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Surgical Rehabilitation of Maxillary and Mandibular Bone Using L-PRF in Cardiac Patients Under Antithrombotic Therapy

Rehabilitación Quirúrgica del Hueso Maxilar y Mandibular Mediante L-PRF en Pacientes Cardíacos en Tratamiento Antitrombótico

Frederico Buhatem Medeiros[1,5]; Raquel D'Aquino Garcia Caminha[1,2]; Tiago Carvalho Santos[1]; Gustavo Hashida[3]; Gabriel Peres[4,5] & Paulo Sergio da Silva Santos[1,6]

MEDEIROS, F. B.; CAMINHA, R. D. G.; SANTOS, T. C.; HASHIDA, G.; PERES, G. & SANTOS, P. S. S. Surgical rehabilitation of maxillary and mandibular bone using L-PRF in cardiac patients under antithrombotic therapy. *Int. J. Odontostomat., 19(3)*:304-314, 2025.

ABSTRACT: The risk of perioperative and postoperative hemorrhage makes oral surgery involving bone tissue in patients receiving antithrombotic therapy difficult, and for the best clinical management, physicians and dentists must always be up to speed. In order to prevent bleeding, less invasive techniques were long considered prohibited. This raised concerns about the increased risk of thromboembolic events and the possibility of stopping antithrombotic medication. Leukocyte- and platelet-rich fibrin (L-PRF) is a new local hemostatic measure that shows promise for reducing bleeding and speeding up healing following exodontia in individuals receiving antithrombotic medication. In order to improve repair, bone regeneration, and control of the local hemostatic process, this case series, which includes an integrative literature review, attempts to demonstrate evidence for the use of fibrin derivatives as a surgical option in the management of patients with heart disease receiving anticoagulant and/or antiplatelet therapy. Oral surgery AND platelet-rich fibrin AND oral anticoagulant were the descriptors used to identify papers for an integrative review that was conducted by scanning the PUBMED/MEDLINE®, SCOPUS®, and BVS databases. In this series of cases we present: Case 1: A person who had a balloon catheter valvuloplasty, a heart murmur, and an unidentified cardiac arrhythmia who also took acetylsalicylic acid every day. Case 2: a patient with a history of rheumatic fever, diabetes, hypertension, a mechanical heart valve prosthesis, several teeth extractions, and a sinus lift who is also on oral anticoagulants. In both cases, L-PRF was used to complete the surgery. Dental surgical operations using platelet aggregate concentrates can be performed safely, with no need to suspend or adjust therapy due to the risk of increased post-operative bleeding. L-PRF has been shown to aid healing and regeneration of soft tissues and bone in the maxillary and mandible areas.

KEY WORDS: platelet-rich fibrin, anticoagulants, platelet aggregation inhibitors, oral surgery, hemostatic techniques.

INTRODUCTION

Surgical procedures in the oral cavity and jaws in individuals under antithrombotic therapy (anticoagulant and/or platelet antiaggregant) remain a challenge because of the increased risk of perioperative and postoperative bleeding (Mourão & Alves, 2019). More recently, with the emergence of direct oral anticoagulants, the risk of bleeding and the lack of a specific reversal agent for these drugs (Constantinides *et al*., 2016), there is still concern about the clinical management of these individuals, and physicians and dentists need to have up-to-date knowledge.

For many years, even minor invasive oral surgical procedures, such as tooth extractions, were contraindicated in patients with a need and indication for anticoagulation, unless their drug regimens were

[1] Department of Dentistry of the Cardiology Society of the State of São Paulo (SOCESP), São Paulo, SP, Brazil.
[2] Bauru State Hospital, SP, Brazil.
[3] University of Guarulhos - UNG /SP, Brazil.
[4] Universidade Paulista - UNIP /SP, Brazil.
[5] Samaritano Hospital.São Paulo, SP, Brazil.
[6] University of São Paulo, Faculty of Dentistry in Bauru, Department of Surgery, Stomatology, Pathology and Radiology. Bauru, SP, Brazil.

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modified for a certain period before and/or after surgery to avoid excessive bleeding (Mourão & Alves, 2019), which arguably increased the risk of a thromboembolic event (Manzano *et al*., 2020). This is still a major concern for dentists and physicians, as discontinuing oral anticoagulant therapy increases the risk of thromboembolism, while maintaining the therapeutic dose increases the risk of bleeding. Several local hemostatic measures have been used to control bleeding in this group of patients, but the efficacy of these measures has not been thoroughly investigated, especially regarding quantity in the transoperative period and subjectivity in the quality of postoperative bleeding (Queiroz *et al*. 2016, Buhatem Medeiros *et al*. 2017).

Leukocyte and platelet-rich fibrin (L-PRF) was a promising natural hemostatic agent for controlling bleeding after tooth extraction, studied in a group of patients receiving platelet antiaggregants and oral anticoagulants (Mourão & Alves, 2019), associated with significant clinical improvements in terms of repair and inflammation, in addition to patients taking medications such as antiresorptive and/or antiangiogenic drugs (Maluf *et al*. 2018). To prove its use and sufficient efficacy, additional controlled clinical trials including bigger patient samples are necessary, particularly with regard to control and efficacy in primary, secondary, or tertiary local hemostasis processes.

In order to improve bone repair and regeneration and halt the local hemostatic process, this case series and an integrative review of the literature seek to provide the recent evidence of the use of fibrin derivatives as a therapeutic option in the management of patients with heart disease undergoing anticoagulant and/or antiplatelet therapy.

CASE SERIES AND REVIEW METHOD

An integrative review was conducted by gathering data from selected papers and describing the findings in a consistent and ordered format. Through a search of the PUBMED/MEDLINE®, SCOPUS® and BVS databases, articles were selected using the descriptors: Oral surgery AND Platelet rich fibrin AND Oral anticoagulant. According to MeSH terms, the descriptor “Oral surgery” covers terms such as “Maxillofacial Surgery; Surgery, Maxillofacial; Oral Surgery; Exodontics”. The descriptor “platelet rich fibrin” includes terms such as: “Fibrin, Platelet-Rich, Platelet Rich Fibrin, L-PRF, Leukocyte- and Platelet-Rich Fibrin, Leukocyte and Platelet Rich Fibrin”; while the descriptor “oral anticoagulant” includes the terms: “Factor Xa Inhibitor; Inhibitor, Factor Xa; Xa Inhibitor, Factor; Direct Factor Xa Inhibitors; Direct-Acting Oral Anticoagulants; Anticoagulants, Direct-Acting Oral; Direct Acting Oral Anticoagulants; Oral Anticoagulants, Direct-Acting; Direct Factor Xa Inhibitor; Direct-Acting Oral Anticoagulant; Anticoagulant, Direct-Acting Oral; Direct Acting Oral Anticoagulant; Oral Anticoagulant, Direct-Acting”.

The inclusion criteria defined were: 1) articles with a case report of dental surgery performed on a patient with heart disease who is using anticoagulant therapy with platelet aggregates; 2) articles published in English, Portuguese and Spanish; 3) articles available online; and 4) articles published in an undetermined period of time. The exclusion criteria were: 1) articles that did not address dental surgery in the patient profile mentioned, 2) review articles (systematic, integrative or narrative) and dissertations or theses. To guide this study, we considered: dental surgery using platelet aggregates in cardiac patients under antithrombotic therapy.

This case series was presented in accordance with the Declaration of Helsinki (1964) and the Resolution No. 466 of the National Health Council (Ministry of Health of Brazil, 2012).

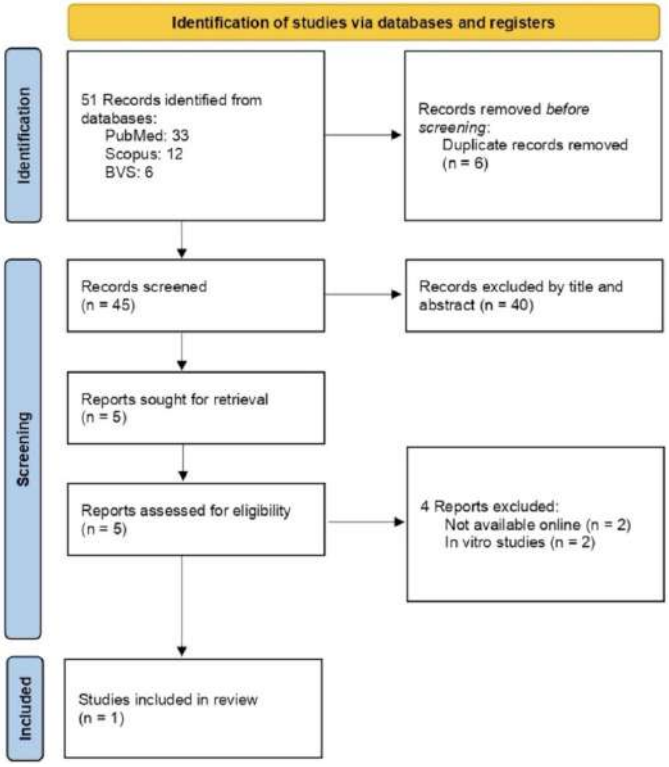

Fig. 1. Flowchart of the stages for selecting the articles available in the databases.

Table I. Laboratory test results of patient of case 2 and reference values.

Parameter		Results	Reference Values
Laboratorial exams	Glycated hemoglobin	6.4 %	5.7 - 6.4 % - pre diabetes
	Calcium - serum	9.2 mg/dL	8.4 - 10.8 mg/dL
	Creatinine - serum	0.82 mg/dL	0.73 - 1.18 mg/dL
Complete blood count	Erythrocytes	5.18 mi/mm^3	4.5 - 6.5 mi/mm^3
	Hemoglobin	15.4 g/dL	13.5 - 18 g/dL
	Hematocytes	48.3 %	40 - 54 %
Laboratorial exams	Prothrombin time-TP	19.4 s	10 - 14 s
	INR	1.75	0.9 - 1.2
	TTPA	30 s	26.4 - 36.8 s
Lipidogram	Triglycerides	243 mg/dL	> 150 mg/dL
	HDL cholesterol	36 mg/dL	< 40 mg/dL

RESULTS

Fifty-one articles were found in the selected databases, 33 of which were in PUBMED/MEDLINE, 12 in SCOPUS and 6 in BVS. After applying the inclusion and exclusion criteria set out in the methodology, 1 article was selected for the final sample (Fig. 1). Prisma Flowchart of databases searched in this literature review

Case report 1

A 19-year-old white woman with an unerupted tooth in the anterior and inferior mandibular base region attended a dental institute that specializes in treating patients with systemic impairment. During clinical examination, the patient revealed a history of congenital pulmonary valve stenosis and balloon valvuloplasty surgery. She had an unspecified cardiac arrhythmia and a heart murmur and was taking acetylsalicylic acid (ASA) 100mg 1x a day and metropolol. An intraoral examination indicated the loss of tooth 32 and the presence of an orthodontic appliance in the lower region. The panoramic reformatting showed an impacted tooth 32 associated with a compound odontoma in the anteroinferior region of the mandible (Fig. 2A). A Cone Beam Computed Tomography scan was requested for three-dimensional evaluation and surgical planning (Fig. 2B).

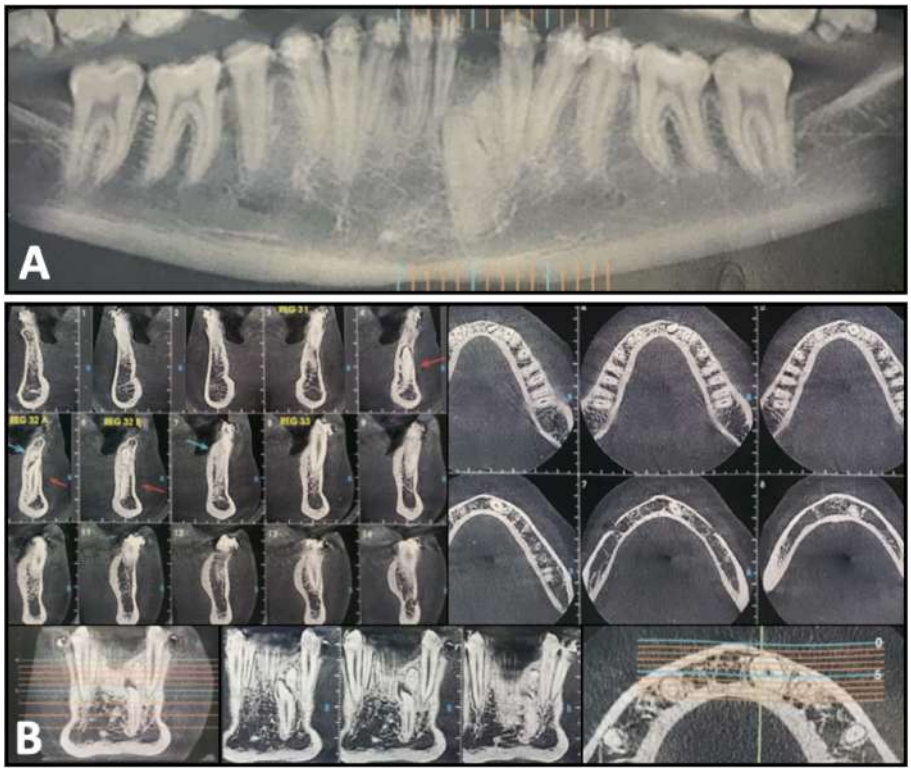

Fig. 2. A. Initial panoramic radiograph. B. Cone Beam Computed Tomography scan.

According to the American Heart Association, antibiotic prophylaxis was performed using 2 g of amoxicillin one hour prior to the procedure in order to prevent infective endocarditis. Thirty minutes before to surgery, a single intramuscular dose of a corticoid (betamethasone dipropionate + betamethasone disodium phosphate) was given to minimize post-operative inflammation.

Initially, approximately 70 mL of blood was drawn from the patient utilizing a closed vacuum collection system using falcon tubes containing silica. The material was centrifuged to obtain platelet concentrates, including stickybone, membranes and L-PRF plugs (Fig. 3). To obtain

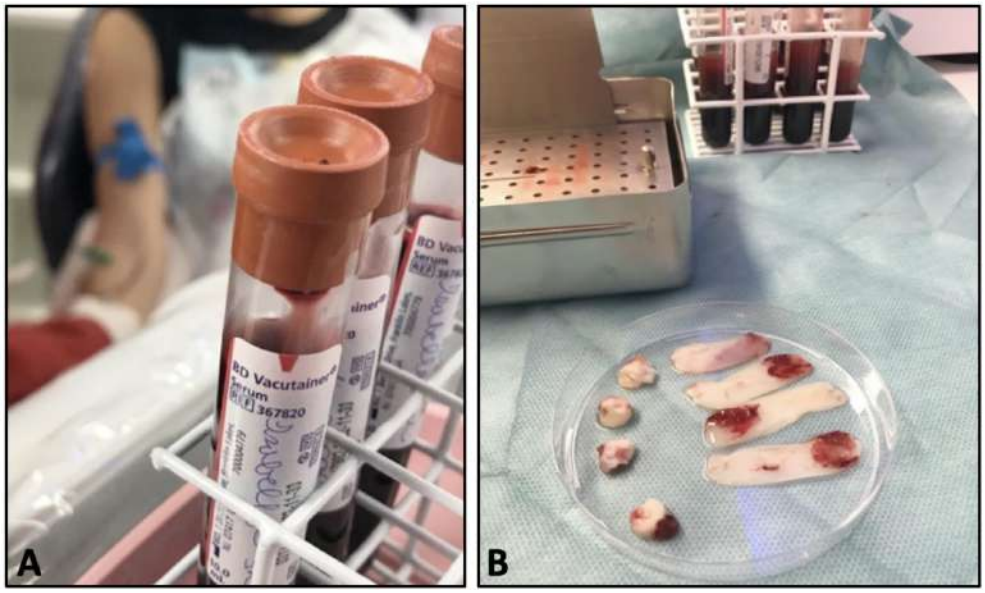

Fig. 3. A y B. Blood collection and obtaining platelet concentrates.

Fig. 5. Macroscopic Tooth 32 and compound odontoma.

the stickybone, bovine bone graft (Lumina-Bone medium 0.5g; Criteria; São Paulo; Brazil) was used in association with autogenous bone graft taken during surgery in the mentual region.

Under local anesthesia using 2 % lidocaine and 1:100,000 epinephrine, the surgery was carried out in an outpatient environment, using the bilateral mentual nerve block technique. The incision was made using a mucoperiosteal flap with two oblique relaxations extending from tooth 34 to tooth 43. Subsequently, an osteotomy and ostectomy were performed for surgical access to the impacted tooth and the lesion (Fig. 4).

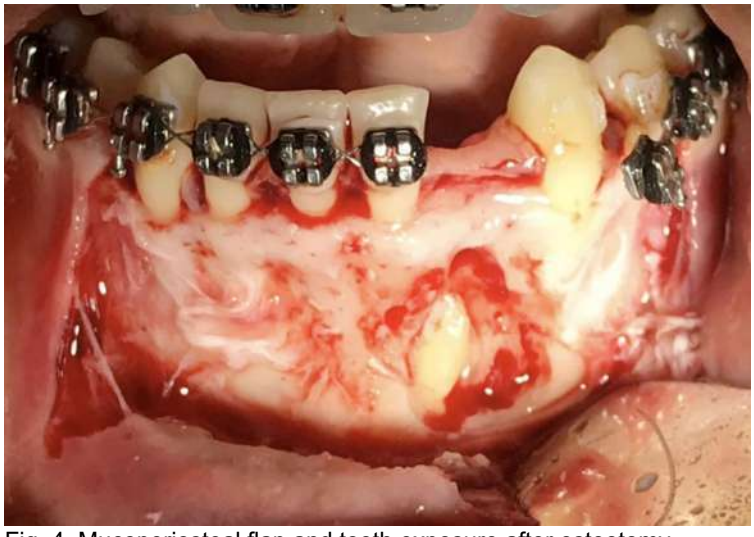

Fig. 4. Mucoperiosteal flap and tooth exposure after osteotomy.

The tooth 32 was extracted and the lesion excised (Fig. 5). After being biopsied, the tissue was put in a 10 % buffered formalin solution and sent for anatomopathological study. The pathologist later verified the diagnostic hypothesis of compound odontoma.

To improve bone regeneration and prepare the surgical site for osseointegrated implant placement in the future, a block of autogenous bone tissue was taken from the mentonian area and broken with a bone crusher (Thimon®; São Paulo, Brazil) (Fig. 6). The entire surgical site was then irrigated with a 0.9 % saline solution.

The autogenous bone was then mixed with bovine bone (Lumina-Bone medium 0.5 g; Criteria; São Paulo; Brazil) and used to make the stickybone. To aid bone neoformation, a non-absorbable synthetic titanium membrane (Surgitime Bionnovation; São Paulo; Brazil) was installed and fixed using titanium membrane fixation tacks (WF cirúrgicos; São Paulo; Brazil). A bovine biological membrane composed of type I collagen (Lumina-coat; Critéria; São Paulo; Brazil) was also placed. L-PRF plugs and membranes were brought into position, filling and covering the surgical site, in order to aid soft tissue and bone repair and promote local hemostasis (Fig. 7). Following these

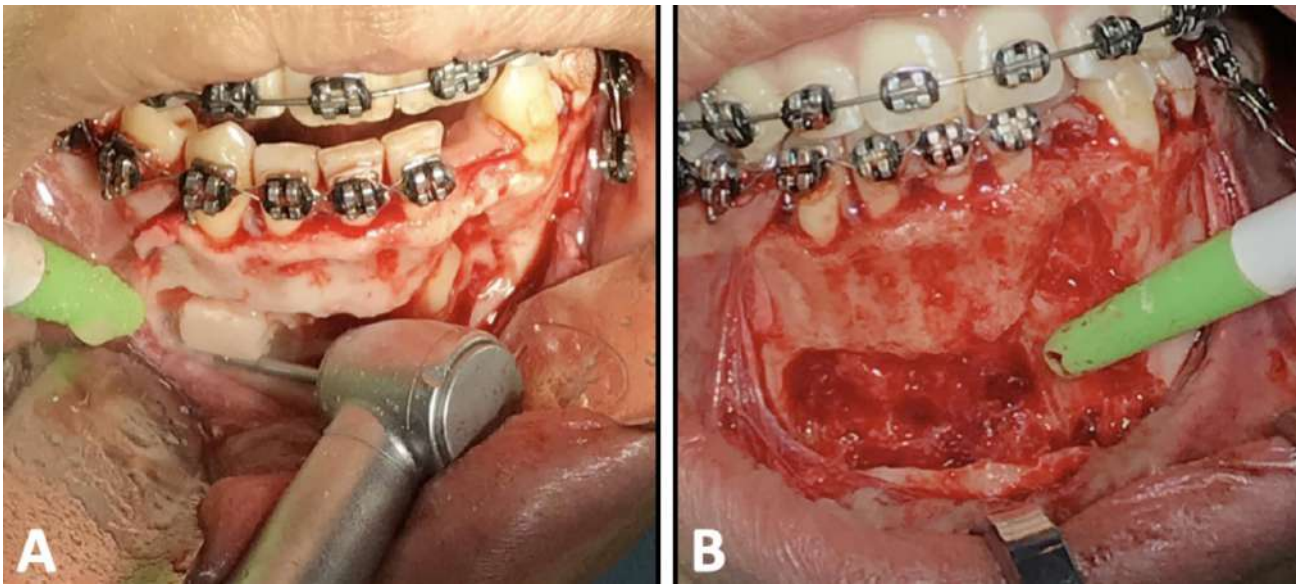

Fig. 6. A y B. Ostectomy and grinding of a bone block in the mental region.

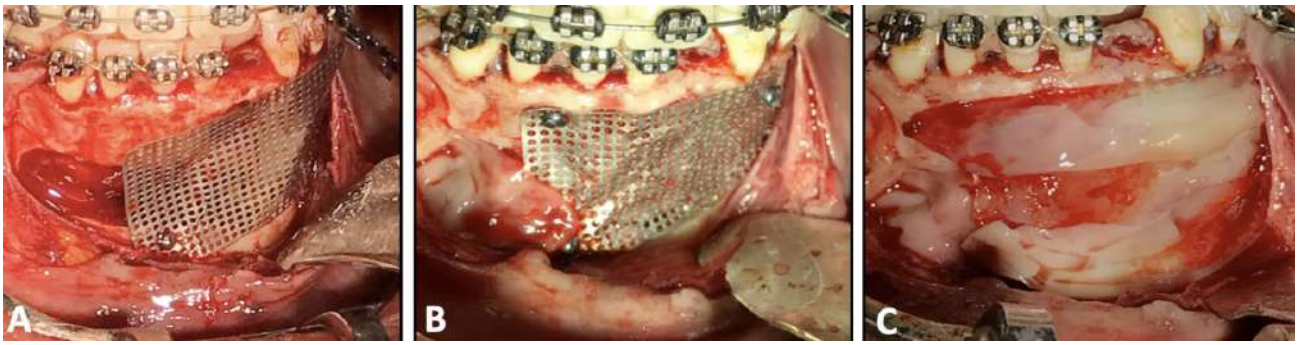

Fig. 7. Preparing the grafts and placing the membranes and L-PRF platelet concentrates. (plugs, membranes and stickbone).

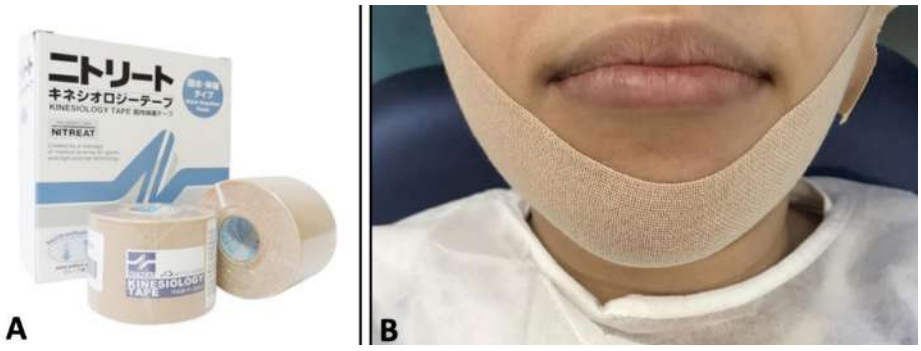

Fig. 8. Installation of an adhesive elastic bandage in the immediate postoperative period (Kinesiology Tape; Nitreat; Japan).

procedures, an adhesive elastic bandage was installed in the immediate postoperative period to provide protection and stabilization of the surgical site, contributing to tissue support and local inflammation control (Fig. 8).

In the Figure 9 depict the patient's post-operative medication and follow-up at 7 days, 30 days, and 5 months. The patient's progress throughout the post-operative follow-up was good, and there were no problems or alterations in the surgical incision.

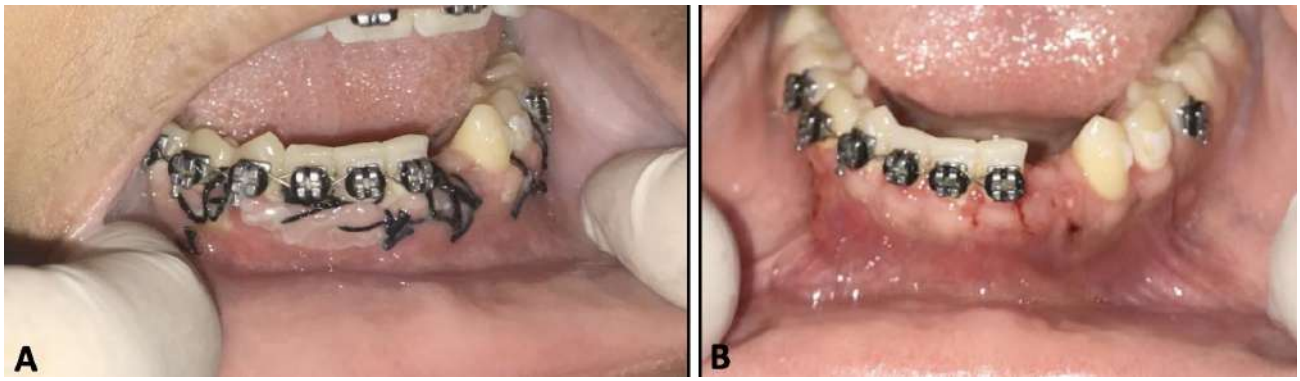

Fig. 9. Postoperative periods at (A) 7 days and (B) 30 days, respectively.

Fig. 10. Panoramic radiograph after 5 months

The tooth was reopened five months after it had fully healed in order to extract the fixation tacks and the synthetic titanium membrane. In order to evaluate surgical planning and the healing phase, a panoramic radiograph was required (Fig. 10).

The subsequent surgical procedure, to remove the membrane and fix tacks, was also performed in an outpatient setting under local anesthetic with 2% Lidocaine and 1:100,000 epinephrine (Alphacaine 100; DFL; São Paulo; Brazil) (Fig. 11).

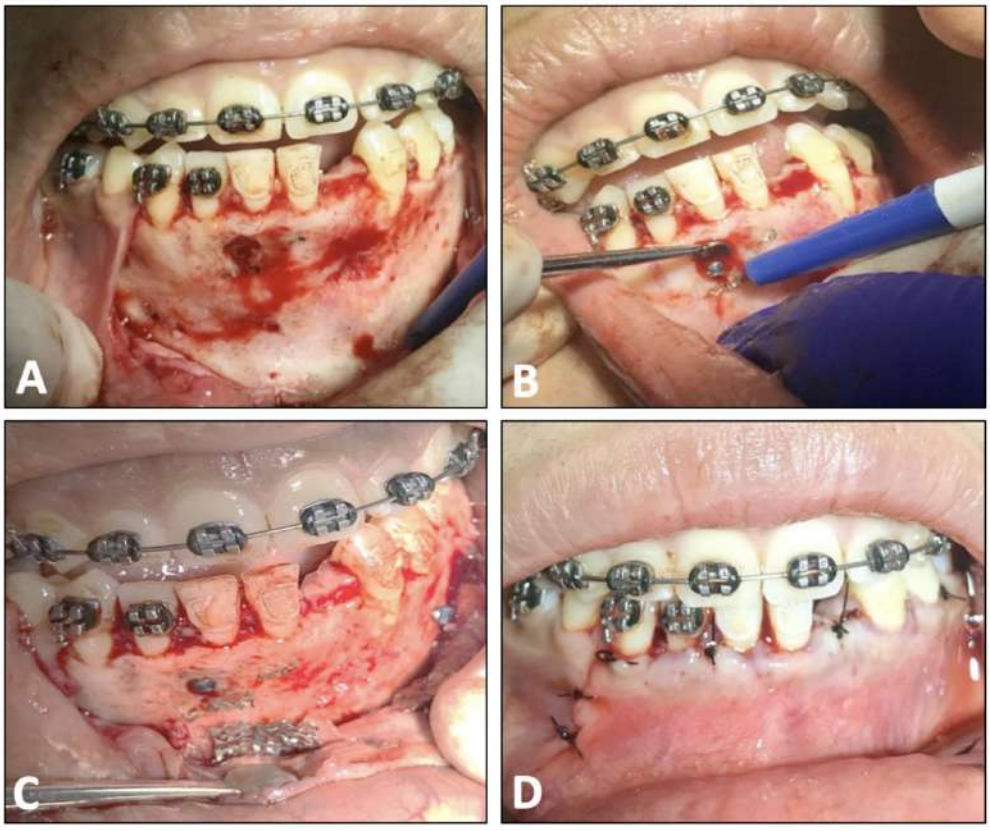

Fig. 11. A-D. Reopening procedure for surgical removal of the titanium membrane and fixation tacks and immediate postoperative period.

The patient reported desensitivity in the right mental region on the second postoperative day, which is indicative of mentual nerve paresthesia. An intramuscular Dexa-citoneurin NFF® solution (dexamethasone phosphate disodium; thiamine hydrochloride; pyridoxine hydrochloride; cyanocobalamin) was prescribed, 1 ampoule of 3 ml every 3 days.

The patient's paresthesia has significantly improved, and she is no longer experiencing any paresthesia-related symptoms. She is being monitored and is prepared to have rehabilitation using an osseointegrated implant for tooth 32.

Case report 2

A 46-year-old Caucasian man with "soft teeth" (S.I.C.) as his primary complaint arrived at the oral surgery course focused on systemically compromised patients at a dental institute. Clinical examination revealed grade 3 mobility in teeth 18, 17, and 16, which was linked with class III furcation involvement. During anamnesis, the patient reported a history of rheumatic fever and mechanical heart valve prosthesis surgery. He reported being diabetic, hypertensive and using antithrombotic therapy with oral anticoagulants (Warfarin sodium®), gliclazide, anlodipine, hydrochlorothiazide and losartan.

In order to evaluate and stratify the dental surgical risk associated with a computed tomography scan for surgical planning (Fig. 12), the patient was asked to perform supplementary laboratory tests 24 hours prior to surgery, such as a blood count, coagulogram, glycated hemoglobin, and lipidogram.

The results are shown in Table I, with normal values for INR (1.75), glycated hemoglobin (Hb; 6.4 %) and prothrombin time (PT; 19.40 seconds), making it possible to perform the surgery.

It was planned to carry out extractions of teeth 18, 17 and 16 and sinus lift surgery at the same time, in order to allow future rehabilitation with osseointegrated implants, under oral anticoagulant maintenance, associated with L-PRF platelet aggregates.

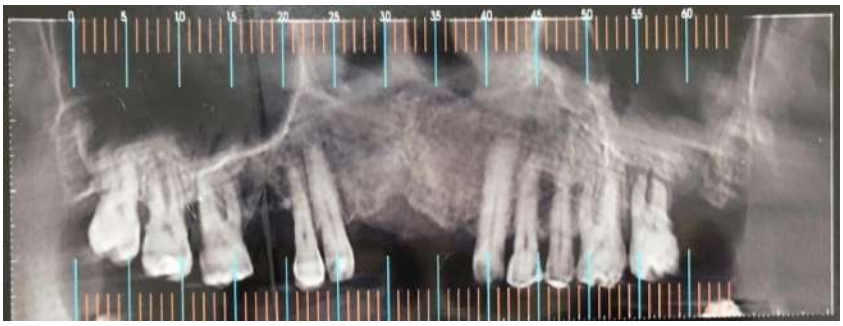

Fig. 12. Computed Tomography.

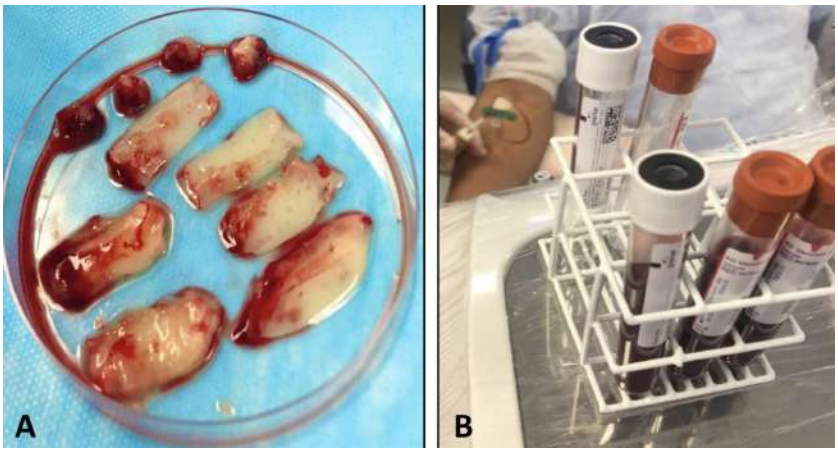

Fig. 13. A y B. Blood collection and making platelet concentrates (stickybone, membranes and plugs).

Preoperatively, antibiotic prophylaxis was carried out with 2 g of amoxicillin 1 hour before surgery and continued therapeutically for 7 days with 500 mg every 8 hours. Dexamethasone 4mg every 8 hours for 3 days and Dipyrone 1g every 6 hours for 3 days were also prescribed.

Approximately 70 mL of the patient's blood was collected preoperatively using a closed vacuum collection system in falcon tubes containing silica. The material was centrifuged to obtain platelet concentrates, including stickybone, membranes and L-PRF plugs (Fig. 13). Lyophilized bovine bone graft (Lumina-Bone medium 0.5 g; Criteria; São Paulo; Brazil) was used to obtain the stickybone.

The surgical procedure was performed in an outpatient setting under local anesthesia using the technique of blocking the middle and posterior superior alveolar nerves

and the greater palatine nerve with 2 % Lidocaine and 1:100,000 epinephrine (Alphacaine 100; DFL; São Paulo; Brazil). An incision was made using a trapezoidal flap, followed by mucoperiosteal detachment. Teeth 18, 17 and 16 were removed, allowing better access to the maxillary sinus (Fig. 14).

Osteotomy and ostectomy were performed in high rotation under refrigeration with a no. 4 spherical drill to access the maxillary sinus (Fig. 15). Schneider's membrane was carefully detached without causing it to rupture, to obtain a space for the placement of the stickybone, ensuring better accommodation of the graft, followed by alveolar filling with plugs and L-PRF membranes, with adequate local hemostasis (Fig. 16).

Finally, occlusive sutures were made with 4.0 nylon thread (Ethicon; São Paulo; Brazil) for first-intensity healing (Fig. 15). Furthermore, three 250 mg tranexamic acid tablets macerated with 0.9% saline solution were applied above the suture (extra-alveolar) as a local hemostatic technique to support primary hemostasis.

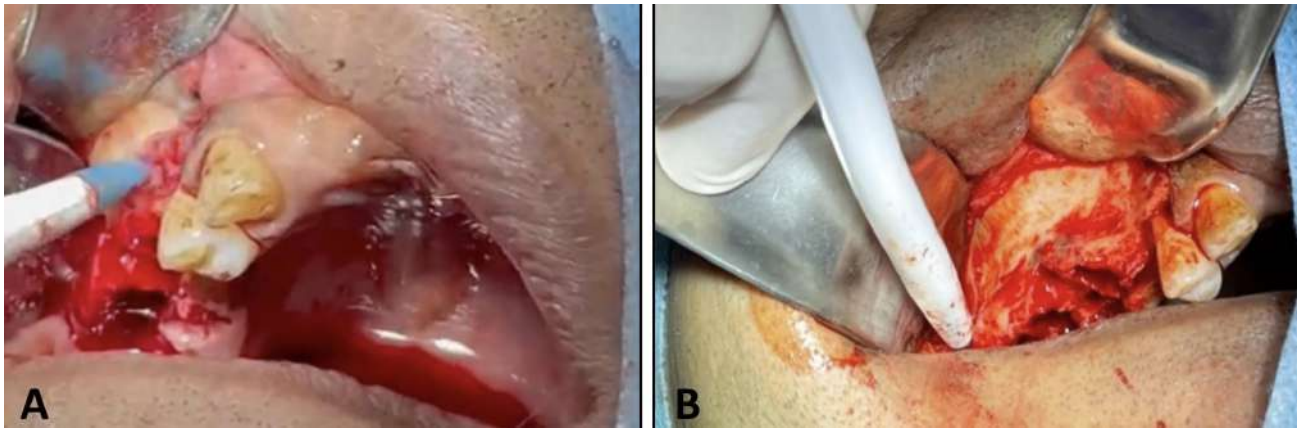

Fig. 14. Extraction of teeth and total detachment of tissue. Exposure of the surgical site for osteotomy.

Fig. 15. Sutures and immediate postoperative period.

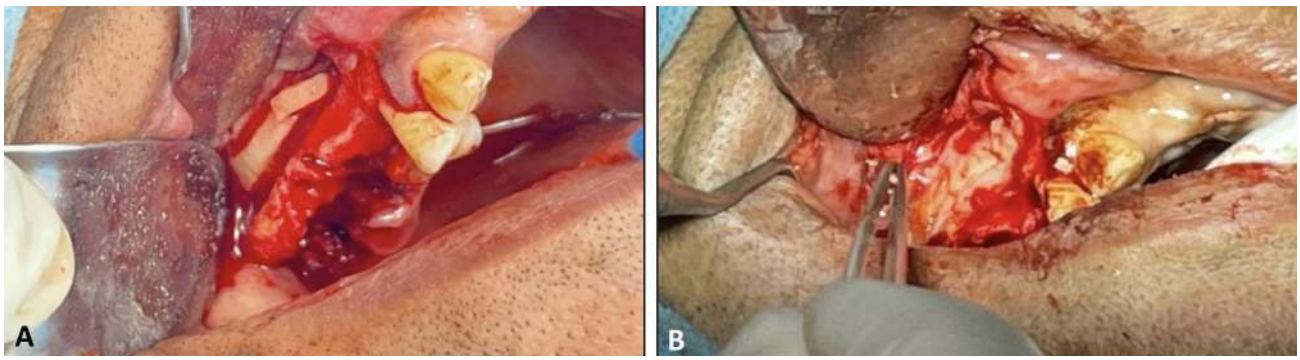

Fig. 16. A y B. Osteotomy and exposure of the maxillary sinus without rupture of the membrane. Stickybone, plugs and L-PRF membranes positioned.

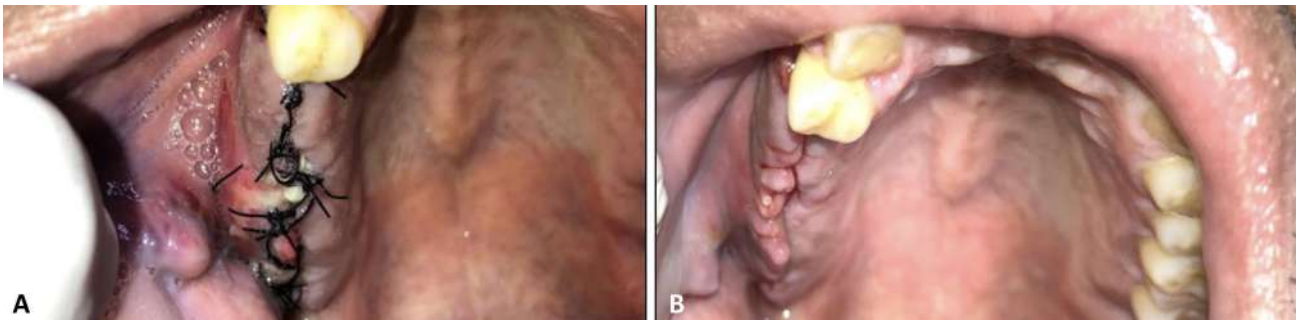

Fig. 17. Post-surgery after 3 days. Post-surgery after 14 days and suture removal.

In the immediate post-operative period, the patient was instructed to eat only a liquid or paste diet for the first 5 days, not to rinse their mouth, to apply ice compresses as soon as possible, to avoid compressing or pressing on the area and not to exert themselves physically for two weeks. Appointments were made after 3 days and 14 days. The patient progressed well, with no painful symptoms or any other complications, and it was possible to remove the suture after 14 days, as shown in Figure 17.

DISCUSSION

The use of L-PRF membranes as a hemostatic maneuver suggests that it is an effective, easy-to-manage and low-cost method in cases of oral surgery related to anticoagulant and antiplatelet drugs in patients with heart disease. It is necessary to evaluate factors that prove this indication, including safety, as well as the correct stratification of the surgery in terms of extent, quality of the membrane and the decision not to suspend antithromboembolic drugs, in association with other alternative methods of stopping local hemostasis.

According to the literature (Guimarães *et al*., 2016; Caminha *et al*., 2018), there is a consensus that anticoagulant and antiplatelet drugs should not be discontinued for oral surgeries, as in the cases reported in this article, because when the medication is discontinued, the possibility of serious thromboembolic events is always a greater risk than hemorrhagic complications, with high morbidity and/or mortality rates.

Regarding the quality of the L-PRF membrane in relation to therapy with antiaggregants and anticoagulants, compared to other hemostatic agents used in these cases, it is still considered a very recent technology (Caminha *et al*, 2024), with primary data, but with promising expectations. However, according to Kuhn *et al*. (2023), the L-PRF membrane had good efficacy in interacting with antiaggregant and anticoagulant therapy drugs, and he described it as follows: “it is an autologous, filling and anti-hemorrhagic biomaterial which, in addition to healing, induces intrinsic growth factors”, confirming that its characteristics are suitable for use in individuals receiving antithromboembolic therapy. In a long-term observational analysis, it was found that L-PRF could reduce post-operative bleeding without the need for medical intervention; however, in contrast to other L-PRF investigations, the group did not report a significant difference in hemorrhage (Berton *et al*., 2023). When anticoagulant-using individuals were included, it was determined that L-PRF is an effective hemostatic technique for dental treatments, particularly when considering its anti-hemorrhagic properties (Sammartino *et al*., 2011).

Regarding the effectiveness of using L-PRF membranes and the extent of the surgical area, in a case of bone neoformation in a post-extraction alveolus, being a small area, L-PRF had excellent effectiveness, and good bone quality could be observed histologically when associated with bone substitute (Canellas *et al*., 2020). L-PRF was also successful in a case of a more extensive maxillary sinus lift; despite the larger surgical area, there was good stimulation of bone neoformation for both preservation and alveolar filling, indicating that the membrane's use is effective but that extension is a significant factor for a positive postoperative period (Tchemra *et al*., 2021).

According to these studies and case reports, the non-suspension of anticoagulants and antiplatelet medications won't have an impact on the membrane's quality. Based on the information gathered, we can say that the L-PRF membrane is a hemostatic technique that has lately been the focus of additional research and has demonstrated positive post-operative outcomes. There is currently minimal information in

scientific databases demonstrating the efficiency of this hemostatic procedure. As a result, more longitudinal and observational studies are required to ensure that the L-PRF membrane may be utilized as a safe hemostatic technique.

CONCLUSION

Dental surgical procedures, such as tooth extractions, sinus lift surgery, and tumor excision, can be performed safely in patients with heart disease who are on antithrombotic therapy (anticoagulants and/or platelet antiaggregants), in conjunction with platelet aggregate concentrates (L-PRF), without the need to suspend or modify therapy due to the risk of increased trans- or post-operative bleeding. To summarize, platelet- and leukocyte-rich fibrin can increase soft tissue and bone regeneration in the maxillary and mandibular areas in a clinical setting. L-PRF has several advantages when used in conjunction with traditional therapeutic resources since it has a high concentration of growth factors, lowers the danger of immunological reactions or infections, and supports the efficient and safe termination of local hemostasis.

MEDEIROS, F. B.; CAMINHA, R. D. G.; SANTOS, T. C.; HASHIDA, G.; PERES, G. & SANTOS, P. S. S. Rehabilitación quirúrgica del hueso maxilar y mandibular mediante L-PRF en pacientes cardíacos en tratamiento antitrombótico. *Int. J. Odontostomat., 19(3)*:304-314, 2025.

RESUMEN: El riesgo de hemorragia perioperatoria y postoperatoria dificulta la cirugía oral en pacientes que reciben tratamiento antitrombótico; así, para una gestión clínica óptima, los médicos y odontólogos deben estar actualizados. Para evitar las hemorragias, durante mucho tiempo se consideró que las técnicas menos invasivas estaban prohibidas. Esto suscitó preocupación por el aumento del riesgo de tromboembolismo y la suspensión del antitrombótico. La fibrina rica en leucocitos y plaquetas (L-PRF) es una nueva medida hemostática local prometedora para reducir las hemorragias y acelerar la cicatrización tras la exodoncia en individuos que reciben antitrombótico. Para mejorar la reparación, la regeneración ósea y el control del proceso hemostático local, esta serie de casos, que incluye una revisión bibliográfica integradora, intenta demostrar la evidencia de derivados de la fibrina como opción quirúrgica en pacientes con cardiopatías recibiendo anticoagulante y/o antiagregante plaquetario. Cirugía oral y fibrina rica en plaquetas y anticoagulante oral fueron los descriptores utilizados para identificar artículos para una revisión integradora mediante la exploración de las bases de datos PUBMED/MEDLINE®, SCOPUS® y BVS. En esta serie de casos presentamos: Caso 1: Mujer que tenía una valvuloplastía con catéter de balón, un soplo cardíaco y una arritmia cardíaca no identificada que además tomaba ácido acetilsalicílico todos los días. Caso 2: Hombre con antecedentes de fiebre reumática, diabetes, hipertensión, una prótesis valvular cardíaca mecánica, varias extracciones dentales y una elevación de seno que también tomaba anticoagulantes orales. En ambos casos, se utilizó L-PRF para completar la cirugía. Las intervenciones quirúrgicas dentales en las que se utilizan concentrados de agregados plaquetarios pueden realizarse con seguridad, sin necesidad de suspender o ajustar el tratamiento debido al riesgo de aumento de la hemorragia postoperatoria. Se ha demostrado que L-PRF ayuda a la cicatrización y regeneración de tejidos blandos y hueso en las zonas maxilar y mandibular.

PALABRAS CLAVE: fibrina rica en plaquetas, anticoagulantes, inhibidores de agregación plaquetaria, cirugía oral, técnicas hemostáticas.

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Corresponding author:
Tiago Carvalho dos Santos
Department of Dentistry of the Cardiology Society of the State of São Paulo (SOCESP)
São Paulo, SP
Rua Doutor Alípio dos Santos – 12-18
9° andar – Jardim Panorama
CEP: 17011-136 – Bauru/SP
BRAZIL

E-mail: odonto.tiagosantos@gmail.com