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Original Article

Effects of concentrated growth factor combined with Bio-Oss bone powder on guided bone regeneration in the maxillary posterior region

Zhe Cheng, Yili Pan, Qin Pan

Songyang Yijia Dental Clinic, Lishui 323400, Zhejiang, China

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Abstract: Objective: To evaluate the clinical effects of concentrated growth factor (CGF) combined with Bio-Oss bone powder on guided bone regeneration for the maxillary posterior region. Methods: This retrospective study included 32 patients with missing maxillary posterior teeth and severe alveolar ridge atrophy requiring implant restoration for retrospective analysis. Sixteen patients received CGF combined with Bio-Oss treatment (CGF/Bio group), while the remaining 16 received Bio-Oss treatment only (Bio group). The Bio group used Bio-Oss bone powder directly. Cone-beam computed tomography (CBCT) was performed preoperatively and at 2, 4, and 6 months postoperatively to evaluate bone mineral density (HU values). The implant retention rate, soft tissue healing time, postoperative pain, and swelling were also evaluated. Results: The 1-year implant retention rate was 100% in the CGF/Bio group and 81.25% in the Bio group ($P = 0.054$). Soft tissue healing time was significantly shorter in the CGF/Bio group ($P = 0.122$). Bone density was significantly higher in the CGF/Bio group at 2, 4, and 6 months postoperatively ($P < 0.05$). Postoperative pain and swelling were significantly lower in the CGF/Bio group ($P = 0.008$ and $P = 0.014$, respectively). Conclusion: The combined application of CGF and Bio-Oss bone powder in maxillary sinus external lift demonstrates superior clinical outcomes, offering improved bone augmentation and enhanced postoperative healing compared to Bio-Oss bone powder alone.

Keywords: Maxillary posterior tooth loss, guided bone regeneration, CGF, Bio-Oss bone powder, maxillary sinus external lift

Introduction

Dental defects in the maxillary posterior region are common in clinical practice, where posterior teeth play an important role in oral chewing function as the main functional teeth [1-3]. However, due to caries, endodontic, periodontal, and periapical diseases, reduced masticatory efficiency, alteration of the lower facial height, and negative impacts on oral function and jaw aesthetics can occur [4, 5]. With growing awareness of oral hygiene, the number of patients receiving implant restorations has increased significantly, particularly for missing teeth in the maxillary posterior region [6, 7]. One of the main challenges for clinicians is to effectively reduce postoperative pain and swelling, thereby improving patients' postoperative quality of life and satisfaction.

As medical technology advances, the use of tissue engineering materials in maxillary sinus bone augmentation surgery has also increased. Bio-Oss bone powder is currently the most widely used artificial bone material in dental implants, demonstrating strong osteogenic capacity and histocompatibility in treating alveolar bone defects and severe deficiencies [8]. Studies [9, 10] on maxillary sinus floor lift in this patient group have shown that the addition of Bio-Oss bone powder improves bone deficiency, although its effectiveness still has room for enhancement. Concentrated growth factor (CGF) is rich in fibrin and growth factors that regulate and promote cell growth and reproduction, enhancing bone tissue regeneration and healing [11]. Dohan et al. [12] applied CGF for guided bone tissue regeneration during maxillary sinus lift and achieved adequate bone volume. Similarly, Sohn et al. [13] applied autogenous bone mixed with CGF as a filler in maxillary sinus lifts, showing good osteogenic results and significantly shortened bone formation time.

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However, the detailed effects of Bio-Oss bone powder combined with CGF in guided bone regeneration specifically in the maxillary posterior region remain underexplored. This study aims to compare the clinical outcomes of using Bio-Oss bone powder and CGF versus Bio-Oss bone powder alone during maxillary external sinus lift, focusing on bone augmentation and postoperative healing outcomes.

Materials and methods

General information

This retrospective study included 32 patients (18 males and 14 females) with missing maxillary posterior teeth and severe alveolar ridge atrophy requiring implant restoration. The patients were treated at Songyang Yijia Dental Clinic from August 2018 to August 2021. Based on their treatment regimen, the patients were divided into two groups: a CGF/Bio group (n = 16, treated with CGF and Bio-Oss), and a CGF group (n = 16, treated with Bio-Oss only). This study was conducted in strict compliance with the Declaration of Helsinki and approved by the Ethics Committee of Songyang Yijia Dental Clinic.

Inclusion criteria: (1) a remaining bone height of 4-6 mm in the alveolar ridge of the missing tooth area confirmed by Cone-beam computed tomography (CBCT); (2) implants of 6 mm long in the supra-maxillary sinus ensured by the Invivo5 implant simulation software; (3) no use of any drugs that interfere with osteogenesis or implant osseointegration; (4) no serious systemic diseases (e.g., heart, lung or brain) or abnormal liver/kidney function; and (5) normal coagulation function.

Exclusion criteria: (1) patients with systemic diseases (e.g., uncontrolled diabetes, severe heart disease) that contraindicated simple surgery; (2) patients with uncontrolled complex periodontal disease; (3) patients with local inflammation and poor oral hygiene; (4) patients with untreated maxillary lesions; (5) patients with severe nocturnal molar disease; and (6) patients with temporomandibular joint disorder syndrome.

Treatment procedures

Preoperative preparation: A comprehensive clinical examination assessed the condition of the missing maxillary posterior teeth, gingiva, health of adjacent teeth, and occlusal relationships. Pre-implantation CBCT was performed to observe the maxillary sinus, measure the width and height of the remaining alveolar bone in the maxillary edentulous area, and determine bone density (in Hounsfield units, HU). Prophylactic antibiotics and analgesics were administered 0.5 h before surgery, including cefaclor extended-release capsule (0.375 g), ornidazole (0.5 g), and aminophenol dihydrocodeine (0.5 g). The patients rinsed their mouth twice with 15 mL of compound chlorhexidine gargle solution for 1 minute each time.

CGF preparation: Ten minutes before surgery, 20 mL of venous blood was drawn from patients and transferred into a tube without anticoagulant. The tube was immediately centrifuged in a Medifuge centrifuge for 12 min, resulting in three distinct layers: the bottom layer of red blood cells and platelets, the middle layer of fibrin clot (i.e., CGF), and the upper layer of serum. A thin layer of red blood cells (2-3 mm) was carefully retained at the junction. The CGF gel was then isolated by precisely removing the underlying red blood cell layer. Subsequently, the CGF membrane was obtained by squeezing out most of the liquid component of the CGF gel with a membrane presser (**Figure 1**).

Surgical method: Routine disinfection and local infiltration anesthesia with articaine were performed. A horizontal incision was made at the top of the alveolar ridge in the edentulous area using a 15-gauge circular blade, with additional vertical incision in the proximal and distal regions. The full mucoperiosteal flap of the lateral wall of the maxillary sinus was turned over to expose the operative area. Based on the number of implants and the size of the window, the lateral wall of the maxillary sinus was opened using an ultrasonic bone knife to reveal the lateral sinus membrane. The implant cavity was then prepared by stripping the top of the posterior alveolar ridge of the maxillary sinus floor mucosa with a sinus membrane elevator. In the CGF/Bio group, the prepared CGF layer was cut and mixed with Bio-Oss bone powder to fill the elevated maxillary sinus mucosa and the implant cavity. The SIC implant was placed at the same time, and the surface of the bone powder was covered with the CGF film. In the

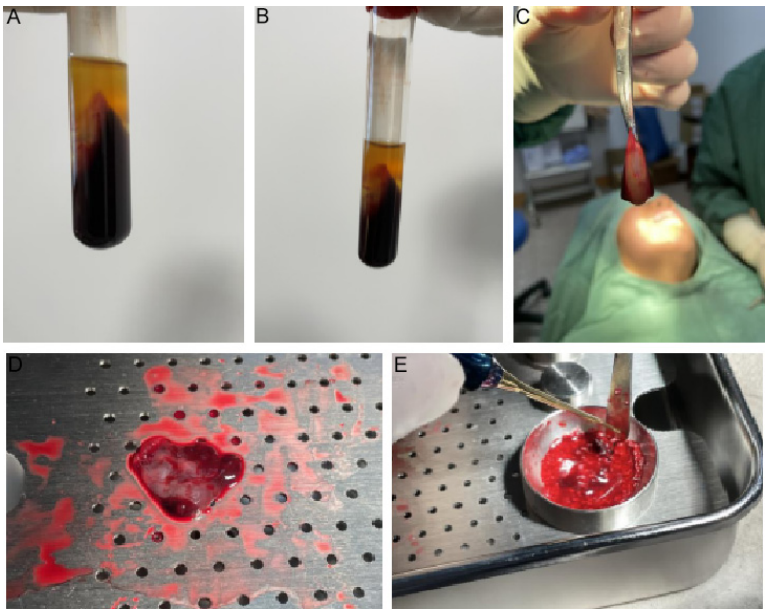

Figure 1. CGF preparation process. A: Initial separation of venous blood after centrifugation, showing three distinct layers; B: CGF layer after centrifugation, with the translucent fibrin clot visible in the middle; C: Processing CGF using membrane presser to create CGF membrane; D: Prepared CGF gel in smaller pieces for mixing with Bio-Oss bone powder; E: Final CGF membrane after compression, ready for clinical application. Note: CGF, concentrated growth factor.

Bio group, Bio-Oss bone powder was placed directly into the elevated maxillary sinus mucosa and implant socket cavity. The SIC implant was then placed, and the wound was tightly sutured. The intervention methods for the Bio group were based on the established protocols described by Esposito et al. [14] and Dottore et al. [15]. The combined use of CGF and Bio-Oss bone powder in the CGF/Bio group followed the techniques reported by Isler et al. [16].

Postoperative management: Antibiotics, oral cefaclor extended-release capsule (0.375 g) and ornidazole (0.5 g) were prescribed twice daily for 3-5 days. Analgesics aminophenedihydrocodeine (0.5 g, for oral administration) was prescribed as appropriate. Compound chlorhexidine gargle (15 ml) was administered 3-4 times daily for 1 week.

Outcome measurements

Osteogenic effect: CBCT was performed at 2, 4, and 6 months postoperatively. Bone density at the proximal-mid, distal-mid, buccal, and palatal sides of the implant end was measured using the EasyDent software provided with the CBCT system. Measurements were obtained 1 mm superior to the maxillary sinus floor, accessed through the alveolar ridge crest. The average of these values was calculated as the bone density (Hounsfield units, HU) for the site. The amount of new bone acquisition and changes in bone mineral density before surgery and at 2, 4, and 6 months postoperatively were compared between the two groups. All measurements were performed by the same examiner, with the mean value of 5 measurements recorded for each site.

Soft tissue healing and implant retention: Soft tissue healing was assessed at 10 days postoperatively. The implant retention rate was evaluated 1 year after surgery using the criteria proposed by Wheeler et al. [17] in 1996. Retention was defined as implants that remained functional without discomfort, excluding dislodged implants and those with degree III loosening on clinical examination.

Postoperative pain: The visual analogue scale (VAS) was used to assess postoperative pain at 24, 48, and 72 hours after surgery. The VAS consists of a 100-mm line, with 0 and 100 at both end of the line, where 0 represents no pain and 100 represents unbearable severe pain. Patients marked their pain level based on their subjective perception. The VAS score was determined by measuring the distance from point 0 to the marker point. The duration of postoperative pain was also recorded, defined as the number of days from surgery until the patient reported a VAS score of 0.

Degree of postoperative swelling: Postoperative swelling was assessed at 48 and 72 hours after surgery and classified into four grades according to the extent of swelling: grade A - no swelling; grade B - mild swelling, limited to the area from the nasal flanks to the corners of the mouth on both sides; grade C - moderate swell-

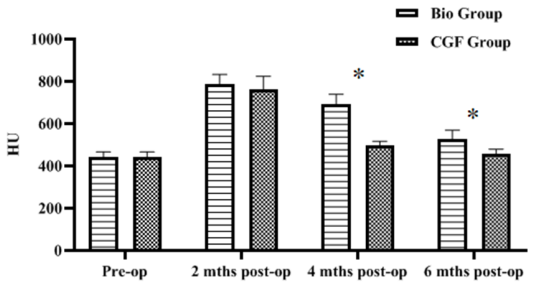

Figure 2. Comparison of BMD between the two groups before operation and at postoperative 2, 4 and 6 months. Note: HU, Hounsfield units; CGF, concentrated growth factor; BMD, bone mineral density. * indicates statistically significant differences between Bio group and CGF group ($P < 0.05$).

ing, within the vertical line connecting the pupils; and grade D - severe swelling, exceeding the aforementioned boundaries.

The primary outcomes included the change in bone mineral density (HU values) at 2, 4, and 6 months after surgery. The secondary outcomes included the implant retention rate at 1 year, soft tissue healing time, postoperative pain, and the degree of postoperative swelling.

Statistical analysis

SPSS 23.0 software was used to analyze the obtained data. Continuous variables (e.g., age, HU value, operation time, VAS scores, pain duration) were expressed as mean ± standard deviation (SD) and compared using independent sample t-tests for between-group comparisons and paired sample t-tests for intragroup comparisons. Categorical variables (e.g., gender, swelling grade) were expressed as n (%) and compared using chi-square test. For multi-time measurement data (e.g., bone density changes at multiple time points), repeated measures ANOVA followed by post hoc Bonferroni tests were used. A two-sided significance level of $\alpha = 0.05$ was applied.

The sample size was calculated to detect a mean difference of 150 HU in bone mineral density between the intervention and control groups, with a standard deviation of 120 HU. Assuming a power of 80% and a significance level of 5%, a sample size of 14 patients per group was required. Finally, we selected 16 cases for each group based on predefined inclusion and exclusion criteria.

Results

Comparison of the treatment efficacy between the two groups

Figure 2 illustrates the changes in bone density before and after implant surgery in the CGF/Bio and Bio groups. Repeated measures ANOVA revealed a significant main effect of time ($F (3, 90) = 58.72$, $P < 0.001$) and a significant interaction between time and group ($F (3, 90) = 10.45$, $P < 0.001$). Post hoc Bonferroni tests demonstrated the following:

1. Early postoperative changes (2 months): Bone density values in the implant area increased significantly compared to preoperative levels in both groups ($P < 0.05$), but the difference between the two groups was not statistically significant ($P > 0.05$). 2. Mid-term outcomes (4 months): The Bio group exhibited significantly higher BMD values than the CGF/Bio group ($P < 0.05$). In the CGF/Bio group, BMD values decreased significantly compared to those at 2 months postoperatively and approached preoperative levels. BMD values in the control group were not significantly changed relative to those at 2 months after surgery and were significantly higher than the preoperative BMD values ($P < 0.05$). 3. Long-term outcomes (6 months): BMD values in both groups returned to levels close to preoperative measurements; in the CGF/Bio group, BMD changes from 4 to 6 months were not statistically significant. The Bio group showed a significant decrease in BMD at 6 months compared to that at 4 months postoperatively ($P < 0.05$), with values approaching preoperative levels.

The patients in the CGF/Bio group demonstrated a 100% retention rate, with no implant loss during follow-up. In the Bio group, three implants were lost, resulting in a retention rate of 81.25%. There was no statistically significant difference between the two groups in terms of implant retention rate at 1 year ($\chi^2 = 3.702$, $P = 0.054$) (**Table 1**).

In terms of soft tissue healing 10 days after surgery, CGF/Bio group had 16 cases of excellent healing, and Bio group had 12 cases of excellent healing, 3 cases of good healing, and 1 case of poor healing. The excellent healing rate in the CGF/Bio group was higher than that in

Table 1. Comparison of soft tissue healing and implant retention rate between the two groups

Group	Retention rate of implants 1 year after surgery			Soft tissue healing 10 days after surgery (cases)		
	Total number of implants (pieces)	Retention	Retention rate (%)	Excellent	Good	Poor
Bio group	16	13	81.25	12 (87.50)	3 (12.50)	1 (0.00)
CGF group	18	18	100	16 (100.00)	0 (0.00)	0 (0.00)
χ^2/z-value	-	3.702			-1.852	
P-value	-	0.054			0.122	

Note: CGF, concentrated growth factor.

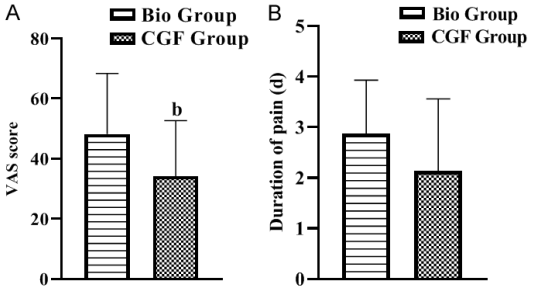

Figure 3. Comparison of postoperative pain between the two groups. A: VAS pain scores at 48 hours post-surgery. B: Duration of postoperative pain. Note: VAS, Visual Analogue Scale; CGF, concentrated growth factor.

the Bio group, but the difference was not significant (z = -1.852, P = 0.122) (**Table 1**).

Comparison of postoperative pain between the two groups

The comparison of postoperative pain levels between the CGF/Bio and Bio groups is shown in **Figure 3**. The postoperative pain score (VAS) at postoperative 48 hours was significantly lower in CGF/Bio group than that in the Bio group (t = -4.528, P < 0.001). The postoperative pain duration was also significantly shorter in the CGF/Bio group compared to that in the Bio group (t = -2.635, P = 0.013).

Comparison of postoperative swelling between the two groups

Postoperative swelling lasted 2.51 ± 1.36 days in the CGF/Bio group, significantly shorter than 4.32 ± 2.17 days in the Bio group (t = 2.827, P = 0.008). The distribution of postoperative swelling severity is shown in **Table 2**. Patients in the CGF/Bio group exhibited significantly less swelling compared to those in the Bio group (z = -2.604, P = 0.014).

Typical case study of CGF/Bio group

A 52-year-old female patient presented with a six-month history of missing right maxillary posterior teeth, resulting in impaired chewing function. She expressed a desire for implant restoration. The patient had previously undergone extraction of the right maxillary teeth due to painful loosening of a fixed denture, with plans for implant restoration six months later. The patient reported no history of systemic diseases such as hypertension, diabetes, or heart disease. She denied any history of infectious diseases, surgeries, trauma, blood transfusions, or allergies to either food or drugs. Her vaccination history was up to date. Her parents were in good health, and there was no known history of major hereditary disease in her family.

General condition: facial symmetry, Oral Examination: normal mouth opening, acceptable occlusal relationship, bilateral mandibular, and left maxillary posterior regions were restored with implants, and the mandibular anterior region had a fixed denture. Teeth 14-17 were missing, with a low but acceptable alveolar ridge width in the 16-17 region. Gingiva appeared healthy, with no significant redness, swelling, or abnormalities.

CBCT imaging suggested that the height of the alveolar ridge at the 16-17 positions in the right maxillary posterior region was approximately 4.20 mm above the maxillary sinus floor (**Figure 4**). Other findings were consistent with the clinical examination. The final diagnosis was partial loss of maxillary dentition (teeth 14-17 missing).

Treatment plan: Placement of dental implants at positions 14-16, with simultaneous maxillary sinus external lift, guided bone regeneration (GBR), and bone grafting. The treatment plan,

Table 2. The distribution of the postoperative swelling degree in the two groups

Group	No swelling	Mild swelling	Moderate swelling	Severe swelling	Duration of swelling (d)
Bio group	1 (6.25)	5 (18.75)	6 (37.50)	4 (25.00)	4.32 ± 2.17
CGF group	3 (18.75)	10 (62.50)	3 (18.75)	0 (0.00)	2.51 ± 1.36
z/t value			-2.604		2.827
P-value			0.014		0.008

Note: CGF, concentrated growth factor.

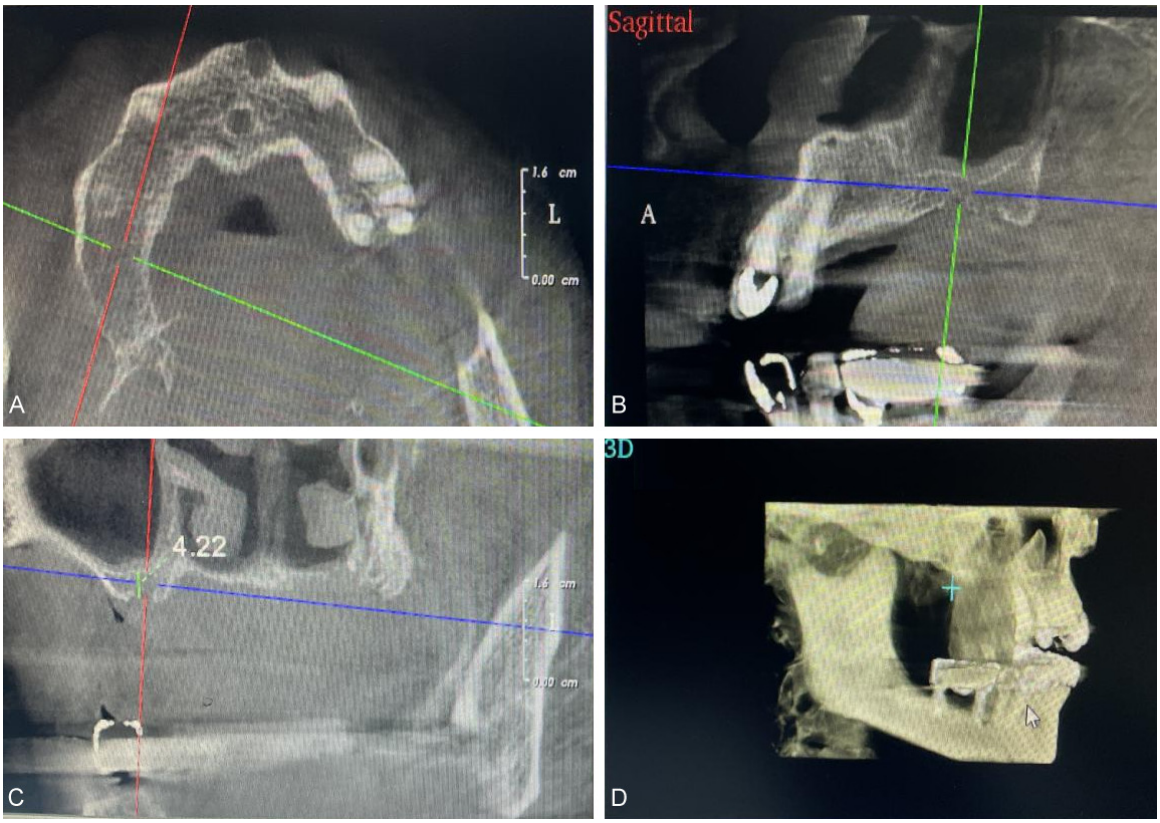

Figure 4. Preoperative CBCT images of the maxillary posterior region. A: Axial view showing the dental arch; B: Sagittal view displaying the maxillary sinus and alveolar ridge; C: Coronal view showing an alveolar ridge height of 4.22 mm; D: 3D reconstruction of the maxillary region. Note: CBCT, Cone-Beam Computed Tomography.

procedure, duration, cost, and expected outcomes were fully explained to the patient. She agreed and signed the informed consent form.

Treatment procedure: The CBCT software was used to design the implant type, position, direction and depth. Then, an appointment was scheduled for the implant surgery and the "right maxillary sinus external lift + implant placement at 14-16". The surgical procedure is illustrated in **Figure 5**.

Follow-up: At the one-week follow-up, the wound was evaluated, and a CBCT scan was performed (**Figure 6**).

Discussion

Patients with tooth loss are often associated with varying degrees of bone deficiency. Guided bone regeneration (GBR) with simultaneous implant placement has become a widely adopted procedure for addressing localized bone defects [18, 19]. The underlying principle of this technique involves: 1) bone defect repair using artificial bone replacement materials (e.g., Bio-Oss bone powder) to reconstruct peri-implant bone defects; 2) restoring barrier function by employing a biological barrier membrane (e.g., Bio-Gide membrane) to prevent

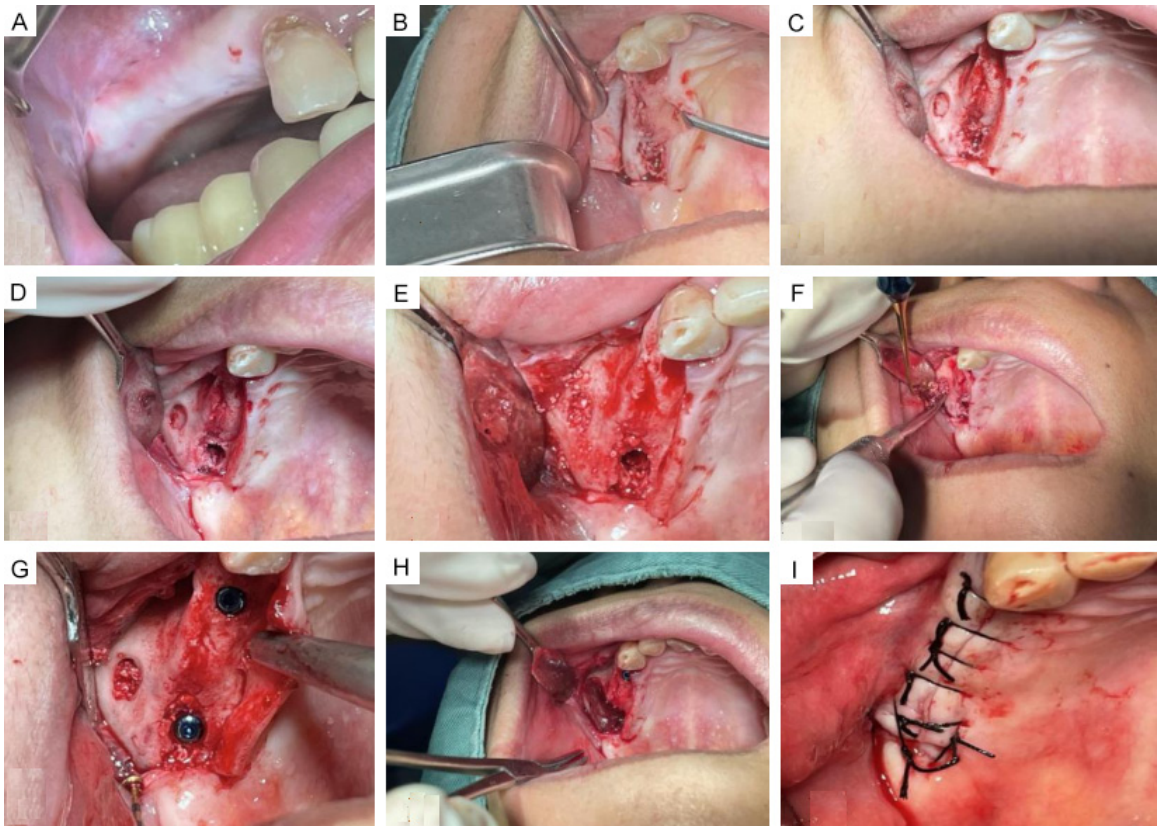

Figure 5. Surgical operation procedures in CGF/Bio group. A: Preoperative intraoral photograph; B: The flap was incised, and the operative area was exposed; C: Lateral wall opening of the maxillary sinus; D: Preparation of the implant cavity on top of the posterior alveolar ridge; E, F: Filling the cavity with CGF and Bio-Oss bone powder mixture; G: Implant placement; H: Bone powder surface covered with CGF membrane; I: Tightly sutured incision. Note: CGF, concentrated growth factor.

apical migration of the gingival epithelium; 3) periodontal tissue regeneration through guiding periodontal ligament cells to preferentially attach to the implant surface, facilitating the formation of new attachments and promoting directional healing of periodontal tissues, thereby enhancing bone regeneration [20-22]. Compared to conventional implant surgery, GBR requires the implantation of a bone substitute, which is more complex and time-consuming due to the additional steps involved in bone grafting and membrane placement. Postoperative pain and facial swelling, which are normal physiological response to surgical trauma, remain as significant concerns. These symptoms can adversely affect patients' quality of life, particularly when lip or cheek swelling interferes with social interactions and daily activities [23]. As a result, how to effectively improve bone volume while minimizing postoperative complications is still a challenge for clinicians.

Concentrated growth factors (CGF) represents a new generation of platelet concentrate products. It is prepared by isolating whole blood from a venous source, completely derived from autologous blood, with no additives introduced during the preparation process. This autologous nature effectively eliminates the risk of immune rejection following implantation. Compared to the first- and second-generation platelet concentrates, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), CGF offers a higher concentration of growth factors and better physical properties such as translucent, more elastic, and easily moldable, making it more easily shaped into various forms using specialized molds to meet specific clinical needs [23, 24]. Studies [25, 26] have shown that CGF and its leachate exhibit potent anti-inflammatory properties. The release of immune-related factors through platelet degranulation effectively inhibits the growth of patho-

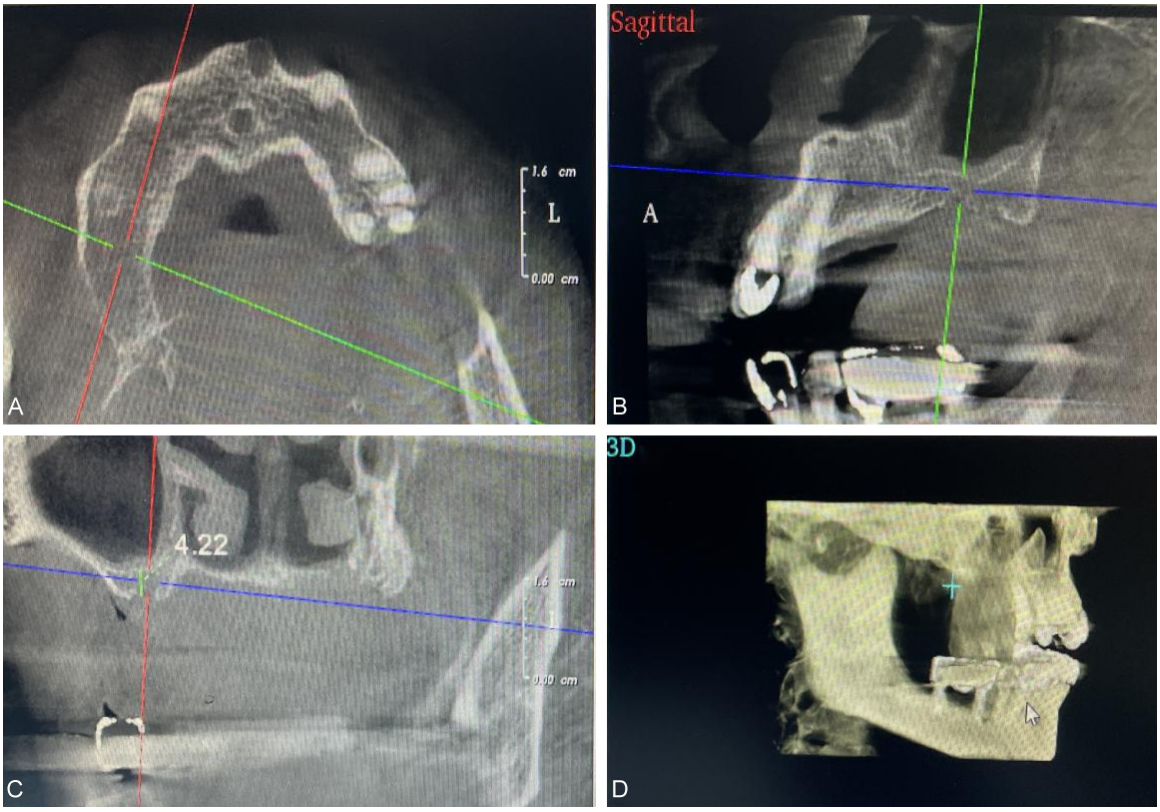

Figure 6. Postoperative CBCT. A: Axial view showing the dental arch with implant in place; B: Sagittal view displaying the maxillary sinus and implant position; C: Coronal view indicating the implant and surrounding bone structure; D: 3D reconstruction of the maxillofacial region post-implantation. Note: CBCT, Cone-Beam Computed Tomography.

genic bacteria and significantly reduces the postoperative pain and swelling.

In this study, we compared two approaches for simultaneous implant placement with maxillary sinus external lift: CGF/Bio vs. Bio alone. The addition of CGF significantly improved the implant retention rate and reduced wound healing time, which is likely attributed to the rich content of growth factors, platelets, and anti-inflammatory factors in CGF; this can effectively reduce postoperative tissue inflammatory response, shorten swelling duration, and promote soft tissue wound healing [27]. In this study, Bone density was evaluated using CBCT (EasyDent software), with results expressed in Hounsfield units (HU). The normal bone density in the maxillary posterior region is approximately 450 HU [28]. Bone substitute materials typically exhibit higher initial density values, which gradually decrease over time as osteogenesis occurs, approaching the natural bone density of 450 HU. In this study, the bone density was significantly higher in both groups at 2 months postoperatively, indicating that the filler has not undergone substantial osteogenesis yet. In the CGF/Bio group, bone density values approached preoperative levels at 4 months postoperatively, suggesting early bone formation around the implant. In contrast, the Bio group only reached preoperative bone density levels by 6 months postoperatively. This suggests that the combination of CGF and Bio-Oss bone powder accelerates new bone formation, demonstrating superior clinical efficacy compared to Bio-Oss alone.

This study also evaluated the degree and duration of postoperative pain and swelling between the two groups. Patients in the CGF/Bio group had lower VAS scores and shorter pain duration than the Bio group. In addition, the duration of postoperative swelling was also significantly shorter in the CGF/Bio group, aligning with the findings of Del Fabbro et al. [29]. The observed reduction in pain and swelling may be attributed to the interaction between CGF fibrin matrices and inflammatory factors. The slow release

of bioactive molecules from CGF fibrin lattices likely modulates the inflammatory response, promoting tissue healing and reducing discomfort [30].

Conclusion

This study demonstrates that CGF combined with Bio-Oss bone powder is highly effective for implant placement in patients with missing teeth and insufficient bone volume in the maxillary posterior region. The combined approach effectively accelerates new bone formation, increases implant retention rates and promotes faster wound healing, while minimizing postoperative complications.

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Disclosure of conflict of interest

None.

Address correspondence to: Zhe Cheng, Songyang Yijia Dental Clinic, Lishui 323400, Zhejiang, China. E-mail: chengzhezj@126.com

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