Journal of Dental Sciences 19 (2024) 865–870

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jds.com

Original Article

Addition of recombinant human bone morphogenic protein-2 to the graft materials improves the clinical outcomes of implants placed in grafted maxillary sinus

Jin-Ho Lee [a], Hyejun Seo [b], Yeong-Cheol Cho [a], Iel-Yong Sung [a], Jang-Ho Son [a*]

[a] *Department of Oral and Maxillofacial Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea*
[b] *Department of Dentistry, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea*

Received 2 August 2023; Final revision received 21 August 2023
Available online 30 August 2023

KEYWORDS
Marginal bone loss;
rhBMP-2;
Sinus graft;
Survival rate

Abstract *Background/purpose:* The long-term outcomes of implants placed in grafted sinuses using recombinant human bone morphogenetic protein-2 (rhBMP-2) are unclear. This study aimed to compare 3- and 5-year implant survival rates and marginal bone loss (MBL) during functional loading.
Materials and methods: In this retrospective study, we analyzed 63 implants inserted after maxillary sinus floor augmentation (MSFA) in 45 patients between January 2016 and April 2019. The outcome variables were: 1) 3- and 5-year cumulative survival rates of the implants and 2) MBL after functional loading. Other assessed variables included patient demographic information, preoperative residual bone height (RBH), surgical site, implant length and diameter, graft material, healing period before loading, prosthetic type, and opposing dentition.
Results: The cumulative 3- and 5-year survival rates of the implants were 100% in the rhBMP-2 group and 95.5% and 86.4% in the non-rhBMP-2 group, respectively. The average 3- and 5-year MBL were 1.14 ± 0.67 mm, 1.30 ± 0.74 mm in the rhBMP-2 group and 1.68 ± 0.90 mm, 2.27 ± 1.29 mm in the non-rhBMP-2 group, respectively. Significant differences were observed between 3 and 5 years between the two groups.

* Corresponding author. Department of Oral and Maxillofacial Surgery, Ulsan University Hospital, 877 Bangeojinsunhwando-ro, Dong-gu, Ulsan, 44033, South Korea.
E-mail address: ribosome@hanmail.net (J.-H. Son).

https://doi.org/10.1016/j.jds.2023.08.020

Conclusion: Addition of the rhBMP-2 to the graft materials positively affects implant placement in the grafted maxillary sinus in terms of implant survival and MBL when preoperative RBH is unfavorable.

Introduction

Bone quality and quantity are major concerns in implant dentistry as they are critical factors for implant stability,[1] decisions regarding loading protocols,[2] long-term implant success and survival,[3] and the need for additional procedures.

The edentulous posterior maxilla is a challenging site for implant placement because of the low bone density in the region, bone quantity resulting from alveolar ridge resorption, and maxillary sinus pneumatization after dental extraction.[4] With improved surgical techniques, devices, and materials, maxillary sinus floor augmentation (MSFA) has become a common surgical option for preparing implant sites in the reduced maxillary posterior ridge with long-term implant success.[5]

Previous studies have indicated that sinus grafting materials promote bone formation in the space created under the elevated sinus membrane by facilitating the three-dimensional stability of the clot against intrasinus pressure.[6,7] To guarantee grafted sinus bone quality and quantity to ensure initial and long-term implant stability, research has focused on ideal space-filling graft materials and utilizing growth factors to accelerate bone formation.

Bone morphogenetic protein-2 (BMP-2) possesses the highest osteoinductive potential among the BMP family.[8] Since many studies have investigated its potential in local bone formation and osseointegration of dental implants, recombinant human BMP-2 (rhBMP-2) has been used in numerous bone augmentation procedures to regenerate new high-quality and high-density bone. Evidence indicates that combining rhBMP-2 with graft materials is a promising alternative to autogenous bone grafts for maxillary sinus augmentation.[9] However, additional quantitative studies are needed to define the long-term outcomes of implants placed in grafted sinuses using rhBMP-2.

Therefore, this study aimed to investigate the outcomes of dental implants placed in the grafted maxillary sinus using rhBMP-2. Our hypotheses were as follows: 1) implants placed in the grafted maxillary sinus with unfavorable residual ridges of less than 5 mm using rhBMP-2 would have sufficient long-term implant stability; 2) rhBMP-2 would be more favorable in terms of implant survival and marginal bone loss (MBL) during functional loading compared with the group that did not receive rhBMP-2. The specific aims of this study were to compare the 3- and >5-year implant survival rates and MBL during functional loading.

Materials and methods

Study design and sample

A retrospective cohort study was conducted to address this research objective. We included 63 implants from 45 patients with MSFA, with or without rhBMP-2, between January 2016 and April 2019 at our institution. The inclusion criteria for the study were as follows: implants with less than 5 mm of preoperative residual bone height (RBH), availability of preoperative radiographs to measure the RBH, immediate postoperative panoramic images, availability of radiographs taken immediately before or after prosthetic loading, and adherence to periodic maintenance checkups. Patients with medical conditions that could compromise bone healing, such as uncontrolled diabetes, long-term steroid use, or preoperative untreated maxillary sinusitis, were excluded. The implants were divided into two groups based on whether rhBMP-2 was used. The study protocol was approved by the Institutional Review Board (IRB File No: 2023-07-025).

Study variables

The outcome variables were: 1) 3- and 5-year cumulative survival rates of the implants and 2) MBL after functional loading. Other assessed variables included patient demographic information, preoperative RBH, surgical site, implant length and diameter, graft material, healing period before loading, prosthetic type, and opposing dentition. Patient demographic and clinical data were obtained from the medical and surgical records. To assess the preoperative RBH, the point corresponding to the center of each inserted implant was measured on preoperative radiographs. MBL was defined as the difference in values between the implant and abutment junction and the most coronal bone-to-implant contact level at the mesial and distal sides of each implant on the follow-up panoramic radiographs.

Surgical procedure

All patients were provided extensive information regarding the advantages and disadvantages of rhBMP-2 before the procedure. Each patient chose whether or not to mix rhBMP-2 with the graft material for sinus floor augmentation. In the rhBMP-2 group, 0.25 mg rhBMP-2 (CGBio, Seongnam, Korea) dissolved in 0.5 mL of normal saline was

mixed with graft material. Deproteinized bovine bone with spongiosa granules (Geistlich Pharma AG, Wolhusen, Switzerland), freeze-dried cancellous bone (CGBio), demineralized dentin matrix, intraoral autograft, and their mixtures were used appropriately. All MSFA procedures were performed using the lateral window technique under local anesthesia. Whenever possible, implants (Osstem®, Seoul, Korea) were installed simultaneously with the MSFA, as per the manufacturer's instructions.

Statistical analysis

Variables were evaluated using descriptive statistics. Categorical variables were expressed as frequencies with percentages, and continuous variables were expressed as the mean ± standard deviation (SD). Comparisons were performed using the chi-square test or Fisher's exact test for categorical variables and Student's t-test for continuous variables, as appropriate. Kaplan-Meier analysis was performed to identify differences in implant failure between the two groups. Kaplan-Meier survival analysis was used to compare the groups in terms of time to implant. Data manipulation and statistical analyses were performed using the SPSS software version 24 (IBM Corp., Armonk, NY, USA). The significance level was set at $P < 0.05$.

Results

A total of 63 implants in 45 patients (19 male and 26 female) met the inclusion criteria. The preoperative RBH was 3.62 ± 1.14 mm in the rhBMP-2 group and 3.31 ± 1.10 mm in the non-rhBMP-2 group.

Parameters such as patient demographic data, surgical site, and duration of prosthetic loading are summarized in Table 1. Other parameters such as preoperative RBH, implant diameter and length, healing period before loading, crown-to-implant ratios, methods of implant placement (simultaneous/staged), prosthetic type (single/splinted), and state of the opposite dentition are summarized in Table 2. The numbers of implants that reached functional loading in 3 and 5 years, respectively, were 28 and 11 in the rhBMP-2 group, and 32 and 21 in the non-rhBMP-2 group.

In the non-rhBMP-2 group, three implants were lost at 2, 55, and 57 months (3.48, 3.6, and 3.46 mm of preoperative RBH, respectively) after prosthetic loading. In contrast, no implants were lost in the rhBMP-2 group. The cumulative 3- and 5-year survival rates for the implants were 100% and 100% in the rhBMP-2 group and 95.5% and 86.4% in the non-rhBMP-2 group, respectively (Fig. 1).

The average 3- and 5-year MBL were 1.14 ± 0.67 mm, 1.30 ± 0.74 mm in the rhBMP-2 group and 1.68 ± 0.90 mm, 2.27 ± 1.29 mm in the non-rhBMP-2 group, respectively. There were significant differences in the 3- and 5-year MBLs between the two groups ($P < 0.05$).

Discussion

This study investigated the effect of rhBMP-2 on MSFA by analyzing short- and long-term implant survival rates and

Table 1 Patient demographics and clinical data.

	Sex (M/F)	Age (year)	Surgical site (P1/P2/M1/M2)	Period of prosthetic loading (months)
rhBMP-2	9/14	60.9 ± 11.9	2/2/13/11	52.9 ± 11.5
Non-rhBMP-2	10/12	59.4 ± 7.83	0/1/17/17	60.7 ± 11.1

Abbreviations: M, male; F, female; P1, first premolar; P2, second premolar; M1, first molar; M2, second molar; rhBMP-2, recombinant human bone morphogenetic protein-2.

Table 2 Clinical data according to other parameters.

	Total (N = 63)	rhBMP-2 (N = 28)	non-rhBMP-2 (N = 35)	*P*
Staged or simultaneous				1.000
Staged	7 (11.7)	3 (10.7)	4 (12.5)	
Simultaneous	53 (88.3)	25 (89.3)	28 (87.5)	
Healing period	8.23 ± 1.29	8.14 ± 2.07	8.31 ± 2.01	0.749
Opposite dentition				0.835
Natural dentition	33 (55.0)	15 (53.6)	18 (56.3)	
Implant	27 (45.5)	13 (46.4)	14 (43.8)	
Prosthetic type				1.000
Single	8 (13.3)	4 (14.3)	4 (12.5)	
Splinted	52 (86.7)	24 (85.7)	28 (87.5)	
Crown-implant ratio	1.29 ± 0.27	1.23 ± 0.30	1.34 ± 0.23	0.147
3-year MBL	1.43 ± 0.84	1.14 ± 0.67(N = 28)	1.68 ± 0.90(N = 32)	0.012*
5-year MBL	1.94 ± 1.21	1.30 ± 0.74(N = 11)	2.27 ± 1.29(N = 21)	0.029*

Abbreviations: MBL, marginal bone loss; rhBMP-2, recombinant human bone morphogenetic protein-2. *$P < 0.05$.

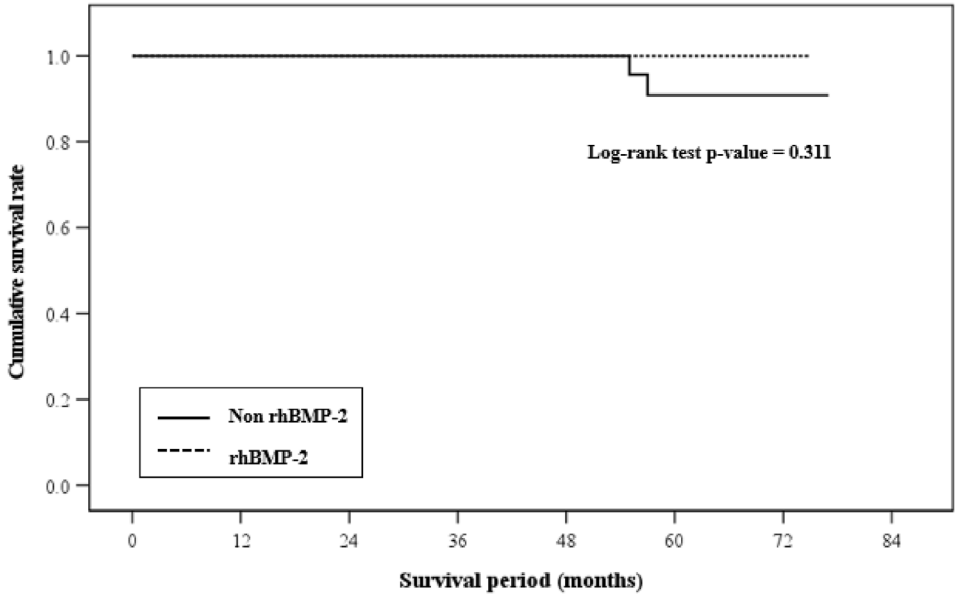

Figure 1 Kaplan-Meier cumulative survival rates. Abbreviation: rhBMP-2, recombinant human bone morphogenetic protein-2.

peri-implant MBL by evaluating changes in crestal bone level over time because progressive marginal bone level alterations are known risk factors for implant success and survival. Thus, we compared implants in the grafted maxillary sinus using bone graft materials and rhBMP-2 with graft materials alone for unfavorable RBH of the posterior maxilla. The 3- and > 5-year implant survival rates were 100% in the rhBMP-2 group and 95.5% and 86.4%, respectively, in the non-rhBMP-2 group, although these were not statistically significant. There were significant differences in the 3- and >5-year MBL between the groups.

Although placing dental implants with MSFA is a reliable procedure with 10-year cumulative survival rates of 86%–97.2%,[10–12] more studies are needed to increase long-term implant survival and maintain peri-implant health. Several studies have shown that survival rates[13,14] and MBL around dental implants placed in the augmented maxillary sinus are affected by RBH. Rosen et al. demonstrated in their multicenter study the implant survival rate was 96% or higher when RBH was ≥5 mm and decreased markedly to 85.7% when the RBH was ≤4 mm.[15] Khouly et al. reported a 90% cumulative implant survival rate during a mean follow-up of 7.2 years.[16] Their multivariate models showed greater implant survival with implants placed with ≥5 mm of RBH than with those placed with <3 mm of RBH. Our previous study using a multivariate model showed that an RBH of <5 mm was a risk factor for long-term implant survival.[17] Therefore, we set RBH <5 mm as the inclusion criterion in this study.

Similar to the effect of RBH on implant survival, a systematic review reported that an RBH <4 mm led to MBL, resulting in a lower success rate with osteotome-mediated sinus floor elevation.[18] According to a study by Gonzalez et al., who used the alveolar crestal approach, MBL was 0.55 mm at an RBH of ≤4 mm and 0.07 mm at an RBH of ≥4 mm over an average of 29.7 months after surgery.[19] A previous study reported that a bone height of 2–4 mm using the lateral approach resulted in the largest change in bone loss.[20]

The stress dispersion around the implant differs depending on the bone quantity and quality. More stress concentration has been reported in low-density cancellous bone, such as the maxillary posterior region.[21] Clinical studies have demonstrated that MBL around implants in grafted sinuses is significantly greater than that in native bone within the first 12 months of functional loading.[22–24]

It is well known that rhBMP-2 effectively promotes bone formation during the early stages of healing compared with control.[25] Studies have demonstrated that rhBMP-2 improves the quality of regenerated bone.[26,27] Terbish et al. reported that injecting rhBMP-2 into a regenerated bone after a distraction osteogenesis procedure significantly increased bone volume at the dentoalveolar distraction site and increased bone density.[28] In MSFA, rhBMP-2, combined with graft material was associated with favorable results that generally outperformed the control groups.[29] However, the use of rhBMP-2 in MSFA remains controversial. It has been concluded that rhBMP-2 does not perform as well as autografts or allografts in MSAF.[30,31] Nevertheless, their results suggest that rhBMP-2 might form adequate bone while decreasing morbidity, making it a reasonable alternative to bone grafting in maxillary sinus floor MSFA.[32]

The need for a carrier has been recognized because BMP are water-soluble proteins that diffuse easily into body fluids. In an experimental setting, BMP delivered without a carrier was not sustained for more than a few hours at the deposition site.[33] Therefore, the binding affinity of BMP to a carrier or the need for a containing material such that it will have a localized effect at the bone graft site appears to be a critical factor for BMP use. Various carriers, including collagen sponges,[34] autogenous bone,[35] and bone substitutes,[36–38] have been investigated for bone graft procedures. Although it is unclear which carrier is more favorable, these studies show that rhBMP-2 combined with autogenous bone or bone substitutes (BS) can achieve predictable results after bone grafting. Furthermore, the maxillary sinus is a pyramidal-shaped cavity with a base

adjacent to the nasal wall, and its contour is favorable for containing BMP-soaked graft materials during MSFA and bone healing. In this study, we used autogenous bone and BS as rhBMP-2 carriers. This result suggests that BMP-2 has a synergic effect with the bone graft material in MSFA, even at a low dose of BMP-2 following the favorable anatomical characteristics of the maxillary sinus.

This study had some limitations. First, the sample size was small. Second, it was a retrospective study, as the medical records and radiographic images did not provide adequate information on buccal/palatal cortical thickness after implantation, the possibility of graft contamination, and the presence of detrimental parafunction. Buccal/palatal cortical thickness is important for preventing bone loss and resultant implant failure. We could not ascertain whether buccal/palatal cortical thickness in the non-rhBMP-2 use group was as high as in the rhBMP-2 group. Additionally, we measured the MBL at the mesial and distal sides of each implant on panoramic radiographs. Buccal/palatal bone loss could be more at the mesial/distal side. Poor bone healing due to graft contamination, such as a sinus membrane tear during MSFA, consequent failure of occlusal load distribution through the peri-implant bone, and failure of osseointegration, cannot be excluded in the non-rhBMP-2 group. Furthermore, previous studies have suggested that bone resorption around implants could be caused by excess occlusal trauma, and bruxism has been suggested to increase the risk of MBL and implant failure over time.[39] However, the presence of detrimental parafunctions, such as night bruxism and clenching, could not be obtained from medical records.

Although this study has some limitations, our results suggest that the addition of the rhBMP-2 to the graft materials has a positive effect on implant placement in the grafted maxillary sinus from the perspective of implant survival and MBL when preoperative RBH is unfavorable. This offers reasonable scientific evidence for clinicians to use rhBMP-2 when preoperative RBH is less than 5 mm. However, the risk factors associated with implant failure and MBL are likely multifactorial, and accordingly allow numerous potential analytical comparisons. Future prospective studies with larger sample sizes and broader range of analytical comparisons should be designed to enhance the overall comprehensiveness of the study of rhBMP-2 use in MSFA.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

The authors are grateful to Eun-Ji Park for the statistical analysis.

References

1. Wirth AJ, Goldhahn J, Flaig C, Arbenz P, Muller R, Lenthe GH. Implant stability is affected by local bone microstructural quality. *Bone* 2011;49:473—8.
2. Muelas-Jimenez MI, Olmedo-Gaya MV, Manzano-Moreno FJ, Reyes-Botella C, Vallecillo-Capilla M. Long-term survival of dental implants with different prosthetic loading times in healthy patients: a 5-year retrospective clinical study. *J Prosthodont* 2017;26:99—106.
3. Goiato MC, dos Santos DM, Santiago JFJ, Moreno A, Pellizzer EP. Longevity of dental implants in type IV bone: a systematic review. *Int J Oral Maxillofac Surg* 2014;43:1108—16.
4. Barone A, Santini S, Sbordone L, Crespi R, Covani M. Clinical study of the outcomes and complications associated with maxillary sinus augmentation. *Int J Oral Maxillofac Implants* 2006;21:81—5.
5. Raghoebar GM, Onclin P, Boven GC, Vissink A, Meijer HJA. Long-term effectiveness of maxillary sinus floor augmentation: a systematic review and meta-analysis. *J Clin Periodontol* 2019;46:307—18.
6. Chen TW, Chang HS, Leung KW, Lai YL, Kao SY. Implant placement immediately after the lateral approach of the trap door window procedure to create a maxillary sinus lift without bone grafting: a 2-year retrospective evaluation of 47 implants in 33 patients. *J Oral Maxillofac Surg* 2007;65:2324—8.
7. Jensen J, Simonsen EK, Sindetpedersen S. Reconstruction of the severely resorbed maxilla with bone-grafting and osseointegrated implants - a preliminary-report. *J Oral Maxillofac Surg* 1990;48:27—32.
8. Cheng HW, Jiang W, Phillips FM, et al. Osteogenic activity of the fourteen types of human bone morphogenetic proteins (BMPs). *J Bone Joint Surg Am* 2003;85:1544—52.
9. de Freitas RM, Spin-Neto R, Marcantonio E, Pereira LAVD, Wikesjo UME, Susin C. Alveolar ridge and maxillary sinus augmentation using rhBMP-2: a systematic review. *Clin Implant Dent R* 2015;17:192—201.
10. Halard JJ. Supercritical CO2 viral-inactivated allogenic bone graft in maxillary sinus augmentation procedures: 10-year retrospective clinical and radiographic results. *Int J Periodont Rest* 2021;41:433—41.
11. Velasco-Ortega E, Sierra-Baztan A, Jimenez-Guerra A, et al. Long-term clinical study of implants placed in maxillary sinus floor augmentation using beta-tricalcium phosphate. *Int J Environ Res Publ Health* 2021;18:9975.
12. Mordenfeld A, Albrektsson T, Hallman M. A 10-year clinical and radiographic study of implants placed after maxillary sinus floor augmentation with an 80:20 mixture of deproteinized bovine bone and autogenous bone. *Clin Implant Dent R* 2014;16:435—46.
13. Zinser MJ, Randelzhofer P, Kuiper L, Zoller JE, De Lange GL. The predictors of implant failure after maxillary sinus floor augmentation and reconstruction: a retrospective study of 1045 consecutive implants. *Or Surg or Med or Pa* 2013;115:571—82.
14. Ferreira CED, Novaes AB, Martinelli CB, Almeida ALG, Batitucci RG. Grafting the nasal cavity with 100% anorganic bovine bone: a clinical and histomorphometric pilot report. *Int J Oral Maxillofac Implants* 2013;28:670—6.
15. Rosen PS, Summers R, Mellado JR, et al. The bone-added osteotome sinus floor elevation technique: multicenter retrospective report of consecutively treated patients. *Int J Oral Maxillofac Implants* 1999;14:853—8.
16. Khouly I, Lopez SP, Aliaga I, Froum SJ. Long-term implant survival after 100 maxillary sinus augmentations using plasma rich in growth factors. *Implant Dent* 2017;26:199—208.
17. Ha J, Son JH, Sung IY, Cho YC, Choi JH. Clinical outcome of implants placed in grafted maxillary sinus via lateral approach: a 10-year follow-up study. *J Dent Sci* 2020;15:270—7.
18. Calin C, Petre A, Drafta S. Osteotome-mediated sinus floor elevation: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants* 2014;29:558—76.

19. Gonzalez S, Tuan MC, Ahn KM, Nowzari H. Crestal approach for maxillary sinus augmentation in patients with <= 4 mm of residual alveolar bone. *Clin Implant Dent R* 2014;16:827—35.
20. Park JH, Kim YG. Longitudinal study of bone height change between two approaches for sinus floor elevation. *Medicina* 2023;59:1132.
21. Kim Y, Oh TJ, Misch CE, Wang HL. Occlusal considerations in implant therapy: clinical guidelines with biomechanical rationale. *Clin Oral Implants Res* 2005;16:26—35.
22. Galindo-Moreno P, Leon-Cano A, Ortega-Oller I, Monje A, O'Valle F, Catena A. Marginal bone loss as success criterion in implant dentistry: beyond 2 mm. *Clin Oral Implants Res* 2015;26:28—34.
23. Galindo-Moreno P, Fernandez-Jimenez A, Avila-Ortiz G, Silvestre FJ, Hernandez-Cortes P, Wang HL. Marginal bone loss around implants placed in maxillary native bone or grafted sinuses: a retrospective cohort study. *Clin Oral Implants Res* 2014;25:378—84.
24. Duan DH, Fu JH, Qi W, Du Y, Pan J, Wang HL. Graft-free maxillary sinus floor elevation: a systematic review and meta-analysis. *J Periodontol* 2017;88:550—64.
25. Alarcon MA, Diaz KT, Aranda L, Cafferata EA, Faggion CM, Monje A. Use of biologic agents to promote bone formation in implant dentistry: a critical assessment of systematic reviews. *Int J Oral Maxillofac Implants* 2017;32:271—81.
26. Seeherman HJ, Li XJ, Smith E, Parkington J, Li R, Wozney JM. Intraosseous injection of rhBMP-2/calcium phosphate matrix improves bone structure and strength in the proximal aspect of the femur in chronic ovariectomized nonhuman primates. *J Bone Joint Surg Am* 2013;95:36—47.
27. Carlisle P, Guda T, Silliman DT, et al. Localized low-dose rhBMP-2 is effective at promoting bone regeneration in mandibular segmental defects. *J Biomed Mater Res B* 2019;107:1491—503.
28. Terbish M, Yoo SH, Kim HJ, et al. Accelerated bone formation in distracted alveolar bone after injection of recombinant human bone morphogenetic protein-2. *J Periodontol* 2015;86:1078—86.
29. del Amo FSL, Monje A. Efficacy of biologics for alveolar ridge preservation/reconstruction and implant site development: an american academy of periodontology best evidence systematic review. *J Periodontol* 2022;93:1827—47.
30. Boyne PJ, Lilly LC, Marx RE, et al. De novo bone induction by recombinant human bone morphogenetic protein-2 (rhBMP-2) in maxillary sinus floor augmentation. *J Oral Maxillofac Surg* 2005;63:1693—707.
31. Triplett RG, Nevins M, Marx RE, et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. *J Oral Maxillofac Surg* 2009;67:1947—60.
32. Kelly MP, Vaughn OLA, Anderson PA. Systematic review and meta-analysis of recombinant human bone morphogenetic protein-2 in localized alveolar ridge and maxillary sinus augmentation. *J Oral Maxillofac Surg* 2016;74:928—39.
33. Manocha Anish, Sachdeva Surinder. Bone morphogenetic proteins: a strategic review. *IP Int J Periodontol Implantol* 2018;3:41—6.
34. de Freitas RM, Susin C, Tamashiro WMDC, et al. Histological analysis and gene expression profile following augmentation of the anterior maxilla using rhBMP-2/ACS versus autogenous bone graft. *J Clin Periodontol* 2016;43:1200—7.
35. Jahanbin A, Zarch HH, Irani S, Eslami N, Kermani H. Recombinant human bone morphogenic protein-2 combined with autogenous bone graft for reconstruction of alveolar cleft. *J Craniofac Surg* 2019;30:209—13.
36. Han JJ, Moon JE, Lee EH, Yang HJ, Hwang SJ. Clinical and radiographic outcomes of dental implant after maxillary sinus floor augmentation with rhBMP-2/hydroxyapatite compared to deproteinized bovine bone. *PLoS One* 2022;17:e0273399.
37. Ku JK, Kim YK, Huh JK, Um IW, Lee ES, Kim C. Allogeneic demineralized dentin matrix as rhBMP-2 carrier: a retrospective clinical study. *Int J Oral Maxillofac Implants* 2022;37:1138—44.
38. Yasuda H, Yano K, Wakitani S, Matsumoto T, Nakamura H, Takaoka K. Repair of critical long bone defects using frozen bone allografts coated with an rhBMP-2-retaining paste. *J Orthop Sci* 2012;17:299—307.
39. Bredberg C, Vu C, Haggman-Henrikson B, Chrcanovic BR. Marginal bone loss around dental implants: comparison between matched groups of bruxer and non-bruxer patients: a retrospective case-control study. *Clin Implant Dent R* 2023;25:124—32.