Role of Leukocyte–Platelet-Rich Fibrin in Endoscopic Endonasal Skull Base Surgery Defect Reconstruction

Liuba Soldatova¹ Raewyn G. Campbell¹ Ahmad H. Elkhatib¹ Thomas W. Schmidt² Nelson R. Pinto³
Jaime M. Pinto⁴ Daniel M. Prevedello^{1,5} Leo F. Ditzel Filho¹ Bradley A. Otto^{1,5} Ricardo L. Carrau^{1,5}

¹ Department of Otolaryngology - Head & Neck Surgery, The Ohio State University Wexner Medical Center, Columbus, Ohio, United States

² Department of Otolaryngology - Head & Neck Surgery, Universidad de Concepción, Concepcion, Chile

³ Graduate School of Periodontics and Implant Dentistry, Research Center for Regenerative Medicine and Tissue Engineering, University of the Andes-Chile, Concepcion, Chile

⁴ Department of Neurosurgery, Universidad de Concepción, Concepcion, Chile

⁵ Department of Neurologic Surgery, The Ohio State University Wexner Medical Center, Columbus, Ohio, United States

Address for correspondence Ricardo L. Carrau, MD, Department of Otolaryngology - Head & Neck Surgery, The Ohio State University Wexner Medical Center, 320 West 10th Avenue, Starling-Loving Hall, B221, Columbus, OH 43210-1282, United States (e-mail: ricardo.carrau@osumc.edu).

J Neurol Surg B 2017;78:59–62.

Abstract

Objective Advancements in endoscopic endonasal approaches have increased the extent and complexity of skull base resections, in turn demanding the development of novel techniques for skull base defect reconstruction. The objective of this pilot study was to investigate the effect of leukocyte–platelet-rich fibrin (L-PRF) on the postoperative healing after endoscopic skull base surgery.

Methods Between January and May of 2015, 47 patients underwent endoscopic endonasal resection of sellar, parasellar, and suprasellar lesions with the application of L-PRF membranes during the skull base reconstruction at two surgical centers. Early postoperative records were retrospectively reviewed.

Results We found that 21 days following the surgery, 17/41 patients (42%) demonstrated improvement in the crusting score as compared with their 7 day postoperative examination. Ten of these patients (23%) showed no crusting. Fourteen (34%) patients had no change in the crusting score. Six patient records were incomplete. A total of 4/47 cases (8.5%) had postoperative cerebrospinal fluid leak requiring surgical repair.

Conclusion This study demonstrates the potential utility of L-PRF membranes for skull base defect reconstruction. Future studies will be conducted to better assess the role of L-PRF in endoscopic skull base surgery.

Keywords

- ▶ leukocyte–platelet-rich fibrin
- ▶ endoscopic endonasal approach
- ▶ endoscopic skull base surgery
- ▶ skull base defect reconstruction

Introduction

Autologous platelet-rich preparations and fibrin glue technologies have been used for many years to promote surgical site healing.^{1–3} In 1970, Matras¹ first described the use of

fibrin glue resulting in improved wound healing in a rat model. This fibrin glue represents one of the first regenerative techniques ever developed and served as the foundation for investigation of the fibrin matrix to promote healing.^{1,4}

received

January 3, 2016

accepted

May 25, 2016

published online

June 28, 2016

© 2017 Georg Thieme Verlag KG
Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0036-1584894>.
ISSN 2193-6331.

Over time, the focus of scientific inquiry has shifted toward the healing properties of platelets concentrated in the fibrin network. Subsequently, the value of circulating growth factors and leukocytes has become evident.^{2,3,5} It is currently accepted that all these elements play a significant role in the healing process. Fibrin, platelets, growth factors, leukocytes, and other cells play a major role in natural healing; therefore, to promote surgical site healing, all these components are combined in modern platelet-rich preparations.⁶

The current classification of platelet-rich concentrates is based on their fibrin architecture and cell content. It consists of two main groups of products, platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), both of which are available in a pure or leukocyte-enriched form (L-PRP and L-PRF).⁹ Each product has a unique biological profile that dictates its clinical applications. L-PRF concentrates provide slow release of many growth factors and can be easily prepared during surgery.^{10–14} They are inexpensive and autologous; therefore, they avoid the complications associated with allogenic blood use.

Multiple surgical specialties have recognized the potential benefits of platelet-rich concentrates. Their use has been described in ophthalmology, neurosurgery, general surgery,⁷ orthopedic surgery, sports medicine,⁶ and oral and maxillo-facial surgery.^{1,8} Several applications of L-PRF concentrate have been described in the literature including postoperative hand wound healing yielding faster reepithelization and in the treatment of androgenic alopecia diminishing hair loss among others.^{15–17} To our knowledge, no studies have been conducted to investigate the effect of L-PRF on the healing of surgical defects following endoscopic skull base resections.

Advancements in endoscopic endonasal approach (EEA) to skull base lesions have resulted in a significant increase in the extent and complexity of skull base defects, in turn, demanding more elaborate and novel reconstruction techniques to expedite healing and prevent postoperative reconstruction failures. The objective of this pilot study was to investigate the effects of L-PRF on postoperative healing of the sinonasal corridor and the rate of postoperative complications following endoscopic endonasal skull base surgery.

Materials and Methods

L-PRF Technique

L-PRF membranes were prepared with IntraSpin L-PRF system (Intra-Lock Inc., Boca Raton, FL)^{11–13,18} using the Xpression preparation box.¹⁴ Blood was drawn into 10-mL anticoagulant-free tubes (red top, BD Vacutainer vacuum tubes) from an arterial line after it was flushed and the first 10 mL of blood was discarded. The tubes were immediately spun in a centrifuge at 2,700 rpm for 12 to 18 minutes according to the patient's coagulation status. This step induces the initiation of the coagulation cascade and platelet activation when they come into contact with the walls of the tube. Fibrinogen is concentrated in the middle of the tube and transformed into fibrin by the circulating thrombin. The fibrin clot formed in the middle of the tube during centrifugation was separated from the red blood cell layer at the bottom of the tube. The fibrin clots were placed into the preparation box and compressed

with a weighted press to create uniform membranes of 1 mm thickness. All membranes were prepared within 2 hours of their application to the surgical skull base defect.

Reconstruction Technique

All reconstructions followed a multilayer technique using a collagen matrix or L-PRF membranes for the intradural (inlay) layer and a mucoperiosteal graft (i.e., sellar or parasellar defect) or flap (i.e., extended approach defect) for the extradural (onlay) reconstruction. L-PRF membranes were laid overlapping the edges of the reconstruction, thus framing the graft or flap. These were bolstered using Nasopore (Stryker Corp., Kalamazoo, MI) as a nonadherent barrier between the reconstruction and sponge nasal packing.

Retrospective Review

Between January and May of 2015, a total of 47 patients, 22 males and 25 females, with mean age of 51, underwent EEA resection of various pituitary and suprasellar masses with L-PRF membrane application during the skull base defect reconstruction at two surgical centers. Following institutional review board approval, their postoperative records were retrospectively reviewed to evaluate the rate of cerebrospinal fluid (CSF) leaks and postsurgical healing. Crusting scale score was used as an indicator of healing progression. Healing was assessed during routine follow-up using a clinically intuitive scale based on sinonasal endoscopy: 0, no crusting; 1, minimal crusting debrided with suction only; 2, moderate crusting requiring forceps debridement; 3, severe crusting causing obstruction. Eight specific areas on each side of the sinonasal corridor were scored using the crusting scale (i.e., septum, floor of the nose, lateral nasal wall, frontal sinus, ethmoid sinus, maxillary sinus, sphenoid sinus, and nasopharynx sites) for a total score that ranged between 0 and 24 (►Table 1). The crusting scale values for the ethmoid and the sphenoid areas were used for this study as these are the areas primarily affected by the L-PRF membrane application. The highest score recorded for these areas was registered as a crusting score. The crusting scores were compared between 7 and 21 days following surgery. Postoperative CSF leaks were recorded.

Table 1 The Ohio State University crusting scale

Site	Right (0–3)	Left (0–3)
Septum		
Floor of the Nose		
Lateral wall of the nose		
Frontal sinus		
Maxillary sinus		
Ethmoid sinuses		
Sphenoid sinuses		
Nasopharynx		
Total:		

0: No crusting. 1: Minimal crusting debrided with suction only. 2: Moderate crusting (i.e., coating) requiring forceps debridement. 3: Severe crusting (i.e., casting) causing obstruction.

Table 2 Indication for endoscopic endonasal surgery

Diagnosis	Count
Macroadenoma (primary and recurrence)	29
Microadenoma	4
Craniopharyngioma (primary and recurrence)	5
Chordoma (primary and recurrence)	2
Inverted papilloma	1
Arachnoid cyst	1
Meningioma	1
Prolactinoma	1
Xanthogranuloma	1
Adenocarcinoma	1
Metastatic carcinoid	1

Results

Indications for EEA in this pilot study included sellar and suprasellar lesions (► **Table 2**), with pituitary adenoma (Hardy score I-IVE) being the most common lesion (► **Table 3**). The surgery itself varied in extent involving transsphenoidal, transplanal, transclival, transcribiform, transthemoidal, or transpterygoid approaches reflecting the extent of the lesion.

Of 47 patients, 4 (8.5%) suffered a postoperative CSF leak, all requiring surgical repair. One patient had recurrent CSF leaks and a total of three repairs, indicating multifactorial etiology for reconstruction failure.

The crusting score assessment revealed that at the second evaluation 21 days following the surgery, 17/41 patients (42%) demonstrated improvement in the crusting score, with 10 (23% of the total cohort) showing no crusting on the examination. Fourteen patients (34%) had no change in the crusting score 21 days postoperatively as compared with the 7-day postoperative evaluation (► **Table 4**). Of 41 patients, 10 (24%) had higher crusting scores during their 21-day postoperative follow-up. Six patient records did not have complete crusting scale information at the time of the record review.

Discussion

This pilot study suggests potential benefits of L-PRF membranes for the reconstruction of skull base defects with encouraging rate of healing progression as measured by the

Table 3 Wilson–Hardy classification of pituitary adenomas

Wilson–Hardy classification	Count
I	7
II, IIA, IIC, IIA&E	12
III, IIIA, IIIB, IIIC, IIIE	10
IVB, IVD, IVE	4

Table 4 Crusting score change at 21 days compared with 7 days postoperative examination

Crusting score change	Count
No crusting on exam	10
Decreased score	17
No change in crusting score	14
Increased Score	10
Not recorded	6

crusting score. However, several variables were not controlled as the study group included different pathologies, surgical approaches, skull base defect size, and methods of reconstruction. Additionally, although recorded during this study, past medical history of the conditions affecting healing process was not taken into account (diabetes, chronic kidney disease, history of smoking, prior surgery, or radiation therapy). Perhaps more importantly, the lack of a control group further limits our ability to draw definitive conclusions. However, the fact that almost a quarter of our patients had no crusting at 21 days after surgery is promising and demands further investigation.

The CSF leak rate of 8.5% found in this study is similar to the overall CSF leak rate quoted in the literature when different surgical approaches and reconstructive techniques are utilized.¹⁹ Two of the CSF leak cases were patients with Hardy IV pituitary adenoma (IVB and IVE). One of the four patients developed a fistula 8 days after the initial resection of Hardy IIA pituitary adenoma. The last of the four patients had a history of diabetes, lupus, and severe sleep apnea, and presented with chordoma eroding clivus and encroaching on the pons. This patient had multiple CSF leaks likely due to multiple factors including complex medical history, high intracranial pressure, and challenging tumor resection.

Despite the fact that the results of this study cannot be generalized, this is the first study to describe the use of L-PRF in the reconstruction of skull base defect. It also provides the foundation for further investigation of L-PRF use in skull base surgery (previously presented by oral communication by T. W. Schmidt and N. R. Pinto).

Recent adoption of EEA for the resection of advanced lesions demands novel reconstruction techniques. Future studies with larger sample size to account for the limitations mentioned previously with multivariate analysis of variables that affect postsurgical healing will better assess the role of L-PRF in the skull base defect reconstruction.

Note

This study was conducted at The Ohio State University Wexner Medical Center, Columbus, OH, and Universidad de Concepción, Concepcion, Chile.

References

- Matras H. Effect of various fibrin preparations on reimplantations in the rat skin [in German]. *Osterr Z Stomatol* 1970;67(9):338–359
- Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;85(6):638–646
- Rosenthal AR, Egbert PR, Harbury C, Hopkins JL, Rubenstein E. Use of platelet-fibrinogen-thrombin mixture to seal experimental penetrating corneal wounds. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1978;207(2):111–115
- Gibble JW, Ness PM. Fibrin glue: the perfect operative sealant? *Transfusion* 1990;30(8):741–747
- Bielecki T, Dohan Ehrenfest DM, Everts PA, Wiczowski A. The role of leukocytes from L-PRP/L-PRF in wound healing and immune defense: new perspectives. *Curr Pharm Biotechnol* 2012;13(7):1153–1162
- Pinto NR, Pereda A, Jiménez P, et al. The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors and fibrin architecture of a leukocyte- and platelet-rich fibrin (L-PRF) clot and membrane. Part 2: macroscopic, photonic microscopy and scanning electron microscopy analysis of 4 kinds of L-PRF clots and membranes. *POSEIDO* 2014;2(2):141–154
- Everts PA, Hoogbergen MM, Weber TA, Devilee RJ, van Monfort G, de Hingh IH. Is the use of autologous platelet-rich plasma gels in gynecologic, cardiac, and general, reconstructive surgery beneficial? *Curr Pharm Biotechnol* 2012;13(7):1163–1172
- Yuan T, Guo SC, Han P, Zhang CQ, Zeng BF. Applications of leukocyte- and platelet-rich plasma (L-PRP) in trauma surgery. *Curr Pharm Biotechnol* 2012;13(7):1173–1184
- Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leukocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol* 2009;27(3):158–167
- Dohan Ehrenfest DM, Bielecki T, Jimbo R, et al. Do the fibrin architecture and leukocyte content influence the growth factor release of platelet concentrates? An evidence-based answer comparing a pure platelet-rich plasma (P-PRP) gel and a leukocyte- and platelet-rich fibrin (L-PRF). *Curr Pharm Biotechnol* 2012;13(7):1145–1152
- Del Corso M, Dohan Ehrenfest DM. Immediate implantation and peri-implant natural bone regeneration (NBR) in the severely resorbed posterior mandible using leukocyte- and platelet-rich fibrin (L-PRF): a 4-year follow up. *POSEIDO* 2013;1:109–116
- Dohan Ehrenfest DM, Sammartino G, Shibli JA, Wang HL, Zou DR, Bernard JP. Guidelines for the publication of articles related to platelet concentrates (platelet-rich plasma – PRP, or platelet-rich-fibrin – PRF): the international classification of the POSEIDO. *POSEIDO* 2013;1:17–27
- Toeroek R, Dohan Ehrenfest DM. The concept of screw-guided bone regeneration (S-GBR). Part 2: S-GBR in the severely resorbed preimplant posterior mandible using bone xenograft and leukocyte- and platelet-rich fibrin (L-PRF); a 5-year follow-up. *POSEIDO* 2013;1:85–92
- Dohan Ehrenfest DM. How to optimize the preparation of leukocyte- and platelet-rich fibrin (L-PRF, Choukroun's technique) clots and membranes: introducing the PRF Box. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110(3):275–278, author reply 278–280
- Cieslik-Bielecka A, Choukroun J, Odin G, Dohan Ehrenfest DM. L-PRP/L-PRF in esthetic plastic surgery, regenerative medicine of the skin and chronic wounds. *Curr Pharm Biotechnol* 2012;13(7):1266–1277
- Chignon-Sicard B, Georgiou CA, Fontas E, et al. Efficacy of leukocyte- and platelet-rich fibrin in wound healing: a randomized controlled clinical trial. *Plast Reconstr Surg* 2012;130(6):819e–829e
- Schiavone G, Raskovic D, Greco J, Abeni D. Platelet-rich plasma for androgenetic alopecia: a pilot study. *Dermatol Surg* 2014;40(9):1010–1019
- Dohan Ehrenfest DM, Kang BS, Del Corso M, et al. The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors and fibrin architecture of a leukocyte- and platelet-rich fibrin (L-PRF) clot and membrane. Part 1: evaluation of the vibration shocks of 4 models of table centrifuges for L-PRF. *POSEIDO* 2014;2(2):129–139
- Harvey RJ, Parmar P, Sacks R, Zanation AM. Endoscopic skull base reconstruction of large dural defects: a systematic review of published evidence. *Laryngoscope* 2012 Feb;122(2):452–459