BMC Oral Health

RESEARCH

Open Access

Stability of alveolar ridge following horizontal guided bone regeneration after implant loading for 1 -2 years: a retrospective comparative study

Zhaoxia Jiang[1†], Dejing Kong[1†], Chuanqing Zhou[2], Yixin Liang[1], Mingli Liu[1] and Zhe Qu[1*]

Abstract

Objective This retrospective comparative study aimed to evaluate the effects of guided bone regeneration(GBR) on horizontal bone augmentation of the alveolar ridge in the mandibular posterior region and bone stability after loading for 1–2 years. We measured and analyzed the changes in alveolar ridge bone width to observe the clinical effect of bone grafting. The RANK/RANKL/OPG concentration in gingival crevicular fluid around the implant was quantitatively analyzed and compared with that of healthy natural teeth to assess the bone condition.

Methods Fifty-two patients admitted to the Department of Implantology of Dalian Stomatological Hospital were selected. 22 implanted dentures of 22 patients that were repaired with soft tissue-level implants after horizontal bone grafting (experimental group). Thirty patients had 30 implanted dentures with the same system of implants without bone grafting (control group). The gingival crevicular fluid around the implant and healthy control natural teeth were collected via the same filter paper strip after loading for 1–2 years. The concentrations and ratios of RANKL and OPG were quantitatively detected via ELISA. The CBCT images taken before bone grafting, on the day after surgery, 6 months after surgery, and after loading were superimposed to measure the horizontal width of the alveolar ridge. Measurements were taken 2 mm apical from the top of the crest at the center of the implant.

Results The average alveolar crest width in the experimental group was 3.72 ± 0.94 mm before surgery, 11.57 ± 1.44 mm on the day after surgery, 8.86 ± 1.37 mm at 6 months after surgery, and 7.62 ± 1.08 mm after 1–2 years of loading. The level of OPG in the experimental group was greater than that in the control group, and greater than that in the natural teeth; however, this difference was not significant ($P > 0.05$). The RANKL concentration in the gingival crevicular fluid of the two groups was similar, and the RANKL/OPG ratio of the implants in the experimental group was slightly lower than that in the control group; whereas the RANKL and ratio of the two groups were lower than that of the natural teeth ($P > 0.05$).

Conclusion GBR application in the horizontal bone augmentation of the mandibular posterior dental region has positive clinical outcomes. After 1–2 years of implant loading, the bone in the neck of the implant in the experimental group is slightly more active than in the control group, and may still be in the process of osteogenesis.

Keywords Guided bone regeneration, Sausage technique, Horizontal ridge augmentation, RANK, OPG

†Zhaoxia Jiang and Dejing Kong contributed equally to this work.

*Correspondence:
Zhe Qu
quzhekq@outlook.com
Full list of author information is available at the end of the article

Introduction

The clinical application of guided bone regeneration (GBR) has expanded the range of patients deemed suitable for dental implant treatment and has improved the long-term success rate and clinical results of dental implants. Several experimental studies have investigated the combination of particulate autogenous bone and DBBM, thereby clinically and histologically confirming the resultant bone quality [1, 2]. It has been reported that implants have been successfully implanted in the regenerated bone area to perform long-term function [3, 4]. Systematic analysis shows that the survival rate of implants is similar regardless of whether the implant area is bone grafting or not [5]. In addition, GBR technology increases the bone quality around the implant to ensure the stability of the implant system under long-term loading [6]. One such method, devised by Urban, is the sausage technique, which uses a 1:1 mixture of xenograft/autogenous grafts and an absorbable collagen membrane fixed with titanium nails [7, 8]. Clinical studies have also shown that the use of the sausage technique for horizontal ridge augmentation can yield satisfactory clinical results [7, 9, 10]. Even this technique got more bone gain than a conventional GBR technique [7].

Most of the current studies evaluating the bone grafting technique are limited in terms of clinical and imaging-based measurements of horizontal bone gain. Objective analyses of microfactor data are also lacking. The discovery of nuclear factor-κB receptor activators (receptor activators of NF-κB, RANK), nuclear factor-κB receptor activator ligands (receptor activators of NF-κB ligand, RANKL), and osteoprotegerin (osteoprotegerin, OPG) pathway activators has facilitated observation and elucidation of the process and mechanism of bone formation and resorption (bone remodeling). Numerous studies have demonstrated that bone remodeling is contingent upon the ratio of RANKL to OPG. Elevated levels of RANKL promote bone resorption, whereas increased levels of OPG induce bone formation [11–13].

The purpose of this study was to analyze the changes in bone width in the bone grafting area 1–2 years after implant loading via CBCT examination and to assess the condition of the augmented bone by measuring the concentration of RANK/RANKL/OPG in the gingival crevicular fluid around the implants. These measurements were compared with those of a control group of conventional implant restorations.

Materials and methods

From December 2019 to June 2021, 22 patients with 22 implant dentures were selected from the Implant Department of Dalian Stomatological Hospital; these patients underwent GBR (absorbable collagen membrane combined with 1:1 autogenous bone particles and xenografted bone replacement materials)in the mandibular posterior dental area (Fig. 1). Thirty implants were included in the control group without bone grafting in the mandibular posterior region. Six months after surgery, all the patients in the study received Straumann soft tissue-level implants (Roxolid® SLActive® Straumann). The implant superstructure was repaired four months later. This clinical study was approved by the Ethics Committee of the hospital (ethics review batch number: DLKQLL2021012), and all patients provided written informed consent.

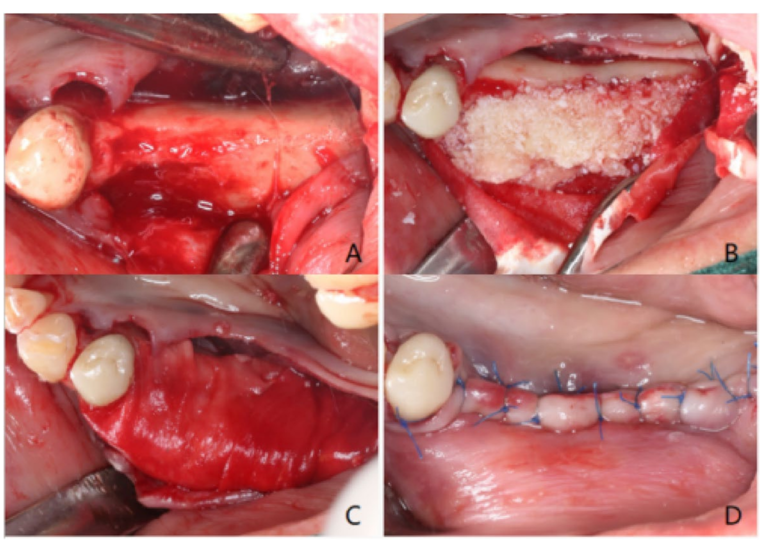

Fig. 1 The process of guided bone regeneration. **A** Exposed surgical area. **B** Placement of absorbable collagen membrane combined with 1:1 autogenous bone particles and xenografted bone replacement materials. **C** Collagen membrane fixation. **D** Close suture

Inclusion criteria: 1.Age of at least 18 years old; 2. Absence of molar teeth in the mandibular posterior region; 3. Duration of 1–2 years after implant loading; 4. Good oral hygiene; 5. Good health and the provision of informed consent; 6. Complete diagnostic and treatment information and imaging data.

Exclusion criteria: 1. History of implants in the missing tooth area; 2. History of severe periodontitis; 3. Periodontal treatment within the previous six months; 4. Systemic or local diseases that may damage healing or osseointegration (e.g., diabetes,angiocardiopathy,and osteoporosis); 5. Systemic condition that makes it difficult to tolerate implant surgery; 6. Use of antibiotics within six months and a long history of drug use; 7. Heavy smoking or bruxism; 8. Pregnancy; and 9. History of head and neck radiotherapy or chemotherapy.

Methods

All implants included in the study were loaded for 1–2 years. If a subject provided multiple implants, one was selected randomly by a toss to represent that individual. Gingival crevicular fluid around the implant included in the study and around one healthy and natural fellow tooth on the contralateral side were collected (if the fellow tooth was missing or abnormal, a nearby healthy natural tooth was selected). Eating and drinking were avoided for at least two hours before sampling. After plaque and tartar were removed and the wet tooth surface was dried and separated, sterilized Whatman No. 3 filter paper strips of the same size were inserted along the tooth surface into the buccolingual side and the proximal and distal gingival grooves; this process was stopped when obstructed, and the strips were removed 30 s later (Fig. 2). We discarded the strips if there was blood or saliva contamination. The collected filter paper strips were placed into EP tubes, which were sealed and stored in a refrigerator at − 70 °C until inspection. RANK, RANKL and OPG were quantitatively detected via enzyme-linked immunosorbent assay (ELISA). Defrost and dilute the sample at room temperature. Capture the target analyte on the microplate. Then warm, wash thoroughly, and use TMB chromogenic substrates. Absorbance (OD value) was measured at 450 nm wavelength by a plate reader. Finally, calculate the sample concentration.

Fig. 2 Gingival crevicular fluid sampling using sterile filter strips

The same machine (NewTom VGi, Italy) was used to perform CBCT before bone grafting, on the day after bone grafting, at 6 months after surgery, and at 1–2 years after loading, using the same parameters. The data were imported into MIMICS software to superimpose and measure the width 2 mm from the crest of the alveolar crest at the center of the implant (Fig. 3). The bone absorption rate is calculated by dividing the bone absorption width by the bone width measured on the day after surgery. All the above data were measured by the same person;each data point was measured three times, and the average was taken (Fig. 4).

Results

Comparison of alveolar crest bone width in the bone grafting area

The horizontal bone widths measured before bone grafting, on the day after surgery, 6 months after surgery,and 1–2 years after loading were 3.72 ± 0.94 mm, 11.57 ± 1.44 mm, 8.86 ± 1.37 mm, and 7.62 ± 1.08 mm, respectively (Table 1). The bone widths at different time points were tested via paired T-tests. The results revealed significant differences in the horizontal bone widths of the bone graft areas during each measurement period (P= 0.000 < 0.05) (Figs. 5). The bone width increased by 7.85 ± 1.63 mm, 5.15 ± 1.30 mm, and 3.9 ± 1.02 mm, respectively. The absorption rate of bone graft material during the healing process from the day after surgery to 6 months after surgery was 0.33 ± 0.16, and the total bone absorption rate after 12–24 months of loading was 0.49 ± 0.14 (Table 2).

Comparison between the two groups in terms of the RANKL and OPG levels in the natural gingival crevicular fluid and implant dentures

The results revealed that the level of RANKL in the gingival crevicular fluid in the two groups was similar(experimental group: 313.34 ± 107.48 pg/mL, control group: 314.13 ± 120.24 pg/mL); while the level in the two groups was lower than that in the natural teeth, but this difference was not statistically significant (P> 0.05) (Table 3). The level of OPG in the gingival crevicular fluid in the experimental group(1764.75 ± 327.89 pg/mL) was greater than that in the control group(1676.00 ± 379.21 pg/mL), as well as that in the natural teeth, but this difference was not significant (P> 0.05). The RANKL/OPG ratio of the implants in both groups was lower than that

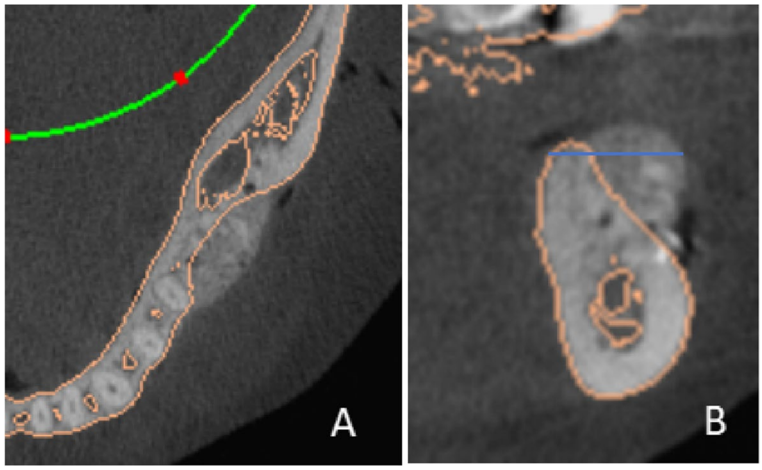

Fig. 3 CBCT matching measurements in different periods. **A** is the cross section after matching, (**B**) is the coronal section after matching

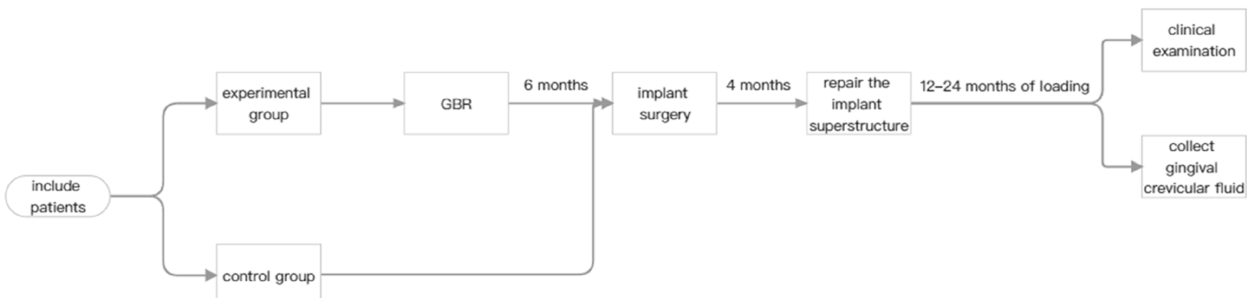

Fig. 4 Experimental technology roadmap

Table 1 The width of horizontal bone in different periods ($n=22$, unit:mm)

	Minimum	Maximum	Mean	Standard deviation
Before bone grafting	1.81	5.32	3.72	0.94
On the day after surgery	8.66	13.82	11.57	1.44
6 months after surgery	6.71	11.89	8.86	1.37
1–2 years after loading	5.64	9.88	7.62	1.08

of natural teeth, and this ratio of the implanted in the experimental group(0.19 ±0.09) was slightly lower than that in the control group(0.21 ±0.10) ($P > 0.05$).

Comparison of RANKL/OPG ratios in gingival crevicular fluid around the implants at different loading times

The experimental group implants that were included in this study were in turn divided into two groups according to the loading time(loaded for 12–18 months or 18–24 months)(Table 4). The independent-sample T-test was used to analyze the difference between the two groups of data. The level of OPG around the implants with short loading times(1776.47 ±370.49 pg/mL) was slightly higher, while the RANKL levels (297.41 ±93.91 pg/mL) and RANKL/OPG ratios (0.18 ±0.08) were slightly lower ($P > 0.05$).

Discussion

With the development of guided bone regeneration technology, researchers have mixed two or more materials to play a complementary role. To date, most studies have focused on the mixed use of autologous bone and xenogeneic bone substitute materials. The reason why this method has a better clinical effect than simple guided bone regeneration is that the inclusion of autologous bone particles brings bone-stimulating growth factors and active osteoblasts to the implanted area, which makes them rapidly vascularized. The 1:1 ratio of sausage bone grafting technology advocated by Urban has been confirmed in numerous clinical studies to have a better and more reasonable effect on repairing the bone augmentation width of the knife-edge alveolar ridge [8, 10,

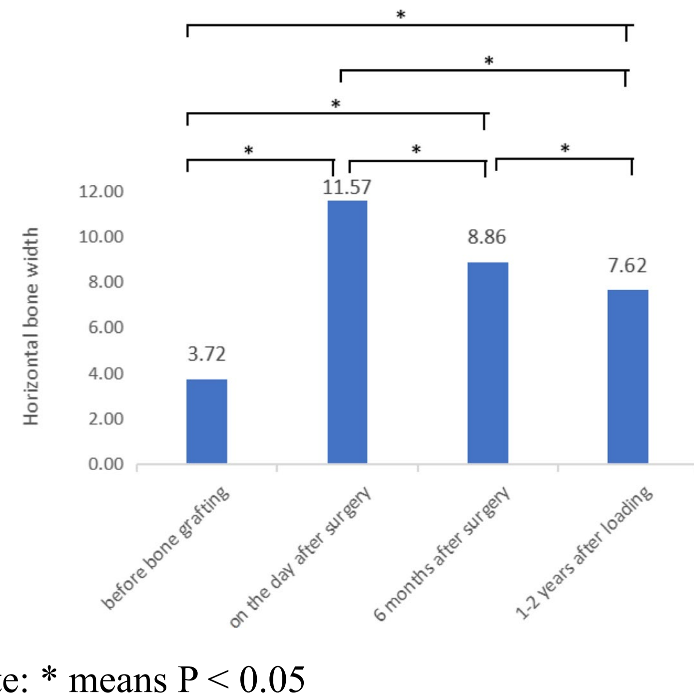

Fig. 5 Horizontal bone width of bone graft area at different periods (*n* = 22, unit:mm)

14]. A comparative test between sausage bone grafts and GBR [7] revealed that the horizontal bone increment of the former was 5.3 ±2.3 mm after 6 months of healing, whereas the horizontal bone increment of the latter was only 2.7 ±1.8 mm. In our study, we used the sausage bone grafting technique. A total of 22 implants were included in the experimental group, and the retention rate of the implants was 100% after 1–2 years of reexamination after loading. The average bone width before surgery was 3.72 ±0.94 mm, 11.57 ±1.44 on the day after bone grafting, and 8.86 ±1.37 mm after 6 months of healing. Similarly, Silvio et al. [9], reported that the average horizontal bone width increased by 5.03 ±2.15 mm from the level of the alveolar crest up to 7 months after bone graft healing.

Regarding the resorption rate during repair of the knife-shaped alveolar ridge, the bone absorption rate during the healing of the bone graft area in this study was 0.33 ±0.16, which was slightly higher than that reported in the study of Helene M et al. (0.29) [7]. One reason was the oppressive influence of muscle activities and the physiological structure and limitations of the materials used; another reason is that bone reconstruction is a continuous dynamic process, and therefore, slight variations may be related to small differences in the recovery time during healing.In addition, maxillary teeth were included in most of the above studies, and previous studies have shown that there is a difference in the healing speed of the upper and lower jaws [15]. Previous studies have shown good bone augmentation results; the researchers hypothesized that these bone gains are due to the composition of the granular grafts used in the study (a 1:1 mixture of granular autografts and DBBM), as xenografts slow the uptake of autografts and promote an increase in volume [14, 16]. Moreover, a meta-analysis reported that

Table 2 Width changes (mm) and absorptivity of horizontal bone in different periods in bone grafting area (*n* = 22)

	Minimum	Maximum	Mean	Standard deviation
Bone augmentation on surgery day	3.34	10.20	7.85	1.63
Bone augmentation 6 months after surgery	3.29	7.69	5.15	1.30
Bone augmentation after loading	2.72	6.22	3.90	1.02
Bone resorption rate at 6 months	0.01	0.62	0.33	0.16
Total bone resorption rate after loading	0.08	0.68	0.49	0.14

Table 3 Comparison of RANKL, OPG and ratio in gingival crevicular fluid around implant and natural teeth between the two groups(pg/mL)

Project	Experimental group			Control group		
	Implant tooth($n=22$)	Natural tooth($n=22$)	*P*	Implant tooth($n=30$)	Natural tooth($n=30$)	*P*
RANKL	313.34 ± 107.48	360.83 ± 90.12	0.120	314.13 ± 120.24	356.90 ± 98.61	0.137
OPG	1764.75 ± 327.89	1684.60 ± 242.47	0.362	1676.00 ± 379.21	1683.81 ± 367.77	0.936
RANKL/OPG	0.19 ± 0.09	0.22 ± 0.07	0.216	0.21 ± 0.10	0.22 ± 0.09	0.479

bone resorption via xenografts was lower (11.6%) than that via autografts alone [17]. In addition, Amorfini's and Gultekin's studies reported similar results, with a positive correlation between graft volume and graft absorptivity when a 1:1 mixture of granular autografts and DBBM was used [18, 19]. However, unlike the other studies, the present study did not reveal a correlation between graft volume and graft material absorption during healing [20]. We believe that the bone formation volume of the jaw is not completely proportional to the amount of bone graft, and the calculation of the resorption rate is closely related to the amount of bone graft on the day of surgery; thus, the resorption rates calculated by various experts differ. On the basis of the results from the above mentioned Urban study, the absorption rate is likely to be stable regardless of the amount of transplanted material [7].

Both the dynamic stability of bone and bone remodeling are joint effects of osteogenic activity and osteoclastic activity, or they balance each other, or one side is more active. Numerous studies have confirmed that the RANK/RANKL/OPG system plays an important regulatory role in alveolar bone metabolism and remodeling and that the expression level and site affect bone resorption and bone formation [21–23]. RANKL plays an important role in the maturation and activation of osteoclasts.The only cell surface receptor activator of RANKL RANK. OPG, a soluble decomposing receptor, is an inhibitor of RANKL, and the two proteins have opposite effects on bone turnover. OPG binds to the activator of the RANKL receptor and reduces the binding of RANKL to RANK, thereby inhibiting the osteoclast process and promoting osteogenesis. In the study of orthodontic tooth movement, Yamaguchi, M et al. reported that RANK-RANKL plays a central role in bone resorption [24]. In addition, H.Tanaka et al. confirmed that the expression of RANKL/OPG was the key factor in bone formation and bone resorption during bone remodeling [25]. Therefore, the total RANKL/OPG ratio may be a reasonable indicator that explains the results of studies on the biological activity of these biomarkers as indicators of tissue change. Multiple studies have shown that a high RANKL/OPG ratio promotes osteoclast activity and subsequent bone loss, suggesting a tendency for bone resorption in patients; a low RANKL/OPG ratio leads to osteogenesis and subsequent bone remodeling, suggesting a tendency toward osteogenesis in patients [26–28]. Reducing RANKL expression or regulating the RANKL/OPG ratio is an effective strategy to prevent alveolar bone resorption and promote bone formation. In tissue engineering therapy, the RANKL/RANK/OPG signaling pathway can be directly and locally promoted to induce osteogenic differentiation to enhance the formation of new bone [29, 30]. In vitro experiments, Qu Z, et al.and Toledano-Osorio M, et al. all found that stimulating osteoblast-like cells on the surface of the implant led to alkaline phosphatase activity and osteocalcin production of cells were increased, while OPG/RANK ratio increased significantly [31, 32]. In the mouse experiment, Akiyama et al. inhibited the expression level of RANKL and increased the expression level of OPG in mouse primary osteoblasts to prevent cell differentiation into osteoclasts and bone resorption [33]. In the clinical study, the RANKL/OPG ratios for healthy implants were 0.10 ± 0.09 and 0.08 ± 0.08 for smoking and non-smoking [34]. The dates are lower than the results of our study. On the one hand, we did not compare smoking and non-smoking groups, and there is a dependent relationship between ratios and the amount and length of the smoking habit. On the other hand, the small sample size could be a limitation of our study. At present, most studies report results at the diseased sites of periodontal, and there is little information about the biomarkers in healthy peri-implant fluids. In addition, studies have shown that a certain amount of bone remodeling occurs at the beginning of the load on the alveolar crest in the neck of the implant restoration, as do changes in cytokine levels [35]. Therefore, in our study, the experimental group

Table 4 Comparison of RANKL/OPG in gingival crevicular fluid around implants in the experimental group at different loading times(unit:pg/mL)

Project	12–18 months($n=10$)	18–24 months($n=12$)	*p*
RANKL	297.41 ± 93.91	326.61 ± 120.07	0.539
OPG	1776.47 ± 370.49	1754.99 ± 304.49	0.883
RANKL/OPG	0.18 ± 0.08	0.20 ± 0.10	0.570

was compared with the control group and natural teeth. The results indicated that the RANKL level in the gingival crevicular fluid of the two groups appeared similar to that of the natural teeth, while the OPG level in the experimental group tended to be higher than that in the control group and natural teeth, although this difference was not statistically significant. The RANKL/OPG ratios of the implants in both groups all tended to be lower than that in the natural teeth,while the ratio of the implants in the experimental group was lower than that in the control group, although the differences were not statistically significant. Therefore, we believe that the osteogenesis process may still be ongoing after 1 to 2 years of loading of the implant in the bone graft area. We also compared implants loaded for 12–18 months with those loaded for 18–24 months and found that the OPG levels were slightly higher around implants that were loaded for a shorter period and were greater than those of healthy natural teeth. The RANKL concentration and the RANKL/OPG ratio were slightly lower. In addition, we also quantitatively measured the levels of several inflammatory factors around the implants and performed routine clinical periodontal examinations [36]. There was no significant difference between the experimental group and the control group. The stability of the surrounding soft and hard tissue was very similar to that of healthy natural teeth when the control group implant was loaded for 12–24 months. However, the levels of IL- 1β, IL- 6, TNF-α and MMP- 8 in the experimental group were slightly greater than those in the control group, which indicated that the peri-implant bone remodeling in the experimental group was to some extent more active than that at the control group. Therefore, we hypothesized that osteogenic activity was more active in 18 months after loading, and decreased after 18 months, but it was still weakly exist. Further investigation should include expanding the sample size, increasing the measurement time point for the gingival crevicular fluid, and increasing genetic testing to confirm the diagnosis and prognosis.

Conclusion

The application of GBR with 1:1 autogenous bone and xenogeneic bone replacement material in the horizontal bone augmentation of the mandibular posterior dental region has achieved positive clinical outcomes. At least in part, after 1–2 years of implant loading, the bone in the neck of the implant in the experimental group appears to be slightly more active than in the control group and may still be in the process of osteogenesis. We recommend the following clinical guidelines: 1). minimize the bite force and lateral force at the beginning of the implant loading process, especially in the bone graft area, and 2). regularly monitor the health of the soft and hard tissues.

Abbreviations

GBR	Guided Bone Regeneration
DBBM	Deproteinized Bovine Bone Mineral
RANK	Receptor Activators of NF-κB
RANKL	Receptor Activators of NF-κB Ligand
OPG	Osteoprotegerin
CBCT	Cone Beam Computed Tomography
ELISA	Enzyme-Linked Immunosorbent Assay

Acknowledgements

Not applicable.

Authors' contributions

Conceptualization, Methodology, Software: Zhaoxia Jiang, Dejing Kong, Mingli Liu and Zhe Qu; Writing- Reviewing and Editing: Zhaoxia Jiang, Chuanqing Zhou and Zhe Qu; Data curation, Writing-Original draft preparation: Zhaoxia Jiang and Yixin Liang; Visualization, Investigation: Chuanqing Zhou and Mingli Liu; Supervision: Zhe Qu. All authors read and approved the final manuscript.

Funding

This work was supported by Dalian Science and Technology Innovation Fund (NO.2019 J13SN98).

Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

The study was voluntary and all respondents provided their written informed consent. The study received approval from the Dalian Stomatological Hospital Ethics Committee (ethics review batch number: DLKQLL2021012) and adhered to the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Implantology, Dalian Stomatological Hospital, NO.935,Changjiang Road, Shahekou District, Dalian, Liaoning Province, China. [2]Department of Stomatology, the Second Hospital of Dalian Medical University, Liaoning Province, China.

Received: 4 September 2024 Accepted: 18 April 2025
Published online: 01 May 2025

References

1. Pieri F, Corinaldesi G, Fini M, Aldini NN, Giardino R, Marchetti C. Alveolar ridge augmentation with titanium mesh and a combination of autogenous bone and anorganic bovine bone: a 2-year prospective study. J Periodontol. 2008;79(11):2093–103. https://doi.org/10.1902/jop.2008.080061.
2. Mordenfeld A, Johansson CB, Albrektsson T, Hallman M. A randomized and controlled clinical trial of two different compositions of deproteinized bovine bone and autogenous bone used for lateral ridge augmentation. Clin Oral Implants Res. 2014;25(3):310–20. https://doi.org/10.1111/clr.12143.
3. Zitzmann NU, Schärer P, Marinello CP. Long-term results of implants treated with guided bone regeneration: a 5-year prospective study. Int J Oral Maxillofac Implants. 2001;16(3):355–66.
4. Hämmerle CH, Jung RE, Feloutzis A. A systematic review of the survival of implants in bone sites augmented with barrier membranes (guided

bone regeneration) in partially edentulous patients. J Clin Periodontol. 2002;29(Suppl 3):226–33. https://doi.org/10.1034/j.1600-051x.29.s3.14.x.

5. Wessing B, Lettner S, Zechner W. Guided bone regeneration with collagen membranes and particulate graft materials: a systematic review and meta-analysis. Int J Oral Maxillofac Implants. 2018;33(1):87–100. https://doi.org/10.11607/jomi.5461.
6. Johnson TB, Siderits B, Nye S, et al. Effect of guided bone regeneration on bone quality surrounding dental implants. J Biomech. 2018;80:166–70. https://doi.org/10.1016/j.jbiomech.2018.08.011.
7. Arnal HM, Angioni CD, Gaultier F, Urbinelli R, Urban IA. Horizontal guided bone regeneration on knife-edge ridges: a retrospective case-control pilot study comparing two surgical techniques. Clin Implant Dent Relat Res. 2022;24(2):211–21. https://doi.org/10.1111/cid.13073.
8. Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: a prospective case series in 22 patients. Int J Oral Maxillofac Implants. 2011;26(2):404–14.
9. Meloni SM, Jovanovic SA, Urban I, Canullo L, Pisano M, Tallarico M. Horizontal ridge augmentation using GBR with a native collagen membrane and 1:1 ratio of particulated xenograft and autologous bone: a 1-year prospective clinical study. Clin Implant Dent Relat Res. 2017;19(1):38–45. https://doi.org/10.1111/cid.12429.
10. Urban IA, Nagursky H, Lozada JL, Nagy K. Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 25 patients. Int J Periodontics Restorative Dent. 2013;33(3):299–307. https://doi.org/10.11607/prd.1407.
11. Yamaguchi M, Aihara N, Kojima T, Kasai K. RANKL increase in compressed periodontal ligament cells from root resorption. J Dent Res. 2006;85(8):751–6. https://doi.org/10.1177/154405910608500812.
12. Boyce BF, Xing L. Functions of RANKL/RANK/OPG in bone modeling and remodeling. Arch Biochem Biophys. 2008;473(2):139–46. https://doi.org/10.1016/j.abb.2008.03.018.
13. Tat SK, Pelletier JP, Velasco CR, Padrines M, Martel-Pelletier J. New perspective in osteoarthritis: the OPG and RANKL system as a potential therapeutic target? Keio J Med. 2009;58(1):29–40. https://doi.org/10.2302/kjm.58.29.
14. Urban I. Vertical and Horizontal Ridge Augmentation: New Perspectives. Quintessence Publishing, 2017. ISBN: 978-1-78698-000-7.
15. Kotze MJ, Bütow KW, Olorunju SA, Kotze HF. A comparison of mandibular and maxillary alveolar osteogenesis over six weeks: a radiological examination. Head Face Med. 2014;10:50. https://doi.org/10.1186/1746-160X-10-50. Published 2014 Nov 28.
16. Jensen SS, Bosshardt DD, Gruber R, Buser D. Long-term stability of contour augmentation in the esthetic zone: histologic and histomorphometric evaluation of 12 human biopsies 14 to 80 months after augmentation. J Periodontol. 2014;85(11):1549–56. https://doi.org/10.1902/jop.2014.140182.
17. Naenni N, Lim HC, Papageorgiou SN, Hämmerle CHF. Efficacy of lateral bone augmentation prior to implant placement: a systematic review and meta-analysis. J Clin Periodontol. 2019;46(Suppl 21):287–306. https://doi.org/10.1111/jcpe.13052.
18. Amorfini L, Migliorati M, Signori A, Silvestrini-Biavati A, Benedicenti S. Block allograft technique versus standard guided bone regeneration: a randomized clinical trial. Clin Implant Dent Relat Res. 2014;16(5):655–67. https://doi.org/10.1111/cid.12040.
19. Gultekin BA, Bedeloglu E, Kose TE, Mijiritsky E. Comparison of bone resorption rates after intraoral block bone and guided bone regeneration augmentation for the reconstruction of horizontally deficient maxillary alveolar ridges. Biomed Res Int. 2016;2016:4987437. https://doi.org/10.1155/2016/4987437.
20. Sterio TW, Katancik JA, Blanchard SB, Xenoudi P, Mealey BL. A prospective, multicenter study of bovine pericardium membrane with cancellous particulate allograft for localized alveolar ridge augmentation. Int J Periodontics Restorative Dent. 2013;33(4):499–507. https://doi.org/10.11607/prd.1704.
21. Boyce AM. Denosumab: an emerging therapy in pediatric bone disorders. Curr Osteoporos Rep. 2017;15(4):283–92. https://doi.org/10.1007/s11914-017-0380-1.
22. Huang X, Li Y, Liao H, et al. Research advances on stem cell-derived extracellular vesicles promoting the reconstruction of alveolar bone through RANKL/RANK/OPG pathway. J Funct Biomater. 2023;14(4):193. https://doi.org/10.3390/jfb14040193. Published 2023 Mar 30.
23. Noguchi T, Kitaura H, Ogawa S, et al. TNF-α stimulates the expression of RANK during orthodontic tooth movement. Arch Oral Biol. 2020;117:104796. https://doi.org/10.1016/j.archoralbio.2020.104796.
24. Yamaguchi M, Fukasawa S. Is inflammation a friend or foe for orthodontic treatment?: Inflammation in orthodontically induced inflammatory root resorption and accelerating tooth movement. Int J Mol Sci. 2021;22(5):2388. https://doi.org/10.3390/ijms22052388. Published 2021 Feb 27.
25. Tanaka H, Mine T, Ogasa H, Taguchi T, Liang CT. Expression of RANKL/OPG during bone remodeling in vivo. Biochem Biophys Res Commun. 2011;411(4):690–4. https://doi.org/10.1016/j.bbrc.2011.07.001.
26. Paula-Silva FWG, Arnez MFM, Petean IBF, et al. Effects of 5-lipoxygenase gene disruption on inflammation, osteoclastogenesis and bone resorption in polymicrobial apical periodontitis. Arch Oral Biol. 2020;112:104670. https://doi.org/10.1016/j.archoralbio.2020.104670.
27. Jiao M, Zhang P, Yu X, et al. Osteoprotegerin/receptor activator of nuclear factor-κB ligand are involved in periodontitis-promoted vascular calcification. Exp Ther Med. 2022;24(2):512. https://doi.org/10.3892/etm.2022.11439. Published 2022 Jun 14.
28. Asif S, Ahmad B, Hamza SA, Taib H, Kassim NK, Zainuddin SLA. Investigation of salivary RANKL and OPG levels in periodontitis patients at hospital universiti Sains Malaysia. Eur J Dent. 2022;16(1):173–8. https://doi.org/10.1055/s-0041-1731930.
29. Ho ML, Hsu CJ, Wu CW, et al. Enhancement of osteoblast function through extracellular vesicles derived from adipose-derived stem cells. Biomedicines. 2022;10(7):1752. https://doi.org/10.3390/biomedicines10071752. Published 2022 Jul 21.
30. Zhang Y, Jia S, Wen G, et al. Zoledronate promotes peri-implant osteogenesis in diabetic osteoporosis by the AMPK pathway. Calcif Tissue Int. 2023;113(3):329–43. https://doi.org/10.1007/s00223-023-01112-0.
31. Qu Z, Andrukhov O, Laky M, et al. Effect of enamel matrix derivative on proliferation and differentiation of osteoblast cells grown on the titanium implant surface. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011;111(4):517–22. https://doi.org/10.1016/j.tripleo.2010.10.011.
32. Toledano-Osorio M, de Luna-Bertos E, Toledano M, et al. Dexamethasone and doxycycline functionalized nanoparticles enhance osteogenic properties of titanium surfaces. Dent Mater. 2023;39(6):616–23. https://doi.org/10.1016/j.dental.2023.05.004.
33. Akiyama T, Dass CR, Shinoda Y, Kawano H, Tanaka S, Choong PFM. PEDF regulates osteoclasts via osteoprotegerin and RANKL. Biochem Biophys Res Commun. 2010;391(1):789–94. https://doi.org/10.1016/j.bbrc.2009.11.139.
34. Negri BM, Pimentel SP, Casati MZ, Cirano FR, Casarin RC, Ribeiro FV. Impact of a chronic smoking habit on the osteo-immunoinflammatory mediators in the peri-implant fluid of clinically healthy dental implants. Arch Oral Biol. 2016;70:55–61. https://doi.org/10.1016/j.archoralbio.2016.05.014.
35. Tumedei M, Piattelli A, Degidi M, Mangano C, Iezzi G. A narrative review of the histological and histomorphometrical evaluation of the peri-implant bone in loaded and unloaded dental implants. A 30-year experience (1988–2018). Int J Environ Res Public Health. 2020;17(6):2088. https://doi.org/10.3390/ijerph17062088. Published 2020 Mar 21.
36. Jiang Z, Kong D, Li Y, Zhe Qu, Liu M. Effect of guided bone regeneration on inflammatory susceptibility of peri-implant soft tissue. J Oral Sci Res. 2023;39(08):715–20. https://doi.org/10.13701/j.cnki.kqyxyj.2023.08.010.

Publisher's Note