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SYSTEMATIC REVIEW

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Bone preservation or augmentation simultaneous with or prior to dental implant placement: A systematic review of outcomes and outcome measures used in clinical trials in the last 10 years

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Abstract

Aim: To evaluate outcome measures and methods of assessment in clinical studies on bone augmentation/preservation procedures for the placement of dental implants.

Materials and Methods: A systematic search was performed on three databases from January 2011 to April 2021 to identify clinical studies reporting on any type of bone augmentation/preservation procedure. The outcomes that have been used to assess efficacy or performance in each study were registered and assigned to different domains (group of outcomes). The review followed the Preferred Reporting Items for Systematic Review and Meta-Analyses statement.

Results: Seven-hundred and eighty-three publications were included. Only 81.8% of the papers had a clear definition of their primary outcome. The rate of complications (59.3%), implant survival (58.2%), 3D radiographic bone gain/change (30%), marginal bone level (MBL; 29%), and histological outcomes (25.5%) were the most frequently reported outcome domains. The most commonly used primary outcome was 3D radiographic bone gain/change (25.8%), followed by implant survival (13.0%). Patient-reported outcome measures (PROMs) were reported in 15.7% of studies. Differences in the reported outcomes were observed among different types of bone preservation/augmentation interventions (i.e., alveolar ridge preservation, immediate implants, horizontal and/or vertical ridge augmentation, and sinus floor augmentation).

Conclusion: Within the past decade, great heterogeneity was observed among the outcomes considered in studies evaluating bone preservation/augmentation procedures. Three-dimensional radiographic bone gain/change was the most routinely reported main outcome variable, while PROMs were rarely reported.

KEYWORDS
alveolar ridge preservation, bone augmentation, dental implants, immediate implants, sinus floor elevation

1 | INTRODUCTION

Insufficient bone volume is a common and important limitation for the placement of dental implants in the optimal position for the future delivery of a prosthetic restoration. A variety of bone augmentation procedures have been evaluated, such as guided bone regeneration, sinus floor elevation, onlay/inlay bone grafting, ridge preservation procedures, or distraction osteogenesis (Naenni et al., 2019; Raghoebar et al., 2019; Thoma et al., 2019; Urban et al., 2019). Bone augmentation is a major topic of interest in the field of implant dentistry. Indeed, in the past decade, approximately 22% of clinical studies in the field of dental implantology were on bone augmentation procedures (Wu et al., 2020).

A variety of outcome measures have been reported to assess the efficacy and effectiveness of bone augmentation procedures, including implant survival, parameters indicative of peri-implant health, clinical and/or radiographic assessments of bone dimensional changes, aesthetic outcomes, patient-reported outcome measures (PROMs), and histological analyses (Castro et al., 2021; R. E. Jung, Brügger, et al., 2021; E. H. Jung, Jeong, & Lee, 2021; Santos et al., 2021). However, the inclusion of outcome measures in many studies is usually based on previous studies or clinical expertise. Moreover, an appropriate selection of outcome measures helps in comprehensively reflecting the treatment effect, although the right combination of outcomes is seldom reported. As an example, it was stated that only 22% of the published trials reported on both clinical findings and PROMs (Fleming et al., 2016). In addition, a large number of studies failed to report all the outcomes they have measured, which might introduce outcome reporting bias (Sendyk et al., 2019) and lead to research waste (Pandis et al., 2021). The inconsistency of outcome measures among studies might bring large heterogeneity when pooling results in meta-analyses, which reflects the importance of reporting appropriate and standardized outcomes, as well as applying unified and reproducible measurements.

The core outcome sets and measurements (COSM) collects minimum sets of outcomes to be measured in any clinical study to improve the efficiency of the research process and the transparency in reporting the results (Clarke, 2007). If the outcomes of a given study are not present in the COSM, or are present but not adequately reported, such issue should be pre-determined and explained in the study protocol (Williamson et al., 2012).

The aim of adopting the COSM is to standardize outcome reporting, increase research relevance, and synthesize more evidence with less heterogeneity. Furthermore, the COSM could be used in daily clinical practice as a tool to assess treatment outcomes and improve patient care (Williamson et al., 2012). In dentistry, several COSMs have been reported in the field of orthodontics (Tsichlaki et al., 2020), traumatic injuries (Kenny et al., 2018), and periodontology (Lamont et al., 2021). However, currently there is no feasible, validated, and ethically approved COSM in implant dentistry.

Thus, the objectives of the present study were (i) to identify the outcomes and domains that have been used in clinical research of bone augmentation/preservation procedures, and (ii) to synthesize such outcomes to provide a background for the development of a COSM in this field of research. The PICO format question for the present review was as follows: "In patients needing one or more dental implants (Population) receiving bone preservation or augmentation procedures alone (Intervention) or in comparison with a control treatment (Control), which outcomes have been used to assess efficacy or performance (Outcome)?"

Clinical Relevance

Scientific rationale for study: It has not been determined which outcomes should be reported in studies on bone augmentation/preservation procedures for the placement of dental implants.

Principal findings: Over the past 10 years, a number of outcomes have been considered. The rate of complications, implant survival, 3D radiographic bone gain/changes, marginal bone levels, and histological outcomes were the most frequently reported, while economic outcomes where almost non-existent.

Practical implications: The establishment of a core set of outcomes and measurements would be valuable for future studies in bone augmentation/preservation procedures.

2 | MATERIALS AND METHODS

2.1 | Protocol development and focused question

This systematic review is reported following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 statement (Moher et al., 2009). The review protocol (no. CRD42021252768) was registered in the International Prospective Register of Systematic Reviews (PROSPERO) hosted by the Centre for Reviews and Dissemination, University of York, National Institute for Health Research (United Kingdom).

2.1.1 | Eligibility criteria

Inclusion criteria (PICOS)

- *Population*: Patients in need of one or more dental implants.
- *Intervention*: Any type of bone preservation/augmentation procedure. These treatments could have been performed at the time of tooth extraction (alveolar ridge preservation [ARP]) or later, and prior to or simultaneous with implant placement.
- *Comparison*: Any type of bone preservation/augmentation procedure different from the treatment received in the intervention, the absence of treatment in non-controlled studies, or the application of the same procedure as in the intervention but without

any graft (e.g., sinus floor augmentation [SFA] procedure without a graft).
- *Outcome*: Any outcome that has been used to assess efficacy or performance.
- *Study design*: Randomized clinical trials (RCTs), controlled clinical trials, prospective/retrospective cohort studies, or prospective/retrospective case series (CS).

Exclusion criteria

- Bone preservation or augmentation procedures performed with purposes other than implant placement (e.g., pontic sites).
- Studies involving fewer than 20 patients (10 patients per group in comparative studies).
- Studies evaluating bone reconstruction procedures at implants diagnosed with peri-implantitis.

2.1.2 | Type of intervention and comparisons

Studies were selected when they included any type of bone preservation or augmentation procedures. The following treatments were considered:

- Ridge preservation/augmentation procedures at the time of tooth extraction;
- Immediate implants (IIs) at the time of tooth extraction with or without simultaneous bone augmentation;
- Horizontal and/or vertical ridge augmentation (HRA/VRA) procedures prior to implant placement after tooth extraction;
- HRA/VRA procedures simultaneous with implant placement after tooth extraction;
- Lateral or transcrestal SFA procedures prior to implant placement;
- Lateral or transcrestal SFA procedures simultaneous to implant placement.

In controlled studies, the comparison was any augmentation procedure different from the treatment provided in the experimental group. Also, the comparison of bone augmentation procedure to no augmentation (negative control) was considered.

2.1.3 | Type of outcomes

The primary aim of this systematic review was to report any variable that has been used to assess the efficacy or performance of the bone preservation or augmentation procedure. Whenever possible, a detailed specification on how the outcome was measured was provided.

The primary outcome considered in each of the included studies was registered when reported and classified into one of the following domains:

- Clinical bone gain/changes: Clinical measurement of vertical and horizontal bone changes from the bone augmentation procedure to a surgical re-entry (implant placement or implant exposure).
- 2D radiographic bone gain/changes: Measurement of vertical bone changes in periapical or panoramic radiographs, assessed between the augmentation procedure and a second time point (e.g., time of implant placement or implant exposure).
- 3D radiographic bone gain/changes: Measurement of vertical and horizontal bone changes in cone-beam computed tomography (CBCT) scans, assessed between the augmentation procedure and a second time point (e.g., time of implant placement or implant exposure).
- Volumetric ridge changes: Measurement of vertical and horizontal ridge changes through conventional or digital casts, assessed between the augmentation procedure and a second time point. This domain referred to clinical measurements and not 3D radiographic assessment.
- Peri-implant clinical parameters: Measurement of surrogate outcomes of peri-implant health and osseointegration (e.g., probing depth [PD], bleeding on probing [BOP], plaque index [PI], implant stability quotient [ISQ] values, etc.). Measurements related to the position of the mucosal margin and soft tissue dimensions were reported in a different domain.
- Rate of surgery-related complications: Reporting of intraoperative sequelae of the bone augmentation procedure (e.g., neurological or vascular lesions), and healing complications at the augmented site (wound dehiscences and infections).
- PROMs: Measurement of PROMs through validated assessment tools (e.g., HRQoL and OHIP-14), or customized satisfaction questionnaires, providing a composite score or a visual analogue scale (VAS) value.
- Aesthetic outcomes: Assessment of the aesthetic performance of the implant-supported restoration, through validated scoring systems (e.g., Pink Aesthetic Score [Furhauser et al., 2005], White Aesthetic Score [Belser et al., 2009]), or based on the presence of patient/clinician complaints.
- Need of re-grafting: Need to perform additional grafting to ensure the presence of adequate bone volume around the implant once placed in an adequate prosthetically driven position.
- Implant survival: Persistence of the implant in the patient's mouth at a given recall.
- Implant success: Fulfilment of specific implant success criteria at a given recall.
- Marginal bone levels (MBLs): Measurement of inter-proximal peri-implant vertical bone changes in periapical or panoramic radiographs assessed between the implant placement/restoration and a follow-up recall. This outcome evaluated inter-proximal bone stability instead of vertical bone gain/changes associated with the procedure.
- CBCT to assess bone stability: Measurement of vertical and horizontal peri-implant bone changes in CBCT images, as assessed between the implant placement/restoration and a follow-up recall. The difference between this outcome and 3D radiographic bone gain/changes was that the latter was used to assess dimensional changes associated with the procedure itself, whereas the former assessed the dimensional changes associated with the follow-up.

- Soft tissue outcomes: Measurement of the apico-coronal position of the soft tissue margin in relation to different reference points, the soft tissue thickness at different reference points, and the apico-coronal width of the buccal keratinized tissue.
- Surgical time: Measurement of the time required to complete the bone augmentation procedure.
- Histological outcomes: Including descriptive histological findings, histomorphometric measurements (e.g., percentage of vital bone, residual graft, and connective tissue), and immunohistochemical measurements (e.g., relative expression of proteins such as vascular endothelial growth factor and matrix metalloproteinases).

Primary and secondary outcomes from each individual study were recorded and merged together to represent the variables analysed in each investigation. No attempt was made to evaluate the magnitude of the effect (e.g., amount of bone regeneration) in this review. In the case where one investigation was published in more than one article, all the publications referring to the same patient population were included and merged into the same group, considering all the different outcomes that have been evaluated. Studies were grouped by the type of intervention in order to explore which outcomes have been used depending on each procedure.

2.2 | Information sources and search

2.2.1 | Electronic search

Three electronic databases were used as sources in the search for studies satisfying the inclusion criteria: (1) MEDLINE via PubMed; (2) Cochrane Library (including Cochrane Database for Systematic Reviews and Cochrane CENTRAL register for Clinical Trials); and (3) Embase. These databases were searched for studies published from January 2011 to April 2021. The search was limited to human subjects and to studies reported in English. Reports in other languages were not considered because of the limited time for the preparation of this systematic review. The detailed search strategy is listed in Table S1.

2.2.2 | Manual search

All reference lists of the selected studies and previously published systematic reviews were checked for cross-references.

2.3 | Screening methods

Two reviewers (Shi-Min Wei and Xin-Yu Wu) screened the titles and abstracts independently and in duplicate. The same reviewers selected the full manuscripts of studies meeting the inclusion criteria, or those with insufficient data in the title and abstract to make a clear decision. Any disagreement was solved by discussion with a third reviewer (Jun-Yu Shi). Reasons for exclusion during full-text screening were reported. The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the full-text analysis was calculated.

2.4 | Data extraction

Three different reviewers performed data extraction (Eduardo Montero, David Palombo, and Ignacio Sanz-Sánchez). When data were incomplete or missing, authors of the studies were contacted for clarification. If agreement could not be reached, such data were excluded until further clarification became available. When the results of a study were published more than once, the data were used when required. If a study was comparing more than two arms, the data from the groups of interest were extracted.

2.5 | Quality assessment

Quality assessment was done to evaluate how the primary outcome was assessed. Domain 4 from RoB2 was used to describe the risk of bias of the outcome measures for all study types (https://training.cochrane.org/handbook/current/chapter-08#section-8-6).

2.6 | Data analyses

Data were presented descriptively. The outcomes evaluated in each included study were provided in tables taking into consideration the domain and the type of treatment (ARP, IIs, HRA/VRA, and SFA). Primary, secondary, and PROM outcomes were merged and the percentage distribution of each outcome considering every study was calculated. The percentage distribution of the reported primary outcomes (when clearly stated in the manuscript) was also calculated by group of intervention. The analyses were carried out using STATA version 13.1 (StataCorp, College Station, TX).

3 | RESULTS

3.1 | Study selection

The initial electronic search identified 3717, 3010, and 501 records in PubMed, Embase, and Cochrane CENTRAL, respectively. After removal of duplicates, 5424 records were screened for title and abstract. Then, 1025 full-text articles were retrieved and screened, of which 302 were excluded (Supporting Information 1). Among the excluded studies, the main reasons for exclusion were the small number of patients <10 (n = 118), the absence of any bone augmentation/preservation procedure (n = 98), or the augmentation/preservation of bone without the purpose of implant placement (n = 86). Hand search yielded another 60 articles. Finally, a

total of 749 studies representing 783 articles were included in the systematic review (Figure 1). The list of the included studies in the review is shown in Supporting Information 2. Kappa coefficient of inter-rater agreement for the full-text analysis was 0.79.

3.2 | Quality assessment of the outcome

Five questions from the Cochrane recommendations RoB 2.0 tool were considered to assess the quality of measurements/assessments of the outcomes on all the included studies. Overall, 654 articles (83.41%) had measured correctly the outcome, 24 articles (3.06%) were considered to present some concerns, and 106 articles (13.52%) did not report the outcome properly.

3.3 | Characteristics of the included studies

From the 783 articles included in the present systematic review, 155 were related to ARP/augmentation procedures, 81 to immediate implants, 208 to HRA/VRA simultaneous with and/or prior to implant placement, 304 to lateral and/or transcrestal SFA simultaneous with and/or prior to implant placement, and 35 to the miscellaneous group, in which different combined approaches (e.g., lateral SFA plus VRA in the posterior maxilla) or different intervention groups (e.g., immediate implant vs. ARP) were evaluated (see Table S2). Owing to the tremendous heterogeneity found between treatment modalities in the miscellaneous group, no attempt was made to include this group either in the description of the results or in the comparisons.

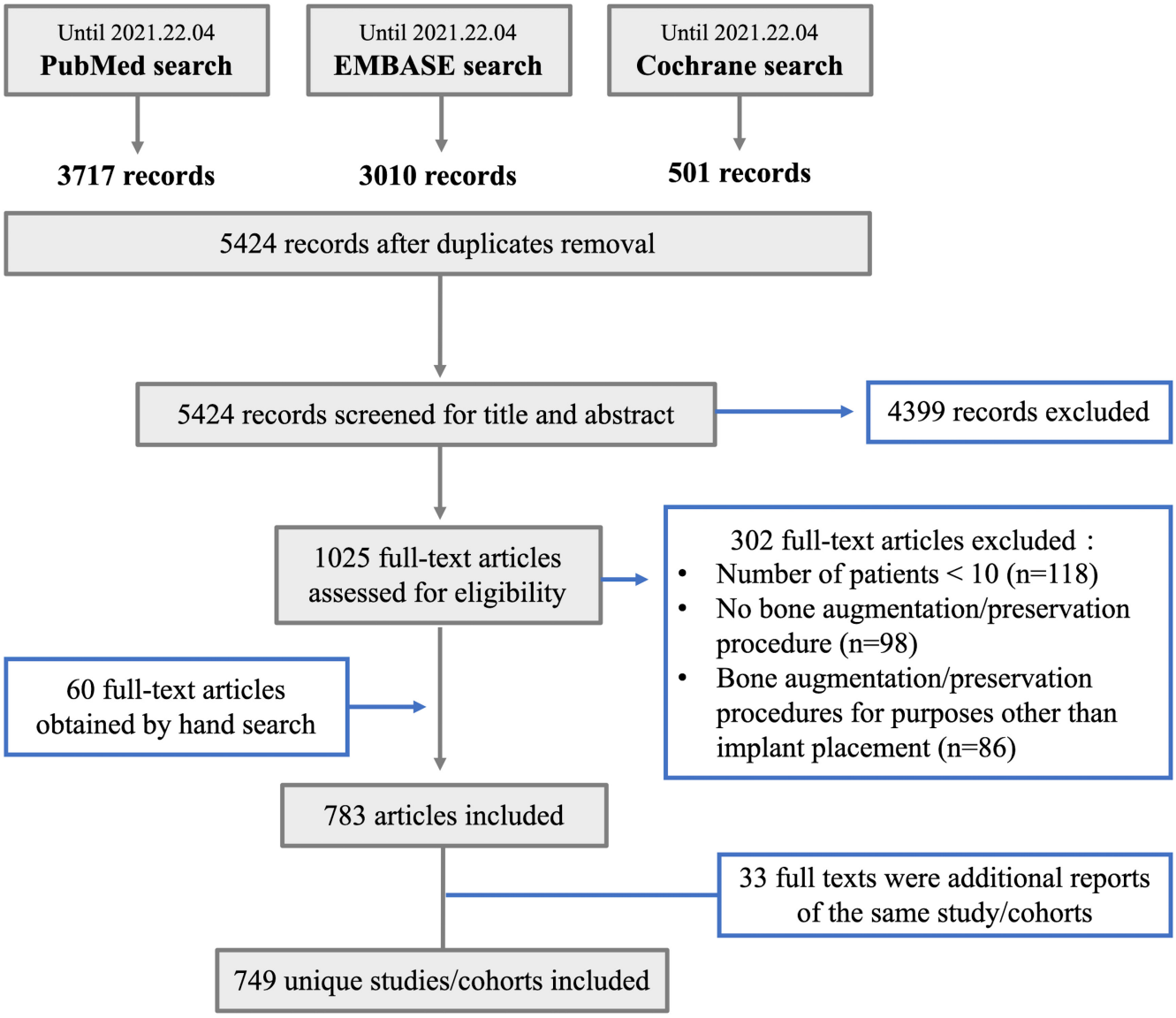

FIGURE 1 Flow chart depicting the article selection process

When taking into consideration all the procedures together, RCTs with a parallel design and retrospective CS were the most frequent study designs used (36.8% and 34.7%, respectively). The primary outcome was clearly stated in a large number of studies (78.5%).

3.3.1 | Alveolar ridge preservation

RCTs with a parallel design was the most frequent study design used (70.3%), followed by prospective and retrospective CS (11.6% and 11%, respectively). The primary outcome was clearly stated in 81.9% of the studies evaluating ARP.

3.3.2 | Immediate implants

Prospective and retrospective CS were the most frequent study designs used (33.3% and 26.9%, respectively). This intervention group showed fewer studies clearly reporting a primary outcome (70.4%) as compared to other treatment modalities (77.1%–81.9%).

3.3.3 | Horizontal and/or vertical ridge augmentation

Retrospective CS were clearly the most frequent study design used (41.8%). The primary outcome was clearly stated in 77.4% of the studies evaluating HRA/VRA.

3.3.4 | Sinus floor augmentation

Retrospective CS were clearly the most frequent study design used (41.5%). The primary outcome was clearly stated in 79.9% of the studies evaluating SFA.

3.4 | Outcome measures reported in the included studies

When taking into consideration all the procedures together, the rate of complications (59.3%) and implant survival (58.2%) were clearly the most frequently reported group of outcomes, followed by 3D radiographic bone gain/changes (30%), MBLs (29%), and histological outcomes (25.5%) (Table 1; Figure 2). On the contrary, volumetric ridge changes (5.6%), aesthetic outcomes (8.6%), CBCT to assess bone stability (8.4%), and surgical time (4%) were the least frequently reported. PROMs were reported only in 15.7% of studies. When comparing the outcomes assessed on each group of interventions, there were statistically significant differences between them for all the domains except for 3D radiographic bone gain/changes ($p = .279$) and surgical time ($p = .083$). Most of the studies assessed ≤5 groups of outcomes (88.8%), whereas only 0.3% assessed >10 domains. Eleven studies (1.4%) did not assess any of the pre-established domains but evaluated different outcomes (Figure S1).

3.4.1 | Alveolar ridge preservation

This intervention group reported more frequently on clinical bone gain/changes (33.6%) and histological outcomes (50.3%) compared to the other groups. Also, the need for re-grafting (21.9%) was more frequently reported as compared to immediate implants (1.2%) or SFA (3.3%). The rate of complications (41.9%) and 3D radiographic bone gain/changes (32.3%) were also frequently reported. On the contrary, implant survival (18.1%) and MBLs (10.3%) were less frequently reported as compared to the other groups, because in many studies the follow-up ended with implant placement. The vast majority of studies (94.8%) reported on five or less group of outcomes.

3.4.2 | Immediate implants

Implant survival (82.7%) and MBLs (50.6%) were the most frequently reported group of outcomes, which at the same time were assessed more frequently than in the other intervention groups. This intervention group also showed the most frequently reported soft tissue outcomes (40.7% vs. 1.6%–16.8%), implant success assessment (23.5% vs. 4.5%–16.5%), aesthetic outcomes (42% vs. 0.7%–8.7%), CBCT to assess bone stability (17.3% vs. 3.9%–11.1%), and peri-implant clinical outcomes (38.3% vs. 6.5%–19.2%). Volumetric ridge changes (11.1%) were more frequently assessed than in the other groups (2.1%–3%). The II group showed the highest percentage of studies reporting on 6–10 domains (22.2%).

3.4.3 | Horizontal and/or vertical ridge augmentation

The rate of complications was the most frequently reported outcome (70.7%), with the highest value among the intervention groups. Implant survival was also frequently reported (63%). The most frequent tool to assess bone gain/changes was 3D radiographic assessment (33.7%) followed by clinical measurements (20.2%). PROMs were reported in 20.2% of the studies. On the contrary, the need for re-grafting was reported only in 17.8% of the studies, MBLs in 33.7%, and peri-implant clinical outcomes in 19.2%. Regarding the number of domains evaluated, 83.2% of the articles reported on ≤5 and 16.4% on 6–10 groups of outcomes.

The timing of implant placement was taken into consideration, and three groups were evaluated: HRA/VRA prior to implant

TABLE 1 Outcome measures reported in the included manuscripts (*N* = 783)

	All (*n* = 783)	ARP (*n* = 155)	II (*n* = 81)	HRA/VRA (*n* = 208)	SFA (*n* = 304)	Miscellaneous (*n* = 35)	*p*-Value
Outcome domain							
Clinical bone gain/changes	105 (13.4%)	52 (33.6%)	4 (4.9%)	42 (20.2%)	1 (0.3%)	6 (17.1%)	<.001
2D Radiographic bone gain/changes	130 (16.6%)	16 (10.3%)	1 (1.2%)	18 (8.7%)	92 (30.3%)	3 (8.6%)	<.001
3D Radiographic bone gain/changes	235 (30.0%)	50 (32.3%)	22 (27.2%)	70 (33.7%)	87 (28.5%)	6 (17.1%)	.279
Volumetric ridge changes	44 (5.6%)	18 (11.6%)	9 (11.1%)	6 (2.1%)	9 (3.0%)	2 (5.7%)	<.001
Peri-implant clinical outcomes[a]	123 (15.7%)	10 (6.5%)	31 (38.3%)	40 (19.2%)	30 (9.8%)	12 (34.3%)	<.001
Complications	465 (59.3%)	65 (41.9%)	33 (40.7%)	147 (70.7%)	194 (63.6%)	26 (74.3%)	<.001
Patient-reported outcome measures	123 (15.7%)	16 (10.3%)	15 (18.5%)	42 (20.2%)	40 (13.1%)	10 (28.6%)	.011
Aesthetic outcomes	67 (8.6%)	4 (2.6%)	34 (42.0%)	18 (8.7%)	2 (0.7%)	9 (25.7%)	<.001
Need of re-grafting	87 (11.1%)	34 (21.9%)	1 (1.2%)	37 (17.8%)	10 (3.3%)	5 (14.3%)	<.001
Implant survival	456 (58.2%)	28 (18.1%)	67 (82.7%)	131 (63.0%)	203 (66.8%)	27 (77.1%)	<.001
Implant success	109 (13.9%)	7 (4.5%)	19 (23.5%)	30 (14.4%)	50 (16.5%)	3 (8.6%)	<.001
MBLs	227 (29.0%)	16 (10.3%)	41 (50.6%)	70 (33.7%)	86 (28.3%)	14 (40.0%)	<.001
CBCT to assess bone stability	66 (8.4%)	6 (3.9%)	14 (17.3%)	23 (11.1%)	19 (6.3%)	4 (11.4%)	.002
Soft tissue outcomes	105 (13.4%)	26 (16.8%)	33 (40.7%)	34 (16.4%)	5 (1.6%)	7 (20.0%)	<.001
Surgical time	31 (4.0%)	1 (0.7%)	3 (3.7%)	11 (5.3%)	16 (5.3%)	0 (0.0%)	.083
Histological outcomes	199 (25.5%)	78 (50.3%)	0 (0.0%)	41 (19.7%)	79 (26.1%)	1 (2.9%)	<.001
Other	11 (1.4%)	0 (0.0%)	0 (0.0%)	5 (2.4%)	5 (1.6%)	1 (2.09%)	<.001
Number of domains considered							
≤5	695 (88.8%)	147 (94.8%)	63 (77.8%)	173 (83.2%)	288 (94.7%)	24 (68.6%)	<.001
6–10	86 (11.0%)	8 (5.2%)	18 (22.2%)	34 (16.4%)	15 (5.0%)	11 (31.4%)	
>10	2 (0.3%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)	

Note: Data expressed as number of studies and percentage of studies in each intervention evaluating the outcome domain.

Abbreviations: ARP, alveolar ridge preservation; CBCT, cone-beam computed tomography; HRA/VRA, horizontal/vertical ridge augmentation; II, immediate implant; MBL, marginal bone level; *n*, number of studies; SFA, sinus floor augmentation.

[a]Peri-implant clinical outcomes included different plaque indices and bleeding indices, probing pocket depth, and implant stability quotient values.

placement (staged approach), HRA/VRA simultaneous with implant placement (simultaneous approach), and a third group in which both procedures were considered together or, when it was not specified, when implants were placed in relation to the augmentation procedure. When comparing the two main groups (simultaneous vs. staged), the simultaneous approach evaluated more frequently clinical bone gain/changes (33.3% vs. 15.8%), peri-implant clinical outcomes (31.8% vs. 14.2%), MBLs (44.4% vs. 27.5%), and soft tissue outcomes (27% vs. 10.8%). On the contrary, the staged approach registered more frequently 2D radiographic bone gain/changes (12.5% vs. 4.8%), PROMs (22.5% vs. 14.3%), and surgical time (6.7% vs. 1.6%) (Table 2).

3.4.4 | Sinus floor augmentation

Implant survival was the most frequently reported outcome (66.8%) followed by the rate of complications (63.6%). However, PROMs were seldom reported (13.1%). The most frequent tool to assess bone gain/changes was 2D radiographic assessment (30.3%), followed by 3D radiographic assessment (28.5%). Whereas histological outcomes were more frequently reported (26.1%) than in the II or the HRA/VRA groups, peri-implant clinical outcomes were barely assessed (9.8%). Moreover, MBLs were evaluated only in 28.3% of the studies. Surgical time was assessed more frequently in this group (5.3%) as compared to the II group (3.7%) or the ARP group (0.7%).

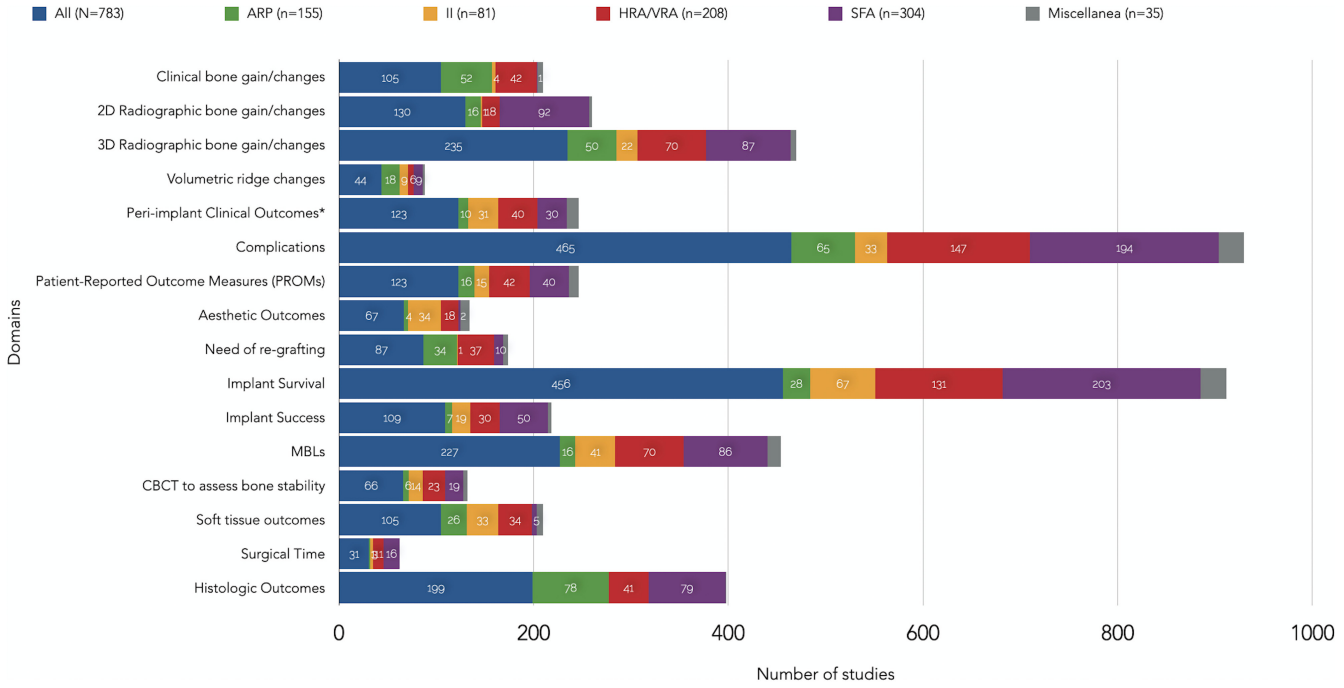

FIGURE 2 Number of studies assessing each domain of outcomes, stratified for clinical interventions. [a]Peri-implant clinical outcomes included different plaque indices and bleeding indices, probing pocket depth and implant stability quotient values. ARP, alveolar ridge preservation; CBCT, cone-beam computed tomography; HRA/VRA, horizontal/vertical ridge augmentation; II, immediate implant placement; MBL, marginal bone level; SFA, sinus floor augmentation

Again, most of the studies evaluated five or fewer groups of outcomes (94.7%).

The timing of implant placement was also taken into consideration, and three groups were evaluated: SFA prior to implant placement (staged approach), SFA simultaneous with implant placement (simultaneous approach), and a third group in which both procedures were considered together or, when it was not specified, when implants were placed in relation to the augmentation procedure. No differentiation was done between the transcrestal and the lateral approach. When comparing the two main groups (simultaneous vs. staged), the simultaneous approach evaluated more frequently 2D radiographic bone gain/changes (48.8% vs. 17.3%), implant survival (84.8% vs. 47.5%), implant success (21.6% vs. 9.4%), and MBLs (47.2% vs. 3%). On the contrary, more articles reporting on the staged approach evaluated 3D radiographic bone gain/changes (36.7% vs. 23.2%) and histological outcomes (47.5% vs. 8%) (Table 2).

3.5 | Primary outcomes reported in the included studies

The primary outcome was clearly stated in 78.5% of the studies, with 573 (73.1%), 37 (4.7%), and 5 studies (0.6%) reporting on 1, 2, and 3 primary outcomes, respectively (Table 3; Figure 3). On the contrary, 19.2% of the studies did not specify which was the primary outcome or which domain it belonged to. Although we pre-established 16 groups of primary outcomes, 1.9% of studies evaluated a primary outcome that did not belong to any of them.

When taking into consideration all the treatment modalities together, the most frequently reported domains representing the primary outcomes were 3D radiographic bone/gain changes (25.8%), histological outcomes (14.3%), and implant survival (13%). On the contrary, peri-implant clinical outcomes and the need of re-grafting were assessed as primary outcome only in 0.5% of the cases, surgical time in 0.3%, and CBCT to assess bone stability in 0.1%. PROMs were considered as the primary outcome only in 2.2% of the cases.

The most frequently reported primary outcomes included in each domain within the 783 articles included in the present systematic review were the following:

- Clinical bone gain/changes: This outcome was frequently reported in ARP or HRA/VRA procedures and was mainly assessed with a periodontal probe or a calliper. In ARP procedures, this domain was represented frequently by the clinical changes in the horizontal and/or vertical dimensions of the bone, assessed immediately after tooth extraction and at implant placement using or not an individualized stent. In HRA/VRA procedures prior to implant placement, this domain was mainly represented by the clinical horizontal bone gain (seven articles) or vertical bone gain (four articles). Studies aimed at evaluating ridge augmentation procedures simultaneous with implant placement established the dehiscence height as the primary outcome in three articles. One study on IIs established as primary outcome the clinical buccal

TABLE 2 Domain of the primary outcome measures reported in the included manuscripts ($n = 783$)

	All ($n = 783$)	ARP ($n = 155$)	II ($n = 81$)	HRA/VRA ($n = 208$)	SFA ($n = 304$)	Miscellaneous ($n = 35$)
Primary outcome domain						
Clinical bone gain/changes	57 (7.3%)	28 (18.1%)	1 (1.2%)	27 (13.0%)	0 (0.0%)	1 (2.9%)
2D Radiographic bone gain/changes	50 (6.4%)	7 (4.5%)	3 (3.7%)	3 (1.4%)	36 (11.8%)	1 (2.9%)
3D Radiographic bone gain/changes	202 (25.8%)	54 (34.8%)	24 (29.6%)	55 (26.4%)	63 (20.7%)	6 (17.1%)
Volumetric ridge changes	21 (2.7%)	10 (6.5%)	6 (7.4%)	3 (1.4%)	1 (0.3%)	1 (2.9%)
Peri-implant clinical outcomes[a]	4 (0.5%)	0 (0.0%)	0 (0.0%)	3 (1.4%)	1 (0.3%)	0 (0.0%)
Complications	61 (7.8%)	2 (1.3%)	1 (1.2%)	24 (11.5%)	29 (9.5%)	5 (14.3%)
Patient-reported outcome measures	17 (2.2%)	0 (0.0%)	1 (1.2%)	7 (3.4%)	7 (2.3%)	2 (5.7%)
Aesthetic outcomes	15 (1.9%)	3 (1.9%)	6 (7.4%)	5 (2.4%)	0 (0.0%)	1 (2.9%)
Need of re-grafting	4 (0.5%)	3 (1.9%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)
Implant survival	102 (13.0%)	2 (1.3%)	15 (18.5%)	24 (11.5%)	52 (17.1%)	9 (25.7%)
Implant success	25 (3.2%)	2 (1.3%)	5 (6.2%)	6 (2.9%)	11 (3.6%)	1 (2.9%)
MBLs	40 (5.1%)	3 (1.9%)	9 (11.1%)	14 (6.7%)	12 (4.0%)	2 (5.7%)
CBCT to assess bone stability	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
Soft tissue outcomes	14 (1.8%)	2 (1.3%)	6 (7.4%)	3 (1.4%)	0 (0.0%)	3 (8.6%)
Surgical time	2 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.7%)	0 (0.0%)
Histological outcomes	112 (14.3%)	39 (25.2%)	0 (0.0%)	14 (6.7%)	58 (19.1%)	1 (2.9%)
Other	15 (1.9%)	2 (1.3%)	0 (0.0%)	4 (1.9%)	9 (3.0%)	0 (0.0%)
Not specified	150 (19.2%)	19 (12.3%)	23 (28.4%)	42 (20.2%)	57 (18.8%)	9 (25.7%)

Note: Data expressed as number of studies and percentage of studies in each intervention evaluating the outcome domain.

Abbreviations: ARP, alveolar ridge preservation; CBCT, cone-beam computed tomography; HRA/VRA, horizontal/vertical ridge augmentation; II, immediate implant; MBL, marginal bone level; *n*, number of studies; SFA, sinus floor augmentation.

[a]Peri-implant clinical outcomes included different plaque indices and bleeding indices, probing pocket depth, and implant stability quotient values.

bone thickness 4 months after implant placement.

- 2D radiographic bone gain/changes: This domain was more frequently reported on SFA procedures, which selected radiographic vertical bone gain or endo-sinus bone gain evaluated by means of periapical radiographs or panoramic x-rays as the primary outcome. This domain was also selected on ARP procedures to determine alveolar bone height and on HRA/VRA procedures to calculate vertical bone gain and/or the rate of bone resorption.
- 3D radiographic bone gain/changes: This domain was the most frequently assessed as the primary outcome, irrespective of the treatment modality. Mainly, CBCT was used to make horizontal and/or vertical linear measurements, representing ridge dimensional changes or bone gain. However, volumetric measurements were less common. In the case of ARP procedures, the most frequently reported primary outcome was the dimensional changes of the alveolar bone, without differentiating between horizontal and vertical measurements. In the case of SFA, the most frequent one was vertical bone gain, whereas for HRA/VRA procedures prior implant placement or horizontal or vertical linear measurements were used to calculate radiographic bone gain. In the case of HRA simultaneous with implant placement and IIs, residual dehiscence height and facial bone thickness were the two most frequently evaluated primary outcomes within this domain. The change in grafted bone volume or the percentage of bone resorption was less frequently reported as the primary outcome.
- Volumetric ridge changes: This domain was seldom chosen as the primary outcome (2.7%), being more frequent in ARP procedures and IIs than in HRA/VRA or SFA interventions. Usually, conventional or digital casts were transferred to a software that allowed the calculation of linear or volumetric ridge dimensional changes.
- Peri-implant clinical parameters: This domain was considered as the primary outcome only in three studies dealing with HRA/VRA procedures and one study in SFA. ISQ, as determined by resonance frequency analysis, was chosen as primary outcome in two studies, while PD and BOP were chosen in just one study.
- Rate of surgery-related complications: Of the included manuscripts, 7.8% considered one main outcome variable that was included within this domain, being more frequently in HRA/VRA and SFA procedures (26.4% and 20.7%, respectively). Healing complications, such as wound dehiscence or exposure of the

TABLE 3 Outcome measures reported in the manuscripts evaluating HRA/VRA and SFA interventions

	HRA/VRA ($n = 208$)						SFA ($n = 304$)					
Timing of implant placement	**Prior to implant placement ($n = 120$)**		**Simultaneous to implant placement ($n = 63$)**		**Both/not specified ($n = 25$)**		**Prior to implant placement ($n = 139$)**		**Simultaneous to implant placement ($n = 125$)**		**Both/not specified ($n = 40$)**	
Outcome domain	**As primary outcome**	**As any outcome**	**As primary outcome**	**As any outcome**	**As primary outcome**	**As any outcome**	**As primary outcome**	**As any outcome**	**As primary outcome**	**As any outcome**	**As primary outcome**	**As any outcome**
Clinical bone gain/changes	11 (9.2%)	19 (15.8%)	15 (23.8%)	21 (33.3%)	1 (4.0%)	2 (8.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2D Radiographic bone gain/changes	3 (2.5%)	15 (12.5%)	0 (0.0%)	3 (4.8%)	0 (0.0%)	0 (0.0%)	5 (3.6%)	24 (17.3%)	29 (23.2%)	61 (48.8%)	2 (5.0%)	7 (17.5%)
3D Radiographic bone gain/changes	34 (28.3%)	45 (37.5%)	17 (27.0%)	20 (31.8%)	4 (16.0%)	5 (20.0%)	21 (22.3%)	51 (36.7%)	26 (20.8%)	29 (23.2%)	6 (15.0%)	7 (17.5%)
Volumetric ridge changes	2 (1.7%)	4 (3.3%)	1 (1.6%)	2 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.6%)	1 (0.8%)	3 (2.4%)	0 (0.0%)	1 (2.5%)
Peri-implant clinical outcomes[a]	1 (0.8%)	17 (14.2%)	2 (3.2%)	20 (31.8%)	0 (0.0%)	3 (12.0%)	0 (0.0%)	11 (7.9%)	1 (0.8%)	18 (14.4%)	0 (0.0%)	1 (2.5%)
Complications	16 (13.3%)	87 (72.5%)	4 (6.4%)	40 (63.5%)	4 (16.0%)	20 (80.0%)	11 (7.9%)	88 (63.3%)	6 (4.8%)	75 (60.0%)	12 (30.0%)	31 (77.5%)
Patient-reported outcome measures	4 (3.3%)	27 (22.5%)	3 (4.8%)	9 (14.3%)	0 (0.0%)	6 (24.0%)	4 (2.9%)	18 (13.0%)	3 (2.4%)	18 (14.4%)	1 (2.5%)	4 (10.0%)
Aesthetic outcomes	3 (2.5%)	9 (7.5%)	2 (3.2%)	8 (12.7%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
Need for re-grafting	1 (0.8%)	30 (25.0%)	0 (0.0%)	3 (4.8%)	0 (0.0%)	4 (16.0%)	0 (0.0%)	6 (4.3%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (5.0%)
Implant survival	12 (10.0%)	68 (56.7%)	5 (7.9%)	45 (71.4%)	7 (28.0%)	18 (72.0%)	11 (7.9%)	66 (47.5%)	29 (23.2%)	106 (84.8%)	12 (30.0%)	31 (77.5%)
Implant success	3 (2.5%)	19 (15.8%)	1 (1.6%)	6 (9.5%)	2 (8.0%)	5 (20.0%)	0 (0.0%)	13 (9.4%)	9 (7.2%)	27 (21.6%)	2 (5.0%)	10 (25.0%)
MBLs	4 (3.3%)	33 (27.5%)	9 (14.3%)	28 (44.4%)	1 (4.0%)	9 (36.0%)	3 (7.5%)	18 (3.0%)	3 (2.2%)	59 (47.2%)	6 (4.8%)	9 (22.5%)
CBCT to assess bone stability	0 (0.0%)	13 (10.8%)	0 (0.0%)	8 (12.7%)	0 (0.0%)	2 (8.0%)	0 (0.0%)	9 (6.5%)	0 (0.0%)	9 (7.2%)	0 (0.0%)	1 (2.5%)
Soft tissue outcomes	1 (0.8%)	13 (10.8%)	1 (3.2%)	17 (27.0%)	1 (4.0%)	4 (16.0%)	0 (0.0%)	4 (2.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Surgical time	0 (0.0%)	8 (6.7%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	2 (8.0%)	1 (0.7%)	8 (5.8%)	1 (0.8%)	8 (6.4%)	0 (0.0%)	0 (0.0%)
Histological outcomes	11 (9.2%)	28 (23.3%)	3 (4.8%)	11 (17.5%)	0 (0.0%)	2 (8.0%)	53 (38.1%)	66 (47.5%)	5 (4.0%)	10 (8.0%)	0 (0.0%)	3 (7.5%)

Note: Data expressed as number of studies and percentage of studies in each intervention evaluating the outcome domain.

Abbreviations: ARP, alveolar ridge preservation; HRA/VRA, horizontal/vertical ridge augmentation; II, immediate implant; MBL, marginal bone level; *n*, number of studies; SFA, sinus floor augmentation.

[a]Peri-implant clinical outcomes included different plaque indices and bleeding indices, probing pocket depth, and implant stability quotient values.

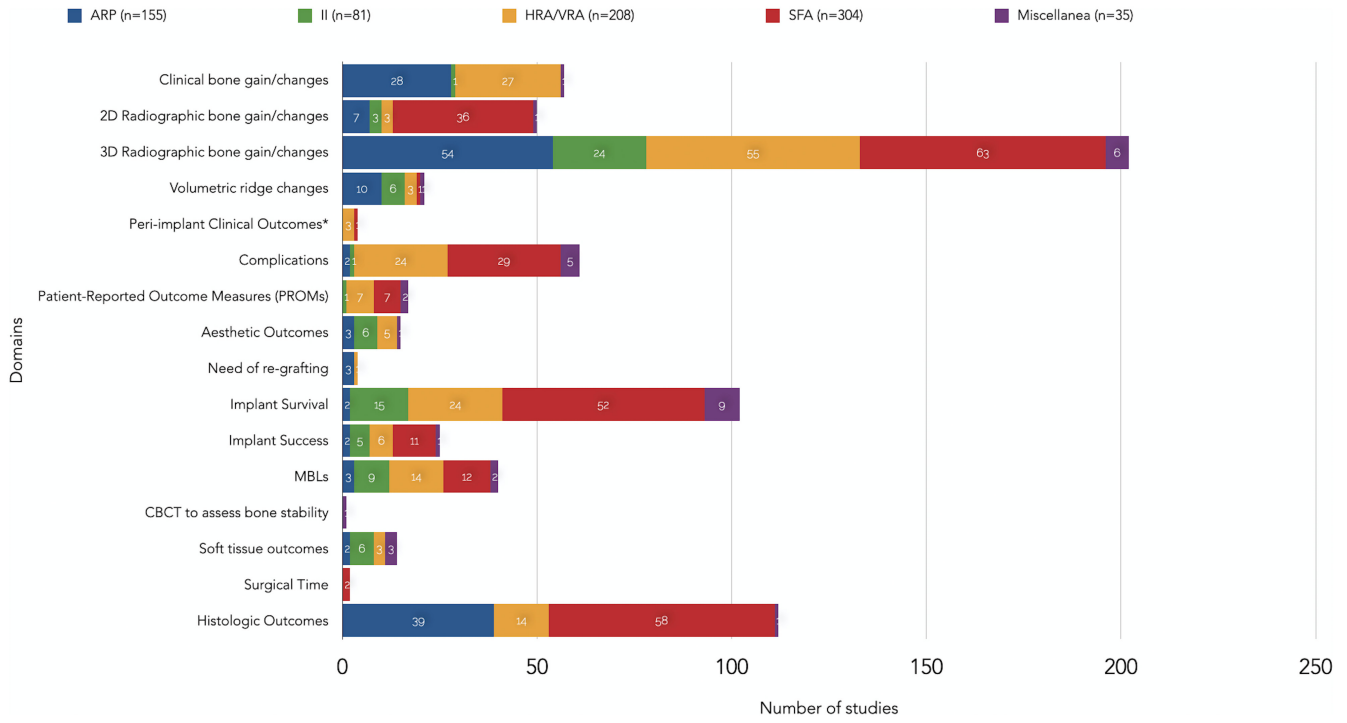

FIGURE 3 Number of studies assessing each domain as primary outcome, stratified for clinical interventions. [a]Peri-implant clinical outcomes included different plaque indices and bleeding indices, probing pocket depth and implant stability quotient values. ARP, alveolar ridge preservation; CBCT, cone-beam computed tomography; HRA/VRA, horizontal/vertical ridge augmentation; II, immediate implant placement; MBL, marginal bone level; SFA, sinus floor augmentation

membrane/Ti-mesh in HRA/VRA procedures and membrane perforation during SFA procedures, were the most frequently reported primary outcomes within this domain. Intra-operative complications or neurosensory disturbances were also reported as primary outcomes.

- PROMs: PROMs were selected as the primary outcome only in 2.2% of the studies. It is remarkable that no single study on ARP and only one on immediate implants considered this domain as the main outcome. The most common tool was a VAS to evaluate post-operative morbidity or pain, through a questionnaire. Other outcomes reported were the dosage of anti-inflammatory drugs required, or the use of some type of Oral Health Impact Profile questionnaire.
- Aesthetic outcomes: Aesthetic outcomes were only rarely considered as the primary outcome ($n = 15$; 1.9%), with II being the intervention in which they were most frequently considered ($n = 6$; 7.4%). Among these outcomes, the most frequently reported was the Pink Aesthetic Score ($n = 8$; Furhauser et al., 2005), followed by the White Aesthetic Score ($n = 3$; Belser et al., 2009).
- Need of re-grafting: The need to perform additional grafting to ensure the presence of adequate bone volume around the implant was considered as the primary outcome only in 0.5% of the studies, with no representation in immediate implants or SFA procedures.
- Implant survival: This domain was the third most frequently reported primary outcome (13.0%). The definition of implant survival/failure basically referred to the presence/absence of the implant in function (Albrektsson & Zarb, 1998). However, some studies referred to the Buser and coworkers' criteria (Buser et al., 1990) requiring radiographic assessments to detect peri-implant radiolucencies.
- Implant success: Implant success was considered as the main outcome variable in 3.2% of the studies. The most commonly reported criteria were (i) the Buser and coworkers' criteria (1997; $n = 5$); (ii) the Albrektsson and coworkers' criteria ($n = 3$); (iii) the Misch criteria (2008; $n = 2$); and (iv) the Karoussis criteria ($n = 1$) (Karoussis et al., 2004).
- MBLs: This domain was considered as the primary outcome in 5.1% of the studies, with a higher representation in the group of immediate implants (11.1%). The most common tool to measure mesial and distal MBLs was periapical X-rays.
- CBCT to assess bone stability: This outcome was considered as the main variable only in one study in the miscellaneous group.
- Soft tissue outcomes: Soft tissue outcomes were only rarely reported as primary variables (1.8%), being significantly more frequently considered in the group of immediate implants (7.4%). Among the outcomes considered in this domain, mid-buccal mucosal level/soft tissue dehiscence was the most frequently reported, followed by the width of the keratinized mucosa.
- Surgical time: The time needed to perform the bone augmentation procedure was considered as the primary outcome only in two studies dealing with SFA.

- Histological outcomes: Histological outcomes were considered as the main outcome variable in 14.3% of the studies, with a higher representation in the groups of ARP (25.2%) and SFA (19.1%). In most of the cases, the histology merely described a histomorphometric analysis evaluating the percentage of newly formed bone, residual graft particles, and soft tissue. Twenty-five studies specifically identified the percentage of newly formed bone or vital bone or mineralized tissue as the main outcome variable. Micro-CT and different immunohistochemical analyses were also the primary outcome variables in a few studies ($n = 6$). Other outcomes considered were the percentage of bone to graft contact, gene expression, and the osteoblastic activity evaluated through scintigraphic analysis.

3.5.1 | Alveolar ridge preservation

Primary outcomes were more homogeneous in this group than in the others, because 78.1% belong to one of the following domains: 3D radiographic bone gain/changes (34.8%), histological outcomes (25.2%), or clinical bone/gain changes (18.1%). Volumetric ridge changes were assessed as the primary outcome in 6.5% of the cases, whereas the remaining domains were equal to 0% or <2%.

3.5.2 | Immediate implants

Again, 3D radiographic bone gain/changes were by far the most frequent domain representing the primary outcome (29.6%). Volumetric ridge changes (7.4%), aesthetic outcomes (7.4%), implant survival (18.5%), MBLs (11.1%), and soft tissue outcomes (7.4%) were the more frequently reported primary outcomes when using IIs than when using the other treatment modalities.

3.5.3 | Horizontal and/or vertical ridge augmentation

The assessment of bone gain/changes with 3D diagnostic methods was the most common primary outcome (26.4%), followed by the clinical dimensional assessment of the bone (13%). The rate of complications was considered as the primary outcome in 11.5% of the cases, which is much higher than when using IIs (1.2%) or ARP (1.3%). Implant survival was considered the primary outcome in 11.5% of the cases and MBL in 6.7% of cases. Although peri-implant clinical outcomes were established to be the primary outcome more frequently on this group than in the others, the value was still low (1.4%). Moreover, the need of re-grafting was considered the primary outcome only in 0.5% of the cases.

When taking into consideration the timing of implant placement, the domains more frequently selected as primary outcome in the simultaneous group were 3D radiographic bone gain/changes (27%), clinical bone gain/changes (23.8%), and MBLs (14.3%). For the staged approach, 3D radiographic bone gain/changes was also the domain more frequently selected as the primary outcome (28.3%). However, clinical bone gain changes was selected less frequently than in the simultaneous approach (9.2%). The rate of complications, implant survival, and histological outcomes were frequently selected as primary outcomes in the staged approach (13.3%, 10% and 9.2%, respectively) (Table 2).

3.5.4 | Sinus floor augmentation

The most commonly reported primary outcome was 3D radiographic bone gain/changes (20.7%), followed by histological outcomes (19.1%) and implant survival (17.1%). Also, 2D radiographs to assess bone gain/changes (11.8%) and the rate of complications (9.5%) were frequently considered as primary outcomes. These five domains represented almost 80% of the primary outcomes in this group.

When taking into consideration the timing of implant placement, the domains most frequently selected as primary outcome in the simultaneous group were 2D radiographic bone gain/changes (23.2%), implant survival (23.2%), and 3D radiographic bone gain/changes. None of the remaining domains was chosen as the primary outcome with a frequency >8%. For the staged approach, histological outcomes were by far the most frequently chosen primary outcome (38.1%), followed by 3D radiographic bone gain/changes (22.3%). The rate of complications, implant survival, and MBLs were the second group of primary outcomes more frequently selected (7.9%, 7.9%, and 7.5%, respectively) (Table 2).

4 | DISCUSSION

The present systematic review aimed to identify the outcome measures of clinical studies reporting bone preservation/augmentation procedures for dental implant placement published in the last decade. From the 783 manuscripts (749 investigations) included, the following four main clinical scenarios were identified: ARP, IIs, HRA/VRA, and lateral and/or transcrestal SFA.

In the present systematic review, risk of bias was assessed based on whether the primary outcomes were appropriate, whether they differed between groups, as well as on the blinding and influence of outcome examiners. A total of 13.2% had not properly assessed the primary outcome, which may be due to several reasons. First, the primary outcomes were not clearly defined in 19.2% articles. Primary outcomes represent the most important objective of a study and are usually used for sample size calculation. The reporting guidelines for trials (Schulz, Altman, Moher, & Group, 2010) and observational studies (von Elm et al., 2007) have emphasized the importance of pre-specifying and reporting the primary outcomes. Second, the measurement of the outcomes was inappropriate or not clearly reported in some studies. Inappropriate measurement or insufficient information on outcome measurement makes it difficult for future

researchers to reproduce the study (Moher et al., 2010) and will introduce bias when pooling existing evidence in systematic reviews. Third, the training, calibration, and blinding of outcome examiners were not fully reported in certain investigations. Thus, consensus guidelines are needed to reduce the bias of outcome assessment, enhance research quality, and make results from similar studies comparable.

Interestingly, an important difference in the type of study design between ARP and IIs was observed. The highest percentage of RCTs (73.5%) and the lowest percentage of CS (22.6%) were found in ARP, while for IIs, the situation was diametrically opposite (29.6% of RCTs and 62.9% of CS). It is also worth pointing out that ARP studies were more frequently conducted in university/hospital settings than in private offices (79.4% vs. 5.8%), while IIs studies were popular in private clinics (56.8% vs. 30.9%). It may reflect that clinicians working in universities/hospitals prefer more conservative treatment options, while those in private clinics prefer the II approach. It is important to note that clinicians should still follow the best clinical evidence rather than personal preferences (Isham et al., 2016).

The main findings of the present review indicate that the rate of complications (59.3%), implant survival (58.2%), 3D radiographic bone gain/changes (30%), MBLs (29%), and histological outcomes (25.5%) were the most frequently reported outcome domains among a relatively extensive list. It is surprising that there is hardly any report on socio-economic outcomes. Several studies have emphasized the necessity and significance of reporting health-economic outcomes (Listl & Weyant, 2019; Shi et al., 2021). The economic outcome measures will certainly influence future treatment decisions in the field of bone augmentation/preservation for both clinicians and patients, and so this type of outcome domain should not be ignored in the future.

Three-dimensional radiographic bone gain/change was the most commonly used primary outcome in all surgical interventions. In addition, among all the four major types of surgical interventions, the proportion of studies reporting 3D radiographic bone change was approximately 30%. In evaluating the efficacy of bone augmentation procedures, 3D radiographic bone gain/change has several advantages over clinical bone gain/change and 2D radiographic bone gain/change, such as accuracy, convenience, the possibility to measure buccal-lingual changes, and the possibility to avoid re-entry surgeries. However, it is important to standardize the measurements to quantify 3D radiographic bone gain/change on CBCTs in order to improve the quality of reporting. In CBCTs from different time points, authors should use the same plane or reference points to improve accuracy and repeatability of the measurements. Anatomical auxiliary reference points (E. H. Jung, Jeong, & Lee, 2021) or 3D reconstruction and superimposition (Li et al., 2019) have been used to reduce errors. Also, some limitations should be considered when using CBCTs. First, repeated CBCTs expose patients to larger radiation dosages, which might raise ethical problems. Second, CBCTs are not appropriate for all purposes in all clinical situations, such as checking the integrity of buccal bone plate in cases of IIs (Sanz et al., 2017), measuring Schneiderian membrane thickness (Insua et al., 2017), or when measuring peri-implant bone level changes, as metal artefacts might influence the outcomes (Schriber et al., 2020). To sum up, methods of measuring bone change should be accurate, feasible in clinical practice, and comparable among studies. Future research should focus on methods of improving and standardizing the measurements of bone gain/change, maybe by using machine learning tools.

For ARP, the most commonly reported outcomes were histological outcomes, complications, clinical bone gain/changes, 3D radiographic bone change/gains, and need of re-grafting, while peri-implant outcomes and aesthetics outcomes were less frequently reported. Histological outcomes were considered as the gold standard to study the progress of socket healing (Araujo & Lindhe, 2009). By combining histological analysis, dimensional changes of the alveolar ridge, and complication rates, the superiority of ARP versus the spontaneous healing of the socket could be demonstrated (Avila-Ortiz et al., 2019; Tonetti et al., 2019). However, different methods of measuring bone changes have been used, including clinical and 2D/3D radiographic bone changes, which makes the comparison of the results among studies difficult. A recent systematic review on ARP reported large heterogeneity when pooling data on bone changes (Avila-Ortiz et al., 2019).

Regarding immediate implants, the most reported outcomes were peri-implant clinical parameters, including implant survival, MBLs, aesthetic outcomes, complications, and soft tissue outcomes. Noticeably, the proportion of studies reporting peri-implant clinical outcomes was higher for immediate implants than for the other three surgical interventions. Compared with implants placed in the healed ridge, immediate implant placement usually has a higher early failure rate and risks of aesthetic failure (Cosyn et al., 2019). In a previous consensus statement, CBCT analyses and mid-facial recession evaluation were recommended in research on immediate implants (Tonetti et al., 2019). In the present systematic review, 3D analysis was the most commonly used outcome measure for bone changes in immediate implants, in accordance with the recommendation from the consensus statement. However, regarding mid-facial recession, the methods (using stents, intra-oral photos, or just a probe) and baseline time points (pre-extraction or immediately after surgery) were different among studies. In addition, most studies reported fewer than five clinical outcomes, failing to comprehensively analyse the outcome in all aspects of tissue volume change, complications, peri-implant health, aesthetics, and PROMs. Thus, we recommend using a series of outcome measures and standardizing the assessment of soft and hard tissue changes, including the use of standard CBCTs and stents for changes in soft tissue parameters.

Regarding HRA/VRA, the most concerned outcomes were the rate of complications, implant survival, 3D radiographic bone gain/changes, MBLs, and clinical bone gain/changes. Notably, the proportion of studies reporting PROMs in HRA/VRA was the highest among the four surgical interventions (20.2%). In those studies in which the bone augmentation procedures were performed before implant placement, the proportion of studies reporting complications and PROMs was higher. However, there are no generally

accepted definitions for most of the surgical complications, including swelling or soft tissue wound healing. Furthermore, details on the severity of the surgical complications were scarce, which limited the information that could be retrieved. As new bone grafting materials are developed, more attention should be paid to the biology of the wound-healing process and the cost–benefit analysis of the different surgical interventions/biomaterials (Sanz et al., 2019).

When it came to SFA, the most concerned outcomes were implant survival, complications, 2D radiographic bone gain/changes, 3D radiographic bone gain/changes, and MBLs, while PROMs and peri-implant clinical parameters were seldom reported. SFA has been reported as a predictable technique in the posterior maxilla with limited bone height (Raghoebar et al., 2019; Shi et al., 2020). Thus, studies on SFA nowadays focus more on detecting potential risks and avoiding complications. Surprisingly, the observations from this systematic review showed that reporting of PROMs was lacking. Surgical complications following SFA usually induce subjective discomfort in patients (Rengo et al., 2021) and PROMs should be reported to comprehensively reflect patient perception (Thoma et al., 2015).

4.1 | Strengths and limitations of the review

The major strength of this review is the comprehensive search strategy in three major databases and cautious handsearching. Approximately 7000 records were screened for potential eligibility, and 749 studies representing 783 manuscripts were included. The data of the present systematic review can be used to develop future consensus in the field of bone augmentation/preservation procedures.

The main limitation of this review is that only studies including more than 20 patients (10 patients per group in comparative studies) were included, and some novel measurement methods may only appear in recent case reports. Further limitations include the exclusive selection of papers published in the English language. These pragmatic decisions were based on the available data sources. However, in view of the vast number of included articles, additional papers would have probably not affected the conclusions. Additionally, considering the volume of the included literature, the quality assessment was only performed for the primary outcome using the Cochrane RoB2 tool Domain 4, despite being designed for RCT only.

5 | CONCLUSIONS

We can conclude that, within the past decade, in clinical studies on the performance of different bone preservation/augmentation procedures for dental implant placement were as follows:

- Nearly one-fourth of the studies did not report primary outcomes. The most frequently reported domain for the primary outcome was 3D radiographic bone gain/changes irrespective of the intervention group.
- The most frequently reported outcomes were radiographic bone change, complications, and implant survival. Health-economic outcomes and PROMs were seldom reported.
- Four types of bone preservation/augmentation procedures were categorized and the outcomes were reported differently. Studies on ARP focused on histological outcomes and complications. Studies on immediate implant placement focused more on implant-related outcomes, while studies on HRA/VRA and SFA focused more on complications and implant survival.
- A core outcome set and measurement should be established in the future. The methods of measuring the outcomes should be developed, verified, and unified. Health-economic outcomes and PROMs should be incorporated. The standard of outcome measurement should be followed by authors and journals.

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CONFLICT OF INTEREST

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

AUTHOR CONTRIBUTIONS

Jun-Yu Shi, Eduardo Montero, Xin-Yu Wu, David Palombo, Shi-Min Wei, and Ignacio Sanz-Sánchez have actively contributed to the conception and design of this work, in the acquisition, analysis, and interpretation of data, and in drafting the work and revising it critically.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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