



A STUDY TO ASSESS THE ROLE OF PLATELET RICH PLASMA AUGMENTATION IN RADIOLOGICAL AND CLINICAL OUTCOME OF ARTHROSCOPIC ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN A TERTIARY CARE CENTRE, BENGALURU

Orthopaedics

Dr Venu R

Dr Ramesh
Krishna K

Dr. Dayanand M

Dr. Kiran

Dr. Lakshmi

Narayana Reddy *Corresponding Author
G*

ABSTRACT

Background: The challenge of anterior cruciate ligament reconstruction is to achieve secure graft attachment between the tendon and bone to allow early range of motion and activity. To enhance Tendon-to-bone healing strategies like Platelet Rich Plasma a form of biological augmentation technique is gaining the importance. Hence this study was done to assess the effect of PRP in enhancing bone to tendon integration, ligamentization and in early rehabilitation of patients. **Materials and Methods:** In this prospective comparative study of 40 patients diagnosed with acute and sub acute ACL tear in the department of Orthopaedics, at Victoria hospital Bengaluru were included. These patients were randomly divided in to 2 Groups, Group A (Test Group) 20 patients were injected with PRP into the graft and tibial tunnel and Group B (Control Group) 20 patients were operated without giving PRP. Patients were followed up and the outcome was assessed both clinically by IKDC and Lysholm knee scoring system and radiologically using MRI. **Results:** Isointense grafts were found in 60% in both groups, Hyper intense grafts were found in 30% and 40% in group A & B respectively and 5% grafts in group A showed Hypo intense signals(P value= 0.319). Synovial fluid at the interface was positive, 30% in group A and 35% in group B(P value=0.736). 90% of the patients in group A and 85% of the patients in group B showed Adequate characterization and good integration of the graft (P value= 0.549). There was no significant difference between the 2 groups in IKDC and Lysholm knee score.

KEYWORDS

Anterior cruciate ligament, Platelet rich plasma, MRI, Lysholm knee scoring system, IKDC scale, tendon to bone healing, synovial fluid interface.

INTRODUCTION

ACL is the primary stabilizer of knee joint limiting anterior tibial translation and internal rotation. Knee joint is one of the most commonly injured joint and most commonly injured ligament in knee joint is ACL. Injury to ACL results in pain, joint effusion, decrease in joint function and instability.

Arthroscopic reconstruction of ACL is the gold standard treatment as Open reconstruction of ACL has many drawbacks like increased post-operative pain, joint stiffness and prolonged rehabilitation phase hence not practised now a days.

Due to advancements made in soft tissue graft fixation techniques and increased incidence of anterior knee pain with bone patellar tendon bone graft, the hamstring graft is increasingly used now in arthroscopic reconstruction of the ACL.² ACL reconstruction is not a "100%-success" procedure as many patients fail to regain their previous level of activity and many factors could influence the clinical outcome.² To enhance Tendon-to-bone healing, to reduce the failure rate and accelerate recovery, many strategies are used.³ Among these biological augmentation is the most exploited strategies in particular the application of PRP.

PRP is produced from centrifugation of peripheral blood, a process that concentrates platelets within autologous plasma. This process of PRP preparation is fundamental n controlling the contents as it influences its therapeutic potential.

Platelets contain alpha granules that store and release a variety of growth factors such as cytokines and chemokines as well as other proteins including IGF-1, TGF-beta and VEGF that may augment the healing environment and also provide added benefit of promoting post surgical hemostasis as well as contributes to a better integration of the graft within bone tunnels thus avoiding their enlargement and failure over time.

Hence this study was done to assess the effect of PRP in enhancing bone to tendon integration and Ligamentization of the graft in Arthroscopic ACL reconstruction using hamstring grafts and the effect

of PRP in early rehabilitation and early return to normal activities following Arthroscopic ACL reconstruction.

MATERIALS AND METHODS

In this prospective comparative study, patients of age ≥ 18 years and ≤ 50 years of either sex who were diagnosed with acute and sub acute complete ACL tear on MRI and underwent Hamstring Quadruple graft for the same from November 2017 – October 2019 in the department of Orthopaedics BMC, Bengaluru were included.

The patients willing to participate in the study were assigned in to Test Group and Control Group by concealment method of randomization, 20 patients in Group A (Test group) and 20 patients in Group B (Control Group).

Group A 20 patients were injected with 6 ml of PRP (Prepared by double spinning method), into the graft and tibial tunnel at the time of Arthroscopic ACL reconstruction using quadruple hamstring graft and Group B of 20 patients were operated without giving PRP. Diagnostic arthroscopy was done before harvesting the graft. Patients were followed up at 6 weeks, 3 months and 6 months.

Same rehabilitation protocol was followed in both groups. At 6 months follow up MRI was taken to assess the graft status and functional outcome was assessed by Lysholm knee scoring system and IKDC score. (The IKDC knee score and Lysholm knee score forms are attached as annexure I and II respectively). The imaging analysis was performed in a blind protocol by the same radiologist.

Evaluated Parameters with MRI Use in ACL-Reconstructed Patients With and Without APC: Hamstring Graft Characterization Criteria according to Figueroa et al.⁷

Score (Points) Integration: Synovial fluid at tunnel-graft interface (femoral or tibial) Positive 1 Negative 2 Ligamentization: Graft signal pattern ($>50\%$) Hypointense 31 isointense 2 Hyperintense 1 Characterization of graft Poor 2 Adequate 3-5

Statistical Analysis

SPSS (Statistical Package For Social Sciences) version 20 was used to perform the statistical analysis. Descriptive statistics was calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Chi square, Un-paired t test and Paired t test were used. The level of significance was set at 5%.

RESULTS

Majority of the patients in both groups of the study belonged to the age group of 19-28yrs (40%) & 29- 38yrs(50%), with 10% between 39-48yrs with no significant difference between the two groups

Majority of the patients in both groups of the study were males with only 2 female patients in PRP group and 1 patient in NON PRP group

The most common mode of injury found was Road Traffic Accidents in both groups with average of 62.5%, followed by sports (average 32.5%) with 1 self-fall in PRP group and 1 fall from height in NON PRP group.

Patients in PRP group presented at an average of 3.7 weeks after the injury and in NON PRP group at average of 3.3 weeks. No significant difference between the 2 Groups was noted.

The Mean final follow up period was 6.2 months in PRP group and 6.25 months in NON PRP group with no significant difference between the 2 groups.

Around 77.5% of the MRIs were done at 6 months and 22.5% of MRIs were done at 7 months after the surgery with no significant difference between the 2 groups.

Table 1synovial Fluid At Tunnel Graft Interface In Mri

Synovial Fluid At Tunnel - Graft Interface	PRP	Non PRP	Total	Chi square test	p value
NEGATIVE	14	13	27	0.114	0.736
	70.0%	65.0%	67.5%		
POSITIVE	6	7	13		
	30.0%	35.0%	32.5%		
TOTAL	20	20	40		
	100.0%	100.0%	100.0%		

Around 67.5% of the patients showed no evidence of fluid in the Tunnel- Graft interface in the MRI and 32.5% showed evidence of fluid in the Tunnel- Graft interface in the MRI with no significant difference between the 2 Groups.

Table 2 Signal Intensity Of The Graft

Signal Intensity Of The Graft	PRP	Non PRP	Total	Chi square test	p value
HYPERINTENSE	6	8	14	2.286	0.319
	30.0%	40.0%	35.0%		
HYPOINTENSE	2	0	2		
	10.0%	0.0%	5.0%		
ISOINTENSE	12	12	24	60.0%	60.0%
	60.0%	60.0%	60.0%		
TOTAL	20	20	40		
	100.0%	100.0%	100.0%		

Around 60% of the patients showed Isointense Grafts, 35% of patients showed Hyper intense Grafts with 2 Grafts showing Hypo intensity only in PRP group with no significant difference between the 2 groups.

Table 3 Scoring Of The Graft

Scoring Of Graft	PRP	Non PRP	Total	Chi square test	p value
2	2	3	5	2.259	0.52
	10.0%	15.0%	12.5%		
3	8	9	17		
	40.0%	45.0%	42.5%		
4	8	8	16	40.0%	40.0%
	40.0%	40.0%	40.0%		
5	2	0	2	10.0%	5.0%
	10.0%	0.0%	5.0%		
TOTAL	20	20	40		
	100.0%	100.0%	100.0%		

Majority of the grafts (average 82.5%) were scored between 3-4,

12.5% of grafts were scored 2 and 2 grafts in PRP Group were scored 5 with no significant difference between the 2 Groups.

Table 4 Integration Of The Graft

Integration Of Graft	PRP	Non PRP	Total	Chi square test	p value
GOOD	18	17	35	0.229	0.633
	90.0%	85.0%	87.5%		
POOR	2	3	5		
	10.0%	15.0%	12.5%		
TOTAL	20	20	40		
	100.0%	100.0%	100.0%		

Around 87.5% of the patients showed Good Integration the Graft and 12.5% of the patients showed poor Integration the Graft with no significant difference between the 2 Groups.

Table 5 Subjective Ikdc Score

IKDC score	PRP		NON PRP			
	Mean	Std. Dev	Mean	Std. Dev	Mean diff	p value#
Pre op	40.15	3.514	39.55	3.052	0.6	0.568
Final follow up	93.85	2.777	92.65	2.084	1.2	0.131
Mean difference	-53.7		-53.1			
p value*	0.001		0.001			

There was an Improvement of IKDC score from 40.15(SD =3.515) in pre op period to 93.85(SD=2.77) with p value= 0.001 at final follow-up in PRP Group and there was improvement from 39.55(SD= 3.052) in pre op period to 92.65 (SD= 2.084) with p value= 0.001 at final follow up in NON PRP Group with no significant difference between the 2 Groups.

Table 6 Lysholm Knee Score At Final Follow Up

Lysholm Knee Score At Final Follow Up	N	Mean	Std. Dev	Mean diff	p value
PRP	20	93.35	2.758	1.600	0.05
NON PRP	20	91.75	2.221		

The PRP Group showed a score of 93.35 (SD= 2.75) and NON PRP Group showed a score of 91.75(SD= 2.221) with no significant difference between the 2 Groups(P value=0.05).

One patient in PRP group showed superficial infection and 2 patients in NON PRP group showed superficial infection.

Around 47.5% of patients returned to pre injury activity level at 6 months post- surgery and 52.5% patients at 7 months (P value= 0.342). In PRP group 55% of patients returned to Pre injury activity level at 6 months post-surgery and 45% at 7 months post-surgery, statistically not significant. In NON PRP group 40 % of patients returned to Pre injury activity level at 6 months post-surgery and 60% at 7 months post-surgery which was statistically not significant between the 2 groups.

DISCUSSION

One of the challenges of anterior cruciate ligament (ACL) reconstruction is to achieve secure graft attachment between the tendon and bone to allow early range of motion and activity. The main healing process leading to bone integration occurs in the bone tunnel and depends on the type of graft and fixation mechanism. Tendon-to-bone healing occurs slowly, which can be a problem to early return to normal activities.

A study by Anderson et al.⁶ indicated that the presence of TGF-beta 1, TGF- beta2, TGF- beta 3, and TGF-1 growth factors directly influences the graft by improving the scarring rate and increasing the tensile force resistance by 65%. In another experimental study, Weiler et al.⁷ indicate that the application of autologous PDGFs applied to the graft during surgery was capable of changing its natural evolution, improving tensile strength and resistance, increasing the maturation rate, and improving collagen quality.

The findings of the our study were that the addition of Platelet rich plasma into Quadruple Hamstring graft and bone tunnels during ACL reconstruction procedure did not lead to an improved knee MRI appearance of graft integration and maturation and did not helps in early return to pre injury activity level.

The possibility to accelerate and improve the integration process and therefore also knee stability is highly desirable nowadays, it is extensively recognized that platelet-derived GFs play a central role in tissue's healing and regeneration processes.⁸

Ventura et al.⁹ performed ACL reconstruction with (n = 10) or without (n = 10) a platelet concentrate, which was placed in both tunnels directly with autologous thrombin: at 6 months there were no significant differences concerning the clinical examination. However, the CT scan highlighted a significant improvement in the ACL density in the platelet-treated group with respect to the untreated group which showed a more heterogeneous nature.

Orrego et al.¹⁰ found 100 % grafts with intensity similar to native posterior cruciate ligament in the platelet group but only 78 % in the control group at 6 months. Figueroa et al.⁵ evaluated the grafts at 6 months postoperatively and found 63.2 % hypo intense grafts in the platelet group but only 42.1 % hypo intense grafts in the control group. The difference was not statistically significant but the trend suggested a better Ligamentization of the graft in the treated group.

Nin et al.¹¹ confirmed these findings at 24 months documenting a 21 % lower intensity on proton density-weighted magnetic resonance images and 23 % lower intensity on T2-weighted magnetic resonance images in the platelet group. Sánchez et al.¹² assessed ACL grafts in terms of gross morphology and histologically. Arthroscopic gross evaluation showed excellent ratings for 57.1 % of platelet-treated ACL grafts, but only 33.3 % in the control group. Whereas these articles almost consistently show an improvement in the graft Ligamentization process, less documented and more controversial is the role of PRP in another key aspect for the success of ACL reconstruction: the integration of the graft.

Orrego et al.¹⁰ showed no significant effect of the platelet concentrate on the osteoligamentous interface or tunnel widening evolution at 6 months. Vadala' et al.¹³ evaluated the efficacy of PRP in reducing femoral and tibial tunnel enlargement at 10–16 months but failed to prove any benefit from this augmentation strategy, which according to Figueroa et al.⁷¹ could even lead to a lower integration, as suggested by the finding of a greater number of cases positive for the presence of synovial fluid at the tunnel-graft interface. Oppositely, a study of Vogrin et al.¹⁴ focused on the MRI analysis of graft vascularization in PRP-treated and control groups. No differences of the intra-articular portion of ACL grafts was found at 12 weeks, but the revascularization was enhanced in the interface zone between the graft and the bone tibial tunnel, and the authors showed that hamstring grafts augmented by platelet-derived GFs had a significantly better anteroposterior knee stability at 6 months.

In this study MRI evaluation was done with respect to graft signal (>50% predominance) which was the first parameter studied showed Isointense grafts in 60% of cases in PRP group and 60% in NON PRP group, Hyper intense grafts were found in 30% of cases in PRP group and 40% in NON PRP group and 5% grafts in PRP group showed Hypo intense signals which was statistically not significant (P value=0.319). Synovial fluid at the interface: negative, 70% in PRP group and 65% in NON PRP group, and positive, 30% in PRP group and 35% in NON PRP group which was statistically not significant (P value=.736)

90% of the patients in PRP group and 85% of the patients in NON PRP group showed Adequate characterization and good integration of the graft, 10% in PRP group and 15% in NON PRP group showed poor characterization and poor integration of the Graft which was statistically not significant (P value=.549).

There was no significant difference between the 2 groups in functional outcome as assessed by IKDC and Lysholm knee score. In PRP group 55% of patients returned to Pre injury activity level at 6 months post-surgery statistically not significant and 45% at 7 months post-surgery. In NON PRP group 40 % of patients returned to Pre injury activity level at 6 months post-surgery and 60% at 7 months post-surgery which was statistically not significant between the 2 groups.

Limitations

- Commercially available PRP preparation system was not used to prepare PRP.
- The PRP was injected into the graft and tibial tunnel without activation and in liquid form which could have resulted in wastage of some amount of PRP while inserting the graft ie. application

modality adopted in the present study may not be the optimal.

- There is the lack of a randomization; however, two consecutive series of patients were compared, the treatment was not a choice of the surgeon in each case, and the outcome was blindly evaluated.

Ethical Requirements: Institutional ethical Committee

Conflicts Of Interests: Nil

REFERENCES

- David Simon, Randy Mascarenhas, Bryan M. Saltzman, Meaghan Rollins, Bernard R. Bach Jr., and Peter MacDonald, "The Relationship between Anterior Cruciate Ligament Injury and Osteoarthritis of the Knee," *Advances in Orthopedics*, vol. 2015, Article ID 928301, 11 pages, 2015. doi:10.1155/2015/928301.
- Signorelli C, Bonanzinga T, Lopomo N et al. "Do preoperative knee laxity values influence post-operative ones after anterior cruciate ligament reconstruction?" *Scandinavian Journal of Medicine and Science in Sports*. 2013; vol. 23, no. 4, pp. e219–e224
- Yuan T, Zhang C Q, and Wang J H. "Augmenting tendon and ligament repair with platelet-rich plasma (PRP)" *Muscle, Ligaments and Tendons Journal*. 2013; vol. 3, no. 3, pp. 139–149.
- Yathiraj BR, Sujit Kadrekar, Dinsha Pardawla, Kulkarni GS eds."ACL deficient knee". *Textbook of Orthopaedics and trauma* .3rd edition. vol 2 .India: Jaypee P-1319 - 1325.
- Figueroa D, Melean P, Calvo R, et al. Magnetic resonance imaging evaluation of the integration and maturation of semitendinosus-gracilis graft in anterior cruciate ligament reconstruction using autologous platelet concentrate. *Arthroscopy* 2010;26:1318-1325.
- Anderson K, Seneviratne AM, Izawa K, Atkinson BL, Potter HG, Rodeo SA. Augmentation of tendon healing in an intraarticular bone tunnel with use of a bone growth factor. *Am J Sports Med* 2001;29:689-698
- Weiler A, Foster C, Hunt P, et al. The influence of locally applied platelet-derived growth factor-BB on free tendon graft remodeling after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2004;32:881–891.
- Tschon M, Fini M, Giardino R, Filardo G, Dallari D, Torricelli P, Martini L, Giavaresi G, Kon E, Maltarello MC, Nicolini A, Carpi A (2011) Lights and shadows concerning platelet products for musculoskeletal regeneration. *Front Biosci (Elite Ed)* 3:96–107
- Ventura A, Terzaghi C, Bordo E, Verdoia C, Gallazi M, Falloni S. Use of growth factors in ACL surgery: Preliminary study. *J Orthop Traumatol* 2005;6:76–79.
- Orrego M, Larraín C, Rosales J, et al. Effects of platelet concentrate and a bone plug on the healing of hamstring tendons in a bone tunnel. *Arthroscopy* 2008;24: 1373-1380.
- Nin JR, Gasque GM, Azcárate AV, Beola JD, Gonzalez MH. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? *Arthroscopy* 2009;25:1206-1213.
- Sánchez M, Anitua E, Azofra J, Prado R, Muruzabal F, Andia I. Ligamentization of tendon grafts treated with an endogenous preparation rich in growth factors: Gross morphology and histology. *Arthroscopy* 2010;26:470-480.
- Vadala A, Iorio R, De Carli A, et al. Platelet-rich plasma: Does it help reduce tunnel widening after ACL reconstruction? *Knee Surg Sports Traumatol Arthrosc* 2013;21:824-829.
- Vogrin M, Rupprecht M, Dinevski D, et al. Effects of a platelet gel on early graft revascularization after anterior cruciate ligament reconstruction: A prospective, randomized, double-blind, clinical trial. *Eur Surg Res* 2010;45: 77-85.