BMC Oral Health

RESEARCH

Open Access

CGF with Bio-Oss collagen as grafting materials for simultaneous implant placement after osteotome sinus floor elevation: a prospective study

Bashar Shahood[1], Seba Harphoush[2], Belal O. M. Muhaisen[1] and Jing Qiu[1,3*]

Abstract

Background Osteotome sinus floor elevation (OSFE) procedure with simultaneous implant placement is known to be an efficient procedure in the atrophic maxilla, where bone regeneration is required the most. The purpose of this study was to radiologically evaluate the efficacy of using Bio-Oss Collagen with Concentrated Growth Factor (CGF) as grafting materials for OSFE with simultaneous implant placement in the atrophic maxilla after one year of functional loading.

Methods A total of 126 implants were placed for 123 patients. Our inclusion criteria were patients with Residual Bone Height (RBH) ≤ 5 whom underwent OSFE procedure and simultaneous implant placement with different grafting materials: Group A with no grafting materials, Group B with Bio-Oss bone graft, and Group C with Bio-Oss Collagen with CGF. The Implants Survival Rate (ISR) was the primary outcome variable. Secondary outcome variables included radiographic measurements assessed at four follow-up time points, the Implant Stability Quotient (ISQ), and bone density (B). Indicators of bone formation were compared at different time points. Appropriate statistical analyses were conducted, with statistical significance set at a *P* value of 0.05 for all tests.

Results ISR was 96%. A significant positive relationship was found between RBH and ISR, [r (126) = .359, *p* = .000]. Endo sinus bone gain indictors increased in both grafted groups as compared to the non-grafted group. Total Bone Resorption (TBR1) and (TBR2) significantly decreased in both grafted groups compared to the non-grafted group (*P* = .004, *P* = .000). Graft size (D) was a positive predictor for ISR at three time points: D0 (odds ratio [OR] 8.06; 95% CI 1.59 to 38.24; *P* = .010); D1 (OR 96.58; 95% CI 1.69 to 5.52; *P* = .027); D2 (OR 4.97; 95% CI 1.29 to 19.19; *P* = .020). Visual Analog Scale (VAS) pain score significantly increased in Group B compared to Groups A and C (*P* = .000).

Conclusion The combination of Bio-Oss Collagen with CGF as grafting material is a reliable protocol after OSFE with simultaneous implant placement in the atrophic maxilla. This approach is accompanied by high patient satisfaction.

Keywords Osteotome sinus floor elevation, Bio-Oss collagen, CGF, Simultaneous implantation, Atrophic maxilla

*Correspondence:
Jing Qiu
qiujing@njmu.edu.cn
Full list of author information is available at the end of the article

Introduction

Residual ridge reduction is a common and fast phenomenon in the edentulous area of the maxilla. This area undergoes a chronic, progressive, and irreversible resorption leading to critical defects in the shape and function of the jaw [1]. The process of bone resorption in the posterior maxilla following tooth loss, coupled with renewed pneumatization of the maxillary sinus, contributes to the vertical and horizontal deficiency of the alveolar bone. These deficiencies are observed in the bilateral maxillary posterior zone, extending from the second premolar to the pterygoid plates, located at the base of the maxillary sinuses. Often, vertical bone augmentation with a sinus lift procedure is required when dental implants are considered for placement in this zone. The bone in this region is also known to have compromised quality (types 3 and 4), which can increase the implant failure rate [2]. Failures in rehabilitation with dental implants should be anticipated when osseointegrated implants are installed in areas of poor bone quality, such as the bilateral maxillary posterior zone, particularly in cases of severe bone resorption [3]. Identifying the most efficient implantation procedure with successful long-term outcomes remains one of the primary concerns in the implant industry.

Osteotome Sinus Floor Elevation (OSFE), as introduced by Summers [4], has proven to be an effective procedure for the atrophic maxilla [5–8]. Furthermore, OSFE is a less invasive surgical technique compared to the previously used lateral approach, offering better cellular viability around the implant and thereby reducing the risk of adverse soft tissue responses [9]. OSFE has been widely applied both with and without grafting materials [10]. Recently, an increasing number of studies have focused on simultaneous sinus elevation and implantation [11–13]. Regardless of whether grafting material was placed, the implant could help preserve the elevated sinus membrane and achieve new bone formation in the sinus [14]. The simultaneous placement of implants contributes to an improved survival rate of implants in the maxilla and helps preserve the alveolar crest volume [15]. Although significant advances have been made in the rehabilitation of the atrophic maxilla using the OSFE procedure, OSFE is not without its limitations, notably the potential risk of membrane perforation. Consequently, alternative methods have been developed to improve clinical outcomes, expand the indications for use, and reduce complications [16]. The newest approaches include: osseodensification, which uses densifying burs to enhance bone density and implant stability; Minimally Invasive Antral Membrane Balloon Elevation (MIAMBE), which employs a balloon for precise and gentle sinus membrane elevation; and the hydraulic sinus lift, which uses fluid pressure for a controlled and less invasive approach [17]. Furthermore, ongoing research into alternative grafting materials is essential for refining OSFE and its alternative techniques, with the goal of improving bone formation, enhancing implant stability, and optimizing clinical outcomes in sinus augmentation procedures [18, 19].

Bio-Oss® is a deproteinated bovine-derived xenograft product, which is widely used in dental practices for ridge augmentation in humans [20–22]. However, concerns about complications and long-term safety associated with bovine-derived xenografts are increasing [23]. Since it lacks osteoinduction and cellular activity, which poses a primary challenge in the field of osteoconductive graft enrichment research, Bio-Oss® presents further concerns. Conversely, Bio-Oss Collagen®, with its 10% collagen formulation, was developed to mimic the role of collagen in promoting rapid vascularization. Recent studies have demonstrated its role in enhancing new bone formation [24, 25]. Collagen is favorable due to its facile application. The interaction between soft tissue and collagen grafting has been extensively described in experimental and clinical research in both animal and human models [26–28]. In a human study, sockets in the molar region of the maxilla and mandible that were filled with Bio-Oss collagen demonstrated new bone synthesis after a healing period of six weeks. This approach resulted in low complication rates and effectively preserved the area for subsequent implant placement [29]. Moreover, bone resorption was significantly less in extraction sockets filled with Bio-Oss collagen combined with early implantation compared to untreated sockets [30]. Recently, Bio-Oss collagen has been demonstrated to achieve a high implant success rate following the OSFE procedure [31, 32]. Alternatively, Concentrated Growth Factors (CGFs), which are obtained from the patient's own blood through specific sequences of centrifuge speed, are considered the newest generation of platelet concentrates. Given its crucial role in bone regeneration through the provision of various growth factors [33], the combination of CGF with other grafting materials has gained increasing interest in the field of bone regeneration [34, 35]. The use of CGF in maxillary sinus augmentation improves clinical outcomes by promoting vascularization and tissue regeneration at the surgical site, enhancing both the quality and quantity of newly formed sinus bone [36]. When combined with graft materials, CGF helps preserve vertical bone height and significantly accelerates osteogenesis, while also reducing postoperative complications and improving implant survival rates [13, 37, 38].

However, research on the combination of CGF and Bio-Oss collagen is limited and has not been reported in the context of OSFE in the existing literature. The purpose of this study was to investigate whether alternative grafting materials, specifically CGF and Bio-Oss collagen,

for OSFE with simultaneous implantation can ensure high implant survival rate after long-term functional loading. Early implant failure typically occurs before the prosthesis is placed, whereas late implant failure is associated with functional loading after the prosthesis has been placed. In our study, the implant survival rate was investigated 6 months after first stage surgery and one year after functional loading with final prosthesis. Moreover, investigating viable techniques for sinus floor elevation and simultaneous implant placement in cases of edentulous posterior maxilla with RBH < 5 mm is of great clinical interest. In addition, this study contributes to the evaluation of patients' postoperative experiences. The null hypothesis is that there are no differences in endo-sinus bone synthesis indicators after OSFE with simultaneous implantation using different grafting materials. The specific objective of this study was to radiographically investigate the efficiency of the combination of Bio-Oss collagen and CGF as grafting materials for OSFE and simultaneous implant placement in the severe atrophic maxilla after one year of functional loading. To our knowledge, there has been no previous research in this area.

Methods

Study design/ sample

This prospective study was conducted in the Affiliated Hospital of Stomatology, Nanjing Medical University, China. This study complies with the Declaration of Helsinki and the Good Clinical Practice guidelines, and was approved by Medical Ethics Committee, School of Stomatology, Nanjing Medical University, China (Approval number: PJ2020-141–001). Informed consent for data evaluation and publishing has been obtained from all included subjects. Patients meeting our inclusion criteria underwent OSFE with simultaneous implantation from March 2021 to January 2022. A detailed medical record was established for each patient, including medical and dental history, oral examination, surgical records, details of bone graft materials, and the type of prosthetic reconstruction. Inclusion criteria for enrollment in this study were as follows: Patient whom underwent OSFE with simultaneous implantation must be at least 18 years of age; have good general health; adequate oral hygiene, indicated by a bleeding index of less than 30% and a plaque score of less than 20%; have been extracted 1 or 2 maxillary molars or pre-molars because of failure of endodontic treatment, root fracture, or after suffering from severe caries for more than 3 months. Radiographic inclusion criteria are as follows: Residual Bone Height (RBH) of the alveolar bone crest measured on CBCT at each implant site is 2–5 mm; an adequate residual alveolar ridge width for implant placement of 6 mm or more; absence of any radiographic signs of maxillary sinus pathology; and length of the inserted implants ranging from 8–10 mm with diameters of 4.1/4.8 mm (Dentium implant/ ICX implant/ MIS). Exclusion criteria were as follows: postoperative CBCT imaging lacking clarity or unclear anatomic references, or incomplete medical history due to the failure of the patient to come for follow up appointments.

Using the R program (R Foundation for Statistical Computing) [39], at least 107 subjects were required to evaluate the association between the primary outcome and three categorial variables. This calculation assumed a medium effect size of 0.3 (measured by Cohen's d), a *P*-value of 0.05, and a power of 80%. Considering the dropout rate of 20%, a total of 134 subjects were needed.

Surgical procedure

Patients were treated according to the designed treatment plan. They were assigned randomized numbers and subsequently divided into three different groups based on those numbers. The surgery consisted of simultaneous implant placement with sinus augmentation via the Osteotome technique (OSFE) by surgeon B.SH. All patients underwent a comprehensive oral examination and received a CBCT scan prior to surgery. Pre-operative CBCT image was used to evaluate RBH and crestal bone width. Those meeting our inclusion criteria were selected for the study. For all subjects, local anesthesia was performed, a mid-crestal incision was made and flap raised, and then the implant site was generated using a pilot drill, maintaining a distance of 1 mm from the sinus floor. Next, the bone of the sinus floor was fractured into the sinus cavity, elevating the Schneiderian membrane, with a vigilant tap of the mallet. The initial sinus elevation was performed with osteotomes, gradually advancing until the final depth was achieved. In the first group (Group A), the implant was placed without any grafting material. In Groups B and C, the elevated sinus was filled with either 0.25 g of Bio-Oss® Bone Graft or 100 mg of Bio-Oss collagen mixed with CGF, respectively. For all groups, the implant was then inserted simultaneously and more palatal, using a submerged technique and using a two-stage procedure. Postoperative CBCT scans were taken immediately for all patients.

Postsurgical care following OSFE with simultaneous implant placement was performed according to standard postsurgical treatment protocols. Patients were instructed to rinse their mouths with a 0.12% chlorhexidine solution for 60 s, five times a day, for 14 days. Additionally, anti-inflammatory drugs and antibiotics were prescribed following the surgery.

Grafting materials

Geistlich Bio-Oss® small granules (0.25 – 1 mm) (Geistlich Pharma AG, Wolhusen, Switzerland); Geistlich Bio-Oss Collagen®, comprised of 90% Geistlich Bio-Oss® granules and 10% of porcine collagen (Geistlich Pharma AG, Wolhusen, Switzerland)); and CGF, which was prepared in the hospital directly before surgery using a previously described method [40], were used as grafting materials. For the CGF with the Bio-Oss group, the extracted CGF layer was then separated and divided into small fragments using sterile scissors, and mixed with 100 mg Geistlich Bio-Oss Collagen® (Fig. 1).

Prosthetic rehabilitation

CBCT was taken for each patient at 3 months (T1) and at six months (T2) after OSFE, followed by the second-stage surgery. Following two weeks secondary healing period, dental impressions were made and implant stability was evaluated. Two weeks later, the final restorations were performed after the insertion of the prosthetic abutments. Each implant was used to hold a single crown.

Variables

The primary predictor variables were three groups according to the type of bone graft used: Group A (control group without any bone graft), Group B (with Bio-Oss bone graft), and Group C (Bio-Oss collagen mixed with CGF). The primary outcome variable was: Implant survival rate. The secondary outcome variables were the changes in the endo-sinus bone gain at different time points which were measured by the following parameters: Height of the apical bone (H, mm), Sinus Lift (SL, mm), Vertical Bone Resorption (VBR, mm), Grafting size (D, mm), Total Bone Resorption (TBR, mm), Implant Stability Quotient (ISQ, between 0 and 100), and Bone density (B, HU). Other secondary outcomes included the post-surgery patient's pain based on VAS score (1 to 100, mm), post-surgery patient's satisfaction VAS score (1 to 10, cm), and willingness to do this procedure again (Yes, No). Covariates included the age by years, sex (male, female), smoking (smoker, non-smoker), Residual Bone Height (RBH, mm), Alveolar Bone Width (ABW, mm), and Implant protrusion length (IPL).

Data collection

Implant survival rate

Implants success was evaluated at two time points: six months after implant placement and one year after functional loading of the upper prosthesis. The survival rate was recorded using the following success criteria: no

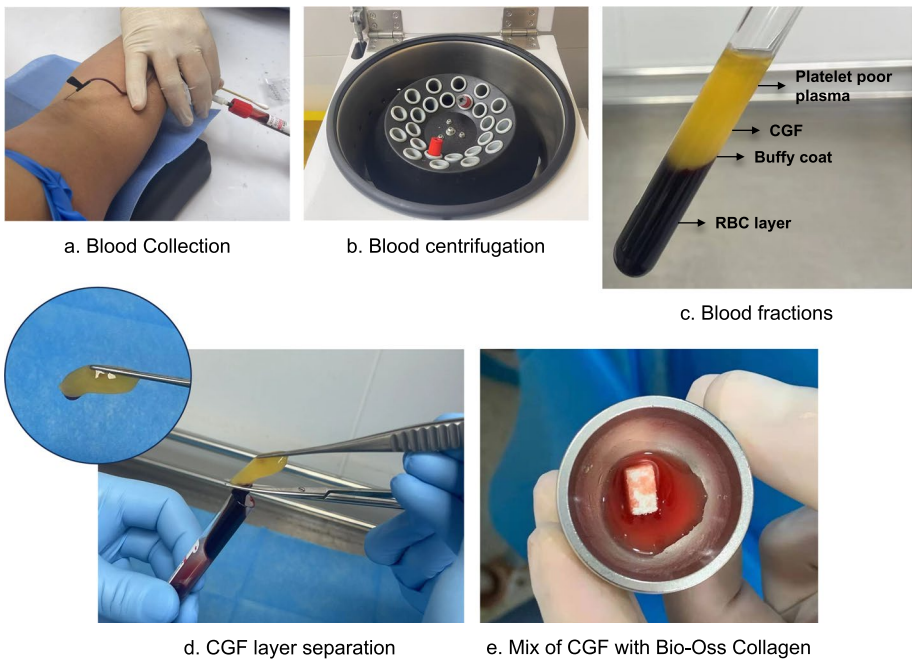

Fig. 1 Preparation of the combination of Concentrated Growth Factor (CGF) and Bio-Oss collagen. **a** Blood collection: IV blood is collected in two 10 mL glass-coated plastic tubes with no anticoagulant addition. **b** Blood centrifugation: Blood is centrifuged with the following programs: 30 s acceleration, 2 min at 2700 rpm, 4 min at 2400 rpm, 4 min at 2700 rpm, 3 min at 3000 rpm, and 36 s deceleration and stop. (Medifuge®, Silfradent Srl, Forli, Italy). **c** Blood fractions: At the end of the centrifugation, four layers are obtained (RBC layer, CGF layer, Buffy coat layer, and Platelet poor plasma with serum). **d** The CGF layer is separated using sterile surgical scissors. **e** Mix of CGF with Geistlich Bio-Oss: CGF is divided into small fragments and mixed with 100 mg Geistlich Bio-Oss Collagen®

implant mobility detected during clinical examination; no pain or any unusual complaint from the patient; no peri-implant radiolucency, infection, or neuropathies; fully functional suited prosthetic constructions without positional change; and an absence of any occlusal malfunctions.

Radiographic evaluation

For each patient, CBCT imaging using GiANO (NewTom, Imola, Italy) with NewTom NNT analysis software was performed at each stage outlined in the study flowchart (Fig. 2) due to its superior spatial resolution. The imaging was conducted at the following time points: preoperative, immediately after first stage surgery T0, 3 months after first stage surgery T1, before second stage surgery T2, and one year after loading with final restorations T3.

All patients received full high-resolution scan: Voxel size 0.075 mm (12.6 mAs, 90 kVp, 3 mA), a field of view (FOV) of 10 (cm)×10 (cm), and 360° rotation around patients in 3.6-s scan time. All the linear variables were measured on the coronal cross-sections parallel to the longitudinal direction of the implant, using the measuring tool of NewTom NNT analysis software. The precision of the measuring system is 0.01 mm. Measurements were assessed by a single operator three times and the average was calculated. The following are definitions of this study linear variables:

RBH: the vertical distance between the alveolar crest and the floor of the maxillary sinus along the maxilla axis was used to measure RBH before surgery.
ABW: the horizontal width of the alveolar bone was measured at 3 mm below the alveolar bone crest. RBH and ABW were only assessed before surgery using preoperative CBCT. IPL was calculated as the implant length IL minus RBH (IPL = IL-RBH).

On postoperative CBCT taken for each implant at four time points, four planes have been indicated orthogonal to the long axis of inserted implant using the previous software, as shown in Fig. 3. Plane 'A' was established passing through highest point of the elevated sinus floor after OSFE, Plane 'B' was established by passing through the vertex of the implant, Plane 'Cp' was established by passing through the bottom level of the maxillary sinus from the palatal side, and Plane 'Cb' was established by passing through the bottom level of the maxillary sinus from the buccal side. The vertical distance (H), representing the height of the augmented sinus floor, between Plane 'A' and Plane 'B' was measured as the at four time points. Immediately after

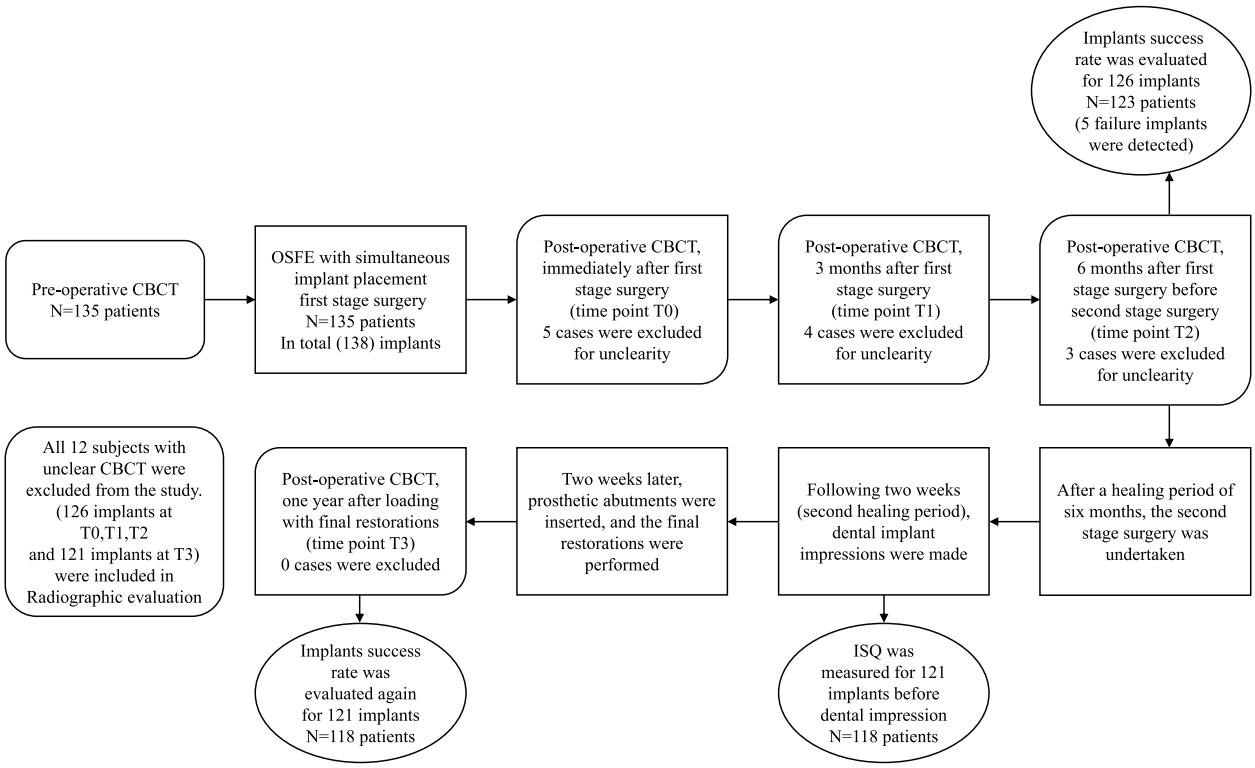

Fig. 2 Flowchart of the study cohort recruitment and completed follow-up

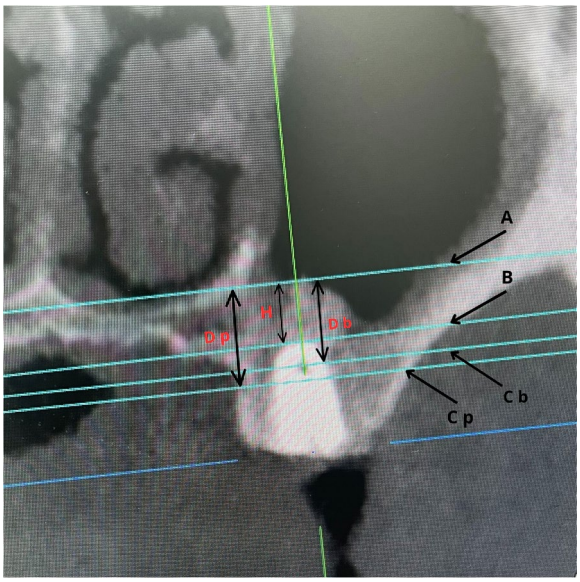

Fig. 3 Imaging measurements: four planes perpendicular to the long axis of the implant were identified, Plane 'A' passed through the highest point of augmented sinus membrane after the OSFE procedure, plane 'B' was perpendicular to the apex of the implant, plane 'Cp' passed through the implant at the level of the bottom of the maxillary sinus from palatal side, and plane 'Cb' passed through the implant at the level of the bottom of the maxillary sinus from buccal side

surgery, the maxillary sinus floor (Plane 'A') was positioned above the apex of all implants, resulting in H0 being greater than 0. At follow-up, when the maxillary sinus floor was on contact with the implant apex, plane 'A' and plane 'B' overlapped, and H was considered to be 0. SL was calculated as H + IPL at four time points. VBR represented the difference in SL between the different follow-up time points. It was calculated twice: first as the difference between SL0 and SL2 (VBR1), and second as the difference between SL0 and SL3 (VBR2). D was defined as the mean vertical distance between the initial sinus floor and the elevated sinus floor assessed at buccal and palatal sides. It was calculated as the average of buccal D (the vertical distance between plane 'A' and plane 'Cb'), and palatal D (the vertical distance between plane 'A' and plane 'Cp'). TBR represented the difference in D between the different follow-up time points. It was calculated twice: first as the difference between D0 and D2 (TBR1), and second as the difference between D0 and D3 (TBR2). H, buccal D, palatal D, D, and SL were measured and calculated four each implant at four time points postoperatively, immediately after the first stage surgery (T0), 3 months after the first stage surgery (T1), 6 months after the first stage surgery and before the second stage surgery (T2), and one year after functional loading (T3).

Implant stability quotient

Implant Stability was measured using The Osstell resonance frequency analyzer (Osstell, Göteborg, Sweden) for each specimen two weeks following the second stage surgery and before dental impression was made. The resonance frequency measurement, an indicator for mechanical implant stability, was assigned a value between 0 and 100. ISQ was measured 3 times for each specimen, and the median was calculated.

Bone density

The bone tissue density was analyzed using NewTom NNT software with a spot diameter of 1 mm at three regions around the center of the measured implant protrusion buccally and lingually. The mean value of the three measurements of the average bone volume was then calculated and expressed in Hounsfield units (HU). B was measured and calculated four each implant at three time points T1, T2, and T3.

Patient's satisfaction

Patient satisfaction was assessed using a simple questionnaire administered three days postoperatively following the first stage of surgery. Initially, patients were asked to rate their pain using a 100-mm Visual Analog Scale (VAS) scale. The pain scores were categorized as follows: 0 to 4 mm indicated no pain, 5 to 44 mm indicated mild pain, 45 to 74 mm indicated moderate pain, and 75 to 100 mm indicated severe pain. Subsequently, patients were asked to rate their satisfaction using 10-cm VAS scale, ranging from 0 meaning not satisfied to 10 meaning very satisfied. Finally, patients were inquired about their willingness to undergo similar procedures in the future if they needed (yes or no question).

Data analysis

Statistical analysis of data was performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corporation, Armonk, New York). The Shapiro–Wilk test was implemented to assess whether the data followed a normal distribution. ANOVA test followed by Tukey's post hoc test was applied to analyze differences in RBH, ABW, IPL, SL, D, B, VBR, TBR, ISQ, pain VAS score and satisfaction VAS score measurements between three groups (A, B and C), and to look at how each group changed over time. The χ^2 test was used to compare ISR, sex, smoking status, and patients' willingness to undergo a similar procedure in the future among the three groups. Fisher's exact test and independent *t*-test were used to conduct bivariate analyses of the covariates versus ISR. The Pearson's correlation coefficient was calculated between primary outcome ISR and variables (RBH, B1 and B2).

Additionally, the Pearson's correlation coefficient and Eta correlation ratio were calculated between the pain VAS score and other variables. Three multiple logistic regressions were implemented to examine the relationship between radiographic measurements (H, D and SL) and ISR at three time points T0, T1, and T2. $P<0.05$ was considered to indicate a statistically significant difference.

Results

This study included 135 patients, with 45 in each group. Twelve subjects were excluded due to unclear CBCT images while 123 patients (126 implants) completed the study assessment follow-up plan. The patients comprised of 79 men and 44 women with a mean age of 58 ± 11.2 (20–78) years. Radiographic assessment of pre-operative CBCT indicated RBH ≤ 5 mm (mean of 4.37 ± 0.75, range 2.6–5) and ABW ≥ 6 (mean of ABW = 11.53 ± 1.89, rang 6–16). Comparison of covariates versus study groups A, B and C is presented in Table 1.

Total implant survival rate was 96%. All 5 failed cases were found at T2 and then removed and rescheduled for retreatment. Comparatively, no implant failure was found at T3 time points, after one year of functional loading. Bivariate analyses of the covariates versus ISR are presented in Table 2.

No significant difference was found for ISR, 95.6% for Group A ($n=45$), 97.6% for Group B ($n=41$), and 95% for Group C ($n=40$) (Table 3). During the follow-up period, four cases of acute sinusitis were documented, three in Group A and one in Group B. These infections were effectively treated with amoxicillin-clavulanate (2,000 mg/125 mg every 12 h for five days) and did not adversely affect the functional performance of the implants. Moreover, no occurrences of Schneiderian membrane perforation were observed throughout the duration of the study.

Radiographic assessment of CBCT after surgery was taken at four time points and is recorded in Table 3. Significant increase of radiographic measurements for H, D and SL were recorded in both grafted Groups B and C compared to Group A at four time points after surgery T0, T1, T2 and T3 ($P<0.001$) with significantly increased D3 (n = 121) in Group C compared to Groups A and B. VBR1 ($n=126$) and VBR2 ($n=121$) had no significant difference between the groups. While TBR1 ($n=126$) and TBR2 ($n=121$) were significantly increased in Group A compared to Groups B and C ($P=0.004$, $P=0.000$), TBR2 also significantly increased in Group B compared to Group C. ISQ measured at the T2 time point ($n=121$) significantly increased in Group B compared to Group A ($P=0.000$), and also increased in Group C compared to Group A as well, but without significant difference. B1 ($n=126$), B2 ($n=126$), and B3 ($n=121$) all significantly increased in Groups B and C compared to Group A ($P<0.001$). The bivariate association between some predictor variables and primary outcome ISR is presented in Table 4. RBH was indicated to have a significant positive relationship with ISR, [r (126) = 0.359, $P=0.000$]. Moreover, there was a significant positive relationship between B1 and ISR, [r (126) = 0.271, $P=0.002$], and there was a significant positive relationship between B2 and ISR, [r (126) = 0.359, $P=0.000$].

Table 1 Comparison of the covariates versus three groups based on grafting materials (Group A, Group B, & Group C)

Covariates	Group A ($n=43$)	Group B ($n=40$)	Group C ($n=40$)	*P* value	Total ($n=123$)
Sex				0.099	
Female %, (n)	32.6% (14)	47.5% (19)	25% (10)		35% (43)
Male %, (n)	67.4% (29)	52.5% (21)	75% (30)		65% (80)
Age	55.88 ± 10.53	59.93 ± 11.94	58.83 ± 11.25	0.24	58 ± 11.21
Smoking				0.009	
Non-smokers %, (n)	65.1% (28)	82.5% (33)	50% (20)		65.9% (81)
smokers %, (n)	34.9% (15)	17.5% (7)	50% (20)		34.1% (42)
	Group A ($n=45$)	**Group B ($n=41$)**	**Group C ($n=40$)**	***P* value**	**Total ($n=126$)**
RBH (mm)	4.49 ± 0.69	4.33 ± 0.73	4.28 ± 0.82	0.385	4.37 ± 0.75
ABW (mm)	12.03 ± 1.8	11.08 ± 1.82	11.42 ± 1.97	0.06	11.53 ± 1.89
IPL (mm)	4.08 ± 0.96	4.41 ± 0.87	4.25 ± 0.97	0.272	4.24 ± 0.94

Sex and Smoking: Chi-Squared Test. Age, RBH, ABW and IPL ANOVA [95% Confidence Interval]. Categorical data are presented as (%), continuous data are presented as mean ± standard deviation

Abbreviations: RBH Residual Bone Height, *ABW* alveolar bone width, *IPL* Implant protrusion length; Group A, with no grafting materials; Group B, with Bio-Oss bone graft; Group C, with Bio-Oss collagen and CGF

Table 2 Comparison of the secondary outcomes versus three groups based on grafting materials (Group A, Group B, & Group C)

Outcomes	Group A (*n* = 45)	Group B (*n* = 41)	Group C (*n* = 40)	*P* value	Total (*n* = 126)
ISR (%)	95.6% (n = 43)	97.6% (n = 40)	95% (n = 38)	0.82	96% (121)
Failure (%)	4.4% (n = 2)	2.4% (n = 1)	5% (n = 2)		4% (5)
H0 (mm)	1.37 ± 0.82[a]	2.35 ± 0.84[b]	2.41 ± 0.99[b]	0.000	2.02 ± 1.00
H1 (mm)	0.72 ± 0.72[a]	1.80 ± 0.89[b]	2.03 ± 1.04[b]	0.000	1.49 ± 1.05
H2 (mm)	0.28 ± 0.50[a]	1.46 ± 0.91[b]	1.38 ± 1.09[b]	0.000	1.01 ± 1.01
SL0 (mm)	5.49 ± 1.17[a]	6.75 ± 1.12[b]	6.62 ± 1.35[b]	0.000	6.26 ± 1.33
SL1 (mm)	4.80 ± 1.25[a]	6.21 ± 1.30[b]	6.28 ± 1.39[b]	0.000	5.73 ± 1.48
SL2 (mm)	4.36 ± 1.10[a]	5.87 ± 1.26[b]	5.63 ± 1.51[b]	0.000	5.25 ± 1.45
D0 (mm)	3.53 ± 0.79[a]	4.63 ± 0.86[b]	4.93 ± 1.14[b]	0.000	4.33 ± 1.11
D1 (mm)	2.63 ± 0.82[a]	3.81 ± 1.09[b]	4.00 ± 1.14[b]	0.000	3.45 ± 1.19
D2 (mm)	1.81 ± 0.84[a]	3.46 ± 1.14[b]	3.64 ± 1.10[b]	0.000	2.93 ± 1.32
VBR1 (SL0-SL2) (mm)	1.13 ± 0.87	0.89 ± 0.79	1.00 ± 0.99	0.455	1.01 ± 0.89
TBR1 (D0-D2) (mm)	1.71 ± 0.65[b]	1.15 ± 0.80[a]	1.29 ± 1.01[a]	0.005	1.39 ± 0.86
B1 (HU)	373.29 ± 231.36[a]	647.22 ± 302.38[b]	627.62 ± 264.15[b]	0.000	543.17 ± 293.39
B2 (HU)	369.27 ± 203.78[a]	763.41 ± 319.04[b]	707.70 ± 296.59[b]	0.000	604.96 ± 325.96
	Group A (*n* = 43)	**Group B (*n* = 40)**	**Group C (*n* = 38)**	***P* value**	**Total (*n* = 121)**
H3 (mm)	0.14 ± 0.33[a]	0.98 ± 0.80[b]	1.09 ± 0.96[b]	0.000	0.71 ± 0.85
SL3 (mm)	5.60 ± 1.42[a]	7.30 ± 1.57[b]	7.44 ± 1.75[b]	0.000	6.74 ± 1.78
D3 (mm)	0.95 ± 0.67[a]	2.89 ± 1.09[b]	3.81 ± 1.09[c]	0.000	2.49 ± 1.54
VBR2 (SL0-SL3) (mm)	1.24 ± 0.87	1.39 ± 0.82	1.33 ± 1.04	0.757	1.31 ± 0.90
TBR2 (D0-D3) (mm)	2.60 ± 0.83[c]	1.77 ± 0.85[b]	1.2 ± 1.45[a]	0.000	1.88 ± 1.21
B3 (HU)	437.39 ± 231.22[a]	1096.82 ± 247.46[b]	972.1 ± 247.44[b]	0.000	832.49 ± 377.5
ISQ (1–100)	72.51 ± 6.20[a]	77.13 ± 4.68[b]	74.76 ± 3.63[ab]	0.000	74.74 ± 5.32
Patient's satisfaction	**Group A (*n* = 43)**	**Group B (*n* = 40)**	**Group C (*n* = 40)**	***P* value**	**Total (*n* = 123)**
Pain VAS score	42.02 ± 20.72[a]	56.43 ± 18.83[b]	37.33 ± 18.05[a]	0.000	45.69 ± 19.86
Satisfaction VAS score	6.84 ± 2.08[b]	5.15 ± 1.73[a]	7.18 ± 1.95[b]	0.000	6.63 ± 1.95
Willing to do similar procedure in the future				0.032	
Positive %, (n)	83.7% (36)	65% (26)	87.5% (35)		78.9% (97)
Negative %, (n)	16.3% (7)	35% (14)	12.5% (5)		21.1% (26)

ISR and Willing to do such kind of procedure in the future: Chi-Squared Test. ISQ, B1, B2, B3, H0, H1, H2, H3, SL0, SL1, SL2, SL3. D0, D1, D2, D3, VBR1, VBR2, TBR1, TBR2, Pain VAS score and Satisfaction VAS score: ANOVA [95% Confidence Interval] followed by Tukey's post hoc test ([a], [b], [ab]). $P < .05$. Categorical data are presented as (%), continuous data are presented as mean ± standard deviation

Abbreviations: *ISR* Implants Survival Rate, *ISQ* Implant Stability Quotient, *B* Bone density measured at three time points T1, T2 and T3, *H* Height of the apical bone measured at four time points T0, T1, T2, and T3, *SL* Sinus Lift calculated at four time points T0.T1.T2.T3; D, Graft Size measured at four time points T0, T1, T2 and T3; *VBR* Vertical Bone Resorption calculated twice, *TBR* Total Bone Resorption calculated twice; T0, immediately after first stage surgery; T1, 3 months after first stage surgery; T2, 6 months after first stage surgery before Second stage surgery and T3, one year after loading with final restorations; Group A, with no grafting materials; Group B, with Bio-Oss bone graft; Group C, with Bio-Oss collagen and CGF

Table 3 Correlation between some of the study variables as secondary predictors and the primary outcome variable ISR

Variables	Correlation Coefficient*	*P* value†
RBH	0.359	0.000
B1	0.271	0.002
B2	0.359	0.000

Abbreviations: *ISR* Implants Survival Rate, *RBH* Residual Bone Height, *B1* Bone density measured at T1, 3 months after first stage surgery, *B2* Bone density measured at T2, 6 months after first stage surgery before Second stage surgery

*Pearson's correlation coefficient. † Independent *t*-test, $P < .05$ (2-tailed)

Three multivariate logistic regression analyses for radiographic measurements (H, D and SL) at T0, T1, and T2 time points as predictors for ISR are presented in Table 4. In the first multivariate regression analyses, implants with higher D0 value were 8.06 times more likely to survive after 6 months of implantation (OR 8.06; 95% CI 1.59 to 38.24; $P = 0.010$). In the second multivariate regression analyses, implants with higher D1 value were 96.58 times more likely to survive after 6 months of implantation (OR 96.58; 95% CI 1.69 to 5.52; $P = 0.027$). In the third

Table 4 Multiple logistic regression for ISR and the radiographic measurements on CBCT at T0, T1 And T2 time points

Variables	**Adjusted Model**	
	OR (95% CI)	*P* Value
H0	1.34 (0.22–8.1)	0.75
D0	8.06 (1.59–38.24)	0.010
SL0	0.25 (0.06–1.06)	0.059
Variables	**Adjusted Model**	
	OR (95% CI)	*P* Value
H1	21.29 (0.26–1.74)	0.174
D1	96.58 (1.69–5.52)	0.027
SL1	0.13 (0.015–1.1)	0.061
Variables	**Adjusted Model**	
	OR (95% CI)	*P* Value
H2	3.1(0.27–36.15)	0.367
D2	4.97(1.29–19.19)	0.020
SL2	0.214(0.4–1.16)	0.074

Abbreviations: *ISR* Implants Survival Rate, *H0* Height of the apical bone measured at T0, *D0* Graft Size measured at T0, *SL0* Sinus Lift calculated at T0, *T0* immediately after first stage surgery, *OR* odds ratio, *H1* Height of the apical bone measured at T1, *D1* Graft Size measured at T1; SL1. Sinus Lift calculated at T1; T1, 3 months after first stage surgery; H2, Height of the apical bone measured at T2; D2, Graft Size measured at T2; SL2, Sinus Lift calculated at T2; T2, 6 months after first stage surgery

multivariate regression analyses, implants with higher D2 value were 4.97 times more likely to survive after 6 months of implantation (OR 4.97; 95% CI 1.29 to 19.19; $P=0.020$).

The results of the patient satisfaction questionnaire, as presented in Table 2, indicate a significant increase in pain VAS scores (mean of pain VAS = 45.18 ± 20.6, range 3–89) in Group B compared to Groups A and C ($P=0.000$). The distribution of pain scores categories between groups are illustrated in Fig. 4. Additionally, there was a significant increase in patient satisfaction VAS scores (mean of satisfaction VAS = 6.4 ± 2.12, range 1–10) in Groups C and A compared to Group B ($P=0.000$). Furthermore, there was a significant increase in the refusal to undergo similar procedures in the future in Group B compared to Groups A and C ($P=0.041$ and $P=0.032$, respectively). After studying the correlation between pain scores and various variables, we identified several significant relationships. There was a significant positive relationship between pain score and age [r (123) = 0.189, $P=0.036$], a significant negative relationship between pain score and RBH [r (123) = -0.324, $P=0.000$], and a significant positive relationship between pain score and IPL [r (123) = 0.207, $P=0.021$]. A significant negative relationship was also found between pain score and satisfaction score [r (123) = -0.752, $P=0.000$]. Furthermore, there was a medium association between pain score and patients' refusal to undergo similar procedures in the future [η (123) = 0.553, $P=0.000$]. Lastly, there was a weak association between pain score and female gender [η (123) = 0.312, $P=0.000$], and no association between pain score and smoking [η (123) = 0.189, $P=0.036$].

Discussion

The purpose of this radiological study was to investigate the ability of the combination of CGF with Bio-Oss collagen as grafting materials to induce osteogenesis in the

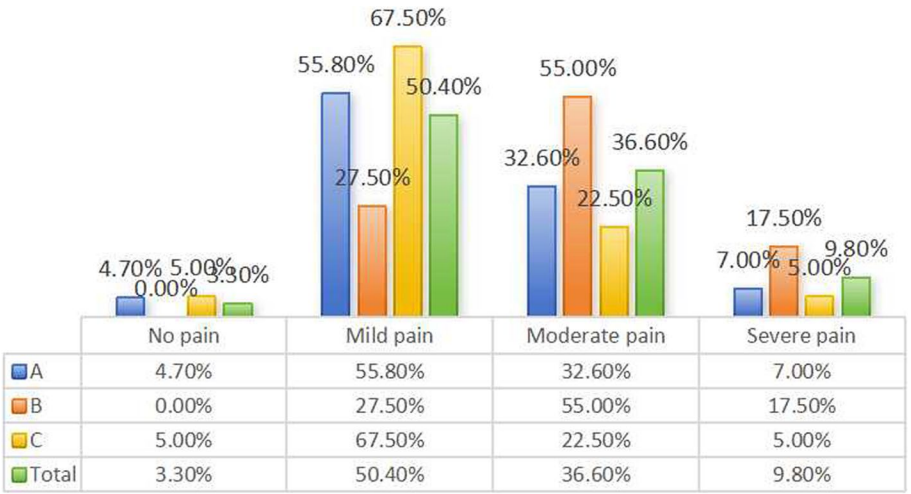

Fig. 4 Distribution of VAS pain scores categories between groups, Group A, with no grafting materials; Group B, with Bio-Oss bone graft; Group C, with Bio-Oss collagen and CGF. The VAS pain scores were categorized as follows: 0 to 4 mm indicated no pain, 5 to 44 mm indicated mild pain, 45 to 74 mm indicated moderate pain, and 75 to 100 mm indicated severe pain

maxillary sinus after OSFE and simultaneous implant placement in patients with severe vertical defects in the alveolar ridge RBH ≤ 5 mm. The null hypothesis posited that no significant difference exists in the long-term intra-sinus osteogenesis process among the various grafting materials utilized following OSFE with simultaneous implantation. The positive correlation between RBH and implant survival rate indicates combined with simultaneous implant placement in the atrophic maxilla can achieve high implant survival rates, under routine clinical practice conditions. In this study, we propose the combination of Bio-Oss Collagen and CGF as grafting materials following OSFE and simultaneous implant placement, a topic not previously investigated in the literature [41]. As shown in our results and in previous studies, sinus floor elevation can be performed without graft material, resulting in sufficient bone development and implant longevity [42]. However, a study conducted by Kim et al. in an animal model demonstrated that bone formation is significantly constrained when sinus lift surgery is performed without the use of grafting materials [43]. Moreover, CGF has shown considerable potential in tissue regeneration, attributed to its capacity to enhance cell proliferation, migration, and differentiation, as well as its ability to stimulate angiogenesis and osteogenesis [44]. The utilization of growth factors has been shown to enhance clinical outcomes by promoting improved vascularization at surgical sites. Furthermore, their application contributes to better postoperative recovery, significantly improving patients' quality of life [36, 45]. The application of CGF membrane as the sole grafting material in conjunction with OSFE and simultaneous implant placement in the atrophic maxilla has been reported to yield favorable outcomes, including significant vertical bone augmentation immediately following surgery [46]. Chen, H., et al. reported that after a 24-month follow-up, there was no significant difference in marginal bone loss between OSFE performed using concentrated growth factors (CGF) alone and OSFE using CGF in combination with bone grafting materials. However, CGF alone was preferred due to its superior patient satisfaction and safety profile [13].

ISR demonstrated a significant positive correlation with grafting size D across three follow-up time points. In the present study, all bone formation indicators showed significant improvement in both grafted groups during follow-up evaluations. While VBR1 and VBR2 did not differ significantly between the groups, TBR1 and TBR2 exhibited a notable increase in the non-grafted Group A. After one year of functional loading, D3 increased in Group C significantly compared to Groups A and B, while TBR2 significantly receded in Group C compared to Groups A and B. Additionally, it was observed that the initial D0 and H0 values were significantly lower in Group A compared to Groups B and C, with Group C exhibiting the highest values. This indicates a notable variation in baseline measurements across the groups, with Group C demonstrating superior initial parameters. Notably, this trend persisted after 12 months of follow-up, as evidenced by the D3 and H3 measurements. These findings suggest that, while collagen combined with CGF may undergo absorption by the six-month mark, as reported in previous research [47], endo-sinus bone gain begins to develop gradually thereafter, effectively slowing the resorption process by the one-year follow-up. This supports the hypothesis that the combination of Bio-Oss collagen with CGF promotes tissue repair and regeneration, offering a sustained and beneficial effect on bone formation over time. Furthermore, this combination may facilitate new bone formation in the sinus when applied following OSFE, potentially improving the outcomes of sinus augmentation procedures. Compatible with these findings, a recent radiographic study reported that the application of Bio-Oss collagen after OSFE and simultaneous implantation achieved a significantly increased initial endo-sinus bone gain compared to the non-grafted group [31]. However, unlike our results, the difference in endo-sinus bone in the aforementioned study diminished after one year of functional loading. In contrast, in our study, bone gain indicators in Group C remained significantly higher than those in the non-grafted group at the T3 time point, suggesting a more sustained enhancement of bone formation over time. Moreover, our findings align with a previous study that successfully employed a combination of CGF and collagen in conjunction with bone grafts for alveolar ridge preservation [48]. This study demonstrated the efficacy of this regenerative approach in promoting tissue healing and enhancing bone regeneration, further supporting the positive outcomes observed in our study. Moreover, simultaneous sinus augmentation and implantation with the presence of grafting material can help assist preserve the augmented sinus membrane and prevent marginal bone loss, as demonstrated in previous studies [49]. This protective effect may contribute to the slower absorption of grafting materials observed in Group C. Most importantly, a reduction in bone absorption coupled with the synthesis of new bone was observed in the sinus. This finding aligns with a previous study, which indicated that alveolar bone levels in extraction sockets were better preserved using collagen in conjunction with early implantation, as compared to collagen alone without implantation [30]. Furthermore, collagen helps maintain the space needed for the osteoinductive properties of the coagulum by enlarging the space, which promotes increased vascularization and stabilization of the coagulum. This

favorable microenvironment supports the recruitment of osteoprogenitor cells and promotes effective bone regeneration. A recent study involving both radiographic and histomorphologic examination demonstrated that the use of collagen alone following OSFE was sufficient to induce proper new bone formation [50]. In our study, the average final sinus lift achieved in Group C was 7.44 mm, which closely approximates the 7.75 mm reported by Yerko, et al., where autologous fibrin glue with a collagen carrier was used during lateral sinus augmentation with simultaneous implantation in the atrophic maxilla with less than 5 mm RBH [51]. This similarity in results further underscores the effectiveness of collagen, either alone or in combination with other materials, in achieving substantial sinus lift and promoting successful bone regeneration in challenging clinical scenarios.

To our knowledge, this is the first study that investigated the functional application of the combination of Bio-Oss collagen with CGF as grafting materials after OSFE. Although previous research has explored the use of collagen combined with CGF membranes for alveolar ridge preservation, demonstrating enhanced soft tissue healing [52], this study uniquely focuses on the application of this combination in the context of OSFE. By addressing this specific clinical scenario, our study contributes new insights into the potential benefits of this grafting combination for promoting bone regeneration and preserving the sinus membrane following sinus augmentation procedures. Moreover, a previous animal study confirmed the positive effects of combining the key growth factor in CGF with Bio-Oss collagen for bone formation [53]. This combination was found to activate the PI3K/AKT signaling pathway in a rat cranial defect model, a mechanism known to play a critical role in regulating osteogenesis and bone remodeling. The activation of this signaling pathway suggests that the synergistic effects of CGF and Bio-Oss collagen may enhance cellular processes involved in bone regeneration, offering a promising therapeutic approach for improving bone healing in clinical settings.

When RBH is severely defected, the implant initial stability is likely to be poor. The application of bone graft materials can strengthen the initial stability, ISQ measured after second stage surgery was significantly increased in Group B compared to Group A, but not compared to Group C. Nevertheless, bone density was increased in Groups B and C compared to Group A at three-time points follow-up, confirming new bone formation in Group C. Bone density was positively correlated with ISR at both T1 and T2. This result is compatible with a previous study which radiographically evaluated bone morphogenetic protein-2 loaded Bio-Oss collagen for OSFE with simultaneous implant placement in atrophic maxilla. The study recorded high levels of bone density, ranging from 643 to 1201 HU with minimal marginal bone loss and good implant stability after 3 years [49]. Another radiographic study indicated a significant increase in bone density with the application of CGF alone after lateral sinus augmentation and simultaneous implantation compared to no grafting in the atrophic posterior maxilla [54].

The promotion of osseointegration and reduction of bone resorption by adding CGF to Bio-Oss bone grafts has been demonstrated in a previous animal study on extracted socket preservation [55]. However, concerns are rising about the long-term safety of bovine-derived xenografts [56]. In this study, we propose the combination of Bio-Oss collagen with CGF to address these concerns and enhance osseointegration and bone formation. Collagen's soft, flexible, and spongy nature, combined with the mechanical solidity of inorganic bone particles, contributes to sustaining the achieved elevation after sinus augmentation. In addition, collagen's plastic cohesive feature after hydration makes it easier to form and use as a grafting material for OSFE, reducing the incidence of Schneiderian membrane perforation. OSFE with the application of Bio-Oss collagen graft has been proven to improve the quality of the postoperative patient experience [57]. Collagen has proven to stimulate bone formation in bone defects, non-healing extraction sockets, and OSFE with simultaneous implant placement [25, 27, 58, 59]. Possibly, CGF may play a role to overcome the degradation and high absorption rate of collagen by stimulating subsequent osteogenesis and bone formation through the PI3K/AKT signaling pathway. A histological study by Ghasemirad et al. indicated a significantly increased amount of endo-sinus newly-formed bone with the application of CGF after lateral sinus augmentation in the atrophic maxilla compared to the bovine xenograft group at the 6-month time point [60]. However, further investigations are needed to verify this pathway in future research. In our study, we sought to enhance the effectiveness of OSFE by introducing a novel combination of grafting materials. While several recent advancements focus on introducing new techniques to improve internal sinus lifting, our approach emphasizes optimizing the regenerative potential of the procedure through the use of innovative grafting materials. In comparison to these newly developed alternatives to OSFE, osseodensification, similarly to OSFE, demonstrated effective membrane lifting and superior endo-sinus bone gain when grafting materials were applied in cases of atrophic maxilla, as observed at the six-month follow-up [61]. Notably, the previous study reported no instances of implant failure, further emphasizing the favorable clinical outcomes associated with this approach. Additionally, MIAMBE

technique has been used in severely atrophic maxilla and proved its safety achieving high patient satisfactions and low pain score with relatively accepted bone gain [62]. Furthermore, hydraulic sinus lift with immediate implant placement—without the use of grafting materials—has achieved a 5–6 mm bone gain at the six-month follow-up, accompanied by a 100% success rate, further underscoring its clinical efficacy and reliability [63]. These findings collectively underscore the potential of various approaches to enhance sinus augmentation outcomes, with the grafting material combination proposed in our study offering a promising alternative for optimizing bone regeneration and improving implant success.

In addition, our results indicated increased patient satisfaction VAS scores, decreased postoperative pain VAS scores, and significantly more positive responses regarding willingness to undergo a similar procedure in the future with the application of Bio-Oss collagen and CGF combination after OSFE in Group C compared to Group B. This is consistent with previous reports indicating that OSFE with Bio-Oss collagen application is accompanied by high patient satisfaction, minimal postoperative pain, and reduced fear of undergoing similar surgical procedures [32, 57]. Additionally, our findings closely align with those of Yan Dai et al.'s study [64], demonstrating that it is highly valuable for alleviating postoperative symptoms and providing pain relief. Moreover, our results indicate a critical need to find alternative procedures that improve patients' postoperative experiences, especially in cases of atrophic maxilla which require careful considerations. The combination of Bio-Oss collagen and CGF after OSFE and simultaneous implantation could be an effective alternative. After radiological evaluation, the indicators of endo-sinus bone diameters and bone density in this study suggest a potential positive impact of the combination of bone collagen with CGF on soft tissue healing and endo-sinus bone formation. This combination contributes to increased implant stability, survival, and longevity, with evidence of improving the postoperative patient experience and providing pain relief.

This research has several constraints. Firstly, the study duration was one year after functional loading of final restorations; therefore, further studies with a larger sample size and a longer-term follow-up are needed to evaluate the lifespan of implants after the application of the Bio-Oss collagen and CGF combination. Secondly, while CBCT offers a precision of 0.01 mm, its capability to accurately represent internal soft tissue structures and lesions is limited. Additionally, there is a limited correlation between CBCT and Hounsfield Units for the standardized quantification of bone density. This discrepancy results in an overestimation of bone quantity when compared to the gold standard of micro-CT [65]. Despite these limitations, the structural pattern of the alveolar bone, which is considered the second most important factor in assessing bone quality, remains consistent across CBCT machines with the highest resolution [66]. Thirdly, this research was based on radiographic evaluation to measure endo-sinus bone formation. Further investigations are needed to elucidate the mechanisms and signaling pathways underlying the endo-sinus osteogenesis process. Another limitation of this study lies in its insufficient consideration of the variability in implant macrogeometry when assessing survival rates. Although three distinct implant designs were utilized, the study did not perform a detailed analysis of specific macrogeometric characteristics such as thread pitch, shape, or diameter and their potential impact on outcomes. This oversight may limit the applicability of the findings to other implant designs, reducing the study's external validity and its relevance to broader clinical contexts. Despite these limitations, the study offers valuable insights into endo-sinus bone formation and implant survival. While further investigations into osteogenesis mechanisms and implant macrogeometry are needed, the findings provide a strong foundation for future research and contribute meaningfully to the field.

Conclusions

Based on the findings and within the limitations of this prospective study, the combination of collagen and CGF as a grafting material has demonstrated reliability as a protocol for OSFE. This method has shown particular efficacy for simultaneous implant placement in the atrophic posterior maxilla with a RBH of 5 mm or less, yielding significant endo-sinus bone gain and high levels of patient satisfaction. Future studies are warranted to elucidate the intrinsic mechanisms driving new endo-sinus bone formation, thereby enhancing our understanding of this approach and its clinical applications.

Abbreviations

OSFE	Osteotome Sinus Floor Elevation
ABW	Alveolar Bone Width
RBH	Residual Bone Height
CGF	Concentrated Growth Factor
CBCT	Cone Beam Computed Tomography
ISQ	Implant Stability Quotient
IPL	Implant Protrusion Length
H	Height of the Apical Bone
D	Graft Size
SL	Sinus Lift
VBR	Vertical Bone Resorption
TBR	Total Bone Resorption
B	Bone Density
VAS	Visual Analog Scale
PI3K	The Phosphoinositide 3-Kinase

AKT Serine-Threonine Kinase

Authors' contributions
The research was conducted by B.SH, who also contributed to the data analyses and authored the manuscript. S.H. contributed to data analysis and edited the manuscript. B.M contributed to data collection. J.Q supervised the research process. All authors reviewed and approved the final text.

Funding
This work was supported by the National Natural Science Foundation of China (Project Number: 82271003), the National Key Research and Development Program sub-project (Project Number: 2023YFC2413605), the Natural Science Foundation of Jiangsu Province (Project Number: BK20241865), and the Jiangsu Province Capability Improvement Project through Science, Technology, and Education-Jiangsu Provincial Research Hospital Cultivation Unit (Project Number: YJXYYJSDW4), Jiangsu Provincial Medical Innovation Center (Project Number: CXZX202227).

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study complies the Declaration of Helsinki and the Good Clinical Practice guidelines, and was approved by Medical Ethics Committee, School of Stomatology, Nanjing Medical University, China (Approval number: PJ2020-141–001). Informed consent for data evaluation and publishing has been obtained from all included subjects.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Oral Implantology, Affiliated Hospital of Stomatology, Nanjing Medical University, Nanjing 210029, PR China. [2]The Key Laboratory of Modern Toxicology of Ministry of Education, School of Public Health, Nanjing Medical University, Nanjing 211166, PR China. [3]Jiangsu Key Laboratory of Oral Disease, Nanjing Medical University, Nanjing 210029, PR China.

Received: 16 April 2024 Accepted: 9 December 2024
Published online: 19 December 2024

References

1. Kondo T, et al. Current perspectives of residual ridge resorption: pathological activation of oral barrier osteoclasts. J Prosthodont Res. 2023;67(1):12–22.
2. Tolstunov L. Implant zones of the jaws: implant location and related success rate. J Oral Implantol. 2007;33(4):211–20.
3. Al-Sabbagh M, Bhavsar I. Key local and surgical factors related to implant failure. Dental Clinics. 2015;59(1):1–23.
4. Summers RB. The osteotome technique: Part 3--Less invasive methods of elevating the sinus floor. Compendium (Newtown, Pa). 1994;15(6):698, 700, 702–4 passim; quiz 710.
5. Nedir R, et al. Osteotome sinus floor elevation technique without grafting: a 5-year prospective study. J Clin Periodontol. 2010;37(11):1023–8.
6. Nedir R, et al. Osteotome sinus floor elevation with and without grafting material in the severely atrophic maxilla A 1-year prospective randomized controlled study. Clin Oral Implants Res. 2013;24(11):1257–64.
7. Yang J, et al. Radiological changes associated with new bone formation following osteotome sinus floor elevation (OSFE): a retrospective study of 40 patients with 18-month follow-up. Med Sci Monit. 2018;24:4641.
8. Tang C, et al. Simultaneous placement of short implants (≤ 8 mm) versus standard length implants (≥ 10 mm) after sinus floor elevation in atrophic posterior maxillae: a systematic review and meta-analysis. Int J Implant Dent. 2022;8(1):45.
9. Si MS, et al. Osteotome sinus floor elevation with or without grafting: a 3-year randomized controlled clinical trial. J Clin Periodontol. 2013;40(4):396–403.
10. Karaca Ç, et al. Evaluation of Sinus Membrane Perforation in Osteotome Sinus Floor Elevation With and Without Grafting. J Oral Implantol. 2022;48(6):550–6.
11. Wang Q, Li D, Tang Z. Sinus floor elevation and simultaneous dental implantation: A long term retrospective study of sinus bone gain. Beijing Da Xue Xue Bao Yi Xue Ban J of Peking University Health Sci. 2019;51(5):925–30.
12. Moraschini V, et al. Maxillary sinus floor elevation with simultaneous implant placement without grafting materials: a systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2017;46(5):636–47.
13. Chen H, et al. Osteotome sinus floor elevation with concentrated growth factor and simultaneous implant placement with or without bone grafting: a retrospective study. Int J Oral Maxillofac Surg. 2022;51(8):1078–84.
14. Cardaropoli D, et al. Soft tissue contour changes at immediate implants: a randomized controlled clinical study. Int J Periodontics Restorative Dent. 2014;34(5):631–7.
15. Marković A, et al. Two-center prospective, randomized, clinical, and radiographic study comparing osteotome sinus floor elevation with or without bone graft and simultaneous implant placement. Clin Implant Dent Relat Res. 2016;18(5):873–82.
16. Kothari N, Jadhav V, Patil S. Different Techniques For Sinus Floor Elevation: A Review Part II–Indirect Techniques. Indian J Contemp Dent. 2021;9(1):1–4.
17. Alsharekh MS, et al. Evolving Techniques and Trends in Maxillary Sinus Lift Procedures in Implant Dentistry: A Review of Contemporary Advances. Cureus. 2024;16(10): e71424.
18. Cao DC, et al. Efficiency of guided bone regeneration in vertical bone augmentation with titanium-reinforced PTFE membrane and platelet-rich fibrin. VNUHCM J Health Sci. 2022;3(2):press-press.
19. Yamada Y, et al. Osteotome technique with injectable tissue-engineered bone and simultaneous implant placement by cell therapy. Clin Oral Implant Res. 2013;24(4):468–74.
20. Zitzmann NU, et al. Alveolar ridge augmentation with Bio-Oss: a histologic study in humans. Int J Periodontics Restorative Dent. 2001;21(3):288–95.
21. Aludden H, et al. Lateral ridge augmentation with Bio-Oss alone or Bio-Oss mixed with particulate autogenous bone graft: a systematic review. Int J Oral Maxillofac Surg. 2017;46(8):1030–8.
22. Sayardoust S, Norstedt W, Shah FA. The long-term impact of alveolar ridge preservation with xenograft bone mineral on peri-implant health after 5 years in function: A retrospective cohort study of 108 patients assessed clinically and radiologically. Clin Exp Dent Res. 2022;8(3):640–9.
23. Rodriguez AE, Nowzari H. The long-term risks and complications of bovine-derived xenografts: A case series. J Indian Soc Periodontol. 2019;23(5):487.
24. Keil C, et al. Histological evaluation of extraction sites grafted with Bio-Oss Collagen: Randomized controlled trial. Ann Anat. 2021;237:151722.
25. Starch-Jensen T, Bruun N, Spin-Neto R. Outcomes following osteotome-mediated sinus floor elevation with Bio-Oss Collagen or no grafting material: a one-year single-blind randomized controlled trial. Int J Oral Maxillofac Surg. 2023;52(9):988–97.
26. Araujo MG, Liljenberg B, Lindhe J. Dynamics of Bio-Oss® Collagen incorporation in fresh extraction wounds: an experimental study in the dog. Clin Oral Implant Res. 2010;21(1):55–64.
27. Tirone F, Salzano S, Pagano M. Histologic and radiographic analysis of nonhealing extraction sockets treated with Bio-Oss Collagen after a 4-month healing period: a prospective descriptive study in humans. Int J Periodontics Restorative Dent. 2019;39(4):561–8.
28. Natto ZS, Parashis AO, Jeong YN. Soft-Tissue Changes After Using Collagen Matrix Seal or Collagen Sponge With Allograft in Ridge Preservation: A Randomized Controlled Volumetric Study. J Oral Implantol. 2020;46(6):588–93.

29. Heberer S, et al. Histomorphometric analysis of extraction sockets augmented with Bio-Oss Collagen after a 6-week healing period: a prospective study. Clin Oral Implant Res. 2008;19(12):1219–25.
30. Heinemann F, et al. Bone level change of extraction sockets with Bio-Oss collagen and implant placement: a clinical study. Ann Anat. 2012;194(6):508–12.
31. Starch-Jensen T, Bruun NH, Spin-Neto R. Endo-sinus bone gain following osteotome-mediated sinus floor elevation with Bio-Oss Collagen compared with no grafting material: a one-year single-blind randomized controlled trial. Int J Oral Maxillofac Surg. 2023;52(11):1205–15.
32. Dai Y, et al. Clinical efficacy of mineralized collagen (MC) versus anorganic bovine bone (Bio-Oss) for immediate implant placement in esthetic area: a single-center retrospective study. BMC Oral Health. 2021;21(1):390.
33. Kim T-H, et al. Comparison of platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factor (CGF) in rabbit-skull defect healing. Arch Oral Biol. 2014;59(5):550–8.
34. Xu Y, et al. One-year results evaluating the effects of concentrated growth factors on the healing of intrabony defects treated with or without bone substitute in chronic periodontitis. Med Sci Monit. 2019;25:4384–9.
35. Zhu Y, et al. The Ability and Mechanism of nHAC/CGF in Promoting Osteogenesis and Repairing Mandibular Defects. Nanomaterials. 2022;12(2):212.
36. Al-Aroomi OA, et al. Effectiveness of concentrated growth factors with or without grafting materials in maxillary sinus augmentation: a systematic review. BMC Oral Health. 2024;24(1):1275.
37. Adalı E, et al. Does concentrated growth factor used with allografts in maxillary sinus lifting have adjunctive benefits? J Oral Maxillofac Surg. 2021;79(1):98–108.
38. Sohn D-S, et al. Bone regeneration in the maxillary sinus using an autologous fibrin-rich block with concentrated growth factors alone. Implant Dent. 2011;20(5):389–95.
39. Park S, et al. Sample size calculation in clinical trial using R. J Minim Invasive Surg. 2023;26(1):9–18.
40. Mijiritsky E, et al. Use of PRP, PRF and CGF in periodontal regeneration and facial rejuvenation—a narrative review. Biology. 2021;10(4):317.
41. Humayun SIH, et al. Regenerative potential of different growth factors (PRP, PRF, AND CGF) in sinus augmentation procedures-a systematic review. Pakistan Oral Dental J. 2022;42(3):141–8.
42. Tamer Y. Evaluation of immediate implant placement with osteotome sinus floor elevation without graft material. Niger J Clin Pract. 2023;26(3):274–9.
43. Kim HR, et al. The use of autologous venous blood for maxillary sinus floor augmentation in conjunction with sinus membrane elevation: an experimental study. Clin Oral Implant Res. 2010;21(3):346–9.
44. Chen L, et al. Efficacy of concentrated growth factor (CGF) in the surgical treatment of oral diseases: a systematic review and meta-analysis. BMC Oral Health. 2023;23(1):712.
45. Malcangi G, et al. Maxillary Sinus Augmentation Using Autologous Platelet Concentrates (Platelet-Rich Plasma, Platelet-Rich Fibrin, and Concentrated Growth Factor) Combined with Bone Graft: A Systematic Review. Cells. 2023;12(13):1797.
46. Chen Y, et al. Inlay osteotome sinus floor elevation with concentrated growth factor application and simultaneous short implant placement in severely atrophic maxilla. Sci Rep. 2016;6(1):27348.
47. Kang J, et al. Comparative analysis of the in vivo kinetic properties of various bone substitutes filled into a peri-implant canine defect model. J Periodontal Implant Sci. 2024;54(2):6–107.
48. 杨婷婷, et al., 两种材料联合 Bio-Oss® 骨粉在后牙区拔牙位点保存术中的应用效果研究. 中国实用口腔科杂志. 2022;15(2):161–166.
49. An X, et al. Immediate nonfunctional loading of implants placed simultaneously using computer-guided flapless maxillary crestal sinus augmentation with bone morphogenetic protein-2/collagen matrix. Clin Implant Dent Relat Res. 2019;21(5):1054–61.
50. Cosola S, et al. Radiographic and Histomorphologic Evaluation of the Maxillary Bone after Crestal Mini Sinus Lift Using Absorbable Collagen—Retrospective Evaluation. Dent J. 2022;10(4):58.
51. Leighton Y, et al. Autologous fibrin glue with collagen carrier during maxillary sinus lift procedure. J Craniofac Surg. 2019;30(3):843–5.
52. Liu Y, et al. Clinical applications of concentrated growth factors membrane for sealing the socket in alveolar ridge preservation: a randomized controlled trial. Int J Implant Dent. 2022;8(1):46.
53. Dong K, et al. The extract of concentrated growth factor enhances osteogenic activity of osteoblast through PI3K/AKT pathway and promotes bone regeneration in vivo. Int J Implant Dent. 2021;7(1):70.
54. Shetty M, Kalra R, Hegde C. Maxillary sinus augmentation with concentrated growth factors: radiographic evaluation. J Osseointegration. 2018;10(4):109–14.
55. Beibei L, Zhiyu C, Shuo Y. Effect of CGF and Bio-oss ratio on site preservation. Chin J Oral Implantol. 2020;25(4):151–4.
56. Rodríguez ÁE, Nowzari H. The long-term risks and complications of bovine-derived xenografts. Revista de la Asociación Dental Mexicana. 2020;77(2):108–16.
57. Starch-Jensen T, Bruun NH. Patient's perception of recovery after osteotome-mediated sinus floor elevation with Bio-Oss collagen compared with no grafting material: a randomized single-blinded controlled trial. Int J Implant Dent. 2021;7(1):20.
58. Wong R, Rabie A. Effect of bio-oss® collagen and collagen matrix on bone formation. Open Biomed Eng J. 2010;4:71–6.
59. Huang J, et al. Dynamics and risk indicators of intrasinus elevation height following transalveolar sinus floor elevation with immediate implant placement: a longitudinal cohort study. Int J Oral Maxillofac Surg. 2021;50(1):109–15.
60. Ghasemirad M, et al. Histological examination of the effect of concentrated growth factor (CGF) on healing outcomes after maxillary sinus floor augmentation surgery. J Med Life. 2023;16(2):267–76.
61. Saglanmak A, et al. Maxillary Sinus Floor Elevation and Simultaneous Implant Installation via Osseodensification Drills: A Retrospective Analysis of Bone Gain in 72 Patients Followed for 6 Months. J Clin Med. 2024;13(8):2225.
62. López-Quiles J, et al. Maxillary sinus balloon lifting and deferred implantation of 50 osseointegrated implants: a prospective, observational, non-controlled study. Int J Oral Maxillofac Surg. 2018;47(10):1343–9.
63. Manekar VS. Graftless crestal hydraulic sinus lift with simultaneous implant insertion. Natl J Maxillofac Surg. 2020;11(2):213–8.
64. Dai Y, et al. Efficacy of concentrated growth factors combined with mineralized collagen on quality of life and bone reconstruction of guided bone regeneration. Regen Biomater. 2020;7(3):313–20.
65. Kamburoğlu K. Use of dentomaxillofacial cone beam computed tomography in dentistry. World J Radiol. 2015;7(6):128–30.
66. Van Dessel J, et al. Accuracy and reliability of different cone beam computed tomography (CBCT) devices for structural analysis of alveolar bone in comparison with multislice CT and micro-CT. Eur J Oral Implantol. 2017;10(1):95–105.

Publisher's Note