



Horizontal ridge augmentation using xenogenous bone graft—systematic review

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Abstract

Purpose This study aimed to perform a systematic review about the use of xenogenous bonegraft in horizontal ridge augmentation to answer the following question: *In implant patients, treated with xenografts for horizontal ridge augmentation, what would be the outcomes in terms of bone gain, bone resorption, implant survival, and complication rates?*

Methods The main search was performed at PubMed, Cochrane, and Scopus databases, and found 2610 articles. After selection and duplicate removal, 29 studies were included in the final review. The collected data were sample size, number and type of graft, site, horizontal gain, resorption rate, and complications.

Results A total of 610 patients were submitted to 853 bone grafts, both in the maxilla and mandible. Most studies ($n = 26$) used particulate grafts, isolated or associated with autogenous bone, and covered by collagen membrane or titanium mesh. The mean of horizontal bone gain was 4.44 mm. In addition, the augmented ridges allowed placement of 1325 successful dental implants. The complication rate was 7.85%, and membrane exposure was the most reported complication.

Conclusions Although the autogenous bone graft remains as the gold standard for alveolar reconstruction, this review suggests that xenogenous bone graft is a feasible alternative for horizontal bone augmentation.

Keywords Alveolar ridge augmentation · Alveolar bone loss · Bone substitutes · Systematic review

Introduction

The alveolar ridge resorption can restrict dental implant placement [1]. Usually, the bone resorption occurs as a consequence of tooth loss, trauma, and pathologies [2]. Therefore, augmentation procedures are performed to provide adequate bone volume for dental implant placement [3]. Residual alveolar ridges according to the main resorbed region are classified as horizontal, vertical, or combined defects. This classification guides the surgeon to the adequate diagnosis and support the treatment decision [4]. Different techniques are available to reconstruct and/or regenerate atrophic alveolar ridges, including ridge split crest, bone block graft, biomaterials, distraction osteogenesis, and guided bone regeneration [5–11].

The autogenous bone is the gold standard for graft procedures due to osteogenesis, osteoinduction, and osteoconduction features. It is used as a block and/or particulate graft [6, 12, 13]. However, the autogenous grafts have some disadvantages includ-

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ing: requirement of a donor site, high morbidity, potential graft resorption, and difficulty to adaptation. Therefore, alternative bone materials from different origins are available, represented by allogenic bone graft (derived from human cadavers), xenogenous bone graft (derived from other animal species), and bone graft substitutes (completely synthetic) [14–16].

The xenogenous bone is used for alveolar ridge augmentation with reliable results, low morbidity, and decreased complication rate [14, 17, 18]. Also, they show a good long-term stability due to the slow resorption characteristic [19]. It is important to highlight that any bone substitute material has osteoinductive feature similar to autogenous bone. Actually, the bone substitute materials support the bone healing process by the osteoconductive characteristic [16, 18–20]. Furthermore, the efficiency of bone substitute materials in augmentation procedures is proved in many studies [17, 19, 21].

The aim of this study was to perform a systematic review of literature on horizontal ridge augmentation using xenogenous bone graft for dental implant placement, to evaluate the bone gain, graft resorption, complication rate, and success.

Materials and methods

This systematic review was directed in accordance for the PRISMA statement (Preferred Reporting Items for Systematic Review and Meta-Analysis) [22], and aimed to

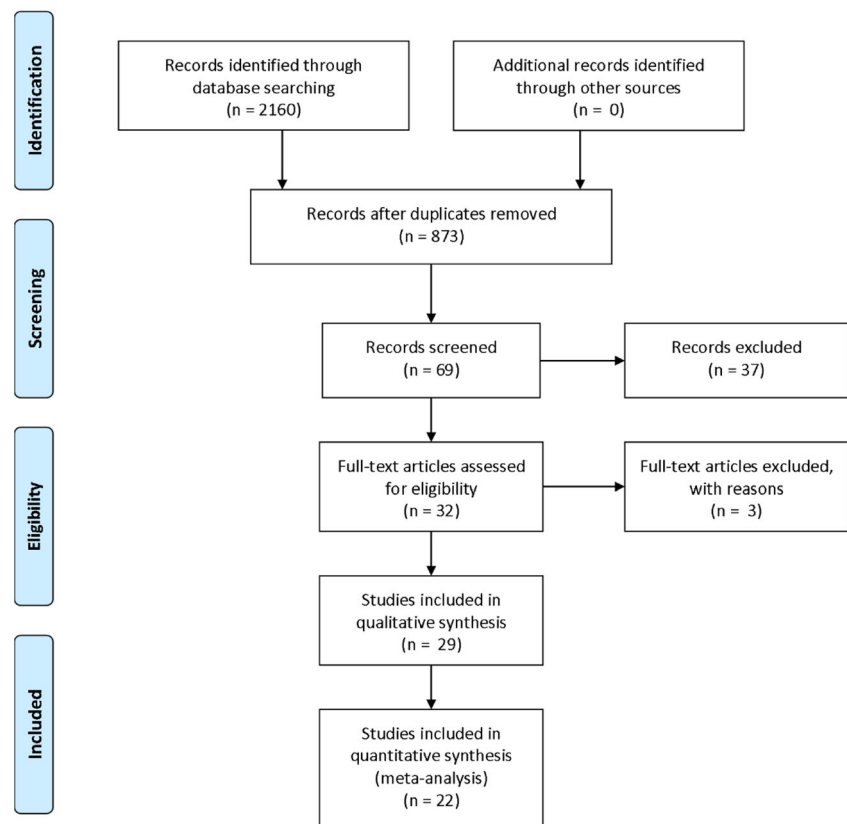
answer the following question: *In implant patients, treated with xenografts for horizontal ridge augmentation, what would be the outcomes in terms of bone gain, bone resorption, implant survival, and complication rates?*

Search strategy and selection criteria

The search strategy was performed in MEDLINE (Medical Literature Analysis and Retrieval System Online, via PubMed), ELSEVIER (via Scopus), and Cochrane Library databases. All possible combinations of the following descriptors were searched: “xenograft,” “Xenogenous,” “bone augmentation,” “bone reconstruction,” “bone particulate,” “bone block,” “bone augmentation,” “bone reconstruction,” “bone particulate,” “bone block,” “lateral augmentation,” “ridge augmentation,” and “horizontal augmentation”.

Three independent reviewers (GC, GST, LBM) analyzed titles and/or abstracts according to the following inclusion criteria: specific studies that evaluated horizontal ridge augmentation using xenogenous bone grafts, studies on humans, reported in the English language, no time restriction regarding to publication date, and study types: case series, retrospective, or prospective clinical trials. The inclusion criteria were broad to bring general results. Technical variations, use of membranes, or type of prosthetic rehabilitation were not considered. Furthermore, bone grafts used in sinus lift procedure or vertical augmentation were not included on this study.

Fig. 1 Flowchart of systematic review process, according to the PRISMA statement



After the initial selection, the researchers evaluated the full-text of the selected articles according to the same inclusion criteria to define the final included studies. Any disagreements between the reviewers were settled by additional discussion.

Data extraction

Data from the included studies was extracted by the reviewers, including the following variables: type of study; augmentation procedure (bone block and/or particulate graft, xenogenous or xenogenous-autogenous mixture); number of patients, age, and gender; number of bone grafts; anatomic region of augmentation; horizontal bone gain; resorption rate; complications; implant viability; and success rate. Again, disagreements between reviewers were solved by further discussion. Data were analyzed by descriptive statistics and horizontal bone gain was evaluated by the confidence interval (95%) from the data.

Quality evaluation

All included studies were evaluated using the PRISMA statement [22] criteria to define the scientific evidence for the clinical decision-making process. This evaluation classifies

the potential risk of bias of each study, analyzing the following criteria: random sample selection, definition of inclusion and/or exclusion criteria, report of losses to follow-up, validated measurements obtained, and statistical analysis. Studies meeting all criteria were classified as low risk of bias, those that did not meet one of the criteria were classified as moderate risk of bias, and those that did not meet two or more criteria were classified as high risk of bias.

Results

The electronic search was performed by two authors (GC and GST) in March 04, 2017 resulting in 2160 articles. After duplicate removal and the reading of titles and/or abstracts, 69 articles were selected. The full-text of all the selected articles was reviewed for the inclusion criteria. Thus, 37 articles did not meet one or more inclusion criteria in title and/or abstract, and three articles were excluded after full reading. Therefore, 29 articles were included in the final selection. A flowchart of the selection and inclusion process is present in Fig. 1.

All the included articles ranged between 2001 and 2017. Among them, 18 studies were prospective, 10 were retrospective,

Table 1 PRISMA quality assessment of bias from selected papers

Year	Author	Randomization	Include/exclude criteria	Loss of follow-up	Valid measurements	Statistical analysis	Risk of bias
2016	Amoian et al.	Yes	Yes	Yes	Yes	Yes	Low
2016	Gultekin et al.	No	Yes	Yes	Yes	Yes	Moderate
2016	Meloni et al.	No	Yes	Yes	Yes	Yes	Moderate
2016	Pelegrine et al.	Yes	Yes	Yes	Yes	Yes	Low
2016	Schwarz et al.	No	Yes	Yes	Yes	No	High
2016	Urban et al.	No	Yes	Yes	Yes	No	High
2016	Wessing et al.	No	Yes	Yes	No	No	High
2015	Merli et al.	Yes	Yes	Yes	Yes	Yes	Low
2015	Monje et al.	No	Yes	Yes	Yes	Yes	Moderate
2014	Kolerman et al.	No	Yes	Yes	Yes	Yes	Moderate
2014	Mordenfeld et al.	Yes	Yes	Yes	Yes	Yes	Low
2014	Pistilli et al.	Yes	Yes	Yes	Yes	Yes	Low
2013	de Stavola et al.	Yes	Yes	Yes	Yes	No	Moderate
2013	Poulias et al.	Yes	Yes	Yes	Yes	Yes	Low
2013	Shalash et al.	No	Yes	Yes	Yes	Yes	Moderate
2013	Urban et al.	No	Yes	Yes	Yes	Yes	Moderate
2012	Block et al.	No	Yes	Yes	Yes	Yes	Moderate
2012	Khammees et al.	No	Yes	Yes	Yes	Yes	Moderate
2012	Pagliani et al.	No	Yes	Yes	Yes	Yes	Moderate
2011	Calvo-Guirado et al.	No	No	No	No	Yes	High
2011	Cordaro et al.	Yes	Yes	Yes	Yes	Yes	Low
2011	Urban et al.	No	Yes	Yes	Yes	Yes	Moderate
2009	Di Stefano et al.	No	Yes	Yes	Yes	Yes	Moderate
2008	Pieri et al.	No	Yes	Yes	Yes	Yes	Moderate
2007	Hammerle et al.	No	No	Yes	Yes	Yes	High
2006	Steigman	No	No	Yes	Yes	No	High
2006	Von Arx et al.	No	Yes	Yes	Yes	No	High
2003	Hellem et al.	No	Yes	Yes	Yes	No	High
2001	Hising	No	Yes	Yes	Yes	Yes	Moderate

Table 2 Data extraction of included papers after full reading screening

Year	Author	Study design	Sample	Grafts	Graft sort	Grafted area	Horizontal gain (mm)	Resorption (mm or %)	Implants (success rate)	Complications	Impossibility of implant/new graft needed	Age (mean \pm SD; range)
2016	Amoian et al.	Prospective	10	13	Particulate xenogenous (CenoBone and Bio-Oss) + collagen membrane	Mandible	2.93 (Cenobone)/3.37 (Bio-Oss)	*	*	*	*	30 to 50
2016	Gultekin et al.	Retrospective	24	28	Particulate autogenous or xenogenous + collagen membrane	Maxilla	5.42 \pm 0.76	12.48 \pm 2.67%	23 (100%)	–	1	48.82 \pm 10.17 (28–67)
2016	Meloni et al.	Prospective	18	22	Particulate autogenous or xenogenous (1:1) + collagen membrane	Posterior maxilla and mandible	5.03 \pm 2.15	*	55 (100%)	Membrane exposure without graft loss (2)	–	56.8 (24–78)
2016	Pelegrine et al.	Prospective	8	8	Particulate xenogenous (control) or particulate xenogenous + aspirated bone marrow (test)	Anterior maxilla	4.34 \pm 1.58 (control) 4.09 \pm 1.33 mm (test)	*	> 16 (100%)	–	–	52.4 \pm 2.2
2016	Schwarz et al.	Retrospective	10	10	Xenogenous block and particulate + collagen membrane	Maxilla and mandible	3.00 \pm 2.20 (<i>n</i> = 10)/3.88 \pm 1.75 (<i>n</i> = 8)	*	8 (80%)	Dehiscence (7); block resorption (4); screw exposure (1).	2	47.4 (34–70)
2016	Urban et al.	Retrospective	16	19	Particulate autogenous and xenogenous (1:1) + d-PTFE or e-PTFE or collagen membrane	Maxilla and mandible	7.0 \pm 1.5	1.4 \pm 1.0 mm	122 (97.6%)	–	–	64.6 \pm 14.6 (48–80)
2016	Wessing et al.	Retrospective	36	49	Particulate xenogenous or xenogenous + autogenous chips (1:1) + collagen membrane	Maxilla and mandible	*	*	103 (100%)	Dehiscence (6); GRAFT loss (2)	1	57.7 \pm 12 (32–76)
2015	Merli et al.	Prospective	50	50	Particulate xenogenous + collagen membrane or β -TCP + collagen membrane	Maxilla and mandible	3.1 \pm 1.2 (Bio-Oss)/3.5 \pm 1.7 (β -TCP)	0.77 \pm 0.36 mm (Bio-Oss)/0.54 \pm 0.45 mm (β -TCP)	61 (100%)	Bio-Oss: dehiscence (1), infection (1), paresthesia (1); β -TCP: dehiscence (1), infection (2)	–	Bio-Oss: 56 \pm 13 (31–76); β -TCP: 53.4 \pm 12.4 (30–76)
2015	Monje et al.	Retrospective	14	19	Autogenous block (mandibular ramus) and particulate xenogenous + collagen membrane; autogenous block (iliac crest) and particulate xenogenous + collagen membrane	Anterior maxilla	3.23 \pm 1.46 (RM); 4.93 \pm 1.84 (CI)	*	*	–	–	18–85
2014	Kolerman et al.	Retrospective	41	122	Split crest + particulate xenogenous + collagen membrane	Maxilla and mandible	3.5 \pm 0.93	*	122 (95.80%)	Dehiscence (15); cover screw exposure (18)	6	(19–77)
2014	Mordenfeld et al.	Prospective	13	28	Particulate autogenous and xenogenous	Maxilla and mandible	4.0 \pm 1.4 (G90:10)/4.5 \pm 1.3 (G60:40)	2.3 \pm 1.7 mm (34.7 \pm 23.5%) (G90:10)/1.8 \pm 1.4 mm (27.2 \pm 18.7%) (G60:40)	71 (97.18%)	Dehiscence (7)	1	59.6 (29–75)
2014	Pistilli et al.	Prospective	20	20	Autogenous block or xenogenous block + collagen membrane	Maxilla and mandible	3.7 \pm 2.1	*(Graft loss in 50% of cases)	53 (64%)	Dehiscence with graft loss (9), severe or total graft resorption (1), graft mobility (1), bone sequestration (1), graft recontouring needed (1).	10	46.8 (21 to 60)

Table 2 (continued)

Year	Author	Study design	Sample	Grafts	Graft sort	Grafted area	Horizontal gain (mm)	Resorption (mm or %)	Implants (success rate)	Complications	Impossibility of implant/new graft needed	Age (mean ± SD; range)
2013	de Stavola et al.	Prospective	10	10	Particulate xenogenous + resorbable membrane	Posterior mandible	5.6 ± 0.3	0.25 ± 0.29 mm	*	–	–	46.6 (20–63)
2013	Poulias et al.	Prospective	12	12	Particulate xenogenous + resorbable membrane	Maxilla and mandible	0.50 ± 0.60	0.30 ± 0.9 mm	23 (100%)	–	–	G1, 52 ± 16 (26–77); G2, 58 ± 11 (38 to 71)
2013	Shalash et al.	Prospective	18	18	β-TCP (G1) or β-TCP and particulate xenogenous (G2) + non-resorbable membrane	Maxilla and mandible	1.96 ± 0.25 (G1)/2.44 ± 0.34 (G2)	*	19 (89.47%)	Membrane exposure (2)	2	31.5 (18–45)
2013	Urban et al.	Prospective	25	76	Particulate autogenous and xenogenous (1:1)+collagen membrane	Maxilla and mandible	5.68 ± 1.42	*	76 (100%)	Infection (1)	1	52.7 (30–72)
2012	Block et al.	Retrospective	12	12	Particulate xenogenous + resorbable membrane	Anterior maxilla	2.8 ± 0.53	< 1 mm	12 (100%)	Dehiscence with partial graft loss (1)	–	42.5 (19–65)
2012	Khamees et al.	Prospective	13	16	Autogenous block + particulate xenogenous + titanium mesh	Maxilla	2.88 ± 0.57	1.67 ± 1.00 mm	23 (100%)	Mesh exposure (4)	–	28.19 ± 11.39 (13–55)
2012	Pagliari et al.	Prospective	19	19	Particulate xenogenous + resorbable membrane	Maxilla and mandible	3.7 ± 1.5	1.0 ± 1.1	34 (97.1%)	–	1	46.3
2011	Calvo-Guirado	Case-control	20	20	Particulate xenogenous + titanium mesh	Posterior mandible	*	*	*	–	–	*
2011	Cordaro et al.	Prospective	17	22	Autogenous block + particulate xenogenous + bi-layer collagen membrane	Maxilla and mandible	3.93 ± 1.36	0.25 ± 0.23	55 (100%)	Dehiscence (1); membrane exposure with partial graft loss (2)	–	42 (19–66)
2011	Urban et al.	Prospective	18	20	Particulate autogenous and xenogenous + resorbable membrane (glycolide and trimethylene carbonate)	Maxilla and mandible	5.56 ± 1.45†	*	43 (100%)	–	–	49.91 (30–60)
2009	Di Stefano et al.	Retrospective	5	5	Particulate xenogenous + Ti-PtFe	Posterior mandible	3.28 ± 0.04	*	15 (100%)	–	–	45.5 (32–59)
2008	Pieri et al.	Prospective	16	19	Particulate autogenous and xenogenous (70:30) + titanium mesh	Maxilla and mandible	4.16 ± 0.59	1.37 ± 0.32 mm	44 (93.18%)	Mesh exposure (1); resorption around implants (3)	–	49.63 ± 10.56 (29–64)
2007	Hammerle et al.	Prospective	12	15	Xenogenous particulate or xenogenous block + resorbable membrane	Maxilla	3.6 ± 1.5	*	15 (100%)	–	–	44 (20–82)
2006	Steigman	Retrospective	8	19	Xenogenous particulate + collagen membrane	Maxilla and mandible	3.04 ± 1.66	*	19 (100%)	Implant threads exposure (1)	1	(35–68)
2006	Von Arx et al.	Prospective	42	58	Autogenous block and xenogenous particulate + collagen membrane	Maxilla and mandible	4.6 ± 1.05	0.36 ± 0.52 mm	*	Hematoma and dehiscence (1). Membrane exposure (3).	2	34 (17–75)
2003	Hellem et al.	Prospective	30	29	Autogenous and xenogenous particulate + fibrinogen	Maxilla and mandible	*	*	82 (95.9%)	Embolism (1) (related to donor site)	–	41.6
2001	Hising	Retrospective	71	92	Autogenous and xenogenous particulate + thrombin	Maxilla and mandible	*	< 1 mm	231 (80.5%)	Infection (2)	2	60 ± 11 (24–84)
Total			608	850								

* Absent information

† Authors presents autogenous bone grafts and autogenous + xenogenous grafts, the mean gain represents the gain for both groups

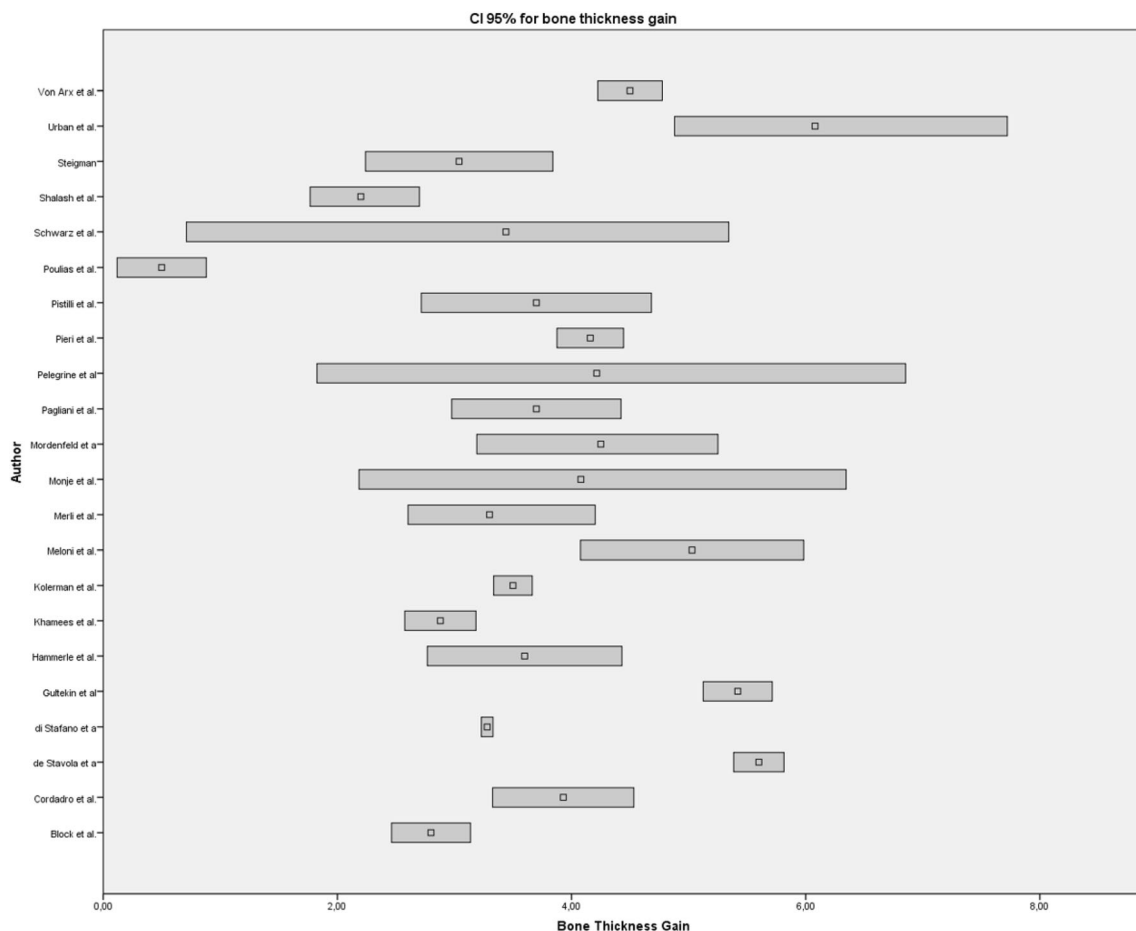


Fig. 2 Horizontal bone gain (in millimeters), 95%CI according to available data

one was case-control, and one was case series. Table 1 shows the quality assessment and bias risk of the selected papers.

Table 2 presents the extracted data for each reviewed article. The mean of horizontal bone gain was 4.44 mm, ranging from 0.11 to 7.72 mm (Fig. 2). In contrast, 18 studies reported resorption data, in millimeters and/or percentage. The means of resorption rate were 1.29 ± 1.11 mm and $24.4 \pm 11.04\%$. The complication rate was 7.95%, and membrane exposure was the most frequent reported one. Furthermore, the achieved horizontal volume allowed implant placement with a success in 96.93% of the cases.

Discussion

This study aimed to aggregate qualified scientific information about horizontal ridge augmentation using xenogenous bone grafts to clarify and discuss its advantages, indications, and complications. In total, 610 patients were submitted to 853 augmentation procedures, involving both the maxilla and mandible. The xenogenous bone grafts were used in different forms, 73.0% of studies used xenografts as particulate graft, alone or associated with autogenous bone. Furthermore,

usually, the grafts were covered by a membrane. Most of the studies used absorbable membrane [2, 14, 23–40], and few studies used titanium mesh [41–43]. Moreover, two studies applied a fibrin sealant—containing fibrinogen, aprotinin, and thrombin—to the grafted area [44, 45]. The application of barriers probably decreases the resorption rates, but the type is not relevant for bone gain [3, 7, 10, 23, 24, 29].

This systematic review was not limited to clinical trials to achieve more data about the use of xenografts. Thus, it was observed that particulate xenograft was the most frequently used, followed by the mixture between autogenous and xenogenous particulate grafts.

Some disadvantages of autogenous bone such as high rates of resorption, harvesting surgery morbidity, and limited amount of volume, stimulated researchers to investigate about bone material substitutes as feasible alternatives [46–48]. Furthermore, most of the studies are from the last 10 years, revealing that this subject is recent and there is a lack of absolute information. The autogenous graft seems to have a significant higher resorption rates when compared with xenografts. In our review, the average resorption for xenografts was 24.4%, while the literature report average resorption rates varying from 10 to 49% for autogenous bone grafts [14, 49–52].

Regarding complications, 13 studies did not report any type [1, 2, 26, 28, 30, 31, 33, 36, 37, 40, 42, 53]. On the other hand, the remaining studies demonstrate dehiscence as the most common complications, however not leading to major problems. Another common complication was membrane exposure with no need of surgical interventions. However, seven studies reported graft infection, failure, and need re-operation.

Horizontal augmentation procedures using xenografts are feasible, presenting significant bone gain and low rates of complications. Esposito et al. [18] published a systematic review evaluating the efficacy of both horizontal and vertical augmentation procedures. However, they found few evidences about horizontal augmentation, with only one clinical trial. In our review, 18 studies were prospective and seven of them presented low risk of bias.

Wessing et al. (2018) [54] published a similar review; however, they have considered any kind of grafts, as fresh frozen bone grafts, autogenous grafts, or xenografts. Beyond our analysis considered only graft procedures with presence of anorganic bone materials, we found a similar treatment success rate, 99.13% (CI, 97.23–99.96) in the Wessing et al. study and 96.43% (CI, 95.43–97.43) in our study.

According to the reviewed studies, xenogenous graft provides proper amount of bone augmentation in thickness (mean 4.44 mm), and high rates of success for implant placement. Just one study presented lower success for implant placement (64%) [14]. However, this study was the only one that used bone blocks from equines and showed 50% of graft loss, which is not reported in any other study [14].

The highest thickness gain was shown by Urban et al. [37] and Gultekin et al. [30], both using a combination of autogenous and xenogenous particulate grafts. These findings agree with the hypothesis that anorganic xenogenous graft could slow the resorption of autogenous bone [7, 25, 30] increasing the volume to the grafted area [1, 2, 27, 52].

The study with the greatest sample size was Kolerman et al. [38] and achieved a mean gain of 3.5 mm (SD 0.93 mm) using a combined technique of split crest and interpositional particulate graft.

The limitation of this systematic review was the impossibility to perform meta-analysis due to the variability and lack of standardization of data. Moreover, despite the number of studies included, only one of them was a randomized clinical trial. Therefore, future studies should explore this lack of clinical trials about the use of bone substitutes in augmentation procedures, especially for horizontal augmentation.

The xenogenous bone grafts, regardless of form of use, presented high success rate without major complications. Those procedures allowed implant placement in 96.63% of the cases. Autogenous block grafts show success rates from 92 to 100% [55]. However, there are few data about

implant installation in grafted areas. Therefore, it is possible to conclude that xenografts are a feasible alternative to autogenous bone grafts in horizontal augmentation. Additionally, we encourage researchers to perform controlled randomized clinical trial in this area due to the lack of strong evidence about implant insertion torque, initial stability, and osseointegration failures in grafted areas.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The work used secondary data, and certified that all procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2008.

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