwarz 2021	0.836	0.709	0.914	
Parvini 2021	0.822	0.701	0.902	
Romito 2022	0.873	0.730	0.946	
Marques 2023	0.855	0.727	0.929	
Pooled	0.843	0.726	0.916	
				0.00 0.25 0.50 0.75 1.00

Appendix Fig 4 One-study removal test of the weighted implant survival of XBB. The data from Angermair et al<sup>29</sup> appeared to be lower than the findings of other studies. With the removal of Angermair's study, the survival rate increased to 86.9%.

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