



TECHNICAL REPORT

Treatment of sinus membrane perforations during sinus lift surgeries using leukocyte and platelet-rich fibrin: A report of three cases

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ABSTRACT

Background and Aim: Schneiderian membrane (SM) perforation is the most frequent intraoperative complication during sinus lifts, which can lead to implant failure or delayed implant treatment. This article aims to show the results of using leukocyte and platelet-rich fibrin (L-PRF) in the treatment of perforations occurring during sinus lifts with a lateral window approach.

Results: Three patients ($n = 5$ implants) with a mean \pm SD age of 57.67 ± 12.12 years were included, in whom perforations of the SM of 3–5 mm and >5 mm occurred. The mean \pm SD preoperative bone height was 4.42 ± 2.96 and, at 6 months it was 9.58 ± 2.41 ($P < 0.05$). All implants had a 100% survival rate at 6–24 months. At the split-mouth, the mean \pm SD baseline height was 5.05 ± 2.99 mm in repaired SM versus 2.92 ± 1.01 in those without any complications ($P > 0.05$). At 6 months, mean \pm SD gains were 10.09 ± 2.44 mm versus 7.73 ± 0.90 mm, respectively, ($P > 0.05$).

Conclusion: L-PRF simplifies SM repair, reducing the need for high surgical experience and/or skills. Although there are no significant differences between repaired and intact SM, at the radiological level, greater bone compactness and maturation were observed in the latter, which may be associated with the presence of air bubbles caused by anaerobic bacterial activity in repaired SM.

Relevance for Patients: The use of L-PRF greatly simplifies the resolution of SM perforations during sinus lift surgeries, reducing treatment times, and providing predictable results. Being of autologous origin, it accelerates and enhances healing, eliminating the possibility of autoimmune rejection reactions.

1. Introduction

The posterior maxilla represents a unique and challenging area for dental implant (DI) placement, osseointegration, survival, and success, mainly due to its often poor bone quality and deficient bone volume as a result of ridge resorption, atrophy, and sinus pneumatization [1]. To counteract these difficulties, a maxillary sinus lift surgery (SLS) is the most predictable procedure in maxillary posterior teeth replacement, with DI survival rates around 97.10% at 15 years of follow-up [2]; however, a Schneiderian membrane (SM) intact and with continuity is deemed “essential” for the successful integration of any grafting materials into the maxillary sinus and subsequently, the high survival rates for DIs placed into augmented sites [1].

In this regard, perforation of the SM is the most frequent surgical complication during the SLS, having been reported to occur in 7–58% of cases [3]. Anatomical, as well as technical factors have been implicated in SM perforation. Conditions such as sinus floor convolutions,

sinus septum, transient mucosa swelling, osteotomy design, and narrow sinus can complicate membrane elevation and increase the risk of perforation during the procedure. Their occurrence can lead to postoperative complications, such as acute or chronic sinus infection, bacterial invasion, inflammation, bleeding, surgical wound dehiscence, loss of graft material, and/or disruption of normal physiological sinus function [4] as well as suspension of the surgical process [5]. Recent research showed that survival rates of DIs placed after SLS with repaired SM are comparable to those placed in sinuses with intact SM (97.68% [$n = 1115$ DIs] vs. 98.88% [$n = 2495$ DIs], respectively) [6].

Collagen membranes (CMs) are commonly used to treat this complication; however, it has been hypothesized that their dense structure may interfere with or block the osteogenic potential of the SM, slowing the formation of new bone in the subsinus cavity [5]. To avoid this, the use of leukocyte and platelet-rich fibrin (L-PRF) has been proposed. L-PRF is a polymerized matrix with a tetramolecular structure containing a large number of leukocytes and platelets (approximately 70% and 95% of the initial clot, respectively) [7,8], as well as monocytes [9] and circulating stem cells [7,8] embedded in a high-density fibrin matrix, obtained autologously from the centrifugation of blood obtained from the patient [10]. Moreover, during this centrifugation, slow and natural polymerization of the fibrin mesh takes place, resulting in a structure with high strength, which would prevent the migration of the bone particles into the maxillary sinus in cases in which SM perforations were repaired [10]. Moreover, due to its molecular characteristics, L-PRF provides an optimal environment for the migration, proliferation and differentiation of endothelial cells, fibroblasts, chondrocytes, and osteoblasts, allowing for accelerated angiogenesis and matrix remodeling [11].

The present article aims to show the results of using L-PRF in combination or isolated in the treatment of SM perforations occurring during SLS with a lateral window approach.

2. Case presentation

Three patients were included, all were male, with a mean \pm SD age of 57.67 ± 12.12 years. None of them had previous sinus pathology. In all cases, SLSs were performed with a lateral window approach for delayed DI placement (at 6 months). In two patients, two DIs were placed and, in one patient, one DI ($n = 5$ DIs). DIs were placed in positions 1.6, 1.7, 2.5, and 2.6 sites ($n = 2$ DIs) (Table 1).

The thickness of the SM before the regenerative procedure was type II (0–2 mm), III (3–4 mm), and IV (>4 mm) according to the classification of Rapani *et al.* [12]. The perforations that occurred were class I ($n = 2$) and IIA ($n = 1$) according to Fugazzotto and Vlassis [13] and their size was 3–5 mm in one case, and >5 mm in two patients.

All cases were operated by the same expert surgeon (A-OS-P). For the treatment of these types of perforations L-PRF was produced through free protocol – that is, to obtain products compatible with the technique separately without depending on a commercial firm, according to a recent study [14] – for which 6 glass-coated plastic

tubes of blood of 10 mL (Process for PRF), without anticoagulants or other additives, are withdrawn and centrifuged at 2700 rpm for 12 min (RCF-clot = $408 \times g$), using an LC-04P centrifugation device (Zenith Lab, Jiangsu, CN) (48° rotor angulation, 50 mm radius at the clot, and 80 mm at the maximum). Six L-PRF clots were produced and dehydrated to obtain membranes in a PRF Box (Salvin, Charlotte, CN, USA) (Figure 1). Depending on the type of perforation and its dimensions, L-PRF was used alone or in combination. In this regard, the small SM perforation (3–5 mm) was treated only with L-PRF and in the other two cases in which there was a >5 mm SM perforation, two different approaches were applied: in one case the SM was sutured to the coronal cortex of the antrostomy and two L-PRF membranes were placed to close the perforation and, in the other case, L-PRF was combined with a resorbable CM (BIOTECK, Arcugnano, Italy) which has a degradation time of 4–6 weeks (Figures 2-4).

The subsinus cavity in all cases was filled with two L-PRF membranes sliced and mixed with a particulate β -tricalcium phosphate bone graft (SynthoGraft, Boston, MA, USA). The antrostomies were sealed with two additional L-PRF membranes.

Measurements were taken at the pre- and 6-month post-operative cone-beam computed tomography (CBCT) using DI planning software (Planmeca Romexis, Helsinki, FI) to evaluate the success of bone regeneration through changes in bone height, as well as the presence/absence of sinus pathology. For this purpose, four measurements were obtained from 4 transverse slices 2 mm distant from each other, taking as a reference the axis of the inserted DI and the adjacent tooth as a standard reference point. Position #1 refers to the most mesial position and position #4 to the most distal with relation to the midline. The overall mean \pm SD bone height preoperatively in the sinuses where SM perforation occurred was 4.42 ± 2.96 and at 6 months, the available bone height to the sinus was 9.58 ± 2.41 mm ($P < 0.05$). In all cases, DIs were placed in a delayed procedure (at 6 months). Insertion torques were not measured electronically; however, they were <50 N•cm (motor marked value). All these DIs had a 100% survival rate at 6–24 months follow-up after loading.

In two patients (cases 2 and 3) in whom a total of 4 DIs were placed, bilateral SLSs were also performed, so in these cases, preoperative bone levels and bone gains at 6 months post-surgery were compared. In these cases, the mean \pm SD pre-operative height in the sinuses in which perforations occurred was 5.05 ± 2.99 mm versus 2.92 ± 1.01 mm in those in which perforations did not occur, with no statistically significant differences ($P > 0.05$). At 6 months, in the sinuses in which the SMs were repaired, bone heights were 10.09 ± 2.44 mm versus 7.73 ± 0.90 mm in those in which they were not ($P > 0.05$) (Table 2). Although there were no significant differences in mean bone height gains between sinuses with repaired and intact SM, radiologically, greater bone compaction was observed in the latter (Figure 5).

3. Discussion

The use of L-PRF makes it very easy to solve cases of perforation of the SM during its elevation, acting as a “patch” [15] due to its

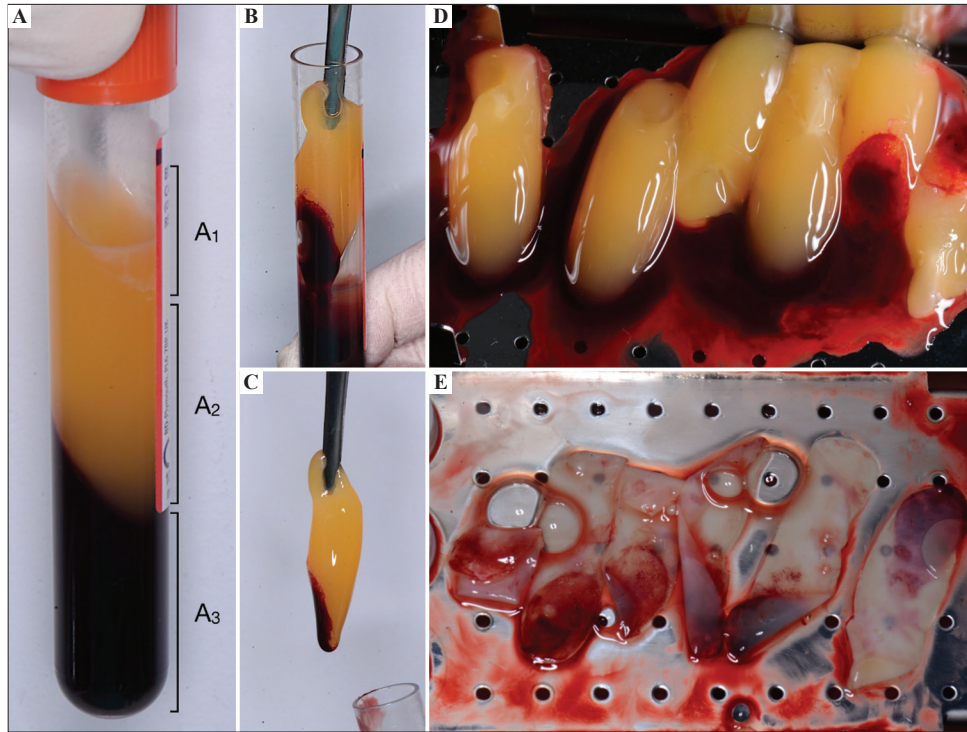


Figure 1. Blood centrifugation produces a 3-layered suspension: erythrocytes at the base of the tube (A_3), a cellular plasma at the top (A_1), and a dense fibrin clot suspended in the middle (A_2), which is extracted with tweezers (B and C). Once all the clots have been obtained, they are deposited in a specific surgical box (D), to dehydrate them by compression and obtain leukocyte and platelet-rich fibrin membranes (E).

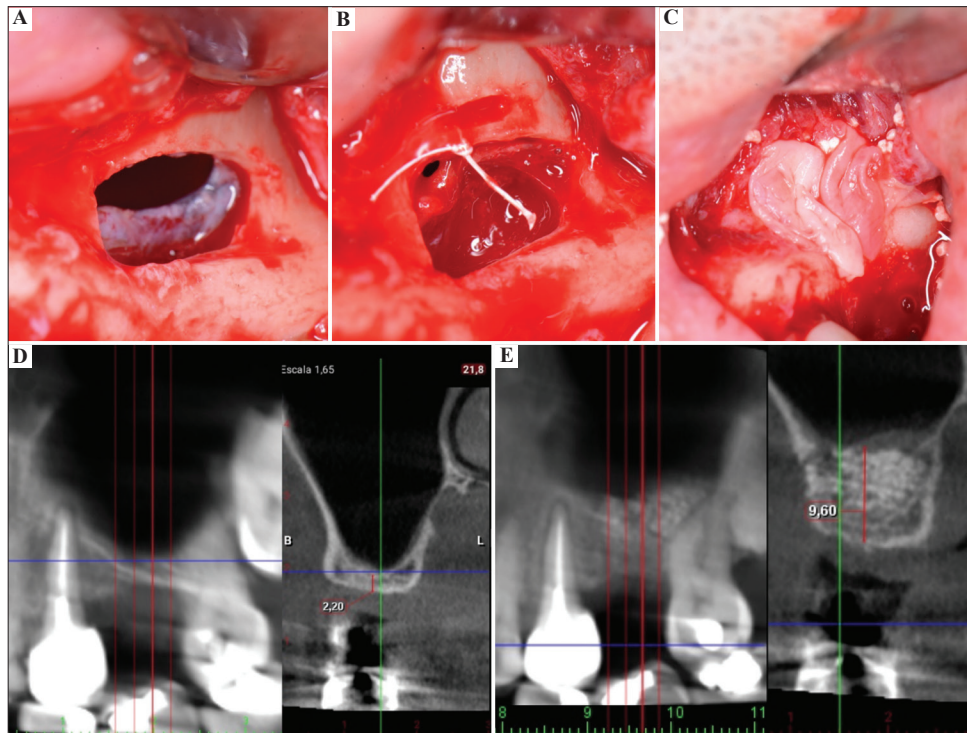


Figure 2. Patient no. 1. (A) Class I perforation of the Schneiderian membrane (SM). (B) The SM was sutured, and the perforation area was sealed with two overlapping leukocyte and platelet-rich fibrin (L-PRF) membranes. (C) Subsequently, the defect was filled with particulate bone graft in combination with two sliced L-PRF membranes and the antrostomy was closed with two additional L-PRF membranes. (D) Initial cone-beam computed tomography (CBCT). (E) CBCT at 6 months post-surgery.

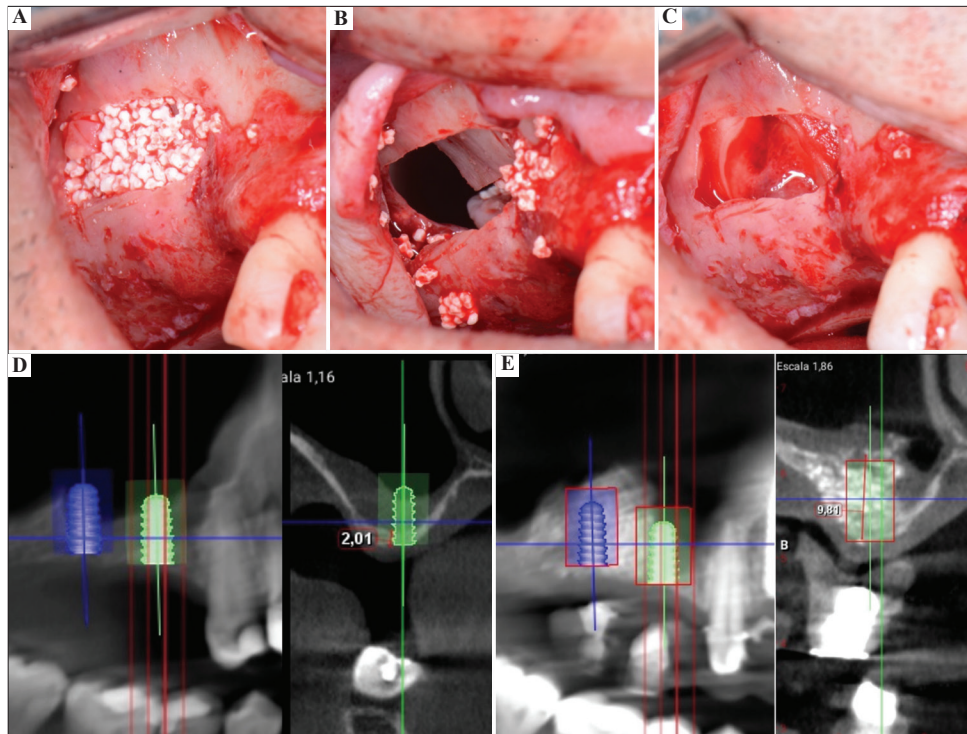


Figure 3. Patient no. 2. (A) After performing SLS and trying to fix a collagen membranes (CM) with a bone tack to seal the antrostomy. (B) The screwdriver was displaced, producing a perforation of the Schneiderian membrane Class IIA. (C) Two leukocyte and platelet-rich fibrin (L-PRF) membranes were immediately placed on the perforation site, and a CM was placed over these membranes to cover the area. (D) Initial cone-beam computed tomography (CBCT). (E) CBCT at 6 months post-surgery.

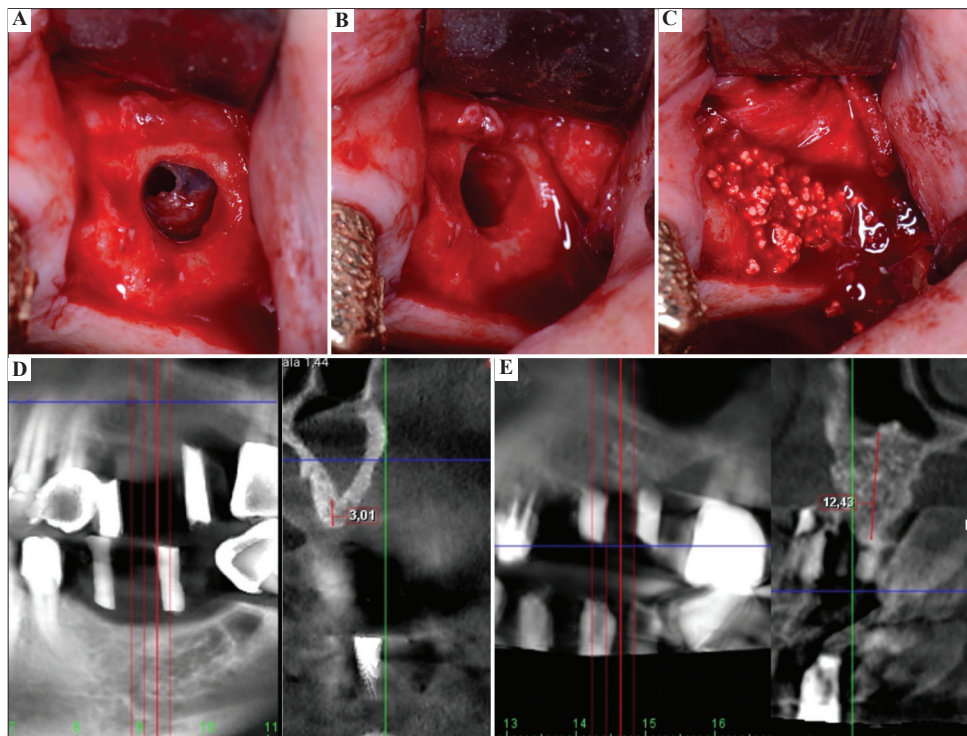


Figure 4. Patient no. 3. (A) A type I perforation of the Schneiderian membrane occurred. (B) Once the detachment was completed, two leukocyte and platelet-rich fibrin (L-PRF) membranes were overlapped to seal it. (C) The subsinusoidal cavity was filled with particulate bone graft and the antrostomy was sealed with two L-PRF membranes. (D) Initial cone-beam computed tomography (CBCT). (E) CBCT at 6 months post-surgery.

Table 1. Characteristics of the patients included

Patient characteristics	Patient number				
	1	2a	2b	3a	3b
Age	54	45	45	74	74
Gender	Male	Male	Male	Male	Male
Smoking habit	No	Yes (10 CPD)	Yes (10 CPD)	No	No
Systemic status	No	No	No	Hyperuricemia Coronary stent	Hyperuricemia Coronary stent
Medication (s)	No	No	No	Zyloric® 100 mg	Zyloric® 100 mg
Allergies	No	No	No	NSAIDs	NSAIDs
Position in the arch	2.6	1.6	1.7	2.5	2.6
Classification of SM perforation	I	IIA	IIA	I	I
Size of SM perforation (mm)	>5	>5	>5	3–5	3–5
Sealing of SM perforation	PRF+SM suture	PRF+CM	PRF+CM	PRF only	PRF only
SM thickness	II	IV	II	III	IV
Initial residual bone height (mm)					
Position 1	2.61	1.60	3.62	15.00	4.20
Position 2	1.40	1.80	3.01	14.17	4.40
Position 3	1.80	1.20	5.80	6.01	5.41
Position 4	1.80	1.00	3.21	3.42	6.85
Mean and individual SD	1.90±0.44	1.40±0.32	3.91±1.11	9.65±5.03	5.22±1.05
Mean and global SD				4.42±2.96	
Bone height 6 m postoperative (mm)					
Position 1	7.61	4.60	10.80	16.00	10.52
Position 2	5.20	8.80	10.40	13.97	10.43
Position 3	8.40	11.21	5.00	13.41	8.60
Position 4	9.00	11.81	5.80	13.60	6.40
Mean and individual SD	7.55±1.45	9.11±2.83	8.00±2.62	14.25±1.03	8.99±1.68
Mean and global SD				9.58±2.41	
Implant length (mm)	6	8	8	10	8
Implant survival rate (%)	100	100	100	100	100
Follow-up after loading (months)	6	6	6	24	24

SD: Standard deviation, SM: Schneiderian membrane, CM: Collagen membrane, mm: Millimetres, CPD: Cigarettes per day, NSAIDs: Non-steroidal anti-inflammatory drugs, PRF: Platelet-rich fibrin

Table 2. Comparison of bone gains between repaired and unrepaired schneiderian membrane at 6 months

Evolution of bone changes	Repaired SM				Unrepaired SM			
	Patient number							
	2a	2b	3a	3b	2a	2b	3a	3b
Initial residual bone height (mm)								
Position 1	1.60	3.62	15.00	4.20	6.00	2.60	8.20	0.80
Position 2	1.80	3.01	14.17	4.40	3.40	2.80	5.80	1.02
Position 3	1.20	5.80	6.01	5.41	2.60	1.22	2.61	2.44
Position 4	1.00	3.21	3.42	6.85	1.20	1.20	1.02	3.82
Mean and individual SD	1.40±0.32	3.91±1.11	9.65±5.03	5.22±1.05	3.30±1.75	1.96±0.75	4.41±2.79	2.02±1.21
Mean and global SD		5.05±2.99				2.92±1.01		
Bone height 6 m postoperative (mm)								
Position 1	4.60	10.80	16.00	10.52	6.80	9.22	8.01	6.60
Position 2	8.80	10.40	13.97	10.43	8.80	8.00	7.60	7.20
Position 3	11.21	5.00	13.41	8.60	9.60	6.60	6.40	10.00
Position 4	11.81	5.80	13.60	6.40	10.80	1.80	7.64	10.02
Mean and individual SD	9.11±2.83	8.00±2.62	14.25±1.03	8.99±1.68	8.64±1.61	6.41±2.82	7.41±0.61	8.46±1.57
Mean and global SD		10.09±2.44				7.73±0.90		

SD: Standard deviation, SM: Schneiderian membrane, mm: Millimetres

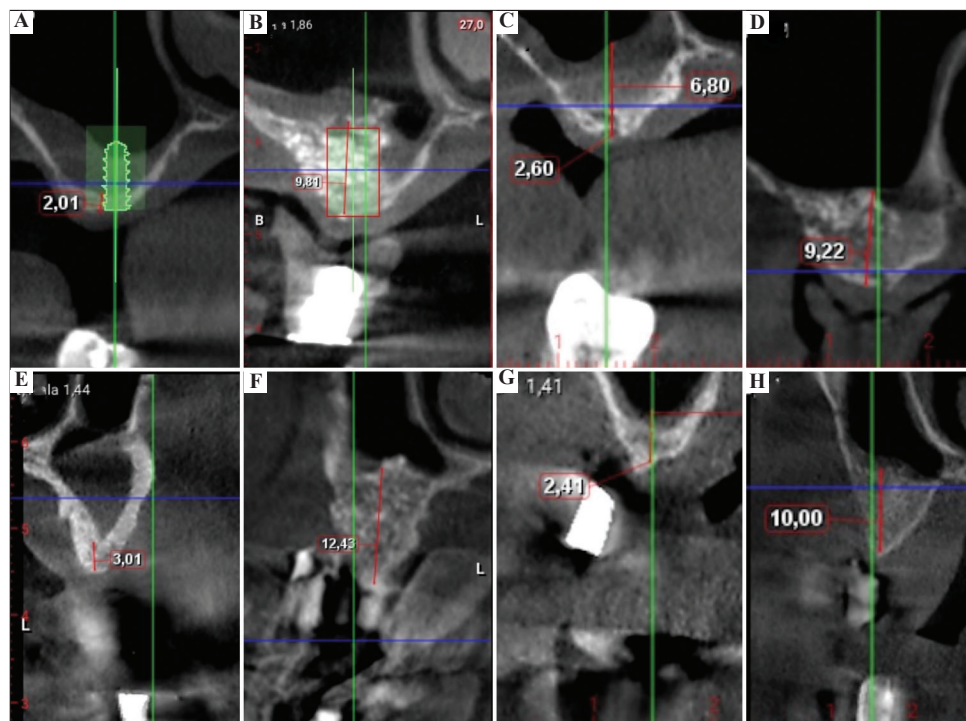


Figure 5. Comparison between test sides and control sides at a radiological level (cone-beam computed tomography [CBCT]). For patient no. 2: repaired Schneiderian membrane (SM) side at baseline (A) and 6 months after sinus lift surgery (B); unrepaired SM at baseline (C) and at 6 months (D). For patient no. 3: repaired SM side at baseline (E) and at 6 months (F); unrepaired SM at baseline (G) and at 6 months (H). In unrepaired SM, there is an apparent increased compaction and maturation of the bone graft.

adhesive properties [16], improving its healing and stimulating its periosteal behavior [15]. Furthermore, in SLSs with a lateral window approach, visualization of the SM perforation is evident, which is not the case in transcresal elevations where a diagnosis is difficult. Using L-PRF as a filling material, alone or in combination with biomaterials, allows the sealing of any perforation that occurs during the procedure.

Current evidence regarding the use of L-PRF for this purpose is limited as it is based on clinical cases, case series or observational studies with small numbers of patients [10,17,18]. Despite this, the observed results are promising. In this regard, Simonpieri *et al.* [17] treated three perforations of the SM with two L-PRF membranes in each case, placing the DIs immediately and only filling the subsinusal cavity with L-PRF membranes, with the DIs remaining stable at 6 months postoperatively, at which time the prosthetic abutments were connected. With a minimum follow-up of 2 years, all cases had a 100% success rate.

Pinto *et al.* [18] showed the treatment of an SM perforation of more than 5 mm in diameter using overlapping L-PRF membranes to seal the defect and a CM on top of them. They filled the subsinusal cavity with deproteinized bovine bone mineral (DBBM) and sealed the anrostomy with a CM. In a delayed approach (8 months) they placed two DIs with a 100% success rate 6 months after prosthetic loading.

An interesting study by Öncü and Kaymaz [10] compared the bone height gain following SLSs on 20 sinuses with ($n = 10$) or without ($n = 10$) the presence of SM perforations. The perforated

SMs were sealed by L-PRF and the filling of the subsinusal cavity in both groups was performed with heterologous cortical bone graft material and the lateral access window was covered with a CM. These authors observed no significant differences between the two groups, having achieved a bone height at 6–8 mm post-surgery of 10.12 ± 1.40 mm and 11.18 ± 1.20 mm, respectively, from an initial mean bone height of 2.41 ± 1.10 mm in both groups, and with DI success rates of 100%.

The use of CMs has proven effective in the repair of SM perforations; however, L-PRF is a valid alternative as it is completely autogenous and is an inexpensive bioactive material. Activated platelets slowly release a wide range of proteins and growth factors including bone morphogenetic proteins, platelet-derived growth factors, insulin-like growth factors, vascular endothelial growth factors, transforming growth factor-beta 1 and 2 that play key roles in bone healing, controlling inflammatory response and infectious processes. In addition, the application of L-PRF is very easy and safe, having positive effects on angiogenesis and wound healing and it stabilizes the graft material and protects the wound [10].

An animal model study evaluated the treatment of these SM perforations with CMs compared to L-PRF membranes. At 1 week, they observed a higher number of inflammatory cells when using CMs and a new osteoid formation significantly greater in the L-PRF group. At 4 weeks, an osteogenic pattern was shown from the periphery to the center of the sinus cavity in the L-PRF group. These findings may be indicative that L-PRF not only does

not interfere but may stimulate the osteogenic potential of SM compared to the use of barrier membranes [5].

Conventionally, SM perforations were classified by their location in relation to the antrostomy [13,19] and, subsequently, by their size, as this was shown to correlate with the rate of DI failure. In this regard, Hernández-Alfaro *et al.* [4] recommended suturing the SM or placing a CM in perforations <5 mm; in those 5–10 mm, shifting the antrostomy bone medially and coronally as a “trap door” and placing a CM apical to it; and in perforations >10 mm, they described several options: sealing the perforation by shifting the antrostomy trap door; by placing an autologous bone block; or using a pedicled buccal fat pad flap. In the present case series, the authors recommend incorporating the L-PRF technique into SLS protocols with a lateral window approach to provide a simple way to resolve a possible perforation of the SM. In this regard, in small perforations (up to 5 mm) whose resolution could be achieved by further detaching the SM and folding it back on itself [13,19], L-PRF could be used in isolation, avoiding the procedure described above, which reduces the need for surgical skill/experience of the operator. Nevertheless, in perforations larger than 5 mm, it is advisable to use L-PRF in combination with CMs or suturing the SM to the coronal cortex of the antrostomy, because L-PRF takes 15 days to resorb [20], which is an insufficient time period considering that SM requires 6–8 weeks for self-healing [21]. In this sense, thanks to the adhesive properties of L-PRF membranes on the SM, it would act as a bridge between the edges of the perforation. In the case of combining it with a CM, this would be placed over the L-PRF membranes ensuring the regeneration of the SM before its degradation.

Regarding SM suturing, Barbu *et al.* [22], combined it with the use of L-PRF in the treatment of perforations >15 mm, placing DIs of 11.5–13 mm in length in one stage. The mean \pm SD initial bone height was 4.48 ± 1.45 mm, with mean gains of 6.43 ± 1.88 mm. Although the initial mean bone height was very similar to that of our study, the subsequent overall gain was 3.15 mm less. This finding was probably due to the fact that they used L-PRF as the only filler biomaterial. Thus, when the L-PRF is resorbed after 15 days, the SM descends to the apex of the DIs acting as a “tent-pole,” forming bone between the SM and the floor of the maxillary sinus. This phenomenon was described by Lundgren *et al.* [23]. However, the DI apex is surrounded by non-osseointegrated connective tissue [24], resulting in a limited bone gain.

In the cases presented, there appears to be greater “compaction” and maturation of the graft material as assessed by CBCTs at 6 months post-surgery. These findings can be explained by the “septic theory.” According to this theory, such “lack of compaction” may be caused by localized air bubbles in the graft, caused by the activity of anaerobic bacteria. Therefore, such vacuoles cannot be due to a “real” lack of condensation in the graft material [25], nor can they be attributed to the use of L-PRF *per se*, but rather to the fact that perforation of the SM occurred, as well as the longer surgical time required to repair them. Both factors may influence increased bacterial colonization of the grafted biomaterial. So far, no author has described this finding, however, de Almeida-Malzoni

et al. [26] 8 months after repairing SM and filling sinus cavities in SLSs with DBBM inserted DIs with low mean torques (30 N•cm), which could confirm our hypothesis. Despite this, the survival rate of DIs was 100% at 3–5 years of follow-up.

Large L-PRF membranes are ideally suited to facilitate the repair of SM perforations. In this respect, it has recently been observed that the material of the blood collection tubes has a more significant influence on the size of the L-PRF clots obtained than the type of centrifuge used, even with 15% differences between various fixed-angle centrifuges. Thus, glass tubes such as those used in the present case series (Process for PRF) make it possible to obtain fibrin clots 200–250% larger than those obtained with plastic tubes (IntraSpin, Intra-Lock) [27,28]. On the other hand, the tubes must be adapted to the ISO 10993-1 standard for clinical use [29], as silica-coated tubes have been shown to contain silica particles that not only leak within PRF tubes but also exert toxic effects on human periosteal cells by adsorbing on the plasma membrane and inducing apoptosis [30], as well as mutagenicity and hemolysis. Furthermore, some plain glass tubes used for laboratory testing incorporate a layer of silicone within the inner tube walls. Their use not only drastically reduces clot size by 200%, but it has also been shown that an excessive silicone coating delays coagulation [28]. This is a critical parameter since, for L-PRF to be obtained, platelet activation and fibrin polymerization must occur physiologically. Hence, platelet activation starts immediately upon contact with the walls of the tube and leads to the formation of a dense fibrin network and usable L-PRF clot [31].

At present, several variations of the L-PRF collection technique have been described to improve the quality of L-PRF with more cells. In this regard, it has been shown that reducing the centrifugation speed prevents cell loss and increases the number of leukocytes embedded in the PRF matrix. Thus, the advanced PRF (A-PRF) (1,500 rpm [230 \times g] or 1300 rpm [200 \times g] for 14 min and glass-based tubes) was developed [32]. Similarly, a variation called A-PRF plus (1300 rpm [200 \times g] for 8 min and glass tubes) was developed, which has shown a significant increase in growth factor release compared to A-PRF and L-PRF [33], which is associated with a higher amount of leukocytes entrapped in fibrin mesh [34].

In short, L-PRF is an adjuvant technique for SLSs, not only because of its interest in repairing SM perforations but also as a filling material alone or in combination with particulate bone grafts, as well as for sealing antrostomies in the case of SLSs with a lateral window approach, as it is effective in preventing mucosal invagination [15], without affecting the proportion of neofomed bone compared to CMs [35]. Thus, their use not only accelerates soft and hard tissue healing processes and reduces postoperative morbidity [36,37], but also reduces associated costs by avoiding or reducing the use of commercially available biomaterials.

4. Conclusions

The use of L-PRF should be considered in SLSs as it simplifies the repair of complications such as small and large SM perforations, reducing the need for high surgical experience and/

or skills. Furthermore, L-PRF might ensure the two osteogenic sources from the SM generate significant new bone formation. Although there are no significant differences between repaired and intact SM, radiologically, greater bone compaction is observed in the latter, which may be associated with the presence of air bubbles caused by anaerobic bacterial activity in repaired SM.

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Conflict of Interest

The authors declare that they have no conflict of interest in relation to this article.

Ethics Approval and Consent to Participate

Consent was obtained from all patients.

Consent for Publication

All patients gave consent for the publication of their images.

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