Effect of the size of the bony access window and the collagen barrier over the window in sinus floor elevation: a preclinical investigation in a rabbit sinus model

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ABSTRACT

Purpose: The aim of this study was to investigate the effect of (1) the size of the bony access window and (2) collagen membrane coverage over the window in sinus floor elevation in a rabbit sinus model.

Methods: Small bony access windows (SW; ø 2.8 mm) were made in 6 rabbits and large windows (LW; ø 6 mm) in 6 other rabbits. Both sinuses in each rabbit were allocated to groups with or without coverage of a collagen membrane (CM) on the window, resulting in 4 groups: SW, LW, SW+CM, and LW+CM. After 4 weeks of healing, micro-computed tomographic, histologic, and histomorphometric analyses were performed.

Results: Bony healing in the window area was incomplete in all groups, but most bone graft particles were well confined in the augmented cavity. Histologically, the pattern of new bone formation was similar in all groups. Histomorphometrically, the percentage of newly formed bone was greater in the groups with CM than in the groups without CM, and in the groups with SW than in the groups with LW (12.92%±6.40% in the SW+CM group, 4.21%±7.73% in the SW group, 10.45%±4.81% in the LW+CM group, 11.77%±3.83% in the LW group). The above differences were not statistically significant (P>0.05).

Conclusions: The combination of a small bony access window and the use of a collagen membrane over the window favored new bone formation compared to other groups, but this result should be further investigated due to the limitations of the present animal model.

Keywords: Animal model; Bone regeneration; Sinus floor augmentation

INTRODUCTION

Maxillary sinus pneumatization is a major challenge in dental implant treatment of the posterior maxillary area [1]. The pneumatized posterior maxilla limits the height of available bone to a varying extent, necessitating sinus floor elevation (SFE) procedures to place implants with adequate length. The mode of SFE can be divided into lateral and transcrestal...
Window size and barrier membrane in sinus floor elevation

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Conflict of Interest
No potential conflict of interest relevant to this article has been reported.

Author Contributions
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Evidence has demonstrated that a bone height of ≤3–4 mm can be successfully overcome with lateral SFE. The reported survival rate of implants placed using lateral SFE was 91.8% in a systematic review [3].

Several factors influencing the success and predictability of lateral SFE have been investigated [4,5]. Among them, the use of a barrier membrane to cover a bony window for accessing the maxillary sinus significantly influenced implant survival. Exclusion of a barrier membrane may result in the following: 1) proliferation of soft tissue into the sinus cavity, 2) less vital bone formation, and 3) spilling or displacement of bone substitute material out of the access bony hole [6-8].

During a lateral SFE procedure, bony window(s) are surgically created on the lateral wall of the sinus to access the sinus cavity. For this, round carbide/diamond burs and piezoelectric devices have been traditionally used [9]. The window(s) serve as a passage for inserting the instruments for the sinus membrane and grafting bone substitute material. Therefore, the size of the window should be large enough to ensure maximum visibility for clinicians and range of motion for instruments [10,11]. These issues regarding the size of the window should be considered in relation to the above-mentioned finding that a barrier membrane is a significant factor in lateral SFE.

A few studies have addressed the size of the bony window [12-15]. Various clinical factors can affect the size of the bony window, such as the anatomical configuration, the number of dental implants to be placed simultaneously with SFE, and the clinician’s level of experience. This may pose a difficulty in standardizing the size of the bony window in every case. Nonetheless, it can be conjectured that a small access window facilitates bone regeneration better in the augmented sinus by forming a cavity mostly surrounded by bone walls [15,16]. This small window then eventually results in a shorter healing period. Moreover, a small bony window might be healed without soft tissue invagination due to faster bone bridge formation in the window, which may exclude the necessity of using a barrier membrane over the window.

The present preclinical study aimed to investigate the effect of 1) the size of the access window and 2) the use of a barrier over the access window on the healing outcomes following SFE in a rabbit sinus model.

MATERIALS AND METHODS

The study was approved by the Institutional Animal Research Committee (KHMC-IACUC 2019-024). The ARRIVE guidelines were followed during the preparation of the manuscript [17]. Surgery was performed between November 26, 2019 and February 7, 2020.

Animals
Twelve male New Zealand White SPF rabbits (2.4−2.9 kg) were used as experimental animals. The rabbits were housed in separate cages under standard laboratory conditions with free access to water and a soft pellet diet. Before surgery, the animals were acclimatized for at least 1 week. Regular monitoring was performed to assess the medical status of the rabbits. The present rabbit sinus model was selected based on its similarity to the human sinus [18].

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Study design
The following treatments were performed according to the size of the bony access window and the membrane coverage on the window. In 6 rabbits, small bony access windows (SW; Ø 2.8 mm) were made on the antral bone to access the bilateral maxillary sinus. In 6 other rabbits, large windows (LW; Ø 6 mm) were made. After inserting bone substitute particles into both sinuses, one access window in each rabbit was covered with a native bilayer collagen membrane (CM) (Biogide; Geistlich Pharma, Wollhusen, Switzerland). Through the above treatments, 4 experimental groups were established, as follows: LW with/without CM coverage (LW+CM and LW), and SW with/without CM coverage (SW+CM and SW). Four weeks of healing were provided to all experimental animals.

Surgical procedures
Throughout the entire surgical procedure, general anesthesia was induced with xylazine hydrochloride (Rompun, Bayer, Seoul, Korea) and Zoletil 50 (Virbac SA, Carros, France). The surgical site was shaved and disinfected with an iodine solution. A local anesthetic agent (2% lidocaine HCl with 1:100,000 epinephrine; Huons, Seoul, Korea) was administered subcutaneously at the site.

A linear incision was made, and full-thickness flaps were reflected to expose the antral bone. In all groups, specially designed sinus step drills (SIS Sinus kit; Shinhung, Seoul, Korea) were used to create a bony access window. The diameter of the window was first set to 2.8 mm in all groups. Using a rubber adapter connected to a hose and a syringe (SIS Sinus kit; Shinhung), hydraulic pressure (saline injection) was applied via the access hole to detach the sinus membrane from the sinus bone walls [19]. Subsequently, for the LW+CM and LW groups, the bony access window was enlarged to 6 mm in diameter using a dome-shaped diamond-coated drill (Dask kit; Dentium, Seoul, Korea).

After the above treatments, 0.35 cc of deproteinized bovine bone substitute material (Maxpore; Shinhung) was gently packed in each sinus. Next, a CM (Bio-Gide; Geistlich Pharma) was placed over the access window in the LW+CM and SW+CM groups. The CM was stabilized using membrane tacks to the antral bone wall near the access window. The CM coverage was extended at least 2 mm beyond the borders of the window. Group assignment was performed according to a computer-generated random sequence by one investigator (S.K.). The flaps were sutured using 4-0 nylon sutures (blue nylon; Ailee, Busan, Korea). Clinical photographs of surgery are shown in Figure 1.

Post-surgical care
An antibiotic (0.3 mL of gentamycin, Komi Gentamicin; Komipharm, Siheung, Korea) and an analgesic (0.3 mL of ketoprofen, KetoPro; Unibitech, Anyang, Korea) were administered intramuscularly for 3 days postoperatively. During the healing period, the rabbits were carefully monitored for diet and weight loss. The animals were sacrificed after 4 weeks. Block tissue sections containing sinuses and adjacent tissues were harvested.

Micro-computed tomographic analysis
Micro-computed tomography (micro-CT) was performed on the harvested specimens (SkyScan 1173 ver. 1.6.0; SkyScan, Aartselaar, Belgium). The conditions of the scans were as follows: 130 kV, 60 μA, pixel size: 13.85 μm, exposure: 500 ms. The scanned images were reconstructed using NRecon ver. 1.7.0.4; SkyScan, Kontich, Belgium). The total augmented volume bordered by bone substitute particles was measured. The grayscale range for the
bone tissue and bone substitute material was between 75 and 255. Due to the overlap of the grayscale range [20], differentiation between the two components was not performed.

**Histologic processing**

The harvested specimens were immersed in 10% neutral-buffered formalin. The specimens were then decalcified, trimmed, and embedded in paraffin. The specimens were serially sectioned at a thickness of 5 μm on the coronal plane. For histologic and histomorphometric analyses, the central sections of the sinuses were chosen. Masson trichrome staining was then performed.

**Histological and histomorphometric analysis**

The stained histological specimens were digitally scanned (Panoramic 250 Flash III; 3DHISTECH, Budapest, Hungary) and observed using computer software (CaseViewer ver. 2.3; 3DHISTECH). Histomorphometric analysis was performed using image analysis software (Photoshop CS6 Extended; Adobe, San Jose, CA, USA) by a blinded investigator (J-E. S).

The following parameters were measured: 1) the area of total augmentation (TA; mm$^2$) bordered by medial/lateral sinus bone walls, the sinus membrane, and the antral bone, including the bony access window; 2) the percentage of newly formed bone (NB; %) within the TA, and 3) the percentage of residual bone substitute material (RM; %) within the TA. In addition, 3 regions of interest (ROIs; size: 0.8 mm×0.8 mm) were established within the TA: the region close to the surgical access window (ROI_W), the center of the augmentation (ROI_C), and the region close to the sinus membrane (ROI_M). NB and RM were measured in these ROIs.

**Statistical analysis**

A sample size calculation was not performed due to the exploratory nature of this study.

Statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Data are shown as mean ± standard deviation and median with interquartile range. The Shapiro-Wilk test was used to determine whether data had a normal distribution. The paired t-test or Wilcoxon sign-rank test was used to determine the statistical significance of differences between the LW+CM and LW groups and between the SW+CM and SW groups.
The independent t-test or Mann-Whitney U test was used to compare the parameters between the LW+CM and SW+CM groups and between the LW and SW groups. The threshold for statistical significance was set at $P<0.05$.

**RESULTS**

**Clinical findings**
Perforation of the sinus membrane was not detected in any of the experimental animals during the SFE procedure. No adverse events, such as infection or swelling, were observed during the entire healing period. Thus, all animals (n=12) were included in the analysis.

**Micro-CT findings**
The areas of augmentation generally had a dome- or U-shaped appearance. Slight spilling of bone substitute particles was observed on the bone surface near the access window in some specimens (1 in the SW+CM group, 2 in the LW+CM group, and 1 in the LW group). Newly formed bone was observed in areas adjacent to the sinus bone wall and between bone substitute particles. The healing of the bony access window was incomplete in all groups to varying extents. No specific healing pattern was observed within the window area (Figure 2).

The total augmented volume (TV) in the SW group was statistically significantly smaller than that in the SW+CM group ($310.77\pm34.71$ mm$^3$ vs. $331.30\pm36.44$ mm$^3$, $P<0.05$). There was no significant difference in TV between the LW and LW+CM groups ($321.17\pm41.22$ mm$^3$ vs. $313.75\pm48.23$ mm$^3$, $P>0.05$) (Table 1).

![Figure 2](https://doi.org/10.5051/jpis.2105560278)

**Figure 2.** Representative reconstructed images from micro-computed tomography. SW: small access window, CM: collagen membrane, LW: large access window.

**Table 1.** Augmented volume in the micro-computed tomographic analysis (in mm$^3$)

| Variables | Without CM | With CM | $P$ value (without vs. with CM) |
|-----------|------------|---------|--------------------------------|
| SW        | 310.77±34.71 mm$^3$ | 331.30±36.44 mm$^3$ | 0.010 |
|           | 315.47 (283.87, 330.08) | 338.00 (310.28, 359.87) |     |
| LW        | 321.17±41.22 mm$^3$ | 313.75±48.23 mm$^3$ | 0.310 |
|           | 326.09 (311.87, 339.07) | 323.90 (286.18, 349.12) |     |
| $P$ value (SW vs. LW) | 0.647 | 0.49 |     |

Data are presented as mean ± standard deviation and median (quartiles).
CM: collagen membrane, SW: small access window, LW: large access window.
**Histological observations**

**General findings**

In all specimens, there was no discontinuity or tearing in the sinus membrane. The shape of augmentation was dome-like or vertically elongated. Newly formed bone was mostly found in areas close to the native bone (near the bony access window and medial/lateral sinus bone walls), but in the center of the augmentation, new bone formation appeared to be less than in other areas within the augmented space (Figures 3 and 4). A varying extent/thickness of bony bridge formation was observed in the access window area. Continuous bony bridge formation was noted in 5 specimens (out of 6) in the SW group, 4 in the SW+CM group, 3 in the LW group, and 5 in the LW+CM group. In cases of incomplete bony bridge formation in the access window, soft tissue invasion was observed. Most of the specimens presented active new bone formation in the area close to the sinus membrane (3 in the SW group, 3 in the SW+CM group, 4 in the LW group, and all specimens in the LW+CM group).

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**Figure 3.** Representative histologic views of the groups with SW. (A-D) SW group; (E-H) SW+CM group; (A, E) total augmentation; (B, F) region of interest close to the surgical access window; (C, G) region of interest at the center of augmentation; (D, H) region of interest close to the sinus membrane. SW: small access window, CM: collagen membrane.

**Figure 4.** Representative histologic views of the groups with LW. (A-D) LW group; (E-H) LW+CM group; (A, E) total augmentation; (B, F) region of interest close to the surgical access window; (C, G) region of interest at the center of augmentation; (D, H) region of interest close to the sinus membrane. LW: large access window, CM: collagen membrane.
Histomorphometric analysis

Entire augmented area

The SW groups presented a greater amount of NB than their LW counterparts (14.21%±7.73% vs. 11.77%±3.83% for groups with CM coverage, 12.92%±6.40% vs. 10.45%±4.81% for groups without CM coverage), but there was no statistically significant difference in each comparison (P>0.05). TA and RM were not also statistically significantly different between the SW and LW groups (15.81±5.97 mm² vs. 12.09±3.16 mm² and 31.70%±5.20% vs. 32.05%±3.66%) and between the SW+CM and LW+CM groups (16.54±4.12 mm² vs. 16.67±2.72 mm² and 26.66%±5.86% vs. 29.08%±5.52%, P>0.05) (Table 2, Figure 5).

The SW+CM and LW+CM groups had a greater NB than their counterparts (the SW and LW groups, respectively), but without a statistically significant difference (P>0.05). TA and RM also did not show statistically significant differences in the above comparisons (P>0.05) (Table 2, Fig. 5).

Table 2. Histomorphometric analysis of the SW, SW+CM, LW, and LW+CM groups

| Variables | Without CM | With CM | P value (without vs. with CM) |
|-----------|------------|--------|-----------------------------|
| TA (mm²)  |            |        |                             |
| SW        | 15.81±5.97 | 16.54±4.12 | 0.790                      |
|           | 13.89 (11.13, 21.22) | 17.23 (14.89, 19.62) |               |
| LW        | 12.09±3.16 | 16.67±2.72 | 0.050                      |
|           | 12.11 (10.41, 14.41) | 17.21 (15.87, 18.67) |               |
| P value (SW vs. LW) | 0.207 | 0.948 |                             |
| NB (%)    |            |        |                             |
| SW        | 12.92±6.40 | 14.21±7.73 | 0.614                      |
|           | 12.43 (7.80, 17.09) | 17.11 (9.46, 19.94) |               |
| LW        | 10.45±4.81 | 11.77±3.83 | 0.475                      |
|           | 10.78 (7.43, 12.89) | 12.34 (9.28, 14.81) |               |
| P value (SW vs. LW) | 0.467 | 0.505 |                             |
| RM (%)    |            |        |                             |
| SW        | 31.70±9.20 | 26.66±5.86 | 0.073                      |
|           | 30.10 (27.61, 32.70) | 26.72 (25.24, 30.71) |               |
| LW        | 32.05±3.66 | 29.08±5.52 | 0.276                      |
|           | 33.12 (30.33, 33.89) | 29.33 (27.01, 30.67) |               |
| P value (SW vs. LW) | 0.932 | 0.479 |                             |

Data are presented as mean ± standard deviation and median (quartiles).

SW: small access window, CM: collagen membrane, LW: large access window, TA: area of total augmentation surrounded by medial/lateral bony walls, the Schneiderian membrane, and the surgical access window, NB: percentage of newly formed bone within the TA, RM: percentage of residual bone substitute material within the TA.

Figure 5. Box and whisker plots of histomorphometric measurements. (A) Total augmented area (mm²); (B) percentage of newly formed bone (%); (C) percentage of residual substitute bone material (%).

SW: small access window, CM: collagen membrane, LW: large access window, TA: area of total augmentation surrounded by medial/lateral bony walls, the Schneiderian membrane, and the surgical access window, NB: percentage of newly formed bone within the TA, RM: percentage of residual bone substitute material within the TA.
For NB in all ROIs, there were no statistically significant inter-group differences ($P>0.05$) except for the comparison between the SW and SW+CM groups in ROI_C (3.12%±2.73% vs. 11.41%±7.81%, $P<0.05$). Despite the absence of a statistically significant difference, the difference in NB of ROI_W and ROI_C was also notable between the LW and LW+CM groups (7.48%±7.10% vs. 22.75%±21.35% in ROI_W, 2.98%±4.10% vs. 7.19%±8.25% in ROI_C) (Table 3).

In terms of RM, there was no statistically significant inter-group difference ($P>0.05$) except for the SW and SW+CM groups in ROI_C ($P<0.05$) (Table 3).

### Table 3. Histomorphometric analysis of the ROI (ROI=0.64 mm$^2$)

| Variables | Without CM | With CM | $P$ value (without vs. with CM) |
|-----------|------------|---------|--------------------------------|
| ROI_W NB (%) |            |         |                                |
| SW        | 15.46±7.77 | 13.32±8.90 | 0.695                          |
|           | 16.91 (10.28, 20.17) | 13.76 (8.91, 18.53) |                         |
| LW        | 7.48±7.10  | 17.08±6.91  | 0.093                          |
|           | 5.98 (1.95, 13.35) | 14.23 (13.98, 14.93) |                         |
| P value (SW vs. LW) | 0.100 | 0.464 |                                |
| RM (%)    |            |         |                                |
| SW        | 29.21±0.03 | 24.33±6.61  | 0.178                          |
|           | 29.37 (28.33, 31.30) | 22.75 (21.35, 28.86) |                         |
| LW        | 34.45±7.24 | 31.59±10.97 | 0.707                          |
|           | 33.84 (28.98, 40.58) | 33.02 (30.51, 34.59) |                         |
| P value (SW vs. LW) | 0.151 | 0.204 |                                |
| ROI_C NB (%) |            |         |                                |
| SW        | 3.12±2.73  | 11.41±7.81  | 0.042                          |
|           | 3.59 (0.87, 4.32) | 12.85 (6.47, 17.46) |                         |
| LW        | 2.98±4.10  | 7.19±8.25   | 0.144                          |
|           | 1.14 (0.30, 4.11) | 5.40 (0.05, 12.77) |                         |
| P value (SW vs. LW) | 0.870 | 0.414 |                                |
| RM (%)    |            |         |                                |
| SW        | 41.46±11.24 | 27.21±11.98 | 0.029                          |
|           | 39.94 (31.74, 48.71) | 27.49 (20.01, 31.83) |                         |
| LW        | 44.87±8.99 | 38.54±5.88  | 0.257                          |
|           | 46.72 (42.79, 48.75) | 38.56 (6.627, 42.12) |                         |
| P value (SW vs. LW) | 0.585 | 0.068 |                                |
| ROI_M NB (%) |            |         |                                |
| SW        | 18.55±13.00 | 15.75±11.07 | 0.306                          |
|           | 22.07 (7.42, 27.50) | 16.68 (7.61, 25.43) |                         |
| LW        | 13.64±9.48 | 19.75±7.64  | 0.205                          |
|           | 14.07 (6.26, 18.48) | 21.66 (14.72, 24.58) |                         |
| P value (SW vs. LW) | 0.497 | 0.443 |                                |
| RM (%)    |            |         |                                |
| SW        | 35.69±19.26 | 35.98±11.49 | 0.976                          |
|           | 35.33 (19.96, 47.63) | 37.25 (34.67, 40.45) |                         |
| LW        | 39.78±5.42 | 35.39±5.48  | 0.242                          |
|           | 39.43 (34.98, 43.98) | 35.53 (34.56, 37.91) |                         |
| P value (SW vs. LW) | 0.642 | 0.899 |                                |

Data are presented as mean ± standard deviation and median (quartiles). ROI: regions of interest, CM: collagen membrane, ROI_W: area close to the surgical access window, NB: percentage of newly formed bone within the ROI, SW: small access window, LW: large access window, RM: percentage of residual bone substitute material within the ROI, ROI_C: area of the center of the augmentation, ROI_M: area close to the Schneiderian membrane.
DISCUSSION

This study investigated the effects of the size of the bony access window and the use of a collagen barrier over the access window on healing outcomes following SFE. The study demonstrated that the combination of a small access window and the use of a collagen barrier led to the most favorable new bone formation.

Several factors related to the success and predictability of SFE have been investigated in a vast amount of research \[4,5\]. Nonetheless, some elements need to be further elucidated, such as the size of the bony access window. Even though some studies clarified the size of the window \[13,21\], the size may be determined on an individual basis for each case because it needs to be suitable for providing the best possible access to the sinus. In the past, forming a large window was recommended to optimize access \[11\]. However, a small window may have the following advantages compared to a large window: (1) less trauma \[13\], (2) establishment of more isolated augmented space \[22\], and (3) faster bone bridge formation on the window \[23\].

In the present study, the SW groups (ø 2.8 mm) presented a greater amount of NB (without a statistically significant difference) than the LW groups (ø 6 mm) at 4 weeks of healing. In another rabbit study, a small window (3×6 mm) also led to greater new bone formation than a large window (5×6 mm) at 2, 4, and 8 weeks \[15\]. In that study, a statistically significant difference was found only at 2 weeks. The bone-forming pattern was not significantly different between the sinuses with small and large windows in both studies.

A few clinical studies demonstrated the histologic and radiographic outcomes following SFE using access windows of different sizes. In a clinical study, the window dimension and the percentage of vital bone in the core biopsy specimen were analyzed, and a strong negative correlation was found between these parameters \[12\]. In other clinical studies on radiographic findings (window size: 6×6 mm vs. 10×8 mm \[13\], 3–5 mm in apico-coronal height vs. 6–8 mm \[14\], respectively), no significant difference in the height of the augmented bone over time was observed in sinuses with large and small windows.

Applying a barrier membrane over the access window is mainly based on a principle of guided bone regeneration, which involves preventing soft tissue infiltration of the augmentation. However, the sinus cavity in SFE is a specific defect resembling a bottle or a bowl, where bone substitute material can easily be inserted, contained, and stabilized. Furthermore, more than half of this defect is surrounded by native bone, which provides an osteogenic source. Thus, some studies investigated the need for a barrier over the access window in lateral SFE \[3,7,8,24-26\]. Interestingly, studies published in the past demonstrated favorable histological bone formation and better implant survival when a barrier was used \[3,25,26\], but relatively recent studies demonstrated no distinct difference between sinuses with access windows covered by a barrier and a non-covered window \[7,8\].

In the present study, using a collagen barrier over the access window led to some increase of NB in both groups with large and small windows. Different sizes of the window appeared to have different influences on new bone formation within the augmentation. The LW+CM group exhibited a greater extent of NB in all ROIs than the LW group (without a statistically significant difference). Inter-group difference in NB of ROI_W was relatively minor for the groups with small window compared to the difference in the groups with large window.
However, there was a statistically significant difference in NB of ROI_C between the SW and SW+CM groups. The bone-forming rate around the osteotomy might play in the above discrepancies. The large window might facilitate unwanted soft tissue invasion in the absence of the CM and subsequently delay new bone formation. The small window seemed to compensate for the influence of the CM in the access window area (ROI_W), but the absence of the CM still had a negative effect in the center of the augmentation. This indicates that soft tissue invasion could not be entirely blocked by a small-sized window.

One of the reasons for using a barrier in SFE is to prevent displacement of bone substitute material out of the access window [6]. However, this could not be evaluated appropriately in the present model due to the different window positions between rabbits and humans. In rabbits, the window was made in the coronal portion to the sinus cavity, but in humans, the lateral side to the sinus cavity [18]. TV was statistically significantly smaller in the SW group than the SW+CM group (310.77±34.71 mm$^3$ vs. 331.30±36.44 mm$^3$) despite the insertion of graft material in a standardized amount, but it seemed that this discrepancy was caused by differences in hydraulic pressure. Moreover, the difference in TV appeared to be clinically negligible considering the shape of the augmentation.

The statistically insignificant difference in NB between groups defined according to window size and the presence of a collagen barrier should be carefully interpreted. Compared to the maxillary sinus in humans, the rabbit sinus has narrow host bone walls. Following sinus membrane elevation, a significant portion of the bone walls is exposed in rabbits, providing more favorable conditions for bone formation than in humans. In the histological sections of the present study, it also appeared that the medial and lateral bone walls markedly contributed to new bone formation. This proximity between the bone walls might attenuate the influence of the collagen barrier and window size in the present animal model.

In the present study, hydraulic pressure was applied to detach the sinus membrane in the SW groups. Considering that the tips of conventionally used hand instruments (i.e., sinus curettes) for detaching the membrane are >2 mm, inserting these instruments into the small window (ø 2.8 mm) and applying appropriate actions was not feasible. Some studies have demonstrated the effectiveness and safety of several types of hydro-pressure systems [27-29], but these systems have generally been utilized for transcrestal SFE. The feasibility of using these systems in lateral SFE should be further investigated.

There are some limitations to the present study. First, the distance between the host bone walls and the border of the access window is short in rabbits, and the window size in all the groups did not reach a critical size that did not heal spontaneously [30,31]. Moreover, using the dome-shaped drill for large windows led to a funnel shape of bone preparation, which means that a smaller diameter was obtained in the internal layer of the antral bone. Those factors could offset the intended effect of the large window. Second, even though hydraulic pressure is a safer and more efficient way to detach the sinus membrane, it might hamper the standardization of the augmentation; for instance, it might induce a discrepancy in the pattern of sinus membrane elevation, the spread of graft material and the apico-coronal levels of the ROIs. Third, the 4-week period of healing in the present study is medium-term healing. Investigations at shorter and later healing timepoints may be needed to obtain more detailed information about bone healing. Fourth, the sample size was small.
In conclusion, the combination of a small bony access window and the use of a CM over the window favored new bone formation, but this result should be further investigated in a larger animal model.

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