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META-ANALYSIS

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Effect of lateral bone augmentation procedures in correcting peri-implant bone dehiscence and fenestration defects: A systematic review and network meta-analysis

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Abstract

Purpose: The aim of the present systematic review was to evaluate the effect of different lateral bone augmentation (LBA) procedures on the complete correction of a peri-implant bone dehiscence (BD) or fenestration (BF) from implant placement to implant surgical uncovering.

Methods: Electronic (Medline, Scopus, and Cochrane databases) and hand literature searches were performed for studies including at least one treatment arm where any LBA had been applied to correct a BD/BF at implant placement (T0). Studies where BD/BF was left untreated were also retrieved as negative control. Data from 24 selected articles were used to perform a network meta-analysis. Based on the proportion of nonresolved BD/BF at implant surgical uncovering (T1), a hierarchy of LBA procedures, and was determined. Spontaneous healing (i.e., exposed implant surface covered by a full-thickness flap; SELF) was also included in the hierarchy. Resorbable membrane + bone graft (RM + BG) was used as reference group. An analysis on the effect of nonhuman (NHBS) vs human (HBS) derived bone substitutes was also performed. NHBS was used as the reference group.

Results: No statistically significant differences were found among treatments for the proportion of nonresolved BD/BF. SELF performed substantially worse compared to RM + BG (OR: 5.78×10, CI: 4.83×10 – 1.3×10^{86}). Treatment based on a combination of a graft material and membrane/periosteum appeared to perform slightly better than treatments using graft material or membrane alone. NHBS appeared to perform better than HBS.

SELF had the worst effect among all treatments for both BD/BF height reduction (BDH) and BD/BF width reduction (BDW). Nonresorbable membrane (NRM) and

patient's own periosteum (PERI) + BG showed greater increases in buccal bone thickness than RM + BG.

Conclusion: Reconstructive treatment (including use of graft alone, membrane alone, or combinations of grafts and either membrane or patient's own periosteum) of a BD/BF at implant placement favorably and significantly impacts on the probability to obtain complete correction of the BD/BF at implant uncovering when compared to full-thickness flap repositioning on the BD/BF. When using a bone substitute, a non-human derived one may be suggested.

KEYWORDS
dehiscence, fenestration, guided bone, implant, lateral bone augmentation

What is known

Two systematic reviews reported a high level of peri-implant bone dehiscence (BD) reduction after lateral bone augmentation (LBA) procedures.Guided bone regeneration (GBR) in the most investigated procedure.The presence of a residual BD after a GBR procedures is associated with higher prevalence of peri-implant diseases

What this study adds

This study is the first systematic review on the effect of LBAs in completely correcting a BD and suggests that the combination of a membrane or patient's periosteum and a bone graft may be the best treatment option.

1 | INTRODUCTION

At healed extraction sites, residual ridge dimensions are often inadequate for the prosthetically-driven placement of dental implants.[1–4] As a consequence, implant placement in native bone may often result in the exposure of the implant surface with the maintenance of the integrity of the marginal bone (bone fenestration, BF) or not (peri-implant bone dehiscence, BD).

Compared to sites with either intact peri-implant bone[5] or surgically treated peri-implant BD,[6] untreated BD is associated with a higher risk for mucosal recession[5] and interproximal bone loss.[6] Moreover, experimentally-induced peri-implantitis progressed more rapidly in presence of a BD.[5]

Collectively, these findings support the rationale for either preventing the formation of a peri-implant bone defect by performing socket preservation/pre-implant lateral bone augmentation (LBA) or correcting the defect at implant placement with an LBA.

Several LBA procedures aimed at correcting a BD/BF simultaneously with implant placement were proposed in the literature. Among these, guided bone regeneration (GBR) is based on the use of barrier membrane with or without an additional bone substitute, and is the most investigated and validated option. Other reconstructive approaches, mainly based on the use of a graft material covered either by a full-thickness flap[7–9] or patient's own periosteum,[10] have been also proposed and investigated. According to two recent systematic reviews, LBA results in a mean vertical reduction of 4.28 mm of BD/BF[11] and a percentage vertical reduction of 81.3% in BD/BF[12] when performed simultaneously to implant placement.

Since the persistence of exposed implant threads following LBA is may favor the occurrence of a biological complication compared to an implant with an intact or fully restored peri-implant bone plate,[5,13] the complete correction of a BD/BF should be preferred to other outcome measures (e.g., mean changes in BD/BF dimensions) when evaluating the clinical effectiveness of an LBA procedure. The rate of complete BD/BF correction following LBA, however, has never been evaluated as the primary outcome measure in a systematic review. The aim of the present systematic review was to evaluate the effect of different LBA procedures on the complete correction of a BD/BF from implant placement to uncovering.

2 | MATERIALS AND METHODS

2.1 | Protocol development and focused question

The manuscript was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.[14] Ethical approval was not required for this systematic review.

The following focused question was addressed: "What is the rate of complete correction of a BD/BF following a LBA procedure performed at implant placement?"

A protocol was developed a priori to collect and summarize the evidence from prospective (i.e., randomized controlled trials; RCTs; controlled clinical trials, CCTs; and case series/reports) and retrospective studies including at least one arm evaluating any intervention for LBA (simultaneous to implant placement) to correct a BD/BF. When available, data derived from the study arm where the BD/BF was left untreated were also retrieved as negative control.

2.2 | Study selection criteria

2.2.1 | Inclusion criteria (PICOS)

1. *P* (*Population*): Adults (≥18 y-o) presenting a BD or a BF, with no restrictions in terms of defect dimensions, immediately after type III or IV implant placement[15];
2. *I* (*Intervention*): Any procedure for LBA to correct a BD/BF, performed concomitantly to implant placement (T0);
3. *C* (*Comparison*): any of the aforementioned interventions, or no treatment of BD/BF.
4. **(***Outcomes***)**: Studies were included if the proportion of implants showing complete defect resolution (i.e., residual defect height = 0 mm) at surgical re-entry (T1) was reported or could be either extracted or derived. The changes in BD/BF height (DH), width (DW) (in mm and/or %), and buccal bone thickness (BBT) (in mm and/or %) between T0 and T1, implant survival rate (ISR), radiographic bone level (RBL), probing depth (PD), and bleeding on probing (BoP) were the secondary outcome variables. The implant was set as statistical unit. For studies where a patient-level analysis was performed, implant-level data were derived or requested to the authors;
5. *S* **(***Study design***)**: Prospective (i.e., RCTs; CCTs; and case series/reports) and retrospective studies including at least one arm evaluating the Intervention or Comparison. Only study arms including at least five patients were considered eligible for this systematic review.

2.3 | Search strategy

2.3.1 | Electronic search

A literature search was conducted on the *Medline* (*Pubmed*) database up to and including September 2021. Also, Elsevier Scopus© (www.scopus.com), and the Cochrane Oral Health Group Specialty Trials' Register (www.thecochranelibrary.com) were consulted (Appendix 1). Only full-text articles written in English were considered. Also, the reference lists of previous systematic reviews on LBA simultaneous to implant placement were hand-searched to identify additional potentially relevant articles. Titles and abstracts from the electronic searches were managed by EndNote® v.X7 software. No attempt to identify possible gray literature was performed.

2.3.2 | Screening methods

Two investigators (Mattia Severi and Anna Simonelli) independently evaluated the titles and abstracts of all identified studies. After this phase, full-text versions were obtained for the studies that appeared to meet the inclusion criteria or for which the title and abstract provided insufficient information to make a clear decision. Disagreements concerning eligibility were resolved by consensus or, if disagreement persisted, by arbitration through a third reviewer (Roberto Farina). Articles that fulfilled all inclusion criteria were processed for data extraction.

2.3.3 | Data extraction: Characterization of the intervention

Data extraction was performed in duplicate by two reviewers (Mattia Severi and Anna Simonelli). Extracted data included details of the population, intervention, comparison outcome, and study characteristics. In particular, the following information were retrieved: study design, population (statistical unit, number of implants), type of LBA procedure (if any), and treatment outcomes. Disagreement between the reviewers was resolved by discussion with a third reviewer (Roberto Farina). If data were missing, the authors of the original article were contacted and asked to provide further details.

2.4 | Quality assessment (risk of bias in individual studies)

For included RCTs, methodological quality assessment was performed according to the revised Cochrane risk-of-bias tool for randomized trials (RoB version2.0, updated October 2018).[16] Five main domains for risk of bias were assessed: randomization process, deviations from the intended interventions, missing outcomes, measurement of the outcomes, and selection of the reported result. A risk-of-bias judgment (among "low risk of bias," "high risk of bias," or "some concerns") was assigned to each domain (depending on the descriptions given for each field) or to the entire study. For nonrandomized studies, methodological quality assessment was performed according to the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I).[17] Seven main domains for risk of bias were assessed: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in the measurement of outcomes, bias in selection of the reported result. A risk-of-bias judgment (among "low risk of bias," "moderate risk of bias," "serious risk of bias," "critical risk of bias," or "no information") was assigned to each domain (depending on the descriptions given for each field) or to the entire study.

2.5 | Statistical methods

Since many studies reported results related to a single treatment arm without a comparator, data could not be analyzed according to the

standard network meta-analysis.[18] An alternative analysis of baseline model to include data from single-arm studies was therefore undertaken.[19]

Treatment arms were grouped as follows:

- spontaneous healing (i.e., exposed implant surface covered by a full thickness flap) (SELF);
- graft material (bone substitute, autogenous bone, or combination) covered by a mucoperiosteal flap (BG);
- resorbable membrane alone (RM);
- resorbable membrane combined with a graft material (RM + BG);
- nonresorbable membrane alone (NRM);
- nonresorbable membrane combined with a graft material (NRM + BG);
- patient's own periosteum combined with a graft material (PERI + BG);

Baseline model was also used to comparatively evaluate the effect of human-derived bone substitutes (HBS) (autogenous bone, allografts, or combination) and nonhuman derived bone substitutes (NHBS) (xenografts, synthetic bone substitutes, or combination). Treatment arms where a HBS and a NHBS were combined together were excluded from the analysis.

A Bayesian approach with the statistical software OpenBUGS was used to undertake all the analyses. Bayesian analysis used Markov Chain Monte Carlo (MCMC) method to obtain posterior distributions of parameters in the model, and 3 sets of noninformative priors were used to initiate 3 chains of simulations, where each chain iterated for 100 000 times and the first 50 000 iterations were burn-ins and discarded. Therefore, 150 000 times in total were used for the calculations of posterior distributions of parameters in the present analysis.

2.6 | Study outcomes

2.6.1 | Primary outcome

The proportion of nonresolved BD/BF at T1 was considered the primary outcome. Among the included studies, RM + BG and NHBS were the most frequently reported treatment and bone substitute,

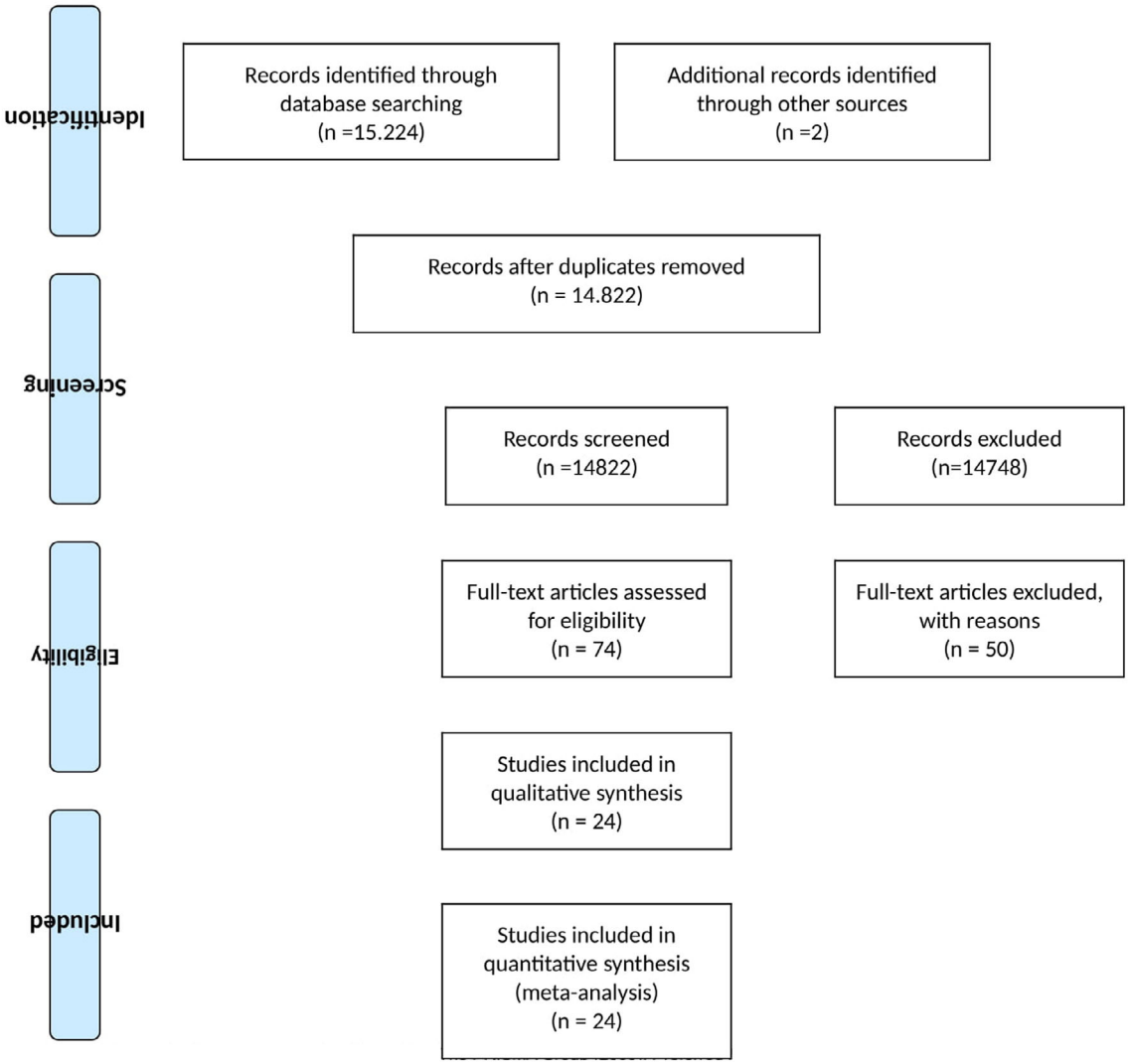

FIGURE 1 PRISMA flowchart for selection process during literature search

TABLE 1 Methodological characteristics of the selected studies, the types of interventions and the outcomes measured

Reference	Publication date	Study design	Test implants (after dropout)	Test implants 2 (after dropout)	Control implants (after dropout)	Intervention test	Intervention test 2	Intervention control	Study outcomes
Dahlin[20]	1991	CCT (split)	7	X	7	ePTFE membrane	X	SH	CDC (%), ΔVDH (%), ISR (%)
Dahlin[21]	1991	Case Series	8	X	X	ePTFE membrane	X	X	CDC (%)
Jovanovic[22]	1992	Case series	14	X	X	ePTFE membrane	X	X	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%), RBL
Mattout[23]	1995	CCT (parallel)	11	X	9	ePTFE membrane + DFDBA	X	ePTFE membrane	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%)
Mayfield[24]	1997	Case series	12	X	X	PLA/PGA membrane	X	X	CDC (%), ISR (%), RBL
Zitzmann[25]	1997	RCT (split)	43	X	39	Collagen membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (%), ISR (%)
Schlegel[26]	1998	CCT (parallel)	14	X	15	PDS membrane + ACBP	X	ACBP	CDC (%), ΔVDH (%), ISR (%)
Majzoub[27]	1999	CCT (parallel)	12	X	10	Laminar bone sheet	X	ePTFE membrane	CDC (%), ΔVDH (%), ISR (%)
Widmark[28]	2000	Case series	9	X	X	ACBP	X	X	CDC (%), ΔVDH (%), ISR (%)
Rosen[29]	2001	Case series	8	X	X	Poly-(DL-lactide) membrane + FDBA/DFDBA	X	x	CDC (%), ISR (%)
Jung[30]	2003	RCT (split)	10	X	10	Collagen membrane + DBBM	X	Collagen membrane + DBBM + rhBMP-2	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
Veis[31]	2004	CCT (parallel)	16	16	14	ePTFE membrane + ACBP (Ramus)	ePTFE membrane + ACBP (Tuberosity)	ePTFE membrane + ACBP (Symphysis)	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
Wang[32]	2004	Case series	6	X	X	Collagen membrane + ACBP + DFDBA + HA	x	X	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
De Boever[33]	2005	Case series	15	X	X	ePTFE membrane + DBBM	X	x	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%), PD, RBL
Van Assche[34]	2013	RCT (split)	14	X	14	Collagen membrane + DBBM	X	Collagen membrane + HA/β-TCP	CDC (%), ΔVDH (%), ISR (%), PD, BoP, RBL
Schneider[35]	2014	RCT	19	X	21	PA/PGA membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔBBT (mm), ISR (%)
Konstantinidis[36]	2015	CCT	9	X	26	Collagen membrane + CPS	X	Titanium mesh + CPS	CDC (%), ΔVDH (mm), ISR (%)

(Continues)

TABLE 1 (Continued)

Reference	Publication date	Study design	Test implants (after dropout)	Test implants 2 (after dropout)	Control implants (after dropout)	Intervention test	Intervention test 2	Intervention control	Study outcomes
Lee[37]	2015	RCT (parallel)	14	X	14	Collagen membrane + DBBM	X	Pericardium membrane + DBBM	CDC (%), ΔVDH (mm), ΔDW (mm), ISR (%)
Jung[6]	2017	RCT (parallel)	15	X	13	Collagen membrane + DBBM	X	SH	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ISR (%), RBL
Naenni[38]	2017	RCT	13	X	13	Collagen membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
Benic[39]	2019	RCT (parallel)	12	X	12	Collagen membrane + DBBM Block	X	Collagen membrane + DBBM	CDC (%), ΔVDH (%), ISR (%)
Temmerman[40]	2019	RCT (parallel)	14	X	14	Collagen membrane + DBBM + ACBP	X	Collagen membrane + DBBM	CDC (%), ΔVDH (%), ΔDW (%), ΔBBT (%), ISR (%), RBL
Trombelli[41]	2019	Case series	15	X	X	Patient's periosteum + DBBM	X	X	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%)
Trombelli[42]	2020	Case series	11	X	x	Patient's periosteum + DBBM	X	x	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%), PD, BoP, RBL

Abbreviations: BoP, bleeding upon probing; β-TCP: beta tri-calcium phosphate; CCT, controlled clinical trial; CDC (%): rate of complete dehiscence coverage; CPS: calcium phosphosilicate; DBBM, deproteinized bovine bone mineral; DFDBA, demineralized freeze-dried bone allograft; ePTFE, expanded polytetrafluoroethylene; FDBA: freeze-dried bone allograft; ISR, implant survival rate; PA/PGA, polyglycolide and polylactide; HA: hydroxyapatite; PD, probing depth; RBL: radiographic bone level; rhBMP-2, recombinant human bone morphogenetic protein 2; RCT, randomized controlled trial; SH, spontaneous healing; ΔVDH (mm): absolute change in vertical dehiscence depth; ΔVDH (%): percentage change in vertical dehiscence depth; ΔDW (mm): absolute change in dehiscence width; ΔDW (%): percentage change in dehiscence width.

respectively. Therefore, they were considered as the reference groups for the respective analysis. The effect size was expressed as odds ratio (OR). If one treatment had an odds ratio greater than 1, this implied a worse treatment effect than the reference group in resolving BD/BF. Treatments were ranked by the surface under the cumulative ranking curve (SUCRA). SUCRA is a numeric presentation of the overall ranking and is presented as a single number associated with each treatment. The higher the SUCRA value, the better is the treatment position in the ranking.

2.6.2 | Secondary outcomes

Absolute and percentage changes in DH, DW, BBT between T0 and T1, ISR, RBL, PD, and BoP were the secondary outcomes. For both absolute and percentage change, mean and standard deviation (SD) were used to perform the analysis. For studies not reporting mean and SD, the mean difference between T0 and T1 was calculated and the SD was obtained by assuming the correlation coefficient between T0 and T1 being 0.5. Data were expressed as mean and standard error (SE), while SUCRA was used for treatment ranking.

3 | RESULTS

3.1 | Summary of the literature search and description of the included studies

The flow of study screening and selection is shown in Figure 1. After the removal of 402 duplicates and the exclusion of 14.748 records out of 14.822 records identified through database search, full-text papers were evaluated for eligibility for 74 records. The list of studies excluded from this review after full-text evaluation (along with the reason for exclusion) is reported in Appendix 2. The screening and

TABLE 2 Distribution of included studies according to LBA procedure and outcome measures

	Treatment							
	RM	RM + BG	NRM	NRM + BG	PERI+BG	BG	SELF	Total
Nonresolved	2	14	4	7	2	2	2	33
DH (mm)	0	11	2	6	2	0	1	22
DH (%)	1	3	1	3	2	2	0	12
DW (mm)	0	6	2	3	2	0	1	14
BBT (mm)	0	5	0	2	2	0	0	9

Abbreviations: BG, bone graft; BBT, buccal bone thickness; DH, BD/BF height; DW, BD/BF width; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane; SELF, spontaneous healing (i.e., exposed implant surface covered by a full thickness flap).

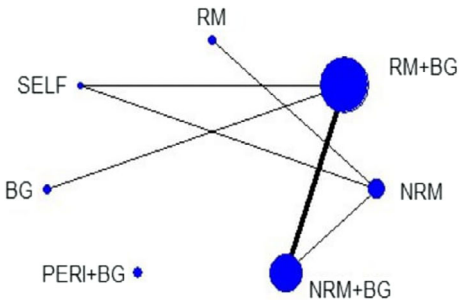

FIGURE 2 Network meta-analysis path graph for the nonresolved bone dehiscence

selection process resulted in the inclusion of 24 studies (nine RCTs, six CCTs, and nine case series). Details of the included studies are reported in Table 1. Twenty-three studies reported data on BD[6,21–42] whereas one study reported data on BF.[20] Quality assessment of the included studies is reported in Appendices 3 and 4.

Mean changes in DH, DW, and BBT were reported or could be retrieved/derived from 18, 10, and seven studies, respectively, whereas percentage change in DH, DW, and BBT could be retrieved from 19, six, and one studies, respectively. ISR was reported or could be retrieved/derived in 23 studies. RBL, PD, and BoP were reported in seven, three and two studies, respectively. The distribution of treatment arms according to evaluated outcome is reported in Table 2.

3.2 | Primary outcome

3.2.1 | Effect of different treatments

The network geometry is illustrated in Figure 2. The results from the baseline model are reported in Table 3. Among the treatment groups, SELF showed a substantial difference in the rate of noncorrection of BD/BF compared to RM + BG (OR: 5.78×10^{38}; CI: 4.83×10^{5} – 1.32×10^{86}), whereas none of the other treatments comparisons showed any significant difference.

The probabilities of treatment ranking and the SUCRA are reported in Table 4. Treatments based on a combination of a graft material and membrane/periosteum (i.e., RM + BG, NRM + BG, and PERI + BG) appeared to perform better than treatments using graft material alone or membrane alone (i.e., BG, RM, and NRM), but the differences were not statistically significant. SELF had the worst effect among all treatments.

3.2.2 | Effect of HBS versus NHBS

Eighteen studies were included for the analysis. NHBS and HBS were employed in 13[6,25,30,33–42] and 5[23,26,28,29,31] studies, respectively. Deproteinized bovine bone mineral and autologous bone were the most used NHBS and HBs, respectively. The results from the baseline model are reported in Table 5. HBS had an odds ratio greater than 1. There were no substantially differences between both treatment effect. The probabilities of treatment ranking and SUCRA are shown in Table 6. NHBS appeared to perform better than HBS.

3.3 | Secondary Outcomes

3.3.1 | BD/BF height

The network geometry for absolute and percentage change in DH is illustrated in Figure 3. The results for absolute change in DH are reported in Table 7. RM + BG and NRM + BG showed 4.03 and 4.66 mm reductions in DH, respectively, while smaller treatment effects were reported for NRM, PERI + BG, and SELF. NRM + BG showed a nonsignificant better effect while NRM and PERI + BG showed a nonsignificant worse effect compared to RM + BG. Only the 2.4 mm difference between SELF and RM + BG was statistically significant (Table 5). Treatment ranking and SUCRA are showed in Table 8. SELF had the worst effect among all treatments.

The results of percentage change are reported in Table 9. For percentage change, BG, RM, and NRM + BG, showed a smaller reduction than RM + BG.

Table 10 provides the probabilities of treatment ranking and SUCRA. Treatments based on a combination of a graft material and membrane/periosteum (i.e., RM + BG, NRM + BG, and PERI + BG) appeared to perform better than treatments using graft material or membrane alone (i.e., BG, RM, and NRM), even though differences were not statistically significant. SELF had the worst effect among all treatments.

TABLE 3 The nonresolved dehiscence odds ratio (reference group = RM + BG)

Item	OR	SE	90% Credible interval	
RM − RM + BG	**1.17**	**3.28**	**0.16**	**7.67**
NRM − RM + BG	0.67	2.20	0.19	2.40
NRM + BG − RM + BG	0.56	1.94	0.19	1.65
PERI+BG − RM + BG	0.17	3.73	0.02	1.39
GRAFT − RM + BG	1.67	3.13	0.26	10.40
SELF − RM + BG	5.78×10^{38}	4.06×10^{25}	4.83×10^{5}	1.32×10^{86}
	Estimate	SE	90% Credible interval	
RM + BG (absolute mean)	0.79	2.66	0.16	3.95
SD of RM + BG	2.54	1.06	2.25	2.71
τ	17.13			

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum;RM, resorbable membrane.

TABLE 4 The probability of rank and surface under the cumulative ranking curve (SUCRA) of the nonresolved dehiscence

	Rank1	Rank2	Rank3	Rank4	Rank5	Rank6	Rank7	SUCRA
NRM	0.00	0.05	0.19	0.36	0.31	0.09	0.00	0.47
RM	0.06	0.13	0.13	0.14	0.23	0.32	0.00	0.45
RM + BG	0.08	0.26	0.27	0.20	0.14	0.06	0.00	0.63
NRM + BG	0.11	0.36	0.26	0.15	0.08	0.03	0.00	0.69
PERI+BG	0.71	0.13	0.07	0.04	0.03	0.02	0.00	0.89
GRAFT	0.04	0.08	0.09	0.11	0.21	0.48	0.00	0.37
SELF	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum;RM, resorbable membrane.

TABLE 5 The nonresolved dehiscence odds ratio (reference group = nonhuman)

Item	Odds ratio	SE	90% Credible interval	
Human	1.17	2.34	0.31	4.13
	Estimate	**SE**	**90% Credible interval**	
Nonhuman (absolute mean)	0.58	2.44	0.13	2.52
SD of nonhuman	2.32	1.13	1.83	2.69
tau	10.61			

TABLE 6 The probability of rank and surface under the cumulative ranking curve (SUCRA) of the nonresolved dehiscence

	Rank1	Rank2	SUCRA
Nonhuman	0.6005	0.3995	0.6005
Human	0.3995	0.6005	0.3995

3.3.2 | BD/BF width

The network geometry for the absolute change in DW is shown in Figure 4. Table 11 shows the results related to the absolute change in DW. PERI + BG showed 1.5 mm greater reduction in defect width than RM + BG, while other treatments showed small, nonsignificant differences.

The probabilities of treatment ranking and SUCRA are reported in Table 12. Treatments based on a combination of a graft material and membrane/periosteum (i.e., RM + BG, NRM + BG, and PERI + BG) appeared to perform better than treatments using graft material or membrane alone (i.e., BG, RM, and NRM), even though differences were not statistically significant. SELF had the worst effect among all treatments.

Since only three studies (Mattout 1995, Trombelli et al. 2019, 2020) reported the mean and SD of the percentage change in DW, no network meta-analysis could be performed for the latter.

3.3.3 | Buccal bone thickness

The network geometry for absolute change in BBT is showed in Figure 5. Results for absolute change in BBT are reported in Table 13. NRM + BG and PERI + BG showed greater increases in BBT than RM + BG. Table 14 provided the probabilities of treatment ranking and SUCRA. Although not statistically significant, RM + BG showed worse effect than other treatments.

Since only one study (Temmerman et al. 2019) reported the percentage change in BBT, without SD, no network meta-analysis could be performed for the latter.

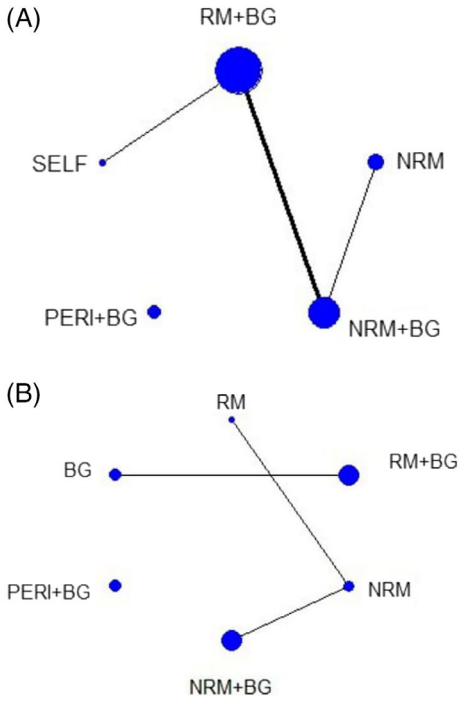

FIGURE 3 Network meta-analysis path graph for the mean difference (3a) and percentage change (3b) of vertical dehiscence height

TABLE 7 The absolute mean difference of vertical dehiscence

Item	Mean	SE	90% Credible interval	
RM + BG	4.03	0.99	2.40	5.65
NRM	2.78	1.74	−0.08	5.63
NRM + BG	4.66	1.52	2.15	7.15
PERI + BG	3.07	1.92	−0.09	6.23
SELF	1.65	2.00	−1.65	4.94

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane.

TABLE 8 The probability of rank and SUCRA of the mean difference of vertical dehiscence

	Rank1	Rank2	Rank3	Rank4	Rank5	SUCRA
RM + BG	0.10	0.72	0.17	0.01	0.00	0.73
NRM	0.01	0.04	0.32	0.50	0.14	0.32
NRM + BG	0.84	0.14	0.03	0.00	0.00	0.95
PERI + BG	0.05	0.10	0.41	0.33	0.11	0.42
SELF	0.00	0.01	0.07	0.16	0.76	0.08

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane; SUCRA, surface under the cumulative ranking curve.

3.3.4 | Implant survival rate

ISR ranged between 80% and 100%. Since ISR was 100% in most study arms, the differences among various treatments could not be

TABLE 9 The Absolute Percentage Change of Vertical Dehiscence

Item	Mean	SE	90% Credible interval	
RM + BG	93.40	1.67	90.64	96.08
RM	74.88	9.42	59.63	90.61
NRM	86.69	7.30	74.72	98.69
NRM + BG	68.99	4.20	61.97	75.79
PERI + BG	94.30	5.01	86.16	100.00
BG	80.04	8.51	65.91	93.85

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane.

TABLE 10 The probability of rank and SUCRA of the percentage change of vertical dehiscence

	Rank1	Rank2	Rank3	Rank4	Rank5	Rank6	SUCRA
RM + BG	0.35	0.55	0.09	0.00	0.00	0.00	0.85
RM	0.01	0.01	0.06	0.24	0.46	0.22	0.24
NRM	0.07	0.08	0.57	0.22	0.05	0.00	0.58
NRM + BG	0.00	0.00	0.00	0.02	0.25	0.73	0.06
PERI+BG	0.56	0.35	0.09	0.01	0.00	0.00	0.89
BG	0.01	0.02	0.19	0.51	0.23	0.05	0.38

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane; SUCRA, surface under the cumulative ranking curve.

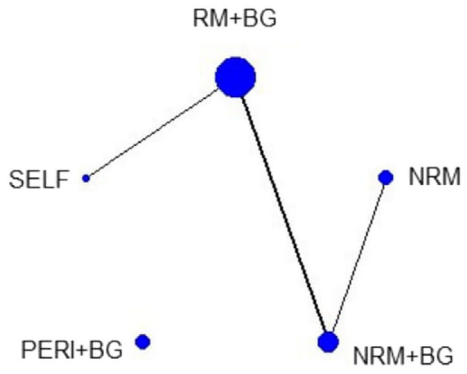

FIGURE 4 Network meta-analysis path graph for the mean difference of defect width

TABLE 11 The absolute mean difference of defect width

Item	Mean	SE	90% Credible interval	
RM + BG	1.95	0.69	0.81	3.05
NRM	1.58	1.24	−0.48	3.57
NRM + BG	2.43	1.03	0.68	4.04
PERI+BG	3.47	1.35	1.25	5.65
SELF	0.91	1.47	−1.51	3.29

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane.

TABLE 12 The Probability of Rank and SUCRA of the Mean Difference of Defect Width

	Rank1	Rank2	Rank3	Rank4	Rank5	SUCRA
RM + BG	0.00	0.07	0.64	0.26	0.02	0.44
NRM	0.00	0.05	0.19	0.55	0.21	0.27
NRM + BG	0.06	0.80	0.11	0.02	0.00	0.72
PERI+BG	0.92	0.06	0.01	0.00	0.00	0.97
SELF	0.01	0.03	0.05	0.16	0.76	0.09

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane; SUCRA, surface under the cumulative ranking curve.

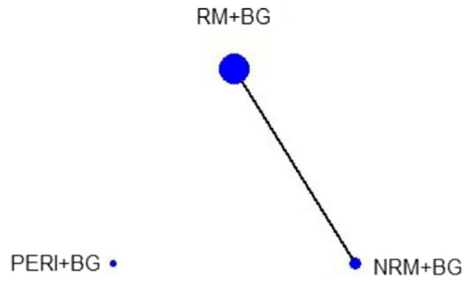

FIGURE 5 Network meta-analysis path graph for the mean difference of buccal bone thickness

TABLE 13 The Absolute Mean Difference of Buccal Bone Thickness

Item	Mean	SE	90% Credible interval	
RM + BG	**−1.47**	**0.70**	**−2.63**	**−0.33**
NRM + BG	−0.11	1.19	−2.06	1.85
PERI + BG	−0.20	1.40	−2.48	2.09

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane.

TABLE 14 The probability of rank and SUCRA of the mean difference of buccal bone thickness

	Rank1	Rank2	Rank3	SUCRA
RM + BG	0.00	0.04	0.96	0.02
NRM + BG	0.55	0.45	0.01	0.77
PERI + BG	0.45	0.51	0.03	0.71

Abbreviations: BG, bone graft; NRM, nonresorbable membrane; PERI, patient's own periosteum; RM, resorbable membrane; SUCRA, surface under the cumulative ranking curve.

reliably estimated (the credible interval would have been extremely wide and not interpretable).

3.3.5 | RBL, PD, and BoP

Due to the paucity of studies reporting data on RBL, PD, and BoP, and the high heterogeneity in observation interval, these parameters were not included in the network meta-analysis and are reported in Appendix 5.

3.3.6 | Heterogeneity and risk of bias in included studies

Among the included RCTs, one resulted at high risk of bias,[30] seven presented some concerns[25,30,34,35,37,38,40] and one was at low risk of bias.[39] Among nonrandomized studies, one study presented a critical risk of bias[31] whereas six studies presented a serious[23,27,36] and moderate[20,26,42] risk of bias.

As the number of studies included in the analysis of each outcome was too few, it was not possible to obtain a robust estimate of heterogeneity. Especially in the Bayesian meta-analysis, the estimate is prone to the influence of prior distribution.

4 | DISCUSSION

In the present systematic review, a network meta-analysis was conducted to evaluate the effect of the type of LBA procedure in completely correcting a BD/BF from implant placement to uncovering. The proportion of nonresolved BD/BF at implant uncovering was considered the primary outcome. Also, based on the primary outcome, a hierarchy of the different surgical options was created, with the combination of resorbable membrane a bone graft being the reference treatment (as the most commonly used option).

4.1 | Key findings

No treatment of BD/BF at implant placement was associated with a markedly higher probability of noncorrected BD/BF compared to the reference treatment (OR: 5.78×10^{38}; CI: 4.83×10^{5} – 1.32×0^{86}). Data related to untreated peri-implant BD/BF were retrieved in two studies,[6,20] both reporting a 100% rate of nonresolved BD/BF at implant placement. Therefore, a very precise estimate for the poor effect of no treatment compared to the reference treatment could not be obtained. However, given its large OR with an extremely wide CI, it is pretty certain that absence of treatment had worse effect than the other treatments.

Compared to the reference treatment, no significant difference in the primary outcome was found for the other treatment options (including graft alone, nonresorbable membrane alone, combinations of graft and nonresorbable membrane or patient's own periosteum) on the proportion of nonresolved BD/BF at implant uncovering. Interestingly, the combination of a graft material and membrane/periosteum showed a nonsignificant tendency to perform better than graft material alone or membrane alone.

NHBS appeared to perform better than HBS in completely correcting a BD/BF. However, no significant differences between HBS and NHBS were found.

4.2 | Overall completeness and applicability of the evidence

The present systematic review was based on all articles reporting data on absence of treatment and/or treatment with a LBA procedure of a BD/BF immediately after type III or IV implant placement.[15] No restrictions were applied in terms of defect dimensions, thus, allowing for heterogeneity in BD/BF configuration and severity among included studies. This methodological aspect supports the generalizability of our findings.

On the other hand, the use of the proportion of nonresolved BD/BF at implant uncovering as the primary outcome was an element of originality of the present review, but led to the exclusion of some RCTs comparing two or more procedures for BD/BF correction where data were not reported or retrievable although.[43–51] This aspect reduced the overall amount of evidence analyzed on the topic within the context of the present review. Also, our literature search was restricted to interventions on LBA procedures, thus, excluding other interventions such as soft tissue grafting. Although soft tissue grafting procedures have been previously proposed to correct small (1.5 mm) peri-implant BDs,[52] no information on the condition of the peri-implant bone plate at re-entry is currently available after soft tissue grafting. Since the repositioning of a mucoperiosteal flap over a peri-implant BD without the adjunctive use of reconstructive devices was not associated with significant reductions in BD at surgical re-entry,[6,20] however, it is reasonable to speculate that the use soft tissue grafts may similarly have a limited impact on hard tissue formation on the exposed implant surface at a peri-implant BD.

4.3 | Potential biases in the review process

Screening, eligibility decisions, and data extraction were carried out in duplicate and independently. The search was also designed to minimize bias, including development of a highly sensitive electronic search strategy of multiple databases. The level of introduced bias seems to be low.

4.4 | Agreements and disagreements with other reviews

Other systematic reviews on the same topic were previously published.[11,12] Both reviews summarized the evidence from RCTs and CCTs on LBA procedures when performed to correct a BD/BF at implant placement. Both reviews considered mean reduction in BD/BF height (as observed from implant placement to surgical re-entry for implant uncovering) as the primary outcome.

However, data deriving from the present network meta-analysis are in accordance with and reinforce those derived from previous systematic reviews on the same topic because, even though no attempt was made to meta-analyze the proportion of cases showing complete correction BD/BF, the data stemming from those reviews clearly showed better outcomes, in terms of BD/BF height reduction, for treatments combining a resorbable/nonresorbable membrane and a bone substitute material compared to spontaneous healing.

4.5 | Implications for practice and policy

Within the limitations of the present systematic review, the results of the analysis indicate that (1) reconstructive surgical treatment of a peri-implant BD/BF with graft alone, resorbable/nonresorbable membrane alone, or combinations of graft and resorbable/nonresorbable membrane or patient's own periosteum, is associated with a lower probability of BD/BF persistence at implant uncovering when compared to repositioning of a full-thickness flap without adjunctive use of reconstructive devices; (ii) the combination of either a membrane (either resorbable or nonresorbable) or patient's own periosteum with a graft material showed a nonsignificant tendency to perform better than other treatments and () NHBS showed a nonsignificant tendency to perform better than HBS.

The best ranking obtained by the combination of patient's own periosteum and a bone substitute among the other treatments included in the present review should be carefully evaluated, since it derives from a case-series and a moderate risk of bias retrospective study. Promising outcomes derived for this treatment, however, should be investigated in further high-quality longitudinal trials to assess its efficacy in completely correcting a BD/BF.

The applicability of the results should be evaluated with caution. Treatment hierarchy, in fact, is based on the SUCRA. This parameter does not take into account the quality of the included study and may be misleading in its interpretation.[53]

4.6 | Implications for further research

Since residual BDs deeper than 1 mm were shown to be associated with greater prevalence of mucositis and peri-implantitis and greater interproximal bone loss over time than implants with either intact peri-implant bone or surgically treated peri-implant BD/BF,[5,6,13] complete BD/BF correction at placement seems to represent a clinically relevant issue for implant prognosis. This consideration supports the use of the rate of complete BD/BF correction as the primary outcome in clinical studies ad systematic reviews evaluating the effectiveness/efficacy of BD/BF treatment.

This review included treatment arms derived from nonrandomized studies, mostly presenting some concerns or higher risk of bias.

Therefore, which bone substitute and which space-making device (barrier membranes or patient periosteum) should be employed to completely correct a BD/BF needs to be investigated further by mean of RCTs with blinded outcomes assessment.

5 | CONCLUSIONS

Within the limitations of the present review, the results indicate that the reconstructive treatment (including use of graft alone, membrane

alone, or combinations of grafts and either membrane or patient's own periosteum) of a BD/BF at implant placement favorably and significantly impacts on the probability to obtain complete correction of the BD/BF at implant uncovering when compared to full-thickness flap repositioning on the BD/BF. Encouraging data were reported for the combination of membrane/periosteum and graft, which showed a tendency to perform better than other treatments, but confirmatory studies are needed for this finding.

Nonhuman bone substitutes showed a tendency to perform better than other treatments to favor the complete correction of a BD/BF.

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CONFLICT OF INTEREST

Mattia Severi, Anna Simonelli, Roberto Farina, Yu-Kang Tu, Cheng-Hsiang Lan, and Ming-Chieh Shih declare no conflict of interest. Leonardo Trombelli received grants and lectured for Geistlich Biomaterials and Thommen Medical.

AUTHOR CONTRIBUTION

Mattia Severi: Concept/design, data collection, drafting article.
Anna Simonelli: Data collection, drafting article.
Roberto Farina: Critical revision of article.
Yu-Kang Tu: Data analysis/interpretation, statistics.
Cheng-Hsiang: Data analysis/interpretation, statistics.
Ming-Chieh Shih: Data analysis/interpretation, statistics.
Leonardo Trombelli: Critical revision of article, approval of article.

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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SUPPORTING INFORMATION

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