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Multivariable analysis of absorbable collagen sponge graft for the maxillary sinus floor elevation and augmentation

상악동저거상술 및 증강술을 위한 흡수성

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- Abstract -

Multivariable analysis of absorbable collagen sponge graft for the maxillary sinus floor elevation and augmentation

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Background: Absorbable collagen is commonly used as a bioscaffold for tissue engineering especially for bone regeneration, given its biocompatibility, biodegradability, and osteoconductive properties. It serves as a physical scaffold for cell attachment and growth by affecting cell behavior through receptor-mediated interactions. The purpose of the present study was to assess the changes in bone height and volume induced by absorbable collagen sponge (ACS) grafted into the maxillary sinus floor elevation procedures and to identify factors associated with these changes.

Materials and methods: After the sinus membrane elevation through a crestal (CA) or lateral (LA) approach, ACS (Ateloplug, Bio-land, Cheong-ju, South Korea) was inserted, and dental implants were placed simultaneously. Changes in bone height and bone volume were evaluated by two- (2D) and three- (3D) dimensional analyses of cone-beam

computed tomography (CBCT) images. Factors associated with these changes were evaluated, including patient factors (age, sex, and smoking status), and implant- and region of interest (ROI)-related factors (implant survival, sinus infection, location, span, implant stability quotients, number of ACS, perforation, sinus membrane elevation height, bone height, bone height change, and bone volume change). Changes in sinus bone height and bone volume at 12 months were the primary outcomes. Variables significantly associated with changes in sinus bone height and bone volume were evaluated by uni- and multivariable analyses based on the generalized estimating equation.

Results: Overall, medical records for 108 patients were collected and evaluated retrospectively, including at 182 implant sites (CA, 53; LA, 129), and 135 ROIs (CA, 45; LA, 90). Implant stability quotients were acceptable in both groups (CA, 82.66 ± 6.61; LA, 81.16 ± 5.41). None of these patients developed sinus infections or showed implant losses. Bone height changes from baseline to postoperative 12 months were 2.16 ± 1.51 mm (residual bone height, 8.11 ± 1.58 mm) in the CA and 4.62 ± 2.04 mm (residual bone height, 5.54 ± 2.52 mm) in the LA ($p < 0.001$). Factors significantly associated with bone height change in the CA group included sex ($p < 0.001$), perforation ($p < 0.001$), and residual bone height ($p < 0.001$), whereas factors significantly associated with bone height change in the LA group included sinus membrane elevation height ($p = 0.013$) and residual bone height ($p < 0.001$). At residual bone heights ≥5 mm, bone height changes were significantly greater in the LA than in the CA group ($p < 0.05$). Bone volume changes from the sinus floor were 159.38 ± 134.52 mm^3 in the CA and 486.83 ± 253.14 mm^3 in the LA group. Bone volume changes in the CA group was significantly affected by the number of ACS ($p < 0.001$) and perforation of sinus membrane ($p < 0.001$),

whereas bone volume changes in the LA group was significantly affected by the number of ACS (p = 0.001).

Conclusions: New bone formation was observed on 2D and 3D analyses after the maxillary sinus floor elevation using ACS. Bone height changes in the CA group were significantly affected by sex, perforation, and residual bone height, whereas bone height changes in the LA group were significantly affected by the sinus membrane elevation height and residual bone height. The number of ACSs affected bone volume change in both the LA and CA groups, with perforation particularly affecting these changes during the CA procedure. Collectively, these findings indicate that the maxillary sinus floor elevation using ACS seemed to be a viable and safe option for patients who require increases in bone height and volume of the maxillary sinus floor for dental implant placement.

Keywords: implant, maxillary sinus, crestal approach, lateral approach, tissue engineering, bioscaffold, bone graft

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CONTENTS

I. INTRODUCTION

Maxillary sinus elevation is regarded as a predictable and effective technique for augmenting atrophic maxillary alveolar ridges. The choice of a crestal (CA) or lateral (LA) approach depends on a number of factors, such as sinus pneumatization, residual alveolar bone volume, and structural sinus anatomy.[1, 2] Various types of bone substitutes (autogenous, xenogeneic, allogeneic, or alloplastic) are available for maxillary sinus elevation and they all provide satisfactory results because Schneiderian membrane serves as encapsulated space insulation for an osteogenic effect.[3, 4]

Factors that should be considered when selecting graft material for sinus augmentation include the length of time the grafted material maintains an adequate volume until the completion of new bone formation, and its efficiency in maintaining factors critical for osteogenesis. Because bone graft in the maxillary sinus after membrane elevation differs fundamentally from bone graft elsewhere in the jaw bones such as alveolar ridge augmentation, biomaterials for sinus augmentation that have even minimal scaffolding benefits may yield satisfactory results.[3, 4] Studies of alternative sinus augmentation techniques have evaluated the use of absorbable collagen sponge (ACS)[5-10], gelatin sponge[11], and oxidized regenerated cellulose,[12] rather than particulate bone substitutes, and even a graftless lateral sinus lift approach (GLSLA) using only blood clot has been proposed.[4, 7, 13-18] These surgical techniques generally eliminate the possibility of allergic reaction and maxillary sinus infections caused by bone substitutes.[6, 8, 9, 19-21] In addition, these graft materials are less expensive than bone substitutes and are technically easy to handle, reducing the operation time.[7] If these techniques have the same efficacy as sinus

augmentation using bone substitutes, they may be satisfactory for both patients and clinicians.

In a GLSLA study, Scala *et al*. emphasized the need for a space maintainer during sinus augmentation to prevent the unsupported Schneiderian membrane from collapsing, thus limiting sinus bone gain.[14] ACS acts as a scaffold in this setting, takes a while to be absorbed, and subsequently maintains sufficient volume to elevate the sinus membrane.[6-8]

Many sinus augmentation studies conducted to date have used ACS as a carrier of bone morphogenetic protein-2 (BMP-2).[9, 22-28] Recently, there have been active investigations of ACS alone.[6-9] Caneva *et al.* have histologically documented the osteoconductive properties of ACS in rabbits.[20] New bone formation and stable results have shown in clinical studies (both prospective and retrospective) about sinus floor elevation using ACS, with or without simultaneous implant placement.[6-9]

Unlike typical bone substitutes, which experience very little change in volume and shape, ACS may be absorbed and its dimensions changed substantially during the postoperative healing phase.[20] For this reason, it is difficult to predict volumetric changes over time or measure quantities of new bone after sinus floor elevation using ACS. To date, there are no precise clinical data to determine the volume of ACS sufficient for new bone formation in the sinus cavity, and no studies have identified factors affecting sinus bone formation. Although ongoing studies are evaluating ACS-based sinus floor elevation technique, most studies to date have been case reports or series with a small number of cases, and the length of implant fixture used for sinus floor elevation has not been uniform. Moreover, no studies to date have compared CA and LA for sinus floor elevation

using ACS.

The purpose of the present study was to assess changes in bone height and volume of the maxillary sinus floor and the degrees of postoperative implant stability achieved when performing sinus floor elevation procedures using ACS grafts through CA and LA. This study hypothesized that ACS could adequately replace bone substitutes, promoting sufficient bone formation and subsequent implant stability after maxillary sinus floor elevation. In addition, the factors affecting changes in bone height and bone volume were evaluated in patients who underwent sinus floor elevation using ACS.

II. MATERIALS AND METHODS

Patient selection

The present study was designed and implemented as a retrospective cohort study. All patient participants underwent posterior maxillary dental implant installation at the Department of Oral and Maxillofacial Surgery of Seoul Metropolitan Government - Seoul National University Boramae Medical Center (SMG-SNU BMC) (Seoul, Korea) between 2017 and 2021. The protocol was approved from the institutional review board of SMG-SNU BMC (IRB No. 20-2017-25), adhering to tenets of the 1964 Declaration of Helsinki and its later amendments. All surgeries were performed by a single experienced oral and maxillofacial surgeon (YSH).

Criteria for study inclusion were as follows: (1) adults who had completed jaw growth; (2) patients who required tooth rehabilitation by implant surgery in the maxillary premolar or molar areas; (3) patients who had intact maxillary sinuses without pathological findings such as tumors, cysts or sinusitis; and (4) patients who underwent simultaneous sinus elevation and implant placement.

Surgical procedures

Bone level implants (TS III SA, Osstem Implant Co., Seoul, Korea) used for implant surgery in the premolar region were 4 mm in diameter and 11.5 mm in length, whereas implants in the molar region were 5 mm in diameter and 11.5 mm in length. The ACS

used in this study was Ateloplug (Bio-land, Cheong-ju, South Korea), which has a sponge block configuration and a bullet-shaped matrix for easy placement at the surgical site. Medium-sized Ateloplug is 15 mm in diameter and 25 mm in length, and has a volume of 4.42 cm^3. Each ACS was divided into four pieces, each of which was used for surgery.

- Lateral approach (LA)

After injection of local anesthetic (2% lidocaine HCl), a full thickness mucoperiosteal flap was raised through one midcrestal and two vertical incisions. A bony window in the lateral sinus wall was created using a low-speed surgical bur to allow access to the sinus membrane (Figure 1A). The bony window was separated from the sinus membrane using sinus curettes, and the sinus membrane was carefully elevated from the surrounding wall to make space for implant fixtures (Figure 1B). After final drilling for implant installation, ASCs were inserted into the space created (Figure 1C). Following installation of the implants (Figure 1D), additional ACSs were inserted into the sinus space (Figure 1E). The bony window was returned to its original configuration, covering the antrostomy (Figure 1F), and the flap was repositioned and sutured using 4-0 Dafilon sutures (B. Braun Medical, Johannesburg, South Africa). Six months after the surgery, implant stability quotient (ISQ) was measured by AnyCheck (Neobiotech, Seoul, South Korea) device, and the prosthetic phase commenced.

- Crestal approach (CA)

After injection of local anesthetic, a midcrestal incision was made, which enabled flap elevation. Drilling was performed to a depth of 1 mm from the sinus floor (pending final

preparations). The sinus floor was elevated using a crestal osteotome technique while cautiously pushing the cut bony segment at least 2 mm into the sinus cavity, thereby elevating the sinus lining (Figure 2A). ACSs were inserted into the newly lifted space (Figure 2B), followed by insertion of the implants and repositioning of the flap (Figure 2C). Six months after surgery, ISQ was determined, and the prosthetic process was performed.

CBCT data acquisition

The progress of bony regeneration at sinus elevation sites was assessed by cone-beam computed tomography (CBCT). CBCT images were obtained before and immediately after surgery, as well as 6 and 12 months after surgery, using a Dinnova 3 scanner (HDX Corp, Seoul, Korea) with a scan time of 7 sec; a voltage of 95 kV; a tube current of 9 mA; a voxel size of 0.3 mm; and a field of view of 9 mm. All images were stored in Digital Imaging and Communication in Medicine (DICOM) format.

Two-dimensional (2D) analysis of bone height

Changes in sinus floor bone height following implant insertion were evaluated by 2D analysis of CBCT images. DICOM data were reconstructed at 0.5 mm thickness using an INFINITT Picture Archiving and Communication System (INFINITT PACS; INFINITT Healthcare, Seoul, Korea). Images were reconstructed in the multiplanar mode, relying on the buccopalatal plane for radiographic evaluations. An arc was drawn along maxillary

arch contour in the axial view, drawing a tangent to the arc where it met the implant center. A plane perpendicular to the tangent and parallel to the long axis of the implant was selected as a buccopalatal plane. The implant center was identified by means of a cover screw (Figure 3A).

The radiographic measurements were performed as follows: (1) Residual bone height (T0) - the distance between the implant platform and the sinus floor at midportion of implant, immediately after the surgery (Figures 3B and C); (2) Sinus membrane elevation height (E) - the distance between the upper border of the elevated sinus membrane and the sinus floor at the midportion of the implant, immediately after surgery (Figure 3C); (3) Bone height, 6 months (T1) and 12 months (T2) postoperatively - the distance between the implant platform and the top of regenerated sinus bone at the midportion of the implant (Figures 3D and E); (4) Bone height change, 6 months postoperatively (G1) - T1 minus T0 (Figure 3D); (5) Bone height change, 12 months postoperatively (G2) - T2 minus T0 (Figure 3E); and (6) Bone height change, 6 to 12 months postoperatively (G3) - T2 minus T1.

Three-dimensional (3D) analysis of bone volume

Volumetric changes in the sinus floor corresponding to each operative site were evaluated by 3D analysis of CBCT images. 3D reconstructions of anatomic structures were generated, and CBCT images obtained before and 12 months after surgery were superimposed using CT-Analyze software v1.11 (Bruker, Kontich, Belgium). Briefly, DICOM data were converted to isotropic voxel size, and images were rendered with

thresholds ranging from 70 to 833 Hounsfield Units (HU) to identify bone structures. The segmented multiplanar images were reconstructed into a 3D virtual model. Preoperative and postoperative 12 months 3D images of anatomical landmarks were superimposed, including the anterior nasal spine (ANS), posterior nasal spine (PNS), and residual teeth. After identifying regions of interest (ROI) on the superimposed images, changes in bone volume in each assessed area were determined by subtracting the volumes on preoperative images from the volumes on postoperative 12 months images (Figure 4).

Intra-rater reliability

Intrarater reliability was evaluated by calculating intraclass correlation coefficients (ICCs). Twenty of the 182 subjects assessed by 2D analyses and 20 of the 135 ROIs assessed by 3D analyses were randomly selected and measured twice.

Statistical analysis

Changes in bone height and volume from before to after sinus floor elevation using ACS were analyzed using the generalized estimating equation (GEE) method. This method does not necessarily depend on a strict covariance structure. The primary outcome measures were changes in bone height (G2) on 2D analysis and changes in bone volume on 3D analysis at postoperative 12 months. GEE-based univariable and multivariable analyses were performed to identify variables significantly associated with changes in

bone height (G2) and bone volume. All statistical analyses were performed using SAS v9.4 statistical software (SAS Institute Inc, Cary, NC, USA), with $p < 0.05$ defined as statistically significant.

III. RESULTS

(1) Patient-related factors

Overall, the present study included 108 patients: 59 (54.6%) male and 49 (45.4%) female. The mean ages of patients in CA and LA groups were 66.55 ± 12.48 years and 62.55 ± 12.44 years, respectively. Of the patients in the CA group, 0 (0%) were smokers, and 38 (100%) were nonsmokers, whereas of the patients in the LA group, seven (9.72%) were smokers, and 65 (90.28%) were nonsmokers (Table 1).

(2) 2D analysis of bone height analysis

Implant-related factors

- Clinical findings

Overall, 182 implant sites, including 53 (29.1%) in the CA group and 129 (70.9%) in the LA group, were included in present study. Implant survival rates over 12 months were 100% in both groups. None of these patients experienced sinus infection, even when the sinus membrane was perforated, and none had any signs and symptoms of sinusitis after surgery, and none had radiographic evidence of sinusitis. ISQ values were acceptable in both the CA (82.66 ± 6.61) and LA (81.16 ± 5.41) groups. Locations of implants were more frequently inserted into molar than into premolar areas in both the CA (84.9% [45/53] vs. 15.1% [8/53]) and LA (84.5% [109/129] vs. 15.5% [20/129]) groups. Of the 53 implants in the CA group, 37 (69.8%) were single implants, and 16 (30.2%) were double implants; of the 129 implants in the LA group, 56 (43.4%) were single, 58 (45.0%) were double, and 15 (11.6%) were triple implants. The numbers of ACS used at surgical site were 0.56 ± 0.16 in the CA group and 1.00 ± 0.30 in the LA group. The sinus membrane perforation rate was higher in the CA (24.5% [13/53]) than in the LA (10.9% [14/129]) group (Table 2).

- Radiographic measures

Immediate postoperative sinus membrane elevation heights (E) were 7.88 ± 3.92 mm in the CA and 13.21 ± 3.96 mm in the LA group, and residual bone heights (T0) in these two groups were 8.11 ± 1.58 mm and 5.54 ± 2.52 mm, respectively. Bone heights in the CA

and LA groups were 10.10 ± 1.51 mm and 9.88 ± 1.92 mm, respectively, at 6 months (T1), and 10.27 ± 1.47 mm and 10.16 ± 1.86 mm, respectively, at 12 months (T2). Significant increases in bone height were observed at all periods (G1, G2, and G3) ($p < 0.01$), but the increase in bone height (G2) at 12 months was significantly lower in the CA (2.16 ± 1.51 mm) than in the LA (4.62 ± 2.04 mm) group ($p < 0.001$) (Table 2). In 33 cases (18.1%), new bone extended beyond the apical ends of implants (T2 >11.5 mm), including two (3.8%) in the CA and 31 (24.0%) in the LA group (Figure 5).

Statistical results

- Univariable analysis

Univariable GEE indicated that factors significantly associated with the bone height change (G2) in the CA group included sex ($p = 0.005$), perforation ($p < 0.001$), and T0 ($p < 0.001$), whereas factors significantly associated with G2 in the LA group included E ($p < 0.001$) and T0 ($p < 0.001$) (Table 3). The number of ACS was not a significant variable influencing G2.

- Multivariable analysis

Multivariable GEE indicated that factors significantly associated with G2 in the CA group included sex ($p < 0.001$), perforation ($p < 0.001$), and T0 ($p < 0.001$), whereas factors significantly associated with G2 in the LA group included E ($p = 0.013$) and T0 ($p < 0.001$) (Table 4).

- Bone height change (G2) relative to residual bone height

The less residual bone height, the more new bone was formed. At residual bone heights ≥5 mm, the increase in sinus bone height was significantly greater in the LA than in the CA group ($p < 0.05$) (Table 5 and Figure 6).

(3) 3D analysis of bone volume

ROI-related factors

- Clinical findings

Overall, 135 ROI images of 125 sinuses were obtained: 45 in the CA and 90 in the LA group. The sinus membrane perforation rate was higher in the CA (26.7% [12/45]) than in the LA (16.9% [13/90]) group. The mean numbers of ACS inserted per ROI were 0.65 ± 0.30 in the CA and 1.42 ± 0.61 in the LA group (Table 6).

- Radiographic measures

The average bone volume changes at the sinus floor were 159.38 ± 134.52 mm^3 in the CA and 486.83 ± 253.14 mm^3 in the LA group (Table 6).

Statistical results

- Univariable analysis

Univariable GEE indicated that factors significantly associated with bone volume changes in the CA group included the number of ACS ($p = 0.005$) and perforation ($p < 0.001$), whereas factors significantly associated with bone volume changes in the LA group included number of ACS ($p = 0.001$) and span ($p = 0.010$) (Table 7 and Figure 7).

- Multivariable analysis

Variables significant in univariable GEE analyses were included in multivariable GEE analyses. To avoid multicollinearity, the final models were chosen by variable selection, such as backward elimination. Multivariable GEE showed that factors significantly associated with bone volume changes in the CA group included the number of ACS ($p < 0.001$) and perforation ($p < 0.001$), whereas the only factor significantly associated with bone volume changes in the LA was the number of ACS ($p = 0.001$) (Table 8).

(4) Intra-rater reliability

ICCs ranged from 0.906 to 0.997, with no significant differences between the two sets of measurements at the 95% confidence level ($p < 0.001$). The ICCs were 0.997 for E, 0.996 for T0, 0.977 for T1, and 0.976 for T2 in 2D analysis, and 0.906 for bone volume change in 3D analysis.

IV. DISCUSSION

Alveolar bone resorption and sinus pneumatization are anatomical situations that hinder implant placement in the posterior maxillary. The role of blood clot in sinus augmentation for the purpose of increasing alveolar bone height is important for new bone formation. The osteoinductive properties thereof in guided bone regeneration and bone grafting have been well established through various studies, involving a wealth of growth factors that initiate and promote bone formation.[29, 30] The blood clot filled in the space formed by Schneiderian membrane elevation also acts as a space maintainer. Given the multiple phases including angiogenesis, migration of osteogenic progenitor cells from adjacent medullary bone to the operative site, and actual bone formation, it is the opinion of certain authors that blood clot alone cannot maintain sufficient space for new bone formation.[16, 30-32]

Absorbable collagen is one of the most common scaffolding materials in bone tissue engineering, providing physical support for cell attachment and growth and influencing cell behavior through receptor-mediated interactions.[1, 33] It is also biocompatible, biodegradable, and osteoconductive in nature.[2] Ateloplug is made of atelocollagen, crosslinked through heat treatment for optimal biocompatibility and minimal antigenicity. It is composed of Type I (85-95%) and Type III (5-15%) collagen derived from porcine skin.[2, 34] The rationale behind its incorporation into ACS is not only preservation of blood clot, but also prevention of the sinus membrane collapse prior to degradation.[34] According to manufacturer, Ateloplug is completely absorbed to the body within 2-4 weeks. Despite its rapid resorption, Ateloplug begins to form new mineralized bone under elevated

Schneiderian membranes within 2 weeks after sinus floor elevation using ACS and serves as a scaffold for space maintenance.[20]

In the present study, ACS placed within the sinus cavity under elevated Schneiderian membrane served as an alternative to bone substitutes in maintaining space. Bone heights 12 months after placement (T2) were 10.27 ± 1.47 mm in the CA and 10.16 ± 1.86 mm in the LA group, providing sufficient new bone to accommodate the 11.5 mm implants. Bone volume changes at 12 months were 159.38 ± 134.52 mm^3 in the CA and 486.83 ± 253.14 mm^3 in the LA group.

Five prior clinical studies and one animal model have evaluated sinus floor elevation using ACS for new bone formation (Table 9).[6-10, 20]. Only two of these studies, however, have involved simultaneous implant placement.[6, 7] Volpe *et al.*[6] performed sinus floor elevation using ACS (36 patients, 36 implants) via CA, confirming new bone formation through periapical radiographs. The mean change in postoperative bone height at 4–6 months was 3.8 ± 1.1 mm (residual bone height, 5.9 ± 1.4 mm) resulting in relatively good stability, as shown by a mean ISQ of 75.8 ± 3.9. Only one patient experienced a sinus perforation, but none experienced a sinus infection. Menassa *et al.*[7] used LA for augmentation, achieving a 12 month sinus bone height increase of 4.4 ± 1.9 mm (residual bone height, 3.5 mm) on periapical radiographs. There were no complications, such as sinus perforation or infection.

Cosola *et al.*[9] and Berberi *et al.*[8] also examined sinus floor elevation using ACS via CA and LA, respectively, both sources confirming new bone formation through CBCT imaging and tissue samples. Core biopsy specimens were collected 6 months after sinus

augmentation during placement of implants. Histologic sections revealed osteocytic activity, vascular ingrowth, and some remnant ACS material (largely absorbed), with well-organized bony trabeculae and marrow (new bone). The sinus bone height increase was 6 mm (residual bone height not determined) and 7.98 ± 1.04 mm (residual bone height, <4 mm) via CA and LA, respectively; and all procedures were free of postoperative complications. Berberi *et al.* recorded a 100% implant survival rate. By comparison, the sinus bone height change in the present study were 3.14 ± 1.60 mm (residual bone height range, 5-7 mm) via CA at postoperative 6 months and 5.68 ± 1.54 mm (residual bone height range, 3-5 mm) via LA at postoperative 12 months. Bone substitutes (autogenous, xenogeneic, allogeneic, or alloplastic) clearly surpass ACS in terms of augmentation volume[20], but the abundance of bone for implantation did not correlate with implant stability or survival.[6, 7, 15, 17, 18, 35] Despite the mean amount of bone height increase in this cohort was inadequate to fully cover the apical ends of fixtures, ISQ scores were acceptable in both groups (CA, 82.66 ± 6.61; LA, 81.16 ± 5.41), and no implant loss was observed during the 12-month follow-up period.

For sinus floor elevation by LA, the handling of window created to access sinus membranes may greatly affect new bone formation. In studies utilizing Bio-Gide membranes[7] or window bone[8] for this purpose, levels of bone height increase have proven satisfactory (4.4 ± 1.9 mm and 7.98 ± 1.04 mm, respectively), whereas histologically verifiable new bone is poorly formed using CollaTape as a barrier membrane or no barrier material at all. Ahn *et al.* found that 11 of 13 specimens lacked any recognizable new bone, and only two specimens harbored small amounts of woven bone.[10] CollaTape is a compressed form of ACS, which, unlike absorbable collagen membrane (ACM), is not

densely structured. It is therefore unable to function as a barrier and is recommended primarily for hemostasis or dressing of wounds. The manufacturer has reported that the duration of intracorporeal resorption of CollaTape is 10–14 days. In contrast, the duration of intracorporeal resorption of an ACM such as Bio-Gide has been reported to be 24 weeks by the manufacturer and 4–8 weeks in another study,[36] largely explaining the failure of CollaTape as a barrier. Use of an ACM barrier in a space intended for new bone growth is already an established technique referred to as guided bone regeneration (GBR) by various clinicians and researchers.[37-39] Significantly more new bone has been found to fill a void in the presence than in the absence of a barrier membrane.[39-44] In the present study, lateral sinus windows were repaired by repositioning window bones, thus increasing the levels of new sinus bone. Complete healing of lateral sinus walls was also confirmed in nearly all cases.

Limitations of these earlier clinical studies[6-10, 20] were the inconsistent or vaguely referenced lengths of installed implants and failures to quantitatively analyze residual bone heights.[7-9, 20] In contrast, the present study analyzed factors likely related to changes in sinus bone height and bone volume, subjecting a number of variables (i.e., residual bone height, number of ACS, sinus elevation height, implant length, change in sinus bone height change, ISQ, survival rate, and postoperative complications) to quantitative analysis. Moreover, to our knowledge, no previous studies had compared changes in sinus bone height and bone volume achieved by the CA and LA methods of sinus floor elevation.

Statistical analyses in the present study showed that parameters affecting changes in

bone height and bone volume differed when using the CA and LA techniques. Analysis of 2D bone height showed that residual bone height (T0) was associated with change in bone height, both by CA and LA. Especially for LA, the less the residual bone height and the higher the sinus membrane elevation (E), the more bone height was increased. Analysis of 3D bone volume demonstrated that the numbers of ACSs affected changes in bone volume in both CA and LA. Sinus perforation was associated with changes in bone height and bone volume via CA, occurring in 24.5% of implants and 26.7% of ROIs, suggesting that overall values were lower when elevations of sinus membranes fell short due to sinus perforation. The perforation rates for LA were lower, occurring in 10.9% of implants and 16.9% of ROIs, and did not significantly affect changes in bone height and bone volume. Because LA allows direct determination of the progress of elevation, a strategically placed ACS may essentially close a perforation site.[45] In contrast, the CA technique is performed blindly, relying on the operator's senses. Sinus perforations are therefore very difficult to recognize intraoperatively and are not easily managed. Postoperative CBCT images in the present study showed ACS migration across a perforated membrane, providing evidence of perforation. Sufficient sinus membrane elevation through retention of graft materials and blood clot was therefore unlikely.

A systematic review reported sinus membrane perforation rates of 19.5% (range, 0–58.3%) using LA and 3.8% (range, 0–21.4%) using CA.[21, 46] However, pinpoint perforations arising during CA are often impossible to detect, suggesting that the actual incidence of these perforations may be higher than reported. A cadaveric CA study found that the sinus membrane perforation rate was 24% (range, 4–25%).[47] Sinus membrane perforations undetected during surgery increase the risk of sinusitis and of implant

failure.[21, 48, 49] The mean incidence of postoperative sinus infection due to graft material has been reported to be 2.9% (range, 0–12%).[21] None of the patients in the present study experienced sinus infection or implant loss due to perforation. Thus, sinus floor elevation using ACS is safe and unassociated with sinus infection.[6, 8, 9]

In the CA group, bone height increases were significantly lower in female than in male (Estimate, -0.940 mm; SE, 0.256; $p < 0.001$). This difference tended to be similar in the LA group, as were bone volume changes after both CA and LA. Because the patients included in the present study were relatively old, with male and female being aged 67.04 ± 13.32 years and 66.30 ± 12.64 years, respectively, impaired bone formation in these women may have been due to hormonal imbalances in postmenopausal women. One of the major changes in postmenopausal women is the reduced ovarian production of estrogens,[50] which act as crucial regulators of osteoblast differentiation and function, and promote the osteogenic differentiation of mesenchymal stem cells. Moreover, estrogens enhance the differentiation of preosteoblasts into osteoblasts, and prolong the lifespan of osteoblasts and osteocytes by suppressing apoptosis.[51] In addition, estrogens stimulate procollagen synthesis as well as IGF1 and TGFβ production by osteoblasts.[52]

Sinus floor elevation using ACS has several advantages, including its relatively shorter operation time and its technical ease of performance. Due to its bullet-shaped matrix, an ACS can be easily inserted deep within sinus cavities. In contrast to particulate-type bone substitutes, ACS is more maneuverable, requiring fewer insertion attempts.

Some may remain skeptical of ACS scaffolding capacity, given its rapid absorption rate [20, 22] and reasoning that inserted implants provide the tenting of the sinus membrane

required for clot maintenance. However, new bone appeared beyond apical ends of inserted implants: 18.1% (n=33) overall, 3.77% (n=2) via CA, and 24.03% (n=31) via LA. In addition, an increased amount of ACS correlated with an increased volume of new bone. New bone has also been observed after sinus membrane elevation and ACS insertion alone, without simultaneous implantation[8, 20]. These findings indicate that ACS acts as scaffolding in this setting.

The results of the present study indicated that sinus membrane elevation height affected the height of new bone formation when sinus membrane perforation was controlled. In addition, the number of ACSs inserted correlated with new bone volume. These findings emphasize the need to insert sufficient quantities of ACS to elevate the sinus membrane as high as possible when performing sinus floor elevation using ACS. The sinus cavity has a three-dimensional structure, differing in the volume of bone augmentation required for each patient and at each implant site. Hence, the aggregate of ACS inserted is not always proportional to the height of sinus membrane elevation. Nevertheless, an increase in the number of ACSs was associated with increased sinus membrane elevation, which may lead to improved outcomes.

A limitation of this study was that although newly formed bones were quantitatively analyzed by CBCT, histological qualitative analysis was not performed. In a previous histological analysis,[8-10] specimens were collected while inserting the implant 6 months after sinus augmentation. However, as in this study, patients undergoing simultaneous sinus floor elevation and implant surgery[6, 7] are reluctant to provide consent for additional surgery for bone biopsy.

V. CONCLUSION

New bone formation was observed on 2D and 3D analyses after the maxillary sinus floor elevation using ACS. Bone height changes in the CA group were significantly affected by sex, perforation, and residual bone height, whereas bone height changes in the LA group were significantly affected by the sinus membrane elevation height and residual bone height. The number of ACSs affected bone volume change in both the LA and CA groups, with perforation particularly affecting these changes during the CA procedure. Collectively, these findings indicate that the maxillary sinus floor elevation using ACS seemed to be a viable and safe option for patients who require increases in bone height and volume of the maxillary sinus floor for dental implant placement.

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Table 1. Patient-related factors in the CA and LA groups

Patient-related factors	CA (n = 38)	LA (n = 72)
Age, yr	66.55 ± 12.48	62.43 ± 12.44
Sex		
Male	16 (42.11)	45 (62.50)
Female	22 (57.89)	27 (37.50)
Smoking		
Smoker	0 (0)	7 (9.72)
Non-smoker	38 (100)	65 (90.28)

Data expressed as n (%) or mean ± SD.

Abbreviations: CA, crestal approach; LA, lateral approach.

Table 2. Implant-related factors in the CA and LA groups

Implant-related factors	CA (n = 53)	LA (n = 129)
Implant survival		
Yes	53 (100)	129 (100)
No	0 (0)	0 (0)
Sinus infection		
Yes	0 (0)	0 (0)
No	53 (100)	129 (100)
Location		
Premolar	8 (15.09)	20 (15.50)
Molar	45 (84.91)	109 (84.50)
Span		
1	37 (69.81)	56 (43.41)
2	16 (30.19)	58 (44.96)
3	0 (0.00)	15 (11.63)
ISQ	82.66 ± 6.61	81.16 ± 5.41
Number of ACSs	0.56 ± 0.16	1.00 ± 0.30
Perforation		
Yes	13 (24.53)	14 (10.85)
No	40 (75.47)	115 (89.15)
Radiographic measures, mm		
E	7.88 ± 3.92	13.21 ± 3.96
Bone height		
T0	8.11 ± 1.58	5.54 ± 2.52
T1	10.10 ± 1.51	9.88 ± 1.92
T2	10.27 ± 1.47	10.16 ± 1.86
Bone height change		
G1	1.99 ± 1.54**	4.35 ± 2.06**
G2	2.16 ± 1.51**	4.62 ± 2.04**
G3	0.17 ± 0.45*	0.28 ± 0.56**

Data expressed as n (%) or mean ± SD.

*$p < 0.01$, ** $p < 0.001$ (based on the generalized estimating equation)

Abbreviations: CA, crestal approach; LA, lateral approach; ISQ, implant stability quotient; ACS, absorbable collagen sponge; E, sinus membrane elevation height; T0, residual bone height; T1, bone height at postoperative 6 months; T2, bone height at postoperative 12 months; G1, bone height change at postoperative 6 months; G2, bone height change at postoperative 12 months; G3, bone height change from 6 to 12 months postoperatively.

Table 3. Univariable analysis of factors associated with bone height changes (G2) (mm) at postoperative 12 months in the CA and LA groups, based on the generalized estimating equation

Predictor variables	CA		LA	
	Estimate (SE)	*p* value	Estimate (SE)	*p* value
Age, yr	0.005 (0.018)	0.781	-0.012 (0.016)	0.447
Sex male (reference) female	-1.082 (0.387)	0.005	-0.731 (0.402)	0.069
Smoking non-smoker (reference) smoker			0.753 (0.949)	0.428
Location premolar (reference) molar	0.675 (0.365)	0.065	0.624 (0.552)	0.259
Span, n	0.191 (0.550)	0.728	-0.372 (0.277)	0.180
Number of ACS, n	1.443 (1.199)	0.229	0.890 (0.734)	0.225
Perforation no (reference) yes	-1.395 (0.402)	< 0.001	0.131 (0.647)	0.840
E, mm	0.131 (0.075)	0.080	0.271 (0.038)	< 0.001
T0, mm	-0.522 (0.095)	< 0.001	-0.553 (0.055)	< 0.001

Abbreviations: CA, crestal approach; LA, lateral approach; SE, standard error; ACS, absorbable collagen sponge; E, sinus membrane elevation height; T0, residual bone height; G2, bone height change at postoperative 12 months.

Table 4. Multivariable analysis of factors associated with bone height changes (G2) (mm) at postoperative 12 months in the CA and LA groups, based on the generalized estimating equation

Predictor variables	CA		LA	
	Estimate (SE)	*p* value	Estimate (SE)	*p* value
Sex male (reference) female	-0.940 (0.256)	< 0.001		
Perforation no (reference) yes	-1.298 (0.282)	< 0.001		
E, mm			0.108 (0.044)	0.013
T0, mm	-0.489 (0.082)	< 0.001	-0.458 (0.075)	< 0.001

Abbreviations: CA, crestal approach; LA, lateral approach; SE, standard error; E, sinus membrane elevation height; T0, residual bone height; G2, bone height change at postoperative 12 months.

Table 5. Bone height changes (G2) (mm) at postoperative 12 months relative to residual bone height (T0) in the CA and LA groups, based on the generalized estimating equation

T0, mm	CA		LA		*p* value
	n	Mean ± SD	n	Mean ± SD	
1–3			18	6.60 ± 1.90	
3–5			38	5.68 ± 1.54	
5–7	18	3.29 ± 1.57	36	4.31 ± 1.52	0.027
7–9	17	1.82 ± 1.18	19	3.74 ± 1.24	< 0.001
9–11	18	1.35 ± 1.00	18	1.96 ± 0.92	0.043
Total	53	2.16 ± 1.51	129	4.62 ± 2.04	

Abbreviations: CA, crestal approach; LA, lateral approach; SD, standard deviation; T0, residual bone height; G2, bone height change at postoperative 12 months.

Table 6. Region of interest (ROI)-related factors in the CA and LA groups

ROI-related factors	CA (n = 45)	LA (n = 90)
Perforation		
Yes	12 (26.67)	13 (16.88)
No	33 (73.33)	77 (83.12)
Span		
1	37 (82.22)	56 (62.22)
2	8 (17.78)	29 (32.22)
3	0 (0.00)	5 (5.56)
Number of ACSs	0.65 ± 0.30	1.42 ± 0.61
Bone volume change, mm^3	159.38 ± 134.52	486.83 ± 253.14

Data expressed as n (%) or mean ± SD.

Abbreviations: CA, crestal approach; LA, lateral approach; ACS, absorbable collagen sponge.

Table 7. Univariable analysis of factors associated with bone volume changes (mm^3) in the CA and LA groups, based on the generalized estimating equation

Predictor variables	CA		LA	
	Estimate (SE)	*p* value	Estimate (SE)	*p* value
Age, yr	1.845 (1.166)	0.114	0.002 (2.193)	0.999
Sex male (reference) female	-7.252 (39.019)	0.853	-41.932 (56.238)	0.456
Smoking non-smoker (reference) smoker	-	-	-38.251 (100.243)	0.703
Perforation no (reference) yes	-128.917 (24.903)	<0.001	-40.094 (82.654)	0.628
Span, n	96.775 (69.024)	0.161	133.489 (51.527)	0.010
Number of ACS, n	180.266 (63.898)	0.005	137.905 (42.335)	0.001

Abbreviations: CA, crestal approach; LA, lateral approach; SE, standard error; ACS, absorbable collagen sponge.

Table 8. Multivariable analysis of factors associated with bone volume changes (mm^3) in the CA and LA groups, based on the generalized estimating equation

Predictor variables	CA		LA	
	Estimate (SE)	*p* value	Estimate (SE)	*p* value
Perforation no (reference) yes	-131.716 (24.254)	< 0.001		
Number of ACS, n	184.757 (52.489)	< 0.001	137.905 (42.335)	0.001

Abbreviations: CA, crestal approach; LA, lateral approach; SE, standard error; ACS, absorbable collagen sponge.

Table 9. Review of sinus floor elevation using absorbable collagen sponge articles.

First author Year	Study design	Patients/implants (n)	Approach method	Implant placement	Outcome method
Present study	Clinical, retrospective	38/53 72/129	CA LA	Immediate	Multivariable analysis, CBCT, ISQ
Volpe[6] 2021	Clinical, retrospective	36/36	CA	Immediate	Periapical radiograph, ISQ
Menassa[7] 2020	Clinical	14/41	LA	Immediate	Periapical radiograph
Cosola[9] 2022	Clinical, retrospective	10/10	CA	After 6 months	CBCT, histological biopsy
Berberi[8] 2017	Clinical, prospective	10/28	LA	After 6 months	CBCT, histological biopsy
Ahn[10] 2011	Clinical	8/13	LA	After 6 months	CBCT, histological biopsy
Caneva[20] 2016	Animal	20 (rabbits)/0	LA	None	Histological biopsy

Data expressed as n (%) or mean ± SD or range.

Abbreviations: CA, crestal approach; LA, lateral approach; ND, not determined; CBCT, cone-beam computed tomography; ACS, absorbable collagen sponge; ISQ, implant stability quotient; NBF, new bone formation; P, sinus membrane perforation; I, sinus infection.

ACS	Follow-up (months)	Implant length (mm)	Residual bone height (mm)
Ateloplug	12	11.5	8.11 ± 1.58 (5.3-11) 5.54 ± 2.52 (0.5-11)
Condress (Smith & Nephew, Agrate Brianza, Italy)	4–6	9–13	5.9 ± 1.4
CollaTape (Zimmer Biomet, FL, USA)	12	8.5–10	3.5 (1.6–6.7)
Condress	6.9 ± 0.67	ND	ND
CollaTape	6	ND	<4
Collaplug (Zimmer Biomet, FL, USA)	6	8	4.5 ± 0.4
Gingistat (GABA Vebas, Milano, Italy)	40 days	-	ND

Bone height change (mm)	Implant survival (%)	ISQ	Histological result	Complication	Lateral window covering
2.16 ± 1.51	100	82.66 ± 6.61	ND	P: 13/I: 0	-
4.62 ± 2.04		81.16 ± 5.41		P: 14/I: 0	Window bone
3.8 ± 1.1	100	75.8 ± 3.9	ND	P: 1/I: 0	-
4.4 ± 1.9	100	ND	ND	ND	Bio-Gide (Giestlich, Pharma, Wolhusen, Switzerland)
6	ND	ND	NBF	P: 0/I: 0	-
7.98 ± 1.04 (middle)	100	ND	NBF	P: 0/I: 0	Window bone
ND	ND	ND	NBF (2 out of 13 specimens)	ND	CollaTape
ND	-	ND	NBF (high soft tissue ratio)	P: 0/I: 0	None

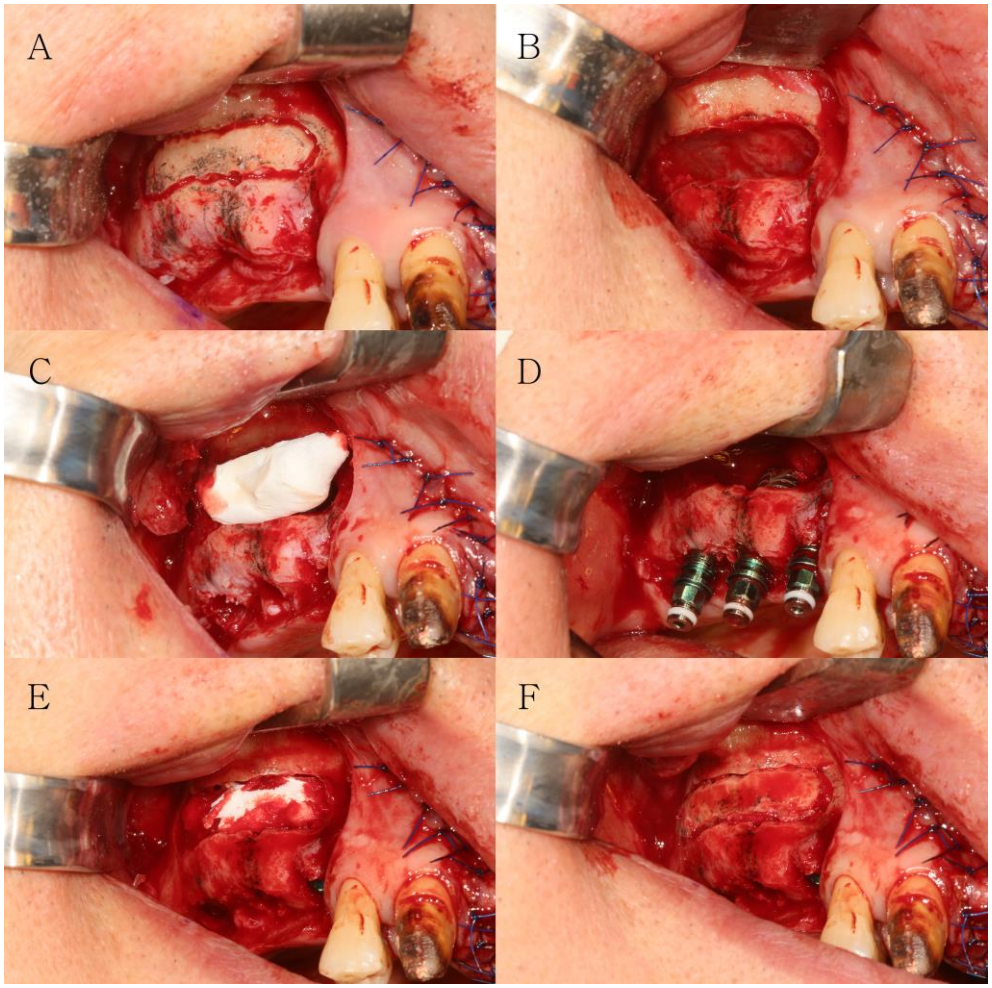


Figure 1. Lateral approach (LA) to sinus floor elevation using absorbable collagen sponge (ACS)

(A) Opening of a window in the lateral sinus wall to access the sinus membrane. (B) Elevation of the sinus membrane upon completion of osteotomy. (C) Insertion of ACSs into the cavity after final drilling for implant installation. (D) Simultaneous placement of implants. (E) Insertion of additional ACSs into the sinus space. (F) Repositioning of the bony window, covering the antrostomy site.

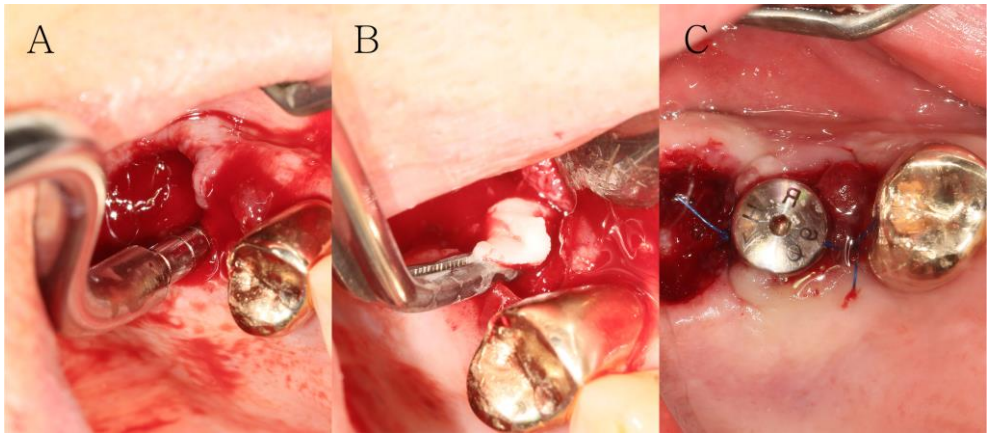
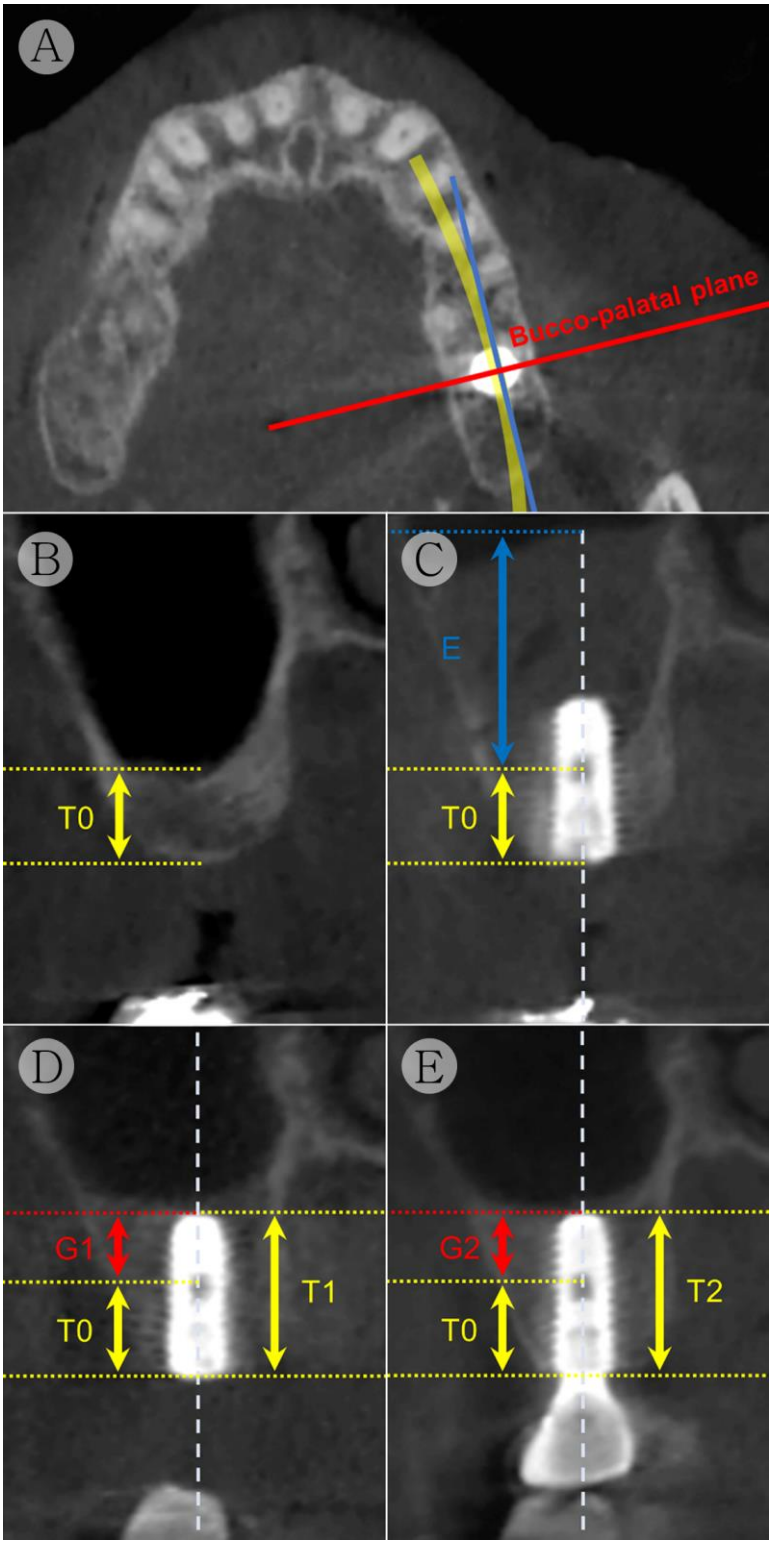


Figure 2. Crestal approach (CA) to sinus floor elevation using absorbable collagen sponge (ACS)

(A) Osteotome elevation of the sinus floor through the ridge crest. (B) Insertion of ACSs into the cavity under the elevated sinus membrane. (C) Simultaneous placement of implants.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Bucco-palatal plane
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G2
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Figure 3. Two-dimensional (2D) bone height analysis of sinus floor elevation using absorbable collagen sponge

(A) Selection of the buccopalatal plane for radiographic evaluation (an arc drawn along the contours of the maxillary arch in the axial view, drawing a tangent to the arc where it meets the center of implant; buccopalatal plane established perpendicular to the tangent line and parallel to the long axis of the implant). (B) Preoperative CBCT view. (C) Residual bone height and sinus membrane elevation height were measured after implant installation. (D) New bone formation at postoperative 6 months. (E) New bone formation at postoperative 12 months.

Abbreviations: CBCT, cone-beam computed tomography; E, sinus membrane elevation height; T0, residual bone height; T1, new bone height at postoperative 6 months; T2, new bone height at postoperative 12 months; G1, bone height change at postoperative 6 months; G2, bone height change at postoperative 12 months.

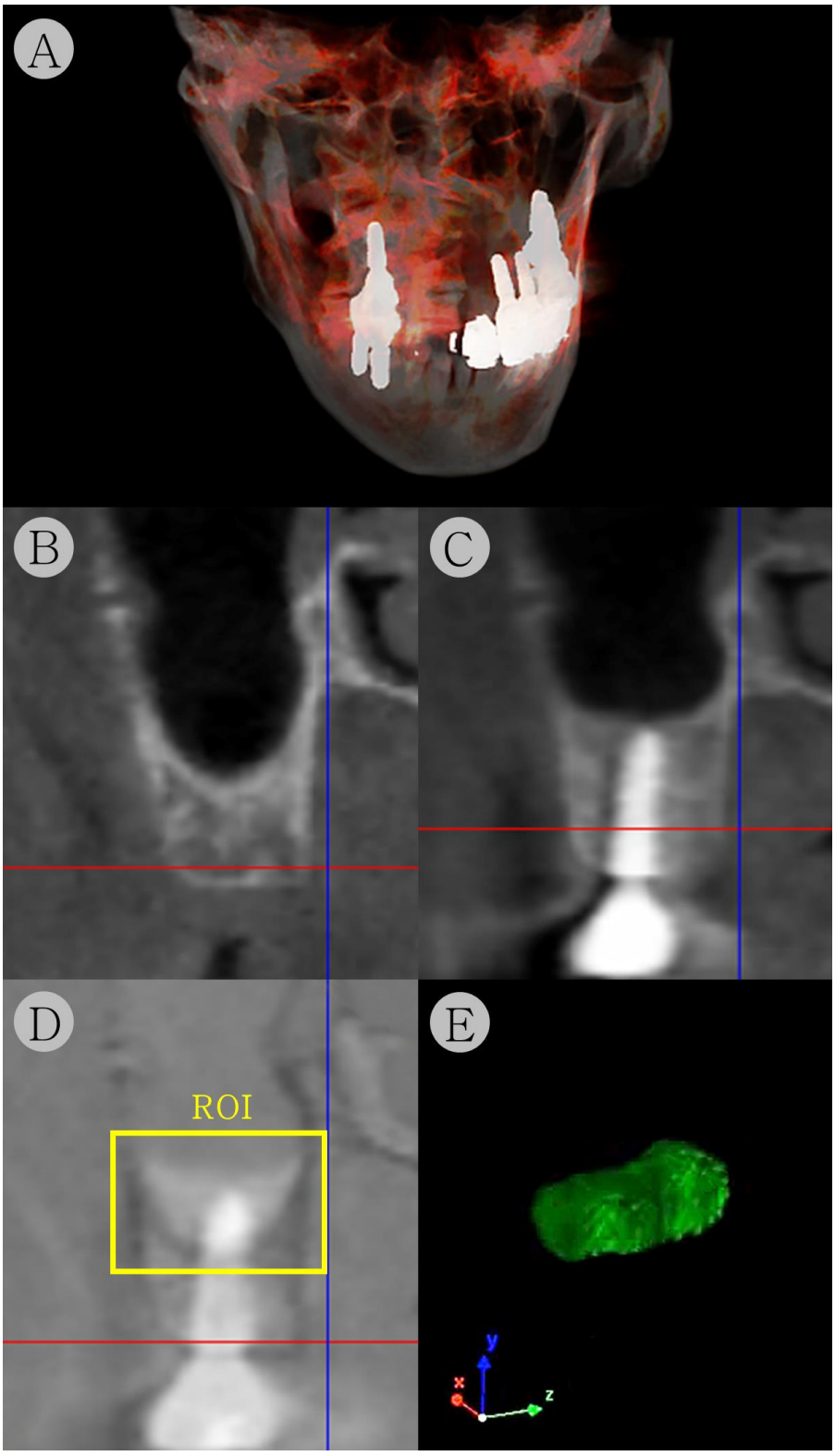
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Figure 4. Three-dimensional (3D) bone volume analysis of sinus floor elevation using absorbable collagen sponge

(A) Reconstruction of DICOM data as a 3D virtual model. (B) Preoperative image. (C) Image at postoperative 12 months. (D) Superimposed images and region of interest (ROI). (E) Volumetric measurement of ROI.

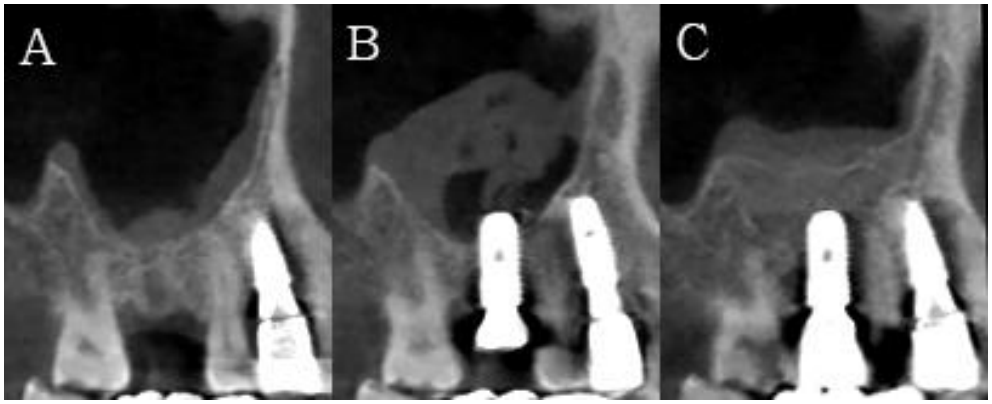

Figure 5. Extension of new bone beyond the apical ends of implants at 12 months after sinus floor elevation using absorbable collagen sponge by crestal approach

(A) Before surgery. (B) Immediately after surgery. (C) 12 months after surgery.

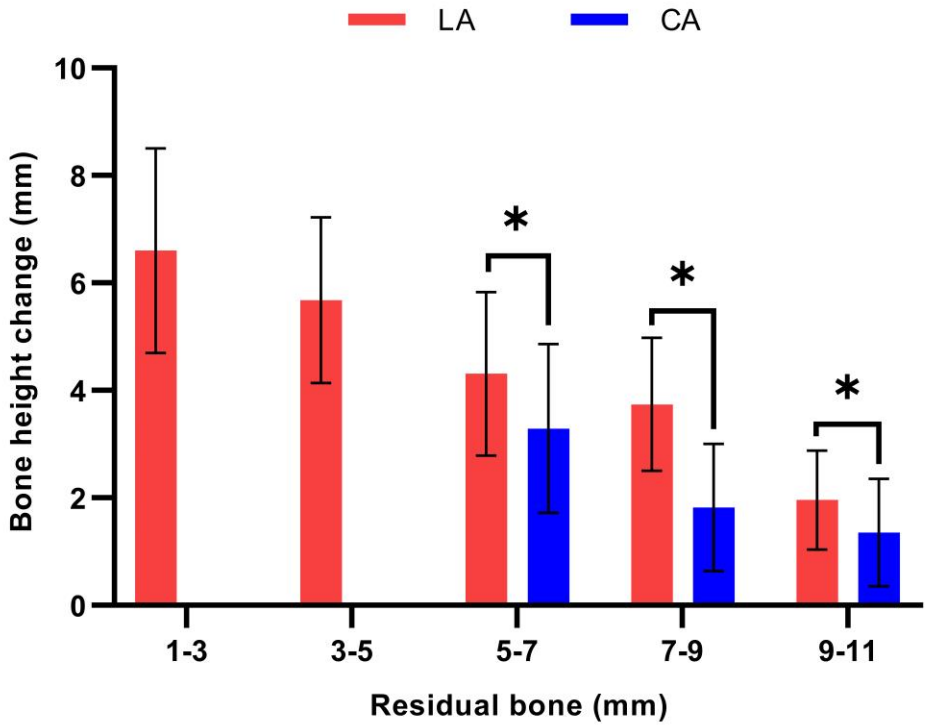

Figure 6. Sinus bone height changed 12 months after sinus floor elevation using absorbable collagen sponge in the CA and LA groups (mean ± SD)

The less residual bone height, the more new bone was formed. At residual bone heights ≥5 mm, the increase in sinus bone height was significantly greater in the LA than in the CA group (*$p < 0.05$).

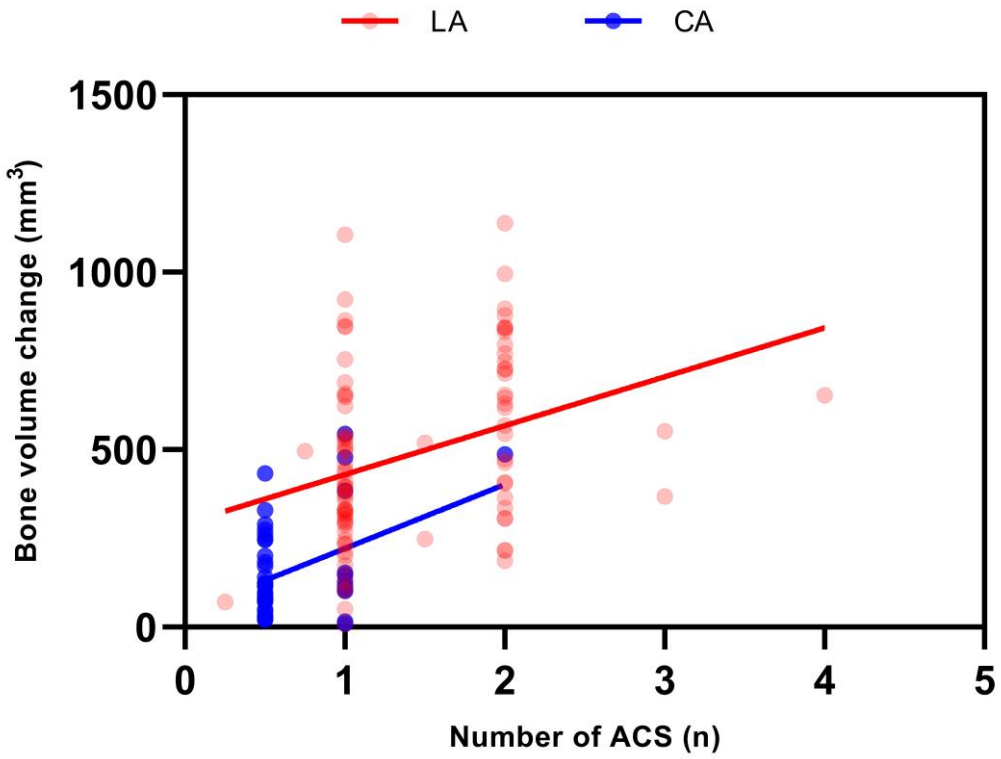

Figure 7. Relationship between bone volume changes and the number of ACS

Results of univariable analysis indicated that bone volume changes were correlated significantly with the number of ACS (CA, estimate = 180.266 mm^3, p = 0.005; LA, estimate = 137.905 mm^3, p = 0.001). As the number of ACSs increased, bone volume changes also increased, showing a linear relationship in both the CA and LA groups.

국문초록

상악동저거상술 및 증강술을 위한 흡수성 콜라겐 스펀지 이식의 다변수 분석

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연구배경: 생체적합성 및 생분해성, 골전도 특성을 가진 흡수성 콜라겐은 골조직 공학에서 가장 일반적인 스캐폴드 재료 중 하나이다. 흡수성 콜라겐은 세포 부착 및 성장을 위한 물리적 구조물 역할을 하며, 수용체에 의해 매개되는 상호작용을 통해 세포 행동에 영향을 미친다. 이 연구의 목적은 흡수성 콜라겐 스펀지를 이용한 상악동저거상술에서 골 높이 및 부피의 변화를 평가하고, 이에 영향을 미치는 요인을 확인하는 것이다.

연구대상 및 방법: 치조정(CA) 또는 측방(LA) 접근법에 의한 상악동막 거상 후, 흡수성 콜라겐 스펀지(Ateloplug)삽입과 임플란트의 식립이 동시에 시행되었다. 골 높이 및 부피의 변화를 평가하기 위해 콘빔 전산화 단층촬영(CBCT) 이미지를 이용한 2 차원 및 3 차원적 분석법이 적용되었다. 환자(나이 및 성별, 흡연) 및 임플란트, 관심영역(ROI)과 관련된

인자(임플란트 생존 및 상악동 감염, 식립 부위, 식립 개수, 임플란트 안정지수, 흡수성 콜라겐 스펀지 개수, 상악동 천공, 상악동막 거상 높이, 골 높이, 골 높이 변화, 골 부피 변화)를 조사했으며, 술 후 12 개월 때의 상악동 골 높이 및 부피 변화량이 주요 평가 지표로 사용되었다. 상악동 골 높이 및 부피 변화와 유의하게 관련된 변수를 확인하기 위해 단변수 및 다변수 분석(일반화 추정 방정식 기반)을 수행했다.

연구결과: 전체 108 명의 환자 및 182 개의 임플란트 식립 부위(53 개의 CA 및 129 개의 LA), 135 개의 관심영역(45 개의 CA 및 90 개의 LA)이 후향적 연구를 위해 선택되었다. 평균 임플란트 안정지수는 두 그룹 모두에서 충분히 높은 값을 보였으며(CA 에서 82.66±6.61, LA 에서 81.16±5.41), 두 방법 모두 상악동 감염이나 임플란트 탈락은 없었다. 술 후 12 개월 때 평균 골 높이 변화는 CA 에서 2.16±1.51 mm)(평균 잔여 골 높이 8.11±1.58 mm), LA 에서 4.62±2.04 mm(평균 잔여 골 높이 5.54±2.52 mm)였다(p < 0.001). CA 의 경우 골 높이 변화에 중요한 인자는 성별(p < 0.001) 및 천공(p < 0.001), 잔존 골 높이(p < 0.001)였다. 반면 LA 의 경우 상악동막 거상 높이(p = 0.013) 및 잔존 골 높이(p < 0.001)가 유의한 인자였다. 잔존 골 높이 5 mm 이상에서의 골 증가는 CA 보다 LA 에서 유의미하게 높게 나타났다(p < 0.05). 평균 골 부피 변화는 CA 에서 159.38±134.52 mm^3, LA 에서 486.83±253.14 mm^3 였다. CA 의 경우 골 부피 변화에 중요한 인자는 삽입된 흡수성 콜라겐 스펀지의 개수(p < 0.001) 및 천공(p <

0.001)이었으며, LA 의 경우 삽입된 흡수성 콜라겐 스펀지의 개수(p = 0.001)가 유의한 인자였다.

결론: 흡수성 콜라겐 스펀지를 이용한 상악동저거상술 후 신생골 형성이 2 차원 및 3 차원적 분석법에서 확인되었다. 골 높이 변화는 치조정접근법의 경우 성별 및 천공, 잔존골의 높이에 영향을 받는 반면, 측방접근법의 경우 상악동막 거상 높이 및 잔존 골 높이에 영향을 받았다. 삽입된 흡수성 콜라겐 스펀지의 개수는 치조정 및 측방 접근 모두에서 골 부피 변화에 영향을 주었으며, 특히 치조정 접근법에서는 상악동막 천공도 영향을 주는 인자였다. 연구 결과에 기반할 때, 흡수성 콜라겐 스펀지를 이용한 상악동저거상술은 골 높이 및 부피 증가가 필요한 환자에게 실행 가능한 안전한 옵션인 것으로 보인다.

주요어 : 임플란트, 상악동, 치조정 접근법, 측방 접근법, 조직 공학, 바이오스캐폴드, 골 이식

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