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Platelet-Rich Fibrin in Membranes and Dental Implants

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A B S T R A C T

Objectives: The aim of this research is to investigate the efficacy of the usage of Platelet Rich Fibrin in the area of dental field when used for implant stability, soft and hard tissue regeneration as well as wound healing.

Material & Methods: For this research, electronic searches were conducted, mostly from PUBMED, Indian journal of dental research and Journal of Applied Oral Science. The electronic literatures that were searched for articles were published up to 10 -15 years. Articles that were chosen for this research mention how Platelet Rich Fibrin aids in dentistry in the fields of oral implantology, soft and hard tissue regeneration and wound healing.

Results: From the articles that were researched, it was found that the use of PRF had a positive effect. In the main topics that were chosen (PRF effect on implants, PRF effect on hard and soft tissue, PRF effect on wound healing), in all of them PRF resulted in an increase and was found to assist in these different fields of dentistry to result in better and faster treatment and comfort for the patient. The increase may not have been major however; no negative results and major complications were found towards PRF.

Conclusion: In conclusion, Platelet Rich Fibrin was shown to improve soft and hard tissue regeneration, wound healing and implant stability when used in dentistry. However further studies and investigations are necessary.

Keywords: Platelet rich fibrin; Oral implant; Hard tissue regeneration; Soft tissue regeneration; Wound healing.

1. Introduction

Platelet-rich fibrin (PRF) t 1membrane is a three-dimensional biodegradable biopolymer, which consists of platelet-derived growth factors enhancing cell adhesion and proliferation. PRF does not require the addition of anticoagulants nor bovine thrombin, it is a second-generation autologous platelet concentrate[13].

Choukroun et al[6]. developed PRF in 2001, it was prepared by withdrawing blood into glass tubes from the patients and then placed into a centrifuge, what happens then is that in the fibrin matrix there are entrapped platelets and leukocytes where a large amount of growth factors are formed from the platelets when they are activated and due do that, the molecules act as cell attractants and increase the proliferation of cells[27,12]. When the centrifugation process is completed, hyper acute serum is collected from the PRF clot, which has very advantageous properties since it has an elevated effect of cell proliferation on the bone marrow mesenchymal stem cells, osteoblasts and osteoarthritic chondrocyte cells[9]. After the hyperactive serum fraction is removed the remaining PRF membrane is a three-dimensional, biocompatible, biodegradable scaffold, which can slowly and sustainably release bioactive molecules, which facilitate cell adhesion and proliferation[4,6].

PRF is widely used in the field of dentistry, especially in oral and maxillofacial surgery and periodontics[7] because it is able to increase the adhesion and proliferate the capacity of gingival fibroblast, it increases new bone formation, improves wound healing, used in sinus lift procedures, soft tissue transplants, post extraction alveolar ridges, bone regeneration for future implants and prosthetic reconstruction[20]. The tissue healing and regeneration takes place when PRF is placed and is caused by the effective creation of new vessels, accelerated wound closure and fast scar tissue remodeling. Despite an increasing use of PRF membranes, there is still no comprehensive review on their efficacy with regard to soft and hard tissue healing after implants insertion. The aim of this study is to evaluate the potential

benefits of using PRF in the soft ad hard tissues implant stability and wound healing.

Thesis objective

For my thesis objective I would like to find out the efficacy of PRF when used as a membrane during implant insertion procedure. To research how PRF aids in soft tissues and hard tissue regeneration also to in the wound healing site.

2. Material and Methods

This article was conducted according to reviews of different articles. PICO question was developed which included definition of the focus question, a P (patient), I (intervention), C (comparison), O (outcome) question. Search strategy, inclusion/ exclusion criteria, data extraction, and outcome measure determination.

2.1 PICO Terms

P: Patients undergoing dental implant surgery.
I: Combining PRF (Platelet Rich Fibrin) while undergoing dental implant surgery.
C: Defined regenerative / reparative approaches with and without the use of PRF.
O: gingival tissues, periodontal tissues, wound healing, Osseo integration.

2.2 Defining the focused questions

For this article, there were different questions concerning the effectiveness of using Platelet rich fibrin (PRF), either it was to be used as a sole treatment or as a combined treatment. The questions were as follows; how would PRF acts as a barrier and as a biological connector when used in implant dentistry (could it improve the Osseo integration process of implant treatment)? How would PRF perform with regard to soft tissue healing?

2.3 Search strategy

For this article, electronic searches were conducted, mostly from PUBMED, Indian journal of dental research and Journal of Applied Oral Science. The electronic literatures that was searched for articles that were published up to 10 -15 years The search terms and strategies that were used were: 1 ((((((platelet rich plasma membrane) OR platelet rich plasma membrane) OR PRP membranes) OR PRP membrane) AND dental) OR platelet rich fibrin membranes) OR platelet rich fibrin membrane. From this combination 219 articles were found, and 42 articles were chosen. 2. ((PRF membranes) AND soft tissue healing) AND dental implants. From this search 3 articles were found and 2 were chosen. 3 (PRF membrane) AND mucosal healing. Here 8 articles were found and 6 selected 4 ((PRF membranes) AND osseointegration) AND dental implants. 4 articles found and 1 chosen.

2.4 Criteria for study selection and inclusion / exclusion

The study selection for this article that was considered were articles that were published only in the English language. Only human studies. (All animal studies were excluded.). Studies that evaluated the clinical effects of PRF (Platelet rich fibrin) in dentistry. The effects of PRF on the gingival tissues and periodontal tissues implant stability, osseointegration process and wound healing.

2.5 Number of included studies

From all of the searched studies, out of 52 articles, 29 articles were chosen for this thesis.

2.6 Data extraction and analysis

Data that was extracted from different articles were general characteristics such as authors, publications (up to 10 years), and reason of study, number of patients, treatment groups, baseline of the studies, PRF preparation techniques, and evaluated parameters, whether implants were placed and complications. Studies were extracted from the collection of articles and summarized into tables based on the topics and discussed accordingly.

2.7 Outcome measure determination

For each of the investigated clinical indication, different primary outcomes were considered. For studies involving wound healing; EHI, GML, Mean Soft Tissue Healing were measured. For studies dealing with implant stability; torque values, ISQ were measured. For studies involving extraction socket management; Alveolar crest height, mean bone density, radiography were being evaluated. For studies involving gingival recessions, KTW, CAL, PD, recession height, GRW were measured.

3. Results

3.1 PRF membranes

3.1.1 PRF membranes definition and preparation

PRF membrane is a patient blood derived and an autogenous living biomaterial that can be utilized as an adjunctive autologous biomaterial to back bone and delicate tissue recuperating and recovery. The critical dynamic components of PRF incorporate the common interaction between a framework (fibrin network), platelets, development variables, leukocytes, and stem cells. So when these elements are combined and arranged legitimately the method of tissue recuperating and recovery cell expansion and separation, extracellular lattice amalgamation, chemotaxis and angiogenesis (neo-vascularization) occurs.

For the PRF preparation, blood is withdrawn from the patient employing a sterile. The tubes with collected blood samples are promptly (within 2 minutes after collecting the blood sample) put within the centrifuge and processed employing a single centrifugation step. Failure to achieve the speedy arrangement of PRF may cause a diffuse polymerization of fibrin, which isn't perfect for tissue.

At the end of the centrifugation spin the caps for A-PRF or L-PRF (not i-PRF) are expelled and the tubes are put in a sterile tube holder. The blood with the clot is put to rest/mature for around 4-8 minutes before removing the clot from the tube.

The centrifugation process activates the coagulation handle and isolates the blood test into three distinctive layers: acellular plasma at the best of the tube; a polymerized fibrin clot is shaped within the center; and blood cells ((red corpuscle base) are accumulated at the end of the tube.

There are diverse centrifugation preparing conventions that are right now being utilized. These incorporate; Unique Choukroun et al. PRF convention (standard convention): 3,000 rpm/10 minutes, Choukroun et al. progressed PRF (A-PRF), enriched with leukocytes: 1,300 rpm/ 8 minutes, Choukroun et al. I-PRF (solution/gel): 700 rpm/3 minutes, Ehrenfest et al. bunch (leukocyte- and platelet-rich fibrin [L-PRF]): 2,700 rpm/12 minutes[6,19].

In vitro studies it appeared that a longer centrifugation speed (2,700 rpm) produce a denser fibrin clot with less inter-fibrous

space containing less cells compared to the shorter centrifugation speed of A-PRF (1300 rpm) that creates a less thick fibrin clot with a looser inter-fibrous structure containing more cells[8].

3.1.2 Biological and mechanical properties of PRF membranes

The key biological functions of PRF are the bioactive barrier and the Competitive interposition barrier. What is meant by these two terms is that in the bioactive barrier, when the PRF membrane is prepared clot forms, which is rich in cells and growth factor, so these components act as a natural bioactive barrier allowing interaction with the tissues below and above it[14.15].

In the competitive interposition barrier such as the GTR (Guided Tissue regeneration) barrier are cell proof barriers against soft tissue invagination, on the other hand PRF membranes allow cells to migrate through it, which allows new blood vessels to form which will lead to regeneration and healing between the tissues below and above the PRF membrane[15].

Advantages and disadvantages of PRF membranes

The main advantages of PRF in repair and recovery processes are that PRF could be a common biomaterial; it is simple and proficient to use, cost effective and successful. It is expected that it is has an expanded clinical performance since it shows a more exhibited expression, concentration of growth factors and matrix proteins. It is safe, it has increased healing potential, reduced morbidity. However there are limitations as PRF lacks rigidity and causes fast degradation, which reduces the application in procedures. Also at present, very little is understood about PRF generated from patients with coagulation disorders or patients on medications that affect blood clotting (heparin, warfarin, or platelet inhibitors)[6].

3.2 Effect on implant stability

3.2.1 Characteristics of included studies

Implant stability is a critical factor resulting in success when setting implants. Four articles considered the connection of PRP layers and embed stability, and to this end they assessed parameters for embed soundness were ISQ (Embed Solidness Remainder), Addition torque and sort of bone quality (**Table 1**). The patients that took portion in these ponders were separated into bunches PRF vs. Non- PRF All ponders utilized comparative arrangement strategies for the layer, pulling back 9-10 ml of persistent blood and centrifuging it for 10 - 12 minutes at 2000 – 3000 rpm. No complications were recorded within the studies during the treatment.

Table 1: Characteristics of studies on PRF membranes and implant stability.

Source		Öncü et al. 2015[21]	Tabrizi et al. 2018[26]	Torkzaban et al. 2018[28]	Hussien et al. 2017[10]
Patient age		44.2+-12.5	39.60±6.74	45.3 (26-60)	28-66
Patients numbers / gender	M	14	9	5	7
	F	6	11	5	12
Implants placed	Type	3.5 x11mm			
	Nr	64	40	50	58 (29 per group)
Length of study		1 month	6 weeks	1 month	12 weeks
Groups		PRF	PRF.	PRF.	PRF
		NON PRF	NON PRF	NON PRF	NON PRF
PRF prep.		9 ml of blood	10 ml of blood	9 ml of blood	10 ml of blood
	Centrifugation	2700rpm, 12 min	28000rpm, 12 min	2000rpm, 10 mins	3000rpm, 12 min
Evaluated parameters		ISQ	ISQ	ISQ	ISQ
		Insertion torque.		Insertion torque	
		Complications	Complications	Complications	Complications

Table legend: rpm rounds per minute, ISQ implant stability quotient.

3.2.2 ISQ values

The results demonstrate that the application of PRF during implant surgery enhances the stability of implants and that is shown by the increased values of the ISQ.

In general there is an increase between all the groups the ISQ measurements, the results show that there is an increase in the PRF as well as in the non- PRF groups however the groups that had the PRF showed higher results.

Table 2: ISQ values with and without PRF membrane over time.

Author	groups	IQS at time of implant placement	IQS Week 1	*P-value*	IQS Week 2	*P-value*	IQS Week 3	*P-value*	IQS Week 4	*P-value*	IQS Week 6	*P-value*	IQS Week 8	*P-value*	IQS Week 10	*P-value*
Öncü et al. 2015[21]	PRF (+)	63.75±11.9	± 78.25 (1) 7.14	*0.001*	± 78.4 a 6.72		± 75.63 3.58		± 74.75 (1) 7.27	*001. 0*						
	(-) PRF	57.2±14.64	± 71.8 (2)4.32	*0.287*	± 71.47 a 5.57		± 70.0 10.08		± 65.5 (2)14.25	*009. 0*						
Tabrizi et al. 2018[26]	PRF (+)				60.60±3.42	*0.04*			70.30±3.36	*0.014*	78.45±3.36	*0.027*				
	(-) PRF				58.25±3.64				67.15±4.33		76.15±2.94					
Torkz-aban et al. 2018[28]	PRF (+)	59.74±5.03	59.85±5.32	*0.004*					66.62±4.77	*0.015*						
	(-) PRF	58.41±3.99	55.99±3.39	*0.004*					63.23±4.74	*0.015*						

Hus-sien et al. 2017[10]	PRF (+)		-						68.1±7.52	*0.023*			71.75±8.08	*0.009*	74.46±8.06	*- 0.001>*
	(-) PRF								68.52±8.84	*0.001*			72.48±0.07	*0.005*	75.04±6.16	*0.001>*

Table legend: P-values denote significant against each other with P<0.001.

3.2.3 Mean insertion torque

In the studies that had used insertion torque as a parameter showed no significant difference between the groups. Nevertheless the group with the PRF had higher values.

Table 3: Mean insertion torque values with and without PRF membrane over time.

Author	Groups	Mean Insertion torque (Ncm)	*P-value*
Öncü et al. 2015[21]	PRF (+)	27.5±11.90	*0.632*
	PRF(-)	24.0±12.45	
Torkzaban et al. 2018[28]	PRF (+)	25.40±3.20	*0.290*
	PRF (-)	24.40±3.33	

3.3 Effect on soft tissues

3.3.1 Characteristics of included studies

In gingival recession the gingiva changes position, exposing more of the tooth or the tooth root. In 6 articles the influence of PRF membranes on gingival recession was studied (**Table 4**).

In the studies found, the patients that had undergone the studies were ranging in age between 18-52 years. In each study the patients were divided into different group treatments but each one included a group that combined PRF into the treatment (VRD+PRF vs. CTG, Gingival recession +LPRF vs. CTG, CAF vs. CAF+PRF, Mucogingival surgery+ PRF, MCAF+PRF and MCAF+SCTG).

Just in two studies minor complications were observed after surgery such as pain, swelling, bleeding, and inflammation of the gingiva. However these kinds of symptoms are normal after a surgery.

For the PRF preparation the blood drawn from the patients that took part in the studies were to be centrifuged. The blood samples that were withdrawn were between 6-10 ml and were being centrifuged at 2700-3000 rpm for 10-12 minutes.

In the different articles the studies were between 3 - 12 months. The evaluated parameters for PRF membranes on gingival recession included the CAL (Clinical attachment level), PD (pocket depth), GT (gingival thickness), recession height and KTW (keratinized tissue width).

Table 4: Characteristics of studies on PRF membranes and gingival recession.

Source		Jankovic et al. 2012[11]	Tunali et al. 2015[29]	Dixit et al. 2018[5]	Kuka et al. 2017[17]	Krismariono et al. 2019[16]	Öncü et al. 2015[21]
Patient age		19-47	25-52	18-50	-	30-40	20-60
Patients numbers / gender	M	5	4	-	11	-	9
	F	10	6	-	13	7	11
Length of study		6 months	12 months	6months	12 months	3 months	6 months
Groups		VRD+PRF	Gingival recession +LPRF	CAF+PRF	CAF+PRF	PRF	MCAF+PRF
		NON PRF	NON PRF	NON PRF	NON PRF	NON PRF	NON PRF
PRF prep.		10 ml of blood	10 ml of blood	6 ml of blood	10 ml of blood	10 ml of blood	9ml of blood
	Centri-fugation	3000 rpm for 10 mins	2700 rpm for 12 mins	2700 rpm for 12 mins	3000 rpm for 10 mins	3000 rpm for 12 mins	2700 rpm for 12 mins
Evaluated parameters		KTW	PD	,VGRD,	Recession height	Recession height	KTW
		CAL	CAL	GRW	KTW		PD
		PD	KTW	CAL	GT		CAL
				GT			GT

3.3.2 Keratinized tissue width

The KTW increased in all the groups that were used as treatment modalities for gingival recessions. The groups that involved PRF showed higher values. Two studies included groups that were PRF vs CTG, and the other study included MCAF+PRF and MCAF+SCTG.

In the study by Jankovic et al. 2012 the KTW in the PRF group increased from 1.32 ± 0.66 mm to 2.20 ± 0.54 mm. In the control group, KTW increased from 1.41 ± 0.58 mm to 2.85 ± 0.45 mm. The gain in KTW was statistically significant for both groups. In a study by Tunali et al[29]. The statistical analyses for the clinical parameters at baseline and 6 months and 12 months post treatment for both groups. Both groups showed a significant increase in the KTW from baseline to 12 months; however, there were no statistically significant differences in the KTW between the two groups at baseline or at 12 months. It goes for the study by Öncü et al[21] where KTW increases in time in both the groups.

Table 5: Keratinized tissue width values with and without PRF membranes over time.

Author	Groups	KTW at basline	P-value	KTW at 1st week	P value	KTW at 6 months	P value	KTW at 12 months	P value
Jankovic et al. 2012[11]	CTG	1.41±0.58	0.00			2.85+0.45	0.013		
	PRF	1.32±0.66	0.00			2.20±0.54	0.013		

Tunali et al. 2015[29]	PRF	2.33±0.56	0.00			2.93±0.70	0.00	2.86±0.69	0.02
	CTG	2.43±0.52	0.00			2.93±0.71	0.00	3.03±0.74	0.00
Öncü et al. 2015[21]	MCAF+PRF	2.70±0.70	0.647	3.80±0.93	0.024				
	MCAF+SCTG	2.60±0.77	0.647	4.33±0.88	0.024				

Table legend: CTG (control group), PRF (platelet Rich Fibrin), MCAF (Modified Coronally Advanced Flap) SCTG (Subepithelial Connective Tissue Graft).

3.3.3 Recession height

Two studies studied difference between CAF vs PRF, and one study studied CTG vs PRF. Kuka et al. 2017 results of the recession height from the baseline in CAF + PRF and CAF groups was 3.15 ± 0.24 and 3.36 ± 0.34 mm, respectively. Intragroup comparisons revealed significant differences at 12 months for all parameters ($p < 0.05$). Recession height reduction was 2.75 ± 0.33 and 2.51 ± 0.33 mm in the CAF + PRF and CAF groups respectively. According to the study by Jankovic et al. 2012[11] the recession height in the PRF group decreased from 3.51±0.70 to 2.83±0.37.and in the CTG group from 3.45±0.84 to 3.07±0.30, it is shown that the differences between the groups were not statistically significant. In Dixit et al. study from baseline to 6 months the recessions height in both the groups also resulted in the decrease, however the results were not statically significant[5].

Table 6: Recession height values with and without PRF membranes over time.

Author	Groups	Recession height [mm]								
		Base-line	P	1 m	P	3 m	P	6 m	P	12 m	P
Kuka et al. 2017[17]	CAF	3.36±0.34	0.126							2.51±0.33	0.134
	CAF+PRF	3.15±0.24	0.126							2.75±0.35	0.134
Jankovic et al. 2012[11]	CTG	3.45±0.84	0					3.07±0.30	0.270		
	PRF	3.51±0.70	0					2.83±0.37	0.270		
Dixit et al. 2018[5]	CAF	2.83±1.12	0.00	0.33±0.78	0.00	0.58±1.00	0.00	0.58±1.00	0.00		
	CAF+PRF	2.92±0.90	0.00	0.08±0.29	0.00	0.33±0.49	0.00	0.50±0.52	0.00		

Table legend: CAF (Coronally Advanced Flap), PRF (Platetlet Rich Fibrin), CTG (control group).

3.3.4 Gingival Thickness

Two studies studied difference between CAF vs PRF, and one study studied MCAF+SCTG vs. MCAF+PRF.

In Dixit et al. 2018[5] results the change in gingival thickness was found to be statistically significant ($P < 0.05$), when the changes are observed from baseline to 6 months in both the groups. In the study by Kuka et al. 2017[17] it is also observed that the Intergroup differences were found to be significant for GT gain ($p < 0.05$). In Öncü et al[21], study results were similar the gingival thickness values increased significantly in both groups after 6 months, respectively. GT was higher in the test group (P = .005), which was the PRF group. So in all of the studies the GT have increased over time[21].

Table 7: Gingival Thickness values with and without PRF membranes over time.

Author	Groups	GT at baseline	P value	GT at 1st week	P value	GT at 1 month	P value	GT at 3rd month	P value	GT at 6th month	P value	GT at 12th month
Dixit et al. 2018[5]	CAF	0.56±0.56	0.102			0.64±0.37	0.102	0.65±0.37	0.072	0.64±0.38	0.108	
	CAF+PRF	0.49±0.31	0.00			1.12±0.42	0.00	1.12±0.43	0.00	0.12±0.43	0.00	
Kuka et al.2017[17]	CAF+PRF	0.78±0.06	0.121									0.53±0.05
	CAF	0.73±0.007	0.121									0.07±0.005
Öncü et al. 2015[21]	MCAF+SCTG	0.69±0.23	0.939	0.85±0.21	0.005							
	MCAF+PRF	0.69±0.21	0.939	0.99±0.20	0.005							

Table legend: CAF (Coronally Advanced Flap), PRF (Platelet Rich Fribrin), MCAF (Modified Coronally Advanced Flap), SCTG (Sub epithelial Connective Tissue Graft).

3.3.5 Clinical Attachment Level

In all of the studies there was a gain in the CAL but there was no significant difference between the intergroup' s that were being studied.

The CAL results in the study by Jankovic et al[11]. showed that in the PRF group, CAL decreased from 4.35 ± 0.67 mm to 1.48 ± 0.40 mm, with an attachment gain of 2.87 mm. In the control group, CAL decreased from4.31 ± 0.61 mm to 1.35 ± 0.38 mm, with an attachment gain of 2.96 mm. The differences between the two groups were not statistically significant for CAL. Sam goes to the rest of the studies by Tunali et al., Dixit et al., Kuka et al., and Öncü et al., there was no significant differences between the groups for CAL[11,29,5,17,21].

Table 8: Clinical Attachment Level values with and without PRF membranes over time.

Author	Groups	CAL at baseline	P-value	CAL at 1st week	P value	CAL at 1st month	p-value	CAL at 3rd month	P value	CAL 6th month	P value	CAL at 12th month	p-value
Jankovic et al. 2012[11]	PRF	4.35±0.67	0.00							1.48±0.40	P<005		
	CTG	4.31±0.61	0.00							1.35±0.38	P<0.05		

Tunali et al. 2015[29]	PRF	5.03±1.94	0.00							2.27±0.92	0.00	2.33±0.90	0.00
	CTG	5.20±1.49	0.00							2.24±0.82	0.00	2.16±0.79	0.00
Dixit et al. 2018[5]	CAF	4.67±1.30	0.00			2.00±0.85	0.00	2.17±0.83	0.00	2.17±0.83	0.00		
	CAF+PRF	4.50±1.00	0.00			1.83±0.72	0.00	2.00±0.74	0.00	2.08±0.67	0.00		
Kuka et al. 2017[17]	CAF+PRF	4.25±0.35	0.063									2.10±0.61	0.119
	CAF	4.54±0.30	0.063									1.74±0.24	0.119
Öncü et al. 2015[21]	MCAF+SCTG	5.53±1.07	0.550	1.77±0.97	0.465								
	MCAF+PRF	5.37±1.07	0.550	2.07±1.17	0.465								

Table legend: CTG (control group), CAF (Coronally Advanced Flap), PRF (Platelet Rich Fribrin), MCAF (Modified Coronally Advanced Flap), SCTG (Sub epithelial Connective Tissue Graft).

3.3.6 Pocket depth

In all of the studies there was a gain in the PD, there was an improvement in the pocket depth as it decreased after the treatments but when comparing to the test and control groups also no significant differences were observed. Tunali et al, found both groups, PDs significantly decreased after treatment (P < .001). The PD values were 1.33 ± 0.59 mm and 1.49 ± 0.50 mm at baseline, 1.24 ± 0.37 mm and 1.13 ± 0.35 mm at 6 months and 1.18 ± 0.33 mm and 1.18 ±0.35 mm at 12 months in the L-PRF and CTG groups, respectively. Between the rest of the studies the changes observed over time between the groups, no statistical significance was observed for the PD[29].

Table 9: Pocket depth Level values with and without PRF membranes over time.

Author	groups	PD at baseline	p-value	PD at 1st week	P value	PD at 6 months	P value	PD at 12 months	P value
Jankovic et al. 2012[11]	PRF	0.74±0.53	0.00			0.95±0.41	0.167		
	CTG	0.86±0.47	0.00			0.92±0.48	0.167		
Tunali et al. 2015[29]	PRF	1.33±0.59	0.00			1.24±0.37	0.57	1.18±0.33	0.44
	CTG	1.49±0.50	0.00			1.13±0.35	0.004	1.18±0.35	0.06
Kuka et al. 2017[17]	CAF+PRF	1.10±0.021	0.396					0.65±0.24	0.515
	CAF	1.18±0.24	0.396					0.78±0.34	0.515
Öncü et al. 2015[21]	MCAF+SCTG	1.33±0.66	0.421	1.17±0.38	1.00				
	MCAF+PRF	1.47±0.51	0.421	1.17±0.38	1.00				

Table legend: CTG (control group), CAF (Coronally Advanced Flap), PRF (Platelet Rich Fribrin), MCAF (Modified Coronally Advanced Flap), SCTG (Subepithelial Connective Tissue Graft).

3.4 Effect on hard tissue

3.4.1 Characteristics of included studies

After tooth extraction, dimensions of the alveolar bone are decreased in vertical as well as horizontal dimensions however that is normal because it is part of the normal healing process. Until today different treatment modalities were used to decrease those changes that occur in the alveolar ridge after the extraction, either for esthetic reasons or for future dental implant placement, such as allograft or xenograft bone grafts material with or without barrier membranes. PRF has many advantages and one of them is that it can be used as an adjunct in extraction socket grafting procedures to improve healing as well as to maintain that alveolar ridge dimension. In 4 articles the influence of PRF membranes on extraction sockets was studied. The results are summarized in **Table 3**.

Table 10: Characteristics of studies on PRF membranes and dental sockets.

Source	Hauser et al., 2013[8]	Shrivastava et.al, 2018[24]	Hussien et al., 2017[10]
Patients+ Age	23 pt. (14 women, 9 men_age (22-75) mean age 47, median age 46.	120 patients	24 patients
Groups	PRF	PRF	PRF
	NON PRF	NON PRF	NON PRF
Length of study	8 weeks	24 weeks	8 weeks
PRF prep.	8ml of blood	10ml of blood	20 ml of blood
Centrifugation	2700rpm for 12 mins.	3000rpm,10 mins	3000 rpm for 10 mins
Evaluated parameters	Alveolar crest height	Mean bone density	Radiographic
Implants placed	Yes 3.5 mm straumann.	none	none
Complications	Mild just sweling	none	none

In the studies found, the patients that had undergone the studies were ranging in age between 19-46 years. In each study the patients were divided into different group treatments but each one included a group that combined PRF into the treatment (PRF vs. Control group (NON-PRF). Mild swellings were recorded as a complication in one study.

For the PRF preparation the blood drawn from the patients that took part in the studies went through the centrifuging process. The blood samples that were withdrawn were between 8-20 ml and were being centrifuged at 2700-3000 rpm for 10-12 minutes.

In the different articles the studies lasted 8 -24 weeks. The evaluated parameters for PRF membranes on extraction sockets included Alveolar crest height, radiographic bone density and mean bone density.

3.4.2 Measured effects

The results show that the PRF membranes had a preventive effect in the radiographic reduction of the alveolar crest height at the mesial and distal sites. As for the radiographic bone fill the result was very positive since it was significantly higher for the PRF group than the NON-PRF group. It is seen that in the mean bone density the results are favorable for the PRF group. It seems that the PRF is a satisfactory alternative with favorable results and low risks in extraction sockets healing.

Table 11: Evaluated parameters of PRF membranes on extracted sockets over time.

Author	groups	Alveolar crest height at baseline	Alveolar crest height at 8 weeks	P-value	Alveolar ridge width at baseline	P-value	Alveolar ridge width at 4 weeks	P-value	Alveolar ridge width at 8 weeks	P-value	Mean Bone Density at baseline	P-value	Mean Bone Density at at 6 weeks	P-value	Mean Bone Density at at 12 weeks	P-value
Hauser et al. 2013[8]	control	11.55±0.47	Mesial (-0.77±0.17) Distal (-2.07±0.81	<0.05												
	PRF (+)	11.55±0.47	Mesial (-1.21±0.40) Distal (-0.76±0.25)	<0.05												
Hussien et al. 2017[10]	control				3.26 ± 2.21	0.141	9.79 ± 6.02	0.012	13.54 ± 6.57	0.036						
	PRF (+)				2.09 ± 0.84	0.141	5.22 ± 0.80	0.012	8.58 ± 1.73	0.036						
Shrivastava et.al , 2018[24]	control										56.26± 3.48	0.1963	58.30 ±3.68	0.0263	75.52 ±5.55	<0.0001
	PRF (+)										57.43 ±3.42	0.1963	60.37± 3.31	0.0263	85.60± 5.15	<0.0001

3.5 PRF membranes and wound healing

When wound healing begins in the oral cavity the rich blood supply helps to speed the recovery, saliva contains proteins that aid in tissue repair, many cells play a role in this process, such as; neutrophils, macrophages, epithelial cells and fibroblasts. PRF may play a specific role in wound healing by increasing cell proliferation and migrations and produce collagen for extracellular matrix to help in repairing the wound.

3.5.1 Characteristics of included studies

In 3 articles the influence of PRF membranes on wound healing was studied. In the studies found, the patients that had undergone the studies were ranging in age between 29-27 years. In each study the patients were divided into different group treatments but each one included a group that combined PRF into the treatment (OFD+PRF vs. PRF, PRF vs. Control group (NON-PRF). In one study complication was observed which included Pus, swelling, erythema, postoperative pain.

For the PRF preparation the blood drawn from the patients that took part in the studies went through the centrifuging process. The blood samples that were withdrawn were between 5-20 ml and were being centrifuged at 2000-3000 rpm for 10-12 minutes.

In the different articles the studies lasted from 1 week to 9 months. The evaluated parameters for PRF membranes on wound healing (**Table 8**), included EHI score (Early Healing Index), GML (gingival marginal level) and the Mean soft tissue healing.

Table 12: Characteristics of studies on PRF membranes and wound healing.

SOURCE	Alpan et al. 2020[18]	Arabacı et al. 2017[3]	Al-Hamed et al. 2016[1]
Patients + Age	40 pt. (Divided 1:1 ratio)	26 pt. (17 males and 9 females) 29-46 years, with mean age +-36.49 (+-7.03 years with chronic periodontitis.	47 (13 M, 34 F), mean age 25.24±7.04
Groups	PRF group and control group	OFD AND OFD+ PRF	PRF +Control
Baseline	30 days	9 months	1 week
PRF prep.	20 ml of blood samples, free of anticoagulant, centrifuged at 2800 rpm for 12 mins	20 ml, centrifuged at 2800rpm for 12 mins	5ml, without A.C, centrifuged at 3000 rpm for 10 mins
Evaluated parameters	EHI score	GML (gingival marginal level)	Mean soft tissue healing
Implants placed	none	none	none
complications	none	none	Pus, swelling, erythema, post-operative pain

3.5.2 Measured effects

The results are summarized in (**Table 13**). As soft tissue healing is in question when used with PRF, one result found by Al-Hamed et al. 2016[1] it was observed that between the two groups (PRF and control group) there was no significance difference. The EHI (early healing index) don't show significant differences between the groups. As for the GML (gingival marginal level) in the PRF group decreases the chances of getting gingival recessions when comparing to the OFD group.

Table 13. Evaluated parameters of PRF membranes on wound healing.

Author	Group	Parameter	P-value
Al-Hamed et al. 2016[1]	PRF VS. NON PRF	Mean soft tissue healing score: PRF group Mean soft tissue healing score= 4.52 (0.71) Non PRF group Mean soft tissue healing score=4.20(0.95)	0.187
Alpan et al. 2020[18]	PRF VS. NON PRF	EHI PRF(+) 1.75±0.85 PRF(-) 2.37±0.68	<0.05
Arabacı et al. 2017[3]	OFD VS. OFD+PRF	GML (mm) Baseline 9 months OFD: 1.37 – 0.26 (Baseline) 1.76 – 0.44(9 months) OFD+PRF 1.30 – 0.29 (Baseline) 1.19 – 0.28 (9 months)	(P = 0.04).

4. Discussion

In the recent years, there is an increase in the use of Platelet rich Fibrin membranes (PRF) in dentistry. The aim of this study is to evaluate the potential benefits of using PRF membranes.

This study shows that PRF membranes are useful in treating gingival recessions, in aiding the soft and hard tissues of the oral cavity, aim in the implant stability and wound healing. For the different issues in question that could occur in the dental treatment, PRF had demonstrated with positive results. Each matter was studied separately in this study to see how PRF could have an effect.

4.1 Basis for the effect of PRF

The use of PRF has a change in the hard and soft tissue regeneration without or with slight signs of inflammation at the wound site. Which in turn aids in haemostasis and increases the positive quality of wound healing. It contains multiple growth factors that improve cellular functions in tissue healing. The platelet growth factor has several biological activities that promote and modulate cell proliferation and regeneration. It increases proliferation of connective tissue progenitors. It contains growth factors such as transforming growth factors (TGF-B), platelet derived growth factor (PDGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF) and insulin like growth factor. All of these mentioned growth factors are important factors for optimal healing[23].

In the following, the influence of PRF membranes on hard and soft tissue as well as implant stability will be considered in more detail.

4.2 How do PRF membranes influence soft tissue healing?

As the effect of PRF membranes performance with regarding to soft tissue was being searched, the KTW, CAL, PD, RECESSION HEIGHT-WIDTH, GT values were used as parameters. In studies it was found that when PRF membranes was applied, there was an increase over time in the KTW values. At the various articles studies, I found that PRF membranes improved soft tissue healing. The improvement was not very significant there were slight increases that proved improvement for the different parameters that were looked at. The results for the different parameters were somewhat similar, however the PRF membranes results were being directly compared to other treatment modalities and PRF membranes always showed a more positive result, again the changes in the results also between the other treatments were not significant. Both treatments showed positive results, but when PRF membranes were used the results were always slightly better[11,29,22].

4.3 Do PRF membranes improve implant stability?

When the effect of PRF membranes on implant stability was being searched, the ISQ and insertion torque values were used as parameters.

In all of the studies there was an increase in the ISQ values when PRF membranes were used. The values are not very significant however in each study the use of PRF membranes ended with an increase.

When the insertion torque values were studied it was observed that when PRF membranes were applied the results were better compared to without the use of PRF membranes, however the results were not significant. Another parameter that was studied was the ISQ; it cannot be compared to the insertion torque since it is a separate parameter. In the ISQ values between the groups that were compared that is, the group with PRF membranes and without PRF membranes, both of the groups showed positive results, it was seen that the PRF membranes group had better results, but again the results between the groups were not significant either.

4.4 What is the effect of PRF membranes on hard tissue?

When the effect of PRF membranes performance with regarding hard tissues was searched the measured parameters were alveolar crest height, mean bone density and radiographic bone width.

The radiographic bone fill for the PRF group was significantly higher than for the non PRF group. As for the other parameters, the alveolar crest height and mean bone density, the results again showed more positive results for the groups that involved PRF membranes, when compared to the non PRF group, but the results were not statistically significant.

4.5 What is the effect of PRF membranes on wound healing?

When the effect of PRF membranes performance with regarding wound healing was searched the measured parameters were EHI, GML and mean soft tissue healing. In all of the studies the results had positive values when PRF membranes were used, although they were not statistically significant.

The factors that influenced the results could be because in each study the speed and time of blood centrifuging was different. In each study the speed and time of blood centrifuging was different, ranging from 2000 to 3000 rpm, and from 10 to 12 minutes centrifugation time. A study by Miron et al[20]. experimented the effect of time between blood draw and centrifugation and the study's findings suggested that clinicians has up to 60 to 90 seconds to draw all the PRF tubes or else the PRF membrane will display in a reduction in size[20].

Also the age of the patients and gender division varied in the studies that could have influenced the results. It was found by the same study that size of outcomes of PRF membranes was significantly larger in females at all investigated time points during the study. It also found in the same article that when age and PRF membranes were studied, it was observed that older patients (male and female) showed larger PRF membranes.

5. Recommendations and Limitations

There are limitations to this study since the results were not significant in the use of PRF membranes and further clinical and histological studies are needed to support the results.

6. Conclusion

In conclusion, the combination use of PRF membranes with regenerative therapy presented in the researched articles had positive outcomes for gingival recession, periodontal regeneration, implant stability, hard tissue coverage and wound healing.

7. Conflicts of Interest

The authors have declares that there are no conflict of interest.

8. List f Abbreviations

Abbreviation	Full Name of Abbreviation
PRF	Platelet Rich Fibrin
CAL	Clinical Attachement Level
KTW	Keratinized tissue width
PD	Pocket Depth
GT	Gingival Thickness
RBF	Radiographic Bone Fill
ISQ	Implant Stability Quotient
EHI	Early Healing Index
GML	Gingival Marginal Level
GCF	Gingival Crevicular Fluid
VRD	Vertical Gingival Recession Depth
CTG	Control Group
CAF	Coronally Advanced Flap
MCAF	Modified Coronally Advanced Flap
SCTG	Subepithelial Connective Tissue Graft
OFD	Open Flap Dbridement

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