The Effectiveness of L-PRF in the Treatment of Schneiderian Membrane Large Perforations: Long-Term Follow-Up of a Case Series

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The perforation of the Schneiderian membrane (SM) is a common surgical complication during the sinus floor augmentation (SFA) procedure. Different approaches have been proposed to completely closer the SM perforation and to avoid graft contamination or migration and postoperative sinus infection. In this context, the leukocyte and platelet-rich fibrin (L-PRF) membranes have been proposed for SM perforation treatment because of their natural adhesive property and resistance. Thus, this case series aims to evaluate the effectiveness of L-PRF in the treatment of SM large perforations during SFA. A total of 9 SM perforations were treated in this case series. The L-PRF membranes were interposed on the perforated SM until the rupture could not be visualized. The maxillary sinus cavities were filled with deproteinized bovine mineral bone (Bio-oss, Geistlich, Switzerland), and a collagen membrane was positioned to cover the lateral access window. After 8 months, 13 implants were placed, achieving satisfactory primary stability. The osseointegration of all implants and absence of infection signs/mucus in the maxillary sinus were observed in cone beam computed tomography or panoramic radiography qualitative analysis after 3–5 years of follow-up. It can be concluded that the use of L-PRF can be considered a viable alternative for the repair of large SM perforations.

Key Words: maxillary sinus, bone substitutes, cone beam computed tomography, maxillary sinus floor augmentation, platelet-rich fibrin

INTRODUCTION

The maxillary sinus (MS) is the largest cavity of paranasal sinus, and it is covered by a respiratory mucosa called the Schneiderian membrane (SM).[1] This mucoperiosteal membrane is thin and has a thickness ranging from 0.3 to 0.8 mm[2]. The epithelial layer, constituted by a ciliated columnar pseudostratified epithelium, is responsible for providing to the maxillary sinus numerous goblet cells that produce mucus.[3] This mucus, besides containing lysozyme (antibacterial), retains bacteria and debris that will later be transported by the cellular cilia towards the ostium,[4] ensuring MS drainage. Any factor that impairs ostium mucus production, ciliary function, or patency may increase the risk of sinusitis.

The MS presence can interfere in dental implant placement in the posterior maxilla because of insufficient bone volume.[5,6] Based on that, the lateral window technique was developed in 1986 by Tatum[7] to access the MS cavity and elevate its floor. Because of the high osteogenic potential of the SM,[8] the lateral window technique can be performed without the association of bone grafts.[9] However, clinical studies have shown that the bone gain is limited, and the implant apex is surrounded by nonosseointegrated connective tissue.[10,11] For this reason, the MS cavity is traditionally filled with particulate bone grafts associated with a collagen membrane to enhance bone formation.[9]

The SM perforation is the most common complication during the sinus floor augmentation procedure (SFA), with a prevalence rate ranging from 3.6% to 56%.[12–15] Large perforations (>1.5 cm) may occur because of operator error,

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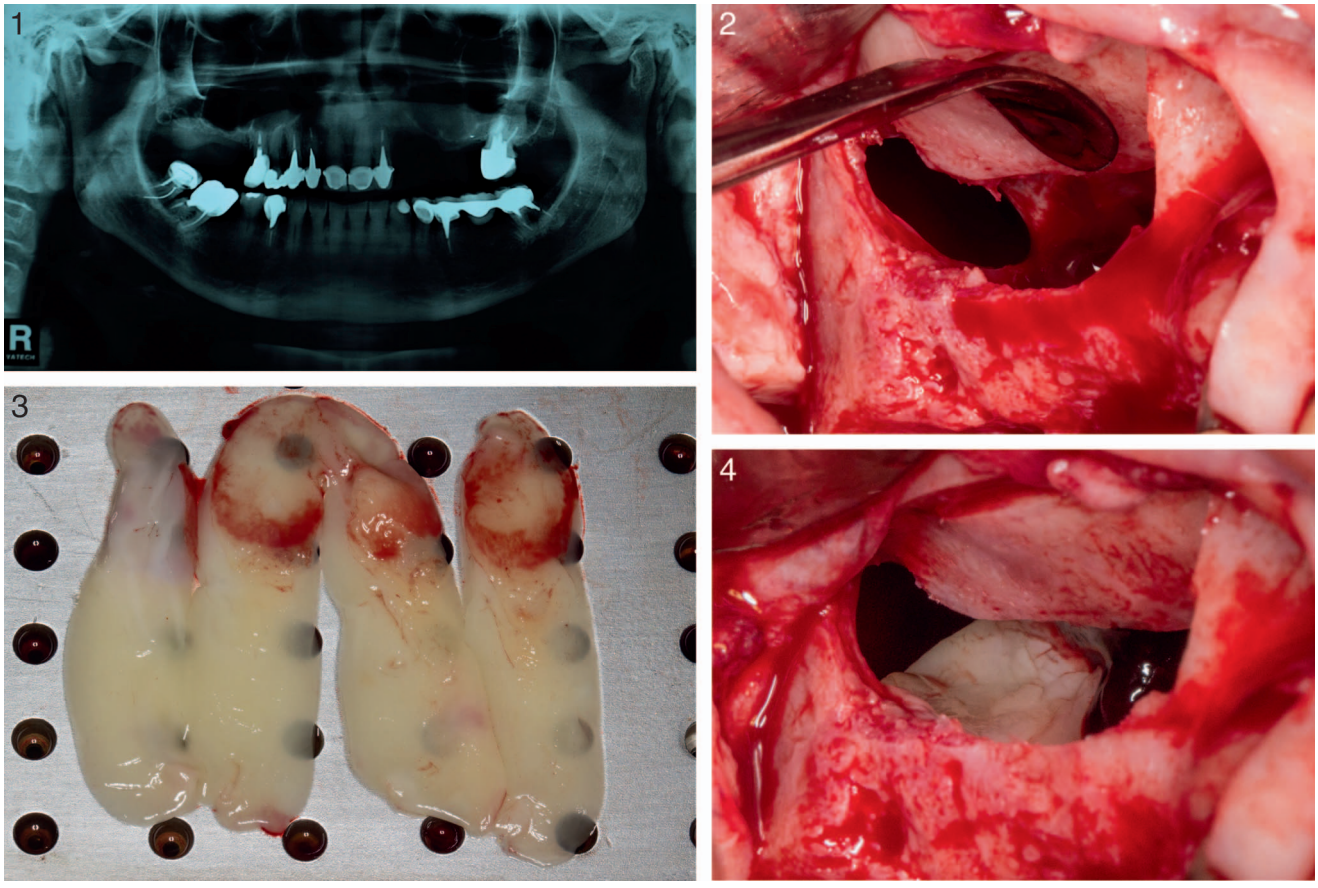
https://doi.org/10.1563/aaid-joi-D-20-00044



Figures 1–4. Figure 1. A representative case illustrating the initial panoramic radiograph indicating the need to maxillary sinus floor augmentation for subsequent implant placement in the region (case E). **Figure 2.** The large perforation of the Schneiderian membrane detected during the sinus floor augmentation procedure in the right maxillary side (case E). **Figure 3.** Leukocyte and platelet-rich fibrin (L-PRF) membranes obtained by centrifuging the patient's blood tubes (case E). **Figure 4.** Interposition of L-PRF membranes on the Schneiderian membrane perforation (case E).

thin-membrane manipulation, presence of bone septum or pathologies, and act secondarily to previous surgery.[16,17] Studies have been shown that SM perforations with a range from 2 mm to 1.5 cm can be closed completely without interfering with bone formation or implant success.[18–22] In this condition, the SM perforation is usually closed by using a collagenous membrane, fibrin adhesive, or oxidized regenerated cellulose and a block graft.[23] However, in some cases of SM large perforations in which the repair does not seem to be sufficiently possible, the procedure needs to be interrupted to avoid graft contamination or migration, which could lead to postoperative sinus infection.[22,24]

Although several techniques have been proposed, no recognized method has been recommended for repairing SM perforations.[25] In this context, the leukocyte and platelet-rich fibrin (L-PRF) membranes are an alternative in the treatment of SM large perforation.[26,27] The L-PRF is a fully autogenous material capable of releasing cytokines and growth factors favorable to the patient's healing and immune response.[28] During L-PRF centrifugation, fibrin network polymerization occurs naturally and slowly, which promotes a high-resistance structure that can avoid graft particle migration into the SM.[27]

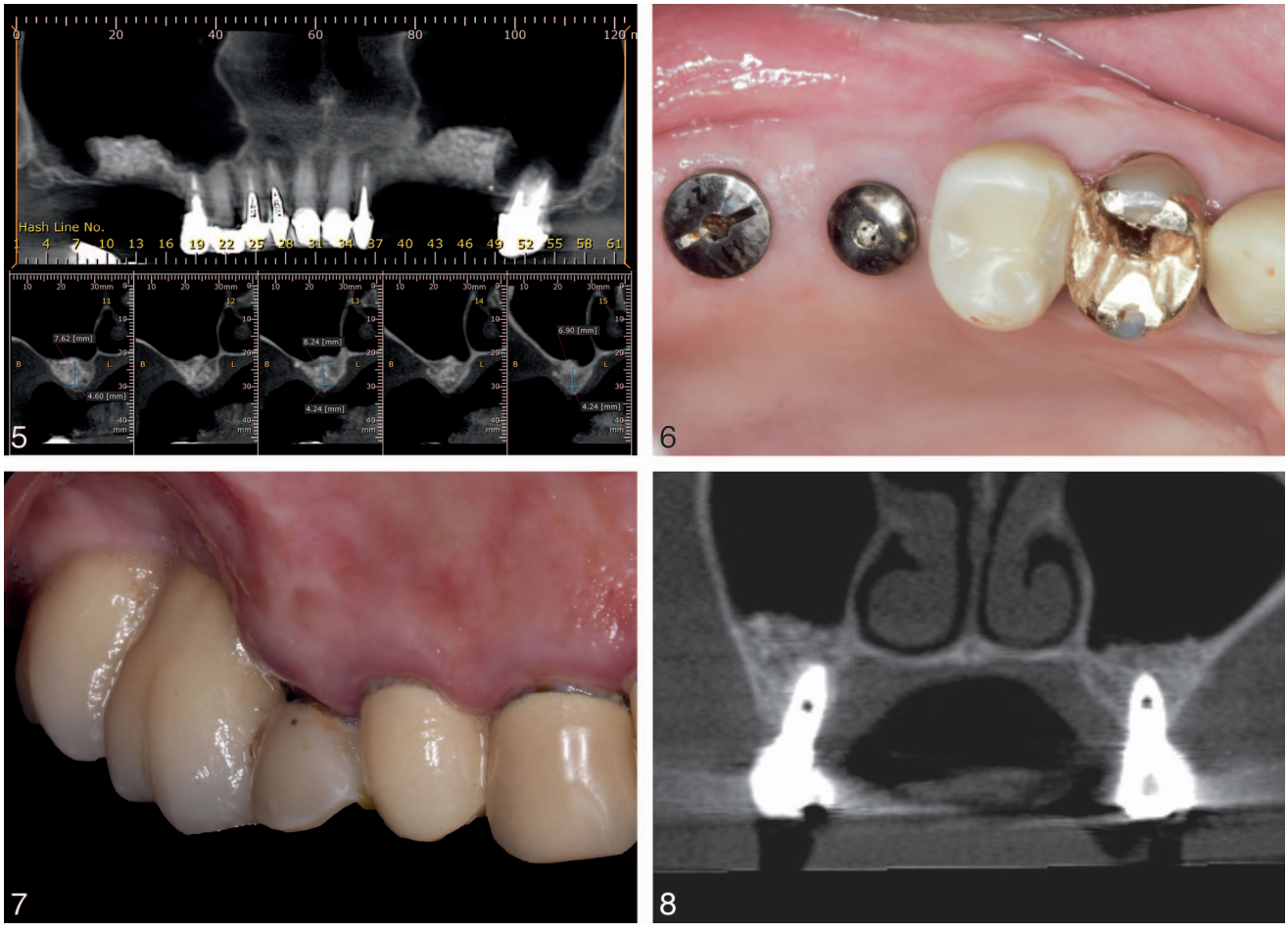
Nonetheless, evidence regarding the use of L-PRF to manage sinus membrane perforations is limited.[26,27] Therefore, this case series aimed to evaluate the use of L-PRF in the treatment of large SM perforations in 9 clinical cases with 2–5 years of follow-up.

Materials and Methods

Surgical technique

From January 2014 to 2017, 9 healthy patients (5 males and 4 females; mean age, 53.22 ± 12.15 years) of the Implantology Clinic at the Araraquara School of Dentistry (UNESP) were evaluated for dental implants rehabilitation. The clinical and radiographic evaluation (panoramic radiography) of the patients showed insufficient bone volume for adequate dental implants placed in the posterior region of the maxilla (Figure 1). Based on that, the patients were submitted to the SFA procedure before dental implant installation.

The SFA was done under local anaesthesia. A linear palatinized incision was made over the bony crest, followed by another vertical incision. A mucoperiosteal flap was retracted to access the lateral wall of the maxillary sinus. The osteotomy was performed with a ball milling cutter until the



Figures 5–8. Figure 5. Cone beam computed tomography 8 months after Schneiderian membrane repair and simultaneous bone graft in the region (case E). **Figure 6.** A representative case illustrating the dental implants after osseointegration (case E). **Figure 7.** A representative case illustrating oral rehabilitation after 5 years of follow-up (case E). **Figure 8.** Coronal section of the cone beam computed tomography exam after 5 years of the Schneiderian membrane perforation treatment (case E).

SM could be visualized by transparency. After that, membrane detachment was performed with specific curettes (Neodent, Curitiba, Paraná, Brasil), and, at this moment, a large disruption of membrane integrity was detected in all patients, making conventional treatment through the interposition of collagen membranes impossible (Figure 2).

Membrane perforation was isolated in all cases, and the interposition of L-PRF membranes was planned because of the perforation dimensions. For L-PRF preparation, six 10-mL glass tubes (without an anticlotting agent) of peripheral blood were collected from each patient. The samples were immediately centrifuged at 400*g*[28] (centrifuge Intra-Spin-Intra-Lock International, Boca-Raton, Fla). Afterward, the tubes were removed from the centrifuge, allowing the visualization of 3 layers. Through a cut, the L-PRF clot was separated from the red corpuscle layer maintaining the buffy coat region. Each fibrin clot was placed in a metal box (Xpression, Intra-lock System, Sao Paulo, Brazil). The fluids present in the fibrin clots were squeezed out to obtain L-PRF membranes (Figure 3). The obtained membranes were interposed on the perforated SM, one over the other until the rupture of the maxillary sinus membrane could not be visualized (Figure 4).

After repair of the sinus membrane perforation, the maxillary sinus cavities were filled with deproteinized bovine mineral bone (Bio-oss, Geistlich, Root Längenbold, Switzerland), and a collagen membrane was positioned to cover the lateral access window. Primary closure was achieved in all cases with 5-0 nylon sutures (Ethicon, Jonhson & Jonhson, New Brunswick, NJ). The patients were instructed to perform gentle mouth rinses with 0.12% chlorhexidine gluconate twice daily for 15 days. The postoperative prescription included antibiotics (amoxicillin, 500 mg, 8/8 hours for 7 days), nonsteroidal anti-inflammatory (nimesulide, 100 mg, 12/12 hours for 3 days), and analgesics (dipyrone, 500 mg, 6/6 hours for 3 days). The sutures were removed 10 days after the surgery.

Implant placement

After 8 months of healing, a cone beam computed tomography (CBCT; patients A, C, D, and E) scan or panoramic radiography (patients B, F, G, H, and L) was requested (depending on the patient's financial condition) to assess the bone graft gain and to identify any possible existing sinus pathology (Figure 5). Adequate bone volume for dental implant placement was

TABLE

Patient demographic data and dental implants primary stability values in N·cm

Patient	Age (yr)	Sex	Perforation Side	Primary Stability (N·cm)
A	63	Male	Left	20
B	35	Female	Left	45
C	55	Female	Right	32
D	68	Male	Left	20
E	71	Female	Right	30
F	45	Male	Left	20
G	51	Male	Left	45
H	49	Female	Right	20
L	42	Male	Right	45

obtained in all patients. A total of 13 implants were placed in the augmented maxillary sinuses with SM perforation treated with L-PRF membranes. The primary stability of implants was measured through implant insertion torque (N·cm). The mean value of the implants primary stability was 30 N·cm (the Table). After 6 months of implant installation, the patients were referred for prosthetic rehabilitation (Figure 6).

Long-term radiologic and clinical assessment

After 3–5 years of the surgical augmentation procedure, the patients were evaluated, and the success of the implants was recorded. A CBTC scan (patients A, C, and E) or panoramic radiography (patients B, D, F, G, H, and L) was performed (depending on the patient's financial condition) to qualitative analyze the SM repair and dental implant osseointegration. No implants were lost after the 3- to 5-year follow-up period (Figure 7). The CBCT or panoramic radiography images showed correct osseointegration of all implants and effective repair of the SM perforations (Figure 8). Bone graft confinement was observed in all maxillary augmented sinuses, and there was absence of signs of infection/mucus.

DISCUSSION

In this cases series, 9 SM perforations during the SLA procedure were effectively treated using L-PRF membranes, and no signs of infection/mucus in the sinus cavity were observed after 3–5 years of follow-up. These SM reparations were made in this case series because unrepaired or improperly repaired SM perforation may result in bacterial penetration, mucus invasion into the bone graft, and even ostium obstruction because of graft leakage to the perforation site, compromising physiologic drainage of the maxillary sinus.[29]

The impact of intraoperative perforations of the SM during SLA on the osseointegration after implant insertion was evaluated in some clinical studies.[21,22,30] Beck-Broichsitter et al[22] showed an implant survival of 98.9% in the perforation group (39 perforations) over an observation period of 2.7 ± 2.03 years compared with 100% in the control group (40 SLA procedures without complications) after 1.8 ± 1.57 years. Similarly, Hernandez-Alfaro et al[21] evaluated the treatment effectiveness of a total of 104 SM perforations with different sizes. After the SM perforation treatment, 278 implants were placed under the repaired membrane, and 247 implants survived. According to these authors, the dental implants survival rates placed under reconstructed membranes correlate inversely with the size of the perforations. In contrast to these results, a study by Nolan et al[30] retrospectively reassessed a total of 359 sinus augmentation procedures with a perforation rate of 41.8% (150 patients) at least 1 year after implant loading and reported a graft failure rate of 6.7%, in which 70.8% of membranes were perforated. In this cases series, a total of 13 implants were placed in the augmented maxillary sinuses with the SM repaired, and no dental implant loss was observed after 3–5 years of follow-up.

Several techniques have been proposed for SM perforation treatment; however, no recognized method has been recommended.[25] L-PRF has been proposed for the repair of large SM perforations based on its natural adhesive properties,[31–33] which guarantee good adhesion of this material to the sinus membrane[34] and good bone graft stabilization capacity because of the mechanical resistance offered by the 3-dimensional fibrin network. Moreover, L-PRF concentrate presents autogenicity, affordable cost, and release of cytokines and growth factors that favor early healing and angiogenesis.[35,36] Based on these properties, the L-PRF membranes were used in this case series for the treatment of 9 SM perforations. None of the patients developed postoperative complications, including wound dehiscence, sinus infection, and exposure or loss of the graft, confirming L-PRF effectiveness in SM perforation treatment in this case series.

A similar result was reported by Oncu et al,[27] which evaluated the bone formation and angiogenesis in 10 SLA procedures with SM perforation repaired with L-PRF membranes in comparison with 10 SLA procedures without SM perforation. No statistical difference was found between the groups for the histologic and radiographic parameters evaluated. Both groups had a similar bone gain, increased area of possible vasculogenesis, and dental implant survival. Similarly, a case report[26] showed that the use of the L-PRF membrane was efficient for the sealing of the SM perforation and enabled bone formation for subsequent dental implant installation. Aricioglu et al[37] compared the effectiveness of resorbable collagen and L-PRF membranes in SM perforations treatment (up to 1 cm) in rats. Both treatments were effective, and no significant difference in the number of lymphocytes, fibroblasts, veins, and collagen fibers was observed between the groups.

The methodologic limitations of the present case series include a relatively low number of participants and the absence of bone formation (volume and height) quantitive analysis. The CBCT bone formation analysis was not made to reduce patient costs; the surgical planning of all steps was made based on panoramic radiographs. The CBCT was requested only in difficult cases where panoramic radiography does not provide all the necessary details for surgical planning.[9–11] However, our finding is promising, and randomized clinical trials including a control group, bone formation analysis, and larger number of patients should be performed to confirm the results obtained in this case series.

In conclusion, the qualitative analysis of the clinical aspects and radiograph/CBCT images of this case series showed that

the L-PRF membrane was effective for the SM large perforation repair, allowing dental implants osseointegration with the absence of infection/mucus signs after 3–5 years of follow-up.

Abbreviations

CBCT: cone beam computed tomography
L-PRF: leukocyte and platelet-rich fibrin
SFA: sinus floor augmentation
SM: Schneiderian membrane

Note

The authors declare no conflicts of interest.

References

1. Rosano G, Taschieri S, Del Fabbro M, Weinstein T, Testori T, Gaudy J. Anatomia chirurgica step by step. Scheda Didattica: Il Seno Mascellare. *Italian Oral Surg*. 2008;7:39–43.
2. Mogensen C, Tos M. Quantitative histology of the maxillary sinus. *Rhinology*. 1977;15:129–140.
3. Watzek G, Bernhart T, Ulm C. Complications of sinus perforations and their management in endodontics. *Dent Clin North Am*. 1997;41:563–583.
4. Santana V. *Anatomia de la Cabeza para Odontólogos*. Madrid, Spain: Editorial Médica Panamericana; 2007.
5. Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. *J Oral Surg*. 1980;38:613–616.
6. Branemark PI, Adell R, Albrektsson T, Lekholm U, Lindstrom J, Rockler B. An experimental and clinical study of osseointegrated implants penetrating the nasal cavity and maxillary sinus. *J Oral Maxillofac Surg*. 1984; 42:497–505.
7. Tatum H Jr. Maxillary and sinus implant reconstructions. *Dent Clin North Am*. 1986;30:207–229.
8. Srouji S, Kizhner T, Ben David D, Riminucci M, Bianco P, Livne E. The Schneiderian membrane contains osteoprogenitor cells: in vivo and in vitro study. *Calcif Tissue Int*. 2009;84:138–145.
9. Chen MH, Shi JY. Clinical and radiological outcomes of implants in osteotome sinus floor elevation with and without grafting: a systematic review and a meta-analysis. *J Prosthodont*. 2018;27:394–401.
10. Sul SH, Choi BH, Li J, Jeong SM, Xuan F. Histologic changes in the maxillary sinus membrane after sinus membrane elevation and the simultaneous insertion of dental implants without the use of grafting materials. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:e1–e5.
11. Sul SH, Choi BH, Li J, Jeong SM, Xuan F. Effects of sinus membrane elevation on bone formation around implants placed in the maxillary sinus cavity: an experimental study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:684–687.
12. Wallace SS, Mazor Z, Froum SJ, Cho SC, Tarnow DP. Schneiderian membrane perforation rate during sinus elevation using piezosurgery: clinical results of 100 consecutive cases. *Int J Periodont Restorat Dent*. 2007; 27:413–9.
13. Schwartz-Arad D, Herzberg R, Dolev E. The prevalence of surgical complications of the sinus graft procedure and their impact on implant survival. *J Periodontol*. 2004;75:511–516.
14. Papa F, Cortese A, Maltarello MC, Sagliocco R, Felice P, Claudio PP. Outcome of 50 consecutive sinus lift operations. *Br J Oral Maxillofacial Surg*. 2005;43:309–313.
15. Toscano NJ, Holtzclaw D, Rosen PS. The effect of piezoelectric use on open sinus lift perforation: a retrospective evaluation of 56 consecutively treated cases from private practices. *J Periodontol*. 2010;81:167–171.
16. Wen SC, Lin YH, Yang YC, Wang HL. The influence of sinus membrane thickness upon membrane perforation during transcrestal sinus lift procedure. *Clin Oral Implants Res*. 2015;26:1158–1164.
17. Zijderveld SA, van den Bergh JP, Schulten EA, ten Bruggenkate CM. Anatomical and surgical findings and complications in 100 consecutive maxillary sinus floor elevation procedures. *J Oral Maxillofac Surg*. 2008;66: 1426–1438.
18. Park WB, Han JY, Kang P, Momen-Heravi F. The clinical and radiographic outcomes of Schneiderian membrane perforation without repair in sinus elevation surgery. *Clin Implant Dent Relat Res*. 2019;21:931–937.
19. Marin S, Kirnbauer B, Rugani P, Payer M, Jakse N. Potential risk factors for maxillary sinus membrane perforation and treatment outcome analysis. *Clin Implant Dent Relat Res*. 2019;21:66–72.
20. Becker ST, Terheyden H, Steinriede A, Behrens E, Springer I, Wiltfang J. Prospective observation of 41 perforations of the Schneiderian membrane during sinus floor elevation. *Clin Oral Implants Res*. 2008;19: 1285–1289.
21. Hernandez-Alfaro F, Torradeflot MM, Marti C. Prevalence and management of Schneiderian membrane perforations during sinus-lift procedures. *Clin Oral Implants Res*. 2008;19:91–98.
22. Beck-Broichsitter BE, Westhoff D, Behrens E, Wiltfang J, Becker ST. Impact of surgical management in cases of intraoperative membrane perforation during a sinus lift procedure: a follow-up on bone graft stability and implant success. *Int J Implant Dent*. 2018;4:6.
23. Fugazzotto PA, Vlassis J. A simplified classification and repair system for sinus membrane perforations. *J Periodontol*. 2003;74:1534–1541.
24. Khoury F. Augmentation of the sinus floor with mandibular bone block and simultaneous implantation: a 6-year clinical investigation. *Int J Oral Maxillofac Implants*. 1999;14:557–564.
25. Ardekian L, Oved-Peleg E, Mactei EE, Peled M. The clinical significance of sinus membrane perforation during augmentation of the maxillary sinus. *J Oral Maxillofac Surg*. 2006;64:277–282.
26. Pinto G, Pigossi SC, Pessoa T, et al. Successful use of leukocyte platelet-rich fibrin in the healing of sinus membrane perforation: a case report. *Implant Dent*. 2018;27:375–380.
27. Oncu E, Kaymaz E. Assessment of the effectiveness of platelet rich fibrin in the treatment of Schneiderian membrane perforation. *Clin Implant Dent Relat Res*. 2017;19:1009–1014.
28. Dohan DM, Choukroun J, Diss A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;101:e37–e44.
29. Pikos MA. Maxillary sinus membrane repair: update on technique for large and complete perforations. *Implant Dent*. 2008;17:24–31.
30. Nolan PJ, Freeman K, Kraut RA. Correlation between Schneiderian membrane perforation and sinus lift graft outcome: a retrospective evaluation of 359 augmented sinus. *J Oral Maxillofac Surg*. 2014;72:47–52.
31. Oncu E, Erbeyoglu AA. Enhancement of immediate implant stability and recovery using platelet-rich fibrin. *Int J Periodontics Restorative Dent*. 2019;39:e58–e63.
32. Oncu E, Bayram B, Kantarci A, Gulsever S, Alaaddinoglu EE. Positive effect of platelet rich fibrin on osseointegration. *Med Oral Patol Oral Cir Bucal*. 2016;21:e601–e607.
33. Sammartino G, Dohan Ehrenfest DM, Carile F, Tia M, Bucci P. Prevention of hemorrhagic complications after dental extractions into open heart surgery patients under anticoagulant therapy: the use of leukocyte- and platelet-rich fibrin. *J Oral Implantol*. 2011;37:681–690.
34. Proussaefs P, Lozada J. The "Loma Linda pouch": a technique for repairing the perforated sinus membrane. *Int J Periodontics Restorative Dent*. 2003;23:593–597.
35. Choukroun J, Diss A, Simonpieri A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;101:299–303.
36. Dohan DM, Choukroun J, Diss A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;101:e45–e50.
37. Aricioglu C, Dolanmaz D, Esen A, Isik K, Avunduk MC. Histological evaluation of effectiveness of platelet-rich fibrin on healing of sinus membrane perforations: a preclinical animal study. *J Craniomaxillofac Surg*. 2017;45:1150–1157.