International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 05 May 2024

Page No: 860-870

DOI: https://doi.org/10.47191/ijmscrs/v4-i05-16, Impact Factor: 7.949

Platelet Rich Fibrin Membrane as Nerve Guidance Conduit for Reconstruction Case with Nerve Repair Based Morphometric and Electrophysiologic Parameters: A Systematic Review and Meta-Analysis

Andi Muh. Octavian Pratama*[1], Pratidina Wulandari[2], Asrofi S. Surachman[3]

[1,2]Plastic Reconstructive and Aesthetic Surgery, Plastic Surgery Subdivision, Department of Surgery, Medical Faculty of Syiah Kuala University/ Zainoel Abidin General Hospital, Aceh, Indonesia

[3]Plastic Reconstructive and Aesthetic Surgery, Plastic Surgery Subdivision, Department of Surgery, Medical Faculty of Syiah Kuala University/ Gatot Soebroto Central Army Hospital, Jakarta, Indonesia

ABSTRACT

Introduction: Motor or sensory nerve injury is a major surgical and clinical challenge, often with disappointing results and impairing sensory and motor function. Now there are some studies to looking for ways to accelerate nerve regeneration. Platelet-rich fibrin (PRF) is made from an autologous platelet concentrate that contains progenitor cells that are essential for the healing process, along with neurotrophic factors and several growth factors. Additionally, PRF can be manufactured in the membrane form that can be wrapped around nerves in the form of tubes which tubulation has many advantages such as guiding growth within the tubular shape to improve regenerative capacity.

Methods: This systematic review and meta-analysis was conducted as per the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. A systematic, detailed search was carried out by the authors in the electronic databases, including PubMed, Cochrane, Research Gate, Elsevier, and PRS Journal. Studies were selected and compared based on outcome measures like Morphometric (Axon Area and Myelin Sheath Thickness) and Electrophysiologic (Amplitude and Nerve Conduction Velocity). Statistical analysis was performed using a random-effect model, pooled standard mean difference and I^2 heterogeneity.

Result: Four randomized studies with analyzed 4 parameters, those are Morphometric (Axon Area and Myelin Sheath Thickness) and Electrophysiologic (Amplitude and Nerve Conduction Velocity). Pooled analysis for the outcome like Myelin Sheath Thickness, Axon Area, and Amplitude showed a significant result in groups with PRF. Pooled analysis for outcome of Nerve Conduction Velocity showed no significant difference between the groups with PRF and without PRF (SMD: 0.01; 95% CI: -0.64. 0.65) with P = 0.99.

Conclusion: This Meta-analysis shows that PRF membrane as nerve guidance conduit is promising method and can improve function outcome in nerve repair specially in Morphometric and Electrophysiologic parameters but outcome of Nerve Conduction Velocity showed no significant in this study.

.

KEYWORDS: Platelet Rich Fibrin Membrane, Nerve Guidance Conduit, Nerve Reconstruction

ARTICLE DETAILS

Published On:
17 May 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Motor or sensory nerve injury is a major surgical and clinical challenge, often with disappointing results and impairing sensory and motor function. Nerve repair is an essential procedure to restore function after nerve injury. The healing process is a multifactorial process, and these factors include the rate of axonal regeneration, the type of injury and damaged nerve, the patient's age and physiological status, the repair technique, and the skill of the surgeon.[1] Despite the advances and evolution of microsurgery, new technologies involved, and the non- tension suturing techniques, the obtained results are disappointing and with difficult complete functional recovery, in addition to development of neuropathic pain in about 45% of cases, especially when there is total nerve transection.[2]

In recent years, the autologous component platelet-rich fibrin (PRF) has attracted the attention of researchers and is used to promote peripheral nerve regeneration after surgical repair or nerve suture. Platelet-rich fibrin (PRF) is produced from autologous platelet concentrates that contain progenitor cells that are essential for the healing process, along with growth factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF)-b, vascular endothelial growth factor (VEGF), and platelet derived endothelial cell growth factor.[3]

Nevertheless, platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) are nearly identical.For growth factor-related components, PRF is considered more advantageous than PRP because itis easier to prepare, has a shorter preparation period, and does not require the addition of foreign materials during preparation. Additionally, PRF can be manufactured in the form of a membrane that can be wrapped around the nerve in the form of a tube. It has many benefits as it enhances regenerative capacity by inducing growth within.[4]

METHOD

Data sources and searches

This systematic review and meta-analysis was conducted as per the Preferred Reporting Items for Systematic Review/and Meta-analysis (PRISMA) guide-lines. The articles were searched conducted using databases such as PubMed, Research Gate, Elsevier, and PRS Journal. In the early stages of searching for journal articles,102 articles were obtained using the keywords“Platelet Rich Fibrin Membrane”, “Nerve Guidance Conduit”, and “Nerve Reconstruction”.

Study selection

Two authors (AP and AM) independently reviewed the abstract and title of the identified articles. After removing any duplicates from the search results, full texts of the potentially eligible studies were retrieved. The authors independently assessed the full-text articles to identify the eligible studies for inclusion. Any disagreement between the authors was resolved through discussion and a third author (AL) was consulted if consensus was not achieved. Excluded studies and the reasons for exclusion were documented. This selection process was presented in the PRISMA flow diagram.

Data extraction

After selecting the relevant studies, two authors independently performed data extraction (AM, AP). Baseline information for each study (information of the author, year of publication), mean/median, Standard Deviation (SD) and total sampling for each parameter (Electrophysiologic and Morphometric) was extracted in a data extraction table using MS Excel (Version 16.16.27) in table 2 and 3. Any discrepancies among the observers were resolved through consensus and in consultation with another author (AL).

Statistical analysis

Data were analyzed using Rev-Man 5.4. software. Continuous variables such as mean operative time were analyzed as mean differences with 95% confidence intervals (CIs). Heterogeneity was identified by visual assessment of the studies’ confidence intervals in the forest plot (eyeball test). Heterogeneity was examined explicitly with I^2 statistics. For quantifying the heterogeneity of the included studies, the following ranges of I2 statistics were used to guide the interpretation:

0% to 40% : might not be important;

30% to 60% : may represent moderate heterogeneity; 50% to 90% : may represent substantial heterogeneity; 75% to 100% : considerable heterogeneity

RESULT

The database search resulted in the identification of 102 records (Figure 1). In total, journals were removed due to (1) Time of publication (more than 10 years), (2) Non English Journal and 73 studies were excluded based on the eligibility criteria. Subsequently, 16 full-text articles were identified, of which 11 articles were removed due to reasons that included the articlenot relate to study outcome. The number of articles include in this scoping review is 4 articles andall articles are Research Articles. We then retained 4 articles for further analysis in describing of Platelet rich fibrin as a nerve guidance conduit for nerve repair and also role of platelet rich fibrinin nerve regeneration process.

Based on table 1, there were 4 articles that became the material in this study with the resultsof using platelet-rich fibrin in nerve repair cases giving good results from several aspects such as the results of histological examination which gave results in the form of remyelenization, vascularization, and repair of axons that better than the other comparison groups. Apart from that,the electromyography examination also gave

good results in the group using PRF for amplitude parameters.

Morphometrics

In this study, 2 parameters highlighted from previous studies regarding the use of Platelet Rich Fibrin Matrix as a nerve guidance conduit in nerve repair are the Morphometric (Axon Area and Myelin Sheet thickness) and electrophysiological (Amplitude and Nerve Conduction Velocity) points. Based on the four articles, not all tested each item. In Morphometrics, there were 3 articles that examined Myelin sheath thickness (Senses et al, Senturk et al, and Torul et al) with significantresults (SMD: -0.57; 95% CI: -1.10. -0.04) with P = 0.04 (Figure 4). There was no statistical hetero-geneity observed between the included studies (I2 = 0%). Whereas in the Continuity of axon.

examination there were only 2 articles that made these points, namely Senses et al and Torul et al with significant results (SMD: -0.80; 95% CI: -1.59. -0.01) P = 0.05 (Figure 5).

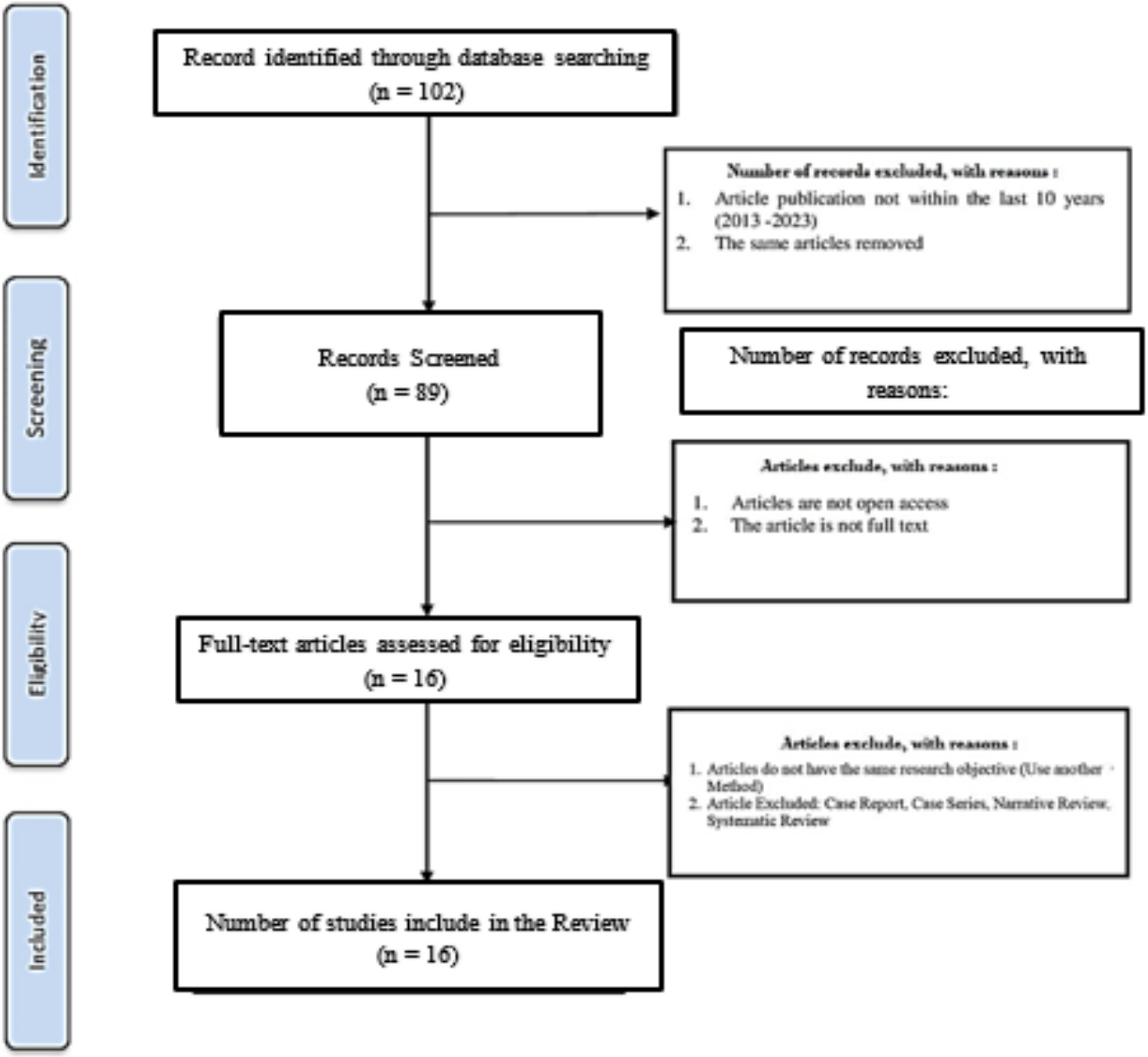

Figure 1. PRISMA Flowchart of the study selection

Table 1. Summary of Clinical Application of PRF Scaffold on Peripheral Nerve Regeneration.

Type of Study	Purposes of Study	Outcome	References
Experimental Study	Evaluate the effect of platelet-rich fibrin (PRF)on peripheral nerve regeneration on the sciatic nerve of rats by using functional, histopathologic, and electrophysiologic analyses	Functional sciatic index analysis and electrophysiologic results showed no signifycantly positive effects on nerve regeneration in PRF-treated rats. The histopathologic results revealed statistically significantly negative effects of nerve regeneration inthe PRF groups.	Senses et al 2016[3]
Experimental Study	Investigated the efficacy of platelet-rich fibrinas a healing enhancer at the region oftransection of the facial nerve.	In PRF Group, the findings of collagen infiltration, Schwann cell proliferation significantly higher than Control group.	Senturk et al 2020[22]
Experimental Study	Evaluate the effect of platelet rich fibrin in enhancing nerve regeneration of the sciatic nerve after end-to-end neurorrhaphy in rat model.	Latency, amplitude, and the reaction of degeneration within each group showed improvement along follow-up periods with a significant difference. Comparison of results between the two groups showed a significant difference along the follow-up periods in favor of PRF Group.	Usama et al. 2022[17]
Experimental Study	Investigate the effects of platelet-rich fibrin(PRF) on peripheral nerve injury in the early period of healing	For Amplitude, Axon number and Myelin SheathThickness values, there was a significant difference between the control and PRF groups	Torul et al2018[21]

Table 2. Summary of Data Extraction for Morphometric Parameter from Each Study

SN	STUDY	MORPHOMETRIC											
		Myelin Sheath Thickness						Axon Area					
		PRFM			Control			PRFM			Control		
		Mean	SD	Total	Mean	SD	Total	Mean	SD	Total	Mean	SD	Total
1	Senses et al 2016	1,8	0,42	10	2,2	0,42	10	1,4	0,52	10	2,1	0,57	10
2	Torul et al 2018	1,64	0,17	10	1,98	0,72	10	7174,71	1013,87	10	7585,15	829,98	10
3	Senturk et al 2020	1,03	0,27	10	1,08	0,29	8	0	0	0	0	0	0
4	Usama et al 2022	0	0	0	0	0	0	0	0	0	0	0	0

Table 3. Summary of Data Extraction for Electrophysiologic Parameter from Each Study

SN	STUDY	ELECTROPHYSIOLOGIC											
		Amplitude						Nerve Conduction Velocity					
		PRFM			Control			PRFM			Control		
		Mean	SD	Total	Mean	SD	Total	Mean	SD	Total	Mean	SD	Total
1	Senses et al 2016	0	0	0	0	0	0	29,5	8,88	9	33,14	12,17	8
2	Torul et al 2018	16,3	2,6	10	13,3	2,5	10	0	0	0	0	0	0
3	Senturk et al 2020	0,22	0,1	10	0,19	0,07	10	37,45	5,48	10	36,06	5,48	10
4	Usama et al 2022	3,38	1,37	10	1,5	0,62	10	0	0	0	0	0	0

ELECTROPHYSIOLOGIC FINDINGS

In Electrophysiologic parameters, there are 2 things that are checked, namely Amplitude and Nerve Conduction Velocity. However, it is the same only with morphometric points where not all of these articles carry out a complete examination of their Amplitude and Nerve ConductionVelocity. For Amplitude, there were 3 articles that carried out this examination (Senturk et al, Usama et al, and Torul et al) with significant results (SMD: 1.01; 95%CI: 0.23. 1.79) with P = 0.01(Figure 2). Whereas in Nerve Conduction Velocity Point, there were 2 articles that carried out thisexamination (Senses et al and Senturk et al) with statistically insignificant results (SMD: 0.01; 95% CI: -0.64. 0.65) with P = 0.99 (Figure 3).

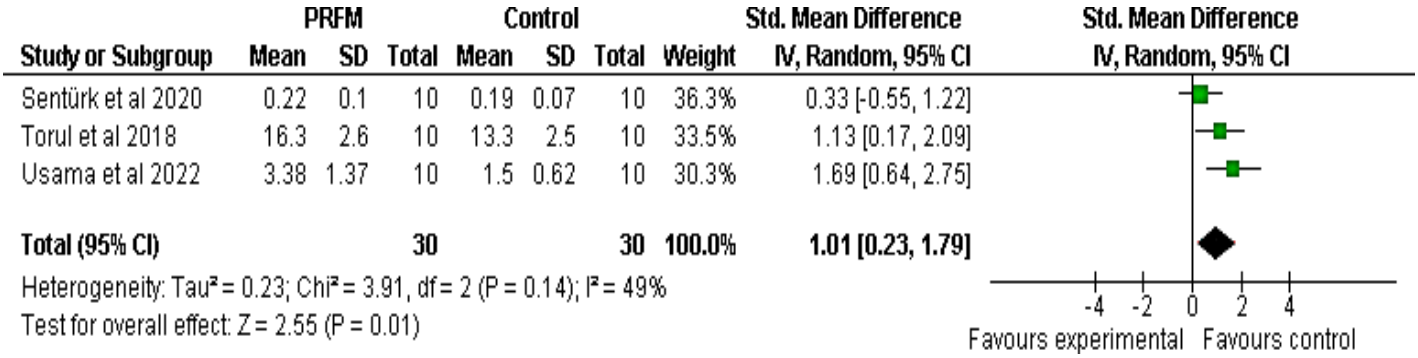

Figure 2. Forest Plot – Amplitude

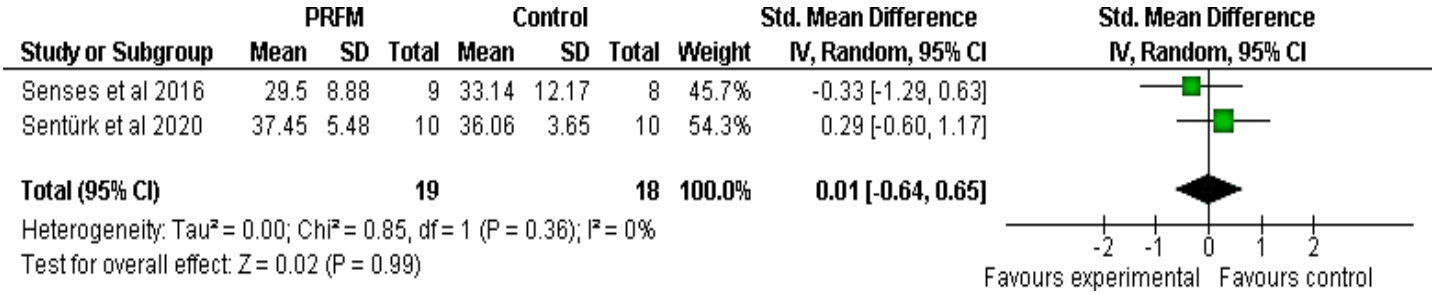

Figure 3. Forest Plot – Nerve Conduction Velocity

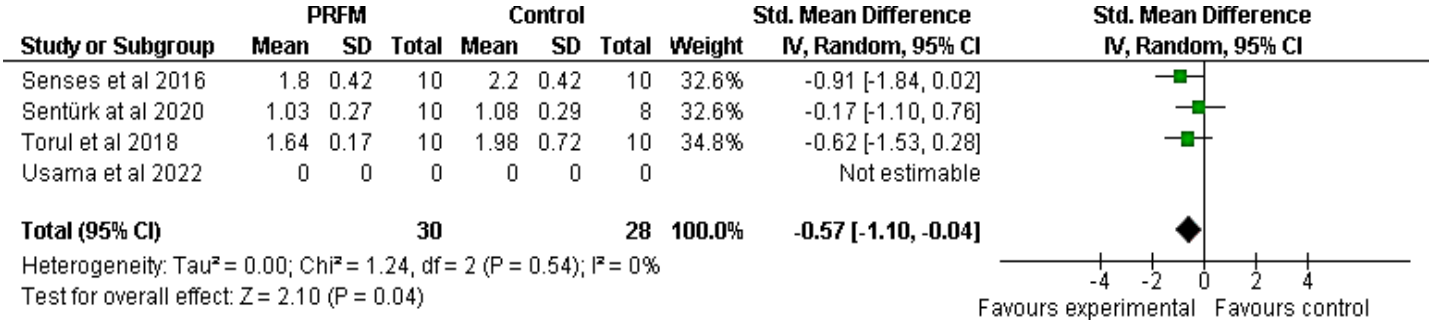

Figure 4. Forest Plot – Myelin Sheath Thickness

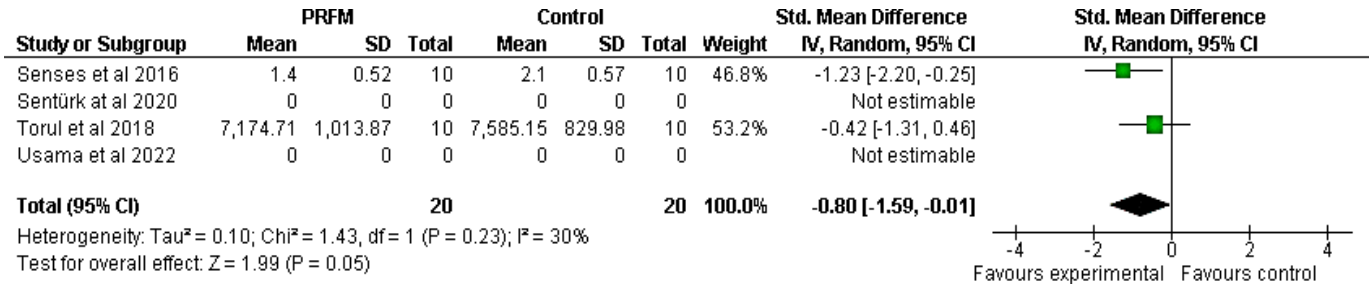

Figure 5. Forest Plot – Axon Area

Mechanism of Peripheral Nerve Regeneration

Nerve injuries are common clinically and the types of injury include open nerve injuries such as glass injuries, mechanical crush injuries, sharp instrument injuries and crush injuries, or nerve compression disorders (carpal tunnel syndrome and cubital tunnel syndrome). Each mechanism of injury can cause different damage to nerve tissue, surrounding soft tissue, and its blood supply, and recovery is also different. Age, gender, patient health status, and underlying disease are also important factors in peripheral nerve regeneration.[5] Nerve injury causes Wallerian degeneration of the distal nerve. Distal myelin sheaths, Schwann cells and axons are disintegrated and cell debris is phagocytosed by macrophages. Phospholipid degeneration of axons and myelinleaves Schwann cells in the basement membrane that encapsulates nerve fibers. The Schwann celllining of the basal layer is called the endoneurial tube or Bunner's ligament. Axonal regeneration occurs along the Bunner zone. Schwann cells are important in processes of nerve regeneration, from Wallerian degeneration to axonal myelination. Schwann cells regulate neuronal regeneration by interacting with various cells in the regenerative microenvironment (Figure 6).[6]

In peripheral nerve injury, injured axons, non-neuronal cells, Schwann cells, nerve terminal fibroblasts, and macrophages provide the microenvironment for nerve regeneration. For example, during vein bridging after sciatic nerve defects, fibrin deposition first occurs in the post-injury nerve space. Red blood cells, granulocytes, platelets, macrophages and endothelial cells then infiltrate the nerve root cavity.[7] Macrophages make up the largest proportion of this cell populationand vascular endothelial cells make up the smallest proportion. Peripheral neurons also respond rapidly after injury, migrating from the nerve stump into the nerve space. Peripheral neuronal migration follows fibrous deposition networks and forms annular channels to control the migration of neuronal fibroblasts and endothelial cells. The number of inflammatory cells gradually decreases over time. VEGF-A release by macrophages promotes the formation of new blood vessels at two nerve endings. The newly formed blood vessel coincides with the long axis of the nerve. Schwann cells migrate by angiogenesis and form Schwann cell cords.[6,8]

Schwann cell regeneration is controlled by SC and is divided into two slow phases (86 μm/day). In the early stages, axonal regeneration does not occur simultaneously with SC regeneration. In the second stage, the velocity was 433 μm/day, with simultaneous migration and axonal development. Netrin1/DCC between Schwann cells and axons is a key signal for axonal regeneration. Netrins, a family of extracellular adhesin-related proteins, play important roles in axonal guidance in the nervous system.[6,9] Schwann cells direct and promote nerve regeneration through the binding of netrin-1 to DCC receptors on axons. Nerve regeneration in defect models requires fibrin deposition and formation of a 3D scaffold for cell crawling. Over time, the fibrin scaffold is gradually replaced by regenerating axons and SC strands

Wallerian Degeneration Mechanism

Nerve injury close to the cell body causes neuron death. Nerve fibers regenerate if the injury is away from the cell body. Axonal disruption and neuronal demyelination at the distal tip is termed Wallerian degeneration. Wallerian degeneration is a unique form of axonal degeneration and a necessary process following peripheral nerve injury. After nerve injury, Schwann cells and neural endothelial fibroblasts undergo gradual apoptosis, and after 2 days Ca2+ and Na+ release lead to axonal degeneration. Injured axons then release neuropeptides such as substance P and calcitonin gene-related peptide (CGRP), leading to neurovasodilation. Neurovascular dilation and chemotaxis through the release of monocyte chemoattractant protein-1 by Schwann cells promote macrophage migration and recruitment. Macrophages phagocytize debris from axons and myelin sheaths, creating a favorable environment for nerve regeneration. Macrophages can also secrete vascular endothelial growth factor (VEGF-A), which promotes the formation of new blood vesselswithin nerves. At this stage, intact Schwann cells release nerve growth factor (NGF), ciliary neurotrophic factor (CNTF), brain-derived neurotrophic factor (BDNF), and glial-derived nerve growth factor (GDNF), thereby Stimulates the formation of new Schwann cells (Figure 7).[6]

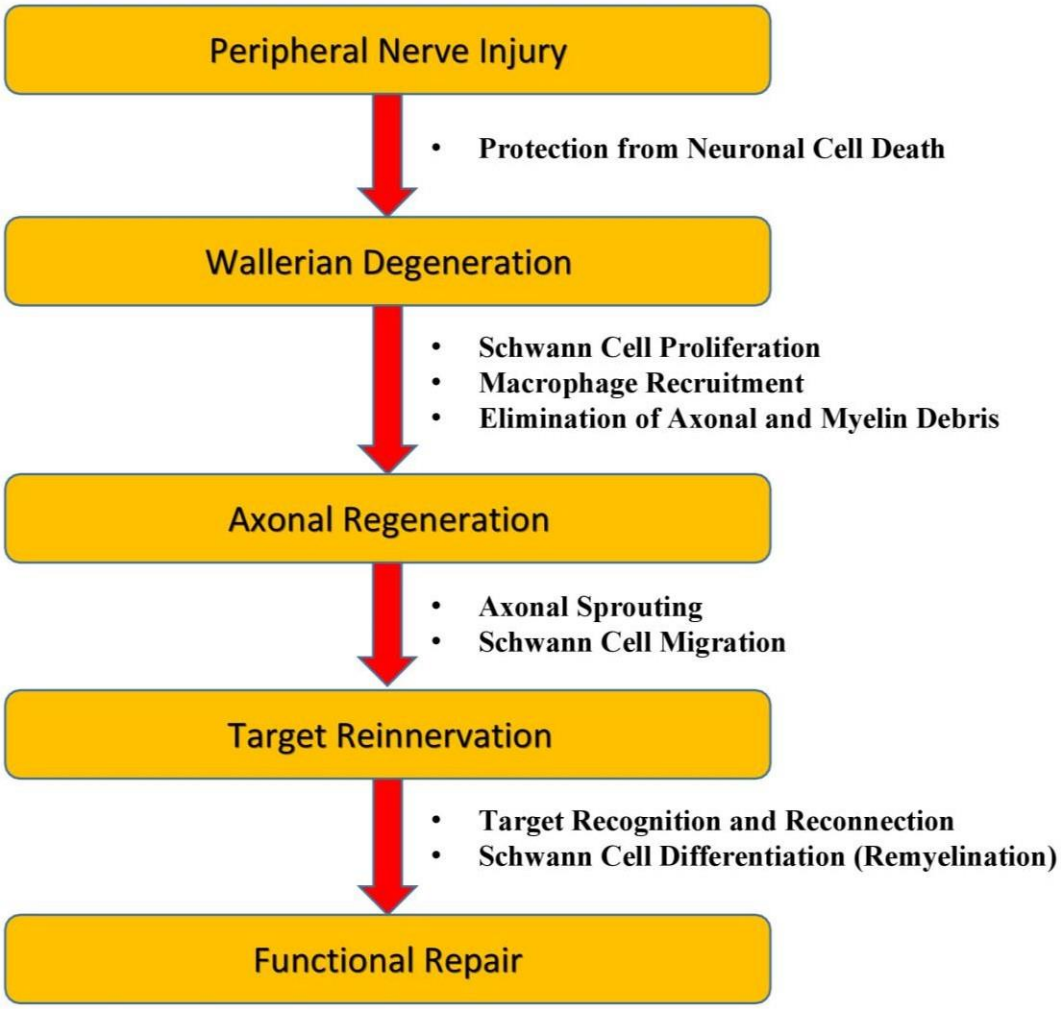

Figure 6. The Process of Peripheral Nerve Regeneration After Injury

Table 4. Biological Activity of Neurotrophic Factors[6]

Growth Factors	Target Cell	Bioactive Effect
Nerve Growth Factor (NGF)	Sensory And Sympathetic Neuron	Promote Survival and Growth
Brain-Derived NeurotrophicFactor (BDNF)	Sensory And Motor Neuron	Promotes Growth and Formation Of Synapses Of Neurons
Neurotrophin 3 (NT-3)	Sensory Neurons	Neurogenesis and Gliogenesis
Glial-Derived Nerve GrowthFactor (GDNF),	Schwann Cells and Motor and Sensory Neurons	Stimulates Proliferation andPromotes Survival
Ciliary Neurotrophic Factor (CNTF)	Sensory and Motor Neurons	Promotes Survival

Platelet Rich Fibrin

Platelet-rich fibrin is a new generation platelet concentrate that promotes the healing process for maximum predictability. It is composed of platelets, cytokines and a fibrin matrix (Table 5). Platelet and leukocyte cytokines play an important role in the biology of this biomaterial.Platelet degranulation involves the release of cytokines that can stimulate cell migration and proliferation within the fibrin matrix and initiate early healing stages.[10] The fibrin matrix that supports it is a key component responsible for the true therapeutic potential of PRF. The biologicalactivity of the fibrin molecule highlights its important ability to form scars. However, a detailed understanding of the components of PRF and their biological roles will help us to understand this biomaterial from a clinical perspective and expand its range of subsequent therapeutic applications.[4,11]

Fibrin is the active form of the fibrinogen molecule present in both plasma and platelet granules. It plays an important role in achieving platelet aggregation and hemostasis. Soluble fibrinogen is converted to insoluble fibrin and polymerized into scar matrix. The slow, spontaneous polymerization of fibrin leads to a uniform three-dimensional organization during the centrifugation performed in PRF preparation. This incorporates platelet cytokines and glycan chains into the fibrin mesh. The fibrin matrix present in PRF is flexible, elastic and extremely strong. Equilateral transitions occur due to the low thrombin concentration. These connected junctions allow the drainage of fine and flexible fibrin networks that can support cytokines and occurring cell migration. The release and use of these cytokines occurs during the initial remodeling of the scar matrix, thus prolonging the longevity of these cytokines.[12]

Platelet Rich Fibrin Promotes Peripheral Nerve Regeneration

As an autologous factor, PRF has high levels of platelets, growth factors, leukocytes, fibrin, and various bioactive factors such as fibronectin, osteonectin, and vitronectin. These componentsare essential for tissue repair. First, platelet activation stops bleeding and releases various growthfactors. Various growth factors influence all aspects of tissue repair. White blood cells help removelocal pathogens and necrotic tissue. Fibrin forms a three-dimensional network structure in damaged tissue and provides a scaffold for tissue regeneration. There are six lines of evidence that PRP may promote nerve regeneration. 1) neuroprotection and prevention of neuronal apoptosis, 2) stimulating revascularization, 3) promoting axonal regeneration, 4) modulating inflammatory responses in the microenvironment, 5) alleviating neural collateral muscle atrophy, and 6) improvement of human nervous system parameters. Here, the effects of PRF on SCs, modulation of the inflammatory environment, and axonal regeneration are presented in detail.[13,20]

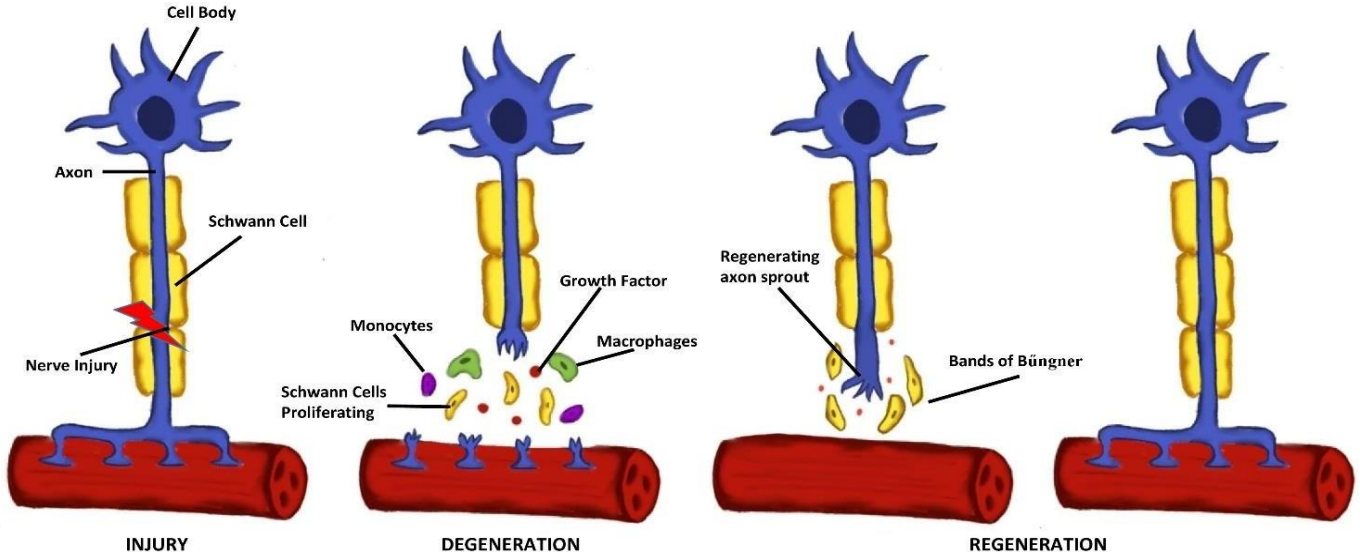

Figure 7. Schematic of The Wallerian Degeneration (Illustrated by Author)

DISCUSSION

Nerves are electrophysiological and directional tissues, suggesting that conduits with a biomimetic microenvironment may be required to promote and guide peripheral nerve regeneration.[14] The repair capacity of peripheral nerves is one of the slowest in the body. Currently, the best treatment for nerve injury is to restore nerve continuity by microsurgical tension-free anastomosis or autologous nerve grafting. This therapeutic approach does not improve slow nerve regeneration and incomplete postoperative functional recovery.

Therefore, regeneration and repairof peripheral nerve injury is the focus of intense research.

In the light of previous evidence, we decided to systematically review the effects of autologous PRF (New Generation Platelet Concentrate) on nerve regeneration. PRF has several advantages over PRP gel, such as shorter duration of generation, easier formation technique underclinical conditions and not requiring any additional heterogeneous agent.[15] As PRP can only be applied in a gel or solution form, a silicon tube is needed for application; PRF, on the other hand,can be applied as an isolated strong membrane. In this study, a PRF membrane was applied and sutured to the crush injury area to act as a tube. It is well known that tubulation techniques improveregenerative capacity from nerve injury. Several tubulization techniques, such as decalcified bone,vein conduit, and silicone tube, have been investigated, with favorable effects reported.[18]

Clinical evidence supports the positive effects of PRF. The duration of growth factor release is longer in PRF than PRP. This is because PRF forms solid membranes that remain intact for morethan 7 days and releases growth factors produced by cell populations formed within the membrane

SC migration after nerve injury is a major mechanism that supports nerve regeneration. Figure 8 explain the significant effect of PRF on SC migration observed in some studies suggeststhat neurotrophic factors such as NT-3 and NGF in PRF play important roles in promoting SC migration. Insulin-like growth factor I (IGF-I) upregulated MBP (myelin basic protein) gene expression in an experimental model, suggesting that IGF-I affected myelin protein synthesis and myelin regeneration. IGF-I acts as a neurotrophic factor that promotes peripheral nerve growth and inhibits neuronal and glial apoptosis.[14]

In another study, Huang et al. successfully used a novel nerve conduction made of platelet-rich fibrin membrane to bridge a 5-mm-long sciatic nerve in nude mice. Histological, morphometric and functional findings showed that PRF-NGC treatment was significantly superiorto the PUR negative control group, with similar levels of regenerated nerves in the ANG group (positive control group). The number of myelinated fibers, fiber diameter, myelin thickness and degree of muscle recovery in the PRF group were significantly superior to the PUR group.[16]

Electrophysiological testing allows the assessment of axon regeneration at different stagesof wound healing and is one of the best methods used to assess peripheral nerve wound healing. Latent prolongation is the minimum increase in stimulus intensity required to activate an action potential in the muscle. In other words, an increase in the stimulus threshold and a decrease in theamplitude of the voltage response to a stimulus of the same magnitude reflect a decrease in neuromuscular function. Looking at the results of this study, it can be seen that the influence of the amplitude parameter has a significant value but is not accompanied by the results of the NerveConduction Velocity parameter. So that it can be an input for further research regarding the specific assessment of the electrophysiological effect of platelet-rich fibrin as a nerve guidance conduit.

The improved axon regeneration rate by PRF-NGC is likely due to the release of growth factors that accelerate outgrowth. Nonetheless, one possible explanation is that PRF is composed of the biopolymer fibrin, and nutrients and oxygen diffused through the permeable PRF conduit tothe regenerating nerve before the tube became vascularized.[16] It's same with the positive result of morphometric parameters outcome in this study. PRF as a coiled membrane to achieve a dual advantage. The first is the channel-like geometry that controls and guides nerve fiber growth during nerve regeneration, and the second is the presence of growth factors that stimulate and promote regeneration.[17]

In contrast, PRP growth factor release is completed within 3 days. The use of PRF is an inexpensive, easy-to-use, and morbidity-reducing alternative to donor sites. In addition, the continuous release of regeneration factors within the line allows for satisfying results.[4]

Table 5. Components of Platelet Rich Fibrin[4]

Growth factors and cytokines presentin PRF	Function
Transforming growth factor-β (TGF-β)	Regulation of Inflammatory; Stimulates angiogenesis, fibronectin, and collagen production; prevents collagen breakdown; induces fibroblastand immune cells chemotaxis
Platelet-derived growth factor (PDGF)	Provokes migration and proliferation of mesenchymatous cell lineage; enables angiogenesis, macrophages chemotaxis, and

	activation; induces TGF-β secretion from macrophages
Insulin growth factor-1 (IGF-1)	Angiogenesis stimulation; induces differentiation and mitogenesis of mesenchymal cells
Vascular endothelial growth factor (VEGF)	Initiates angiogenesis; enhances permeability of the vessels; induces endothelial cell proliferationand migration
Epidermal growth factor (EGF)	Promotes angiogenesis; stimulates proliferation and differentiation of epithelial cells; increases cytokine secretion in epithelial and mesenchymal cells
Cytokines	Promote regeneration process

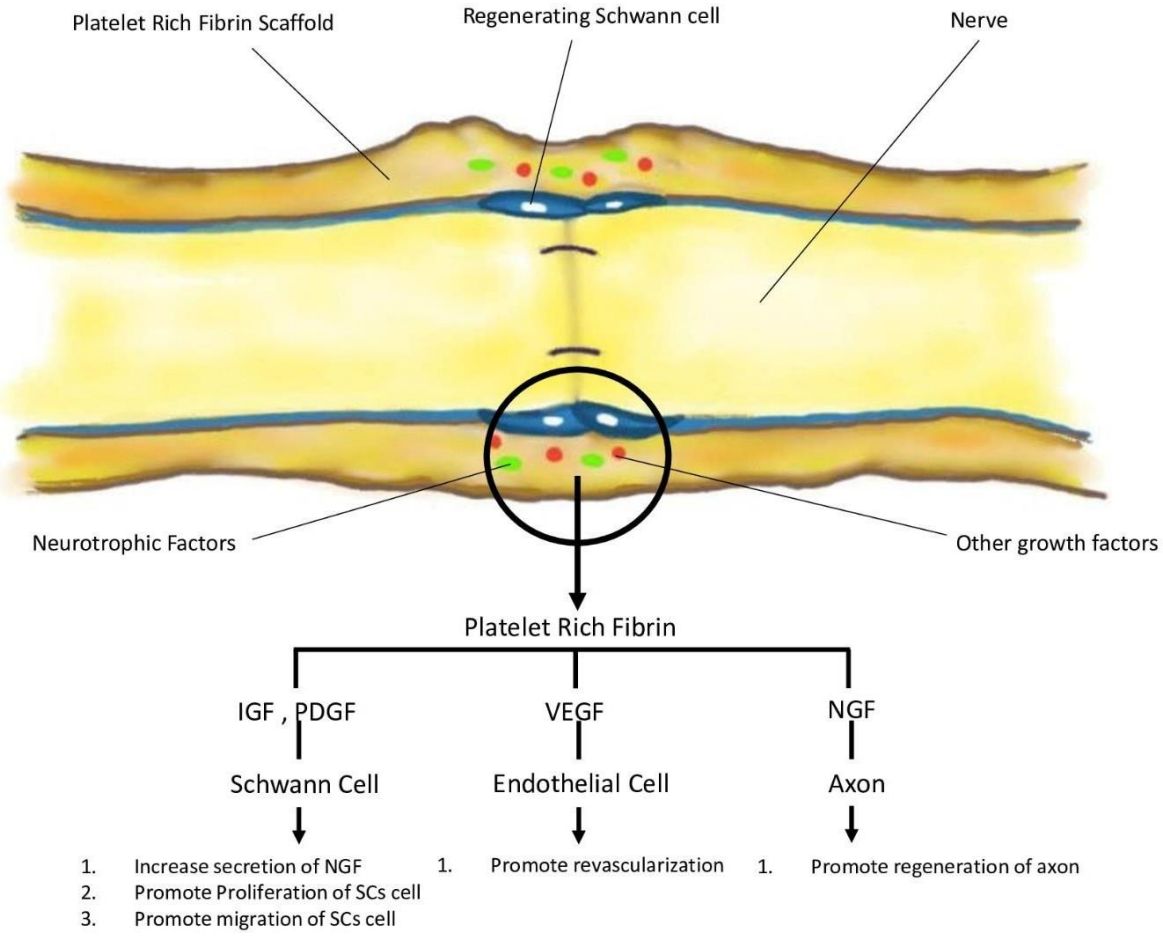

Figure 8. PRF contain high concentration of various growth factor which can promote effectively biological activity of Schwann cells, such as migration, secretion of NGF and proliferation. Additionally, high concentration of VEGF in PRP can improve revascularization. (Illustrated by Authors)

CONCLUSION

This Meta-analysis shows that PRF membrane as nerve guidance conduit is promising method and can improve function outcome in nerve repair specially in Morphometric and Electrophysiologic parameters but outcome of Nerve Conduction Velocity showed no significantin this study.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES

I. Aberg M., Ljungberg C., Edin E., Millqvist H., Nordh E., Theorin A., Terenghi G., Wiberg

II. M. Clinical evaluation of a resorbable wrap-around implant as an alternative to nerve repair: a prospective, assessor-blinded, randomised clinical study of sensory, motor and functional recovery after peripheral nerve repair. J Plast Reconstr Aesthet Surg, 2009. 62(11): p. 1503-9

III. Zhu X., Wei H., Zhu H. Nerve wrap after end-to-end and tension-free neurorrhaphy attenuates neuropathic pain: A prospective study based on cohorts of digit replantation. SciRep, 2018. 8(1): p. 620.

IV. Şenses F., Önder M.E., Koçyiğit I.D., Kul O., Aydin G., Inal E., Atil F., Tekin U. Effect of Platelet-Rich Fibrin on Peripheral Nerve Regeneration. J Craniofac Surg, 2016. 27(7): p. 1759-1764.

V. Pratama, A. M. O., & Anwar Lewa. (2023). The Role of Platelet Rich Fibrin for Closure of Oronasal Fistula Post Palatoplasty through Abilities to Keep Growth Factor Activity for a Relatively Longer Period and Stimulate Tissue Regeneration Effectively . *International Journal Of Medical Science And Clinical Research Studies*, *3*(3), 388–393. https://doi.org/10.47191/ijmscrs/v3-i3-20

VI. Kufflfler, D. P., and Foy, C. (2020). Restoration of Neurological Function Following Peripheral Nerve Trauma. Int. J. Mol. Sci. 21 (5). doi:10.3390/ijms21051808

VII. Wang S, Liu X and Wang Y (2022) Evaluation of Platelet-Rich Plasma Therapy for Peripheral Nerve Regeneration: A Critical Review of Literature. Front. Bioeng. Biotechnol. 10:808248. doi: 10.3389/fbioe.2022.808248

VIII. Min, Q., Parkinson, D. B., and Dun, X. P. (2021). Migrating Schwann Cells Direct Axon Regeneration within the Peripheral Nerve Bridge. Glia. 69 (2), 235–254. doi:10.1002/glia.23892

IX. Cattin, A.-L., Burden, J. J., Van Emmenis, L., Mackenzie, F. E., Hoving, J. J. A., Garcia Calavia, N., et al. (2015). Macrophage-Induced Blood Vessels Guide Schwann Cell- Mediated Regeneration of Peripheral Nerves. Cell 162 (5), 1127–1139. doi:10.1016/j.cell.2015.07.021

X. Dun, X. P., and Parkinson, D. B. (2017). Role of Netrin-1 Signaling in Nerve Regeneration. Int. J. Mol. Sci. 18 (3). doi:10.3390/ijms18030491

XI. Kapse S, Surana S, Satish M, Hussain SE, Vyas S, Thakur D.Autologous platelet-rich fibrin: Can it secure a better healing? OralSurg Oral Med Oral Pathol Oral Radiol 2019;127:8-18

XII. D. M. Dohan, J. Choukroun, A. Diss et al., "Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part III: leucocyte activation: a new feature for platelet concentrates?"Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology, vol. 101, no. 3, pp. E51–E55.

XIII. Masuki H, Okudera T, Watanebe T, et al. Growth factor and pro-inflammatory cytokine contents in platelet-rich plasma (PRP), plasma rich in growthfactors (PRGF), advanced platelet-rich fibrin (A-PRF), and concentrated growth factors (CGF). Int J Implant Dent 2016;2(1):1–6.

XIV. Sánchez, M., Anitua, E., Delgado, D., Sanchez, P., Prado, R., Orive, G., et al. (2017). Platelet-rich Plasma, a Source of Autologous Growth Factors and Biomimetic Scaffold for Peripheral Nerve Regeneration. Expert Opin. Biol. Ther. 17 (2), 197–212. doi:10.1080/14712598.2017.1259409

XV. Kim JW, Kim JM, Choi ME, et al. Platelet-rich plasma loaded nerve guidance conduit as implantable biocompatible materials for recurrent laryngeal nerve regeneration. *NPJ Regen Med*. 2022;7(1):49. Published 2022 Sep 14. doi:10.1038/s41536-022-00239-2

XVI. Caruana A, Savina D, Macedo JP, Soares SC. From Platelet-Rich Plasma to Advanced Platelet-Rich Fibrin: Biological Achievements and Clinical Advances in Modern Surgery. *Eur J Dent*. 2019;13(2):280-286. doi:10.1055/s-0039-1696585

XVII. Huang ML, Zhai Z, Chen ZX, Yang XN, Qi ZL. Platelet-rich fifibrin membrane nerve guidance conduit: a potentially promising method for peripheral nerve injuries. Chin MedJ 2020;133:999–1001. doi: 10.1097/CM9.0000000000000726

XVIII. Dakrory, U., Hegazy, R. The Effect of Using of Platelet Rich Fibrin on Sciatic Nerve Regeneration After End-to-End Neurorrhaphy in Rat Model. *Egyptian Dental Journal*, 2022; 68(2): 1413-1421. doi: 10.21608/edj.2022.121317.1982

XIX. Bayram B, Akdeniz SS, Diker N, Helvacioğlu F, Erdem SR. Effects of Platelet-Rich FibrinMembrane on Sciatic Nerve Regeneration. J Craniofac Surg. 2018 May;29(3):e239-e243.

doi: 10.1097/SCS.0000000000004256. PMID: 29381631

XX. Giannessi E, Coli A, Stornelli MR, Miragliotta V, Pirone A, Lenzi C, Burchielli S, Vozzi G, De Maria C, Giorgetti M. An autologously generated platelet-rich plasma suturable membrane may enhance peripheral nerve regeneration after neurorraphy in an acute injurymodel of sciatic nerve neurotmesis. J Reconstr Microsurg. 2014 Nov;30(9):617-26. doi: 10.1055/s-0034-1372483. Epub 2014 May 16. PMID: 24838385.

XXI. V. Neves Atti, M. Fernandes, G. Santiago de Lima Figueiredo, F. Roth, S. Gomes Valente,

XXII. L.R. Nakachima, C.H. Fernandes, J.B. Gomes dos Santos, Peripheral nerve regeneration in rats using nerve graft in a vein conduit pre-filled with platelet-rich fibrin (PRF), Hand Surgery and Rehabilitation, 10.1016/j.hansur.2022.12.001, **42**, 1, (61-68), (2023).

XXIII. Torul D., Bereket M.C., Onger M.E., Altun G. Comparison of the Regenerative Effects ofPlatelet-Rich Fibrin and Plasma Rich in Growth Factors on Injured Peripheral Nerve: An Experimental Study. J Oral Maxillofac Surg, 2018. 76(8): p. 1823 e1-1823 e12

XXIV. Şentürk F, Bahadır O, Aktaş O, et al (2020) platelet rich fibrin on facial nerve regeneration: an experimental study. Braz J Otorhinolaryngol.