Egypt, J. Plast. Reconstr. Surg., Vol. 47, No. 1, January: 7-12, 2023

Enhancement of Gliding after Repair of both Flexor Tendons Zone II by Injection of Activated Platelet-Rich Plasma (PRP)

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ABSTRACT

Background: Flexor tendon injury is a common kind of trauma and often challenging injury presented to hand surgeons.

Aim of Study: In this study, we aim to test the influence of activated PRP injection on the functional outcomes after repair of both flexor tendons zone II, especially the decline in gliding resistance through avoidance of adhesion formation.

Patients and Methods: 40 patients with injury of both Flexor Digitorum Superficialis (FDS) and Flexor Digitorum Profundus (FDP) tendons zone II were included in this study. Random distribution of the patients into two groups was done, according to whether activated PRP is injected or not. Group I: In which 20 patients had activated PRP injection in the tendon at the site of repair and Group II: It is control group, in which 20 patients had placebo saline injection. Both groups were evaluated at 8 weeks, 6 and 12 months postoperatively as regards: The Range of Motion (ROM), Grip Strength and Finger Pinch measurements.

Results: Group I showed a better Range of Motion, Grip Strength and Finger Pinch strength of the injured side in comparison to Group II.

Conclusion: Activated PRP injection improved the functional outcomes after repair of both FDS and FDP tendons zone II.

Key Words: *Platelet -Rich Plasma (PRP) – Flexor Digitorum Superficialis (FDS) – Flexor Digitorum Profundus (FDP) – Gliding – Range of Motion (ROM).*

Ethical Committee Approval: The study was approved by the Faculty of Medicine, Ain Shams Faculty of Medicine, Research Ethics Committee.

Conflicts of Interest: There are no conflicts of interest.

INTRODUCTION

Healing of the tendons usually goes through 3 overlapping phases: Inflammatory, proliferative and remodeling. Regulation of these phases was controlled by many growth factors that are connected through complex cellular signaling cascades. These exert anabolic effects, increase chemotaxis of bone marrow cells, and improve histologic organization **[1]**.

PRP is a biological product that is defined as a portion of plasma fraction of a patient's own blood with high platelets and growth factors concentration. Activated PRP brings many types of growth factors (GFs) to the injury sites, by degranulation of platelets to release growth factors from α ' granules. These GFs include Platelet-Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Transforming Growth Factor-beta (TGF-β), Epidermal Growth Factor (EGF), Fibroblastic Growth Factor (FGF), Insulin-like Growth Factor-I (IGF-I) and Hepatocyte Growth Factor (HGF) **[2]**.

Throughout the previous two decades, PRP had emerged to be used as a biological treatment to regenerate and repair damaged or non-functional tissues in various medical conditions **[3]**. Many studies had supported the use of activated PRP in tendon injuries treatment as it might enhance type I collage expression **[4]**, promote angiogenesis **[5]**, and show greater maturation in tendon callus formation **[6]**.

Any affection of repaired tendon gliding due to excess surgical knots or scar tissue formation was found to have an undesirable effect on the postoperative function of the patients. Repair of flexor tendons zone II represents a surgical competition due to the complex anatomy in this area **[7]**. Poor outcomes and a higher risk of adhesions usually encountered, due to fibro-osseous tunnel tightness especially if both tendons were injured and poor vascular supply in this zone that's why it was named no man's land **[8]**.

Various agents as Hyaluronic acid **[9]**, lubricin **[10]**, 5-fluorouracil **[11]** and oral ibuprofen **[12]** have been tested to modify adhesion formation around

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tendon repair sites and they showed improved tendon gliding and substantial reductions in synovial thickening.

Contrary to many studies concerning tendon injuries of the hand, no one has discussed the consequences of activated PRP injection on the functional outcomes after both tendons repair zone II, especially the decline in gliding resistance through avoidance of adhesion formation.

PATIENTS AND METHODS

A comparative prospective controlled randomized study was conducted in the Plastic, Burns and Maxillofacial Surgery Department at Ain-Shams University Hospitals. 40 patients were involved, 4 females and 36 males, age ranging from 15-45 years old and an average 30 years old, with acute isolated sharp injury of both FDS and FDP tendons zone II, in a solitary digit of the hand, during a period from November 2018 to February 2020.

Exclusion criteria included: Age less than 15 or more than 45 years old, crush type of injuries, multiple digits, previous injury, or surgery, associated fractures, open joint capsule, injury of neurovascular bundles, skin loss and polytraumatized patients with bad general condition. Before participation in this study, written informed consent was obtained from all patients. This study was approved by the Ethical Committee of the Faculty of Medicine, Ain Shams University.

A venous blood sample of (30cc) was drawn from all patients involved in the study, then the blood sample was dispensed into tubes containing citrate dextrose before doing the repair, then simple randomization of patients was done to be listed in one of the comparison groups; the patients were equally distributed into two groups. Group I; 20 patients had activated PRP injected to the tendon at the site of repair while in Group II; control group, in which 20 patients had placebo saline injected. The blood samples from the control group patients were discarded, while the other samples were used to prepare activated PRP to make the patient blinded to the injection material in the study.

Preparation of PRP was described by Sonnleitner et al., **[13]**; first centrifugation of blood sample (soft spin at 3600 rpm for 3 minutes) resulted in blood separation into three layers; an acellular plasma layer known as platelet-poor plasma (PPP) which is the uppermost layer, and it represents 40% of entire volume. A middle PRP layer known as the "buffy coat" and it represents 5% of the entire volume. At the end a bottom layer known as RBC layer, and it represents 55% of entire volume. A second centrifugation of the tube was commenced (hard spin at 2400 rpm for 15 minutes) resulting in settlement of the platelets at the bottom of the tube with little RBC. Bovine thrombin was mixed with PRP in the following amount of every 1cc PRP 0.2ml should be added and 10% (0.1ml) of calcium chloride during the application time.

If the approach to the tendon was insufficient, the original wound was extended into the sheath. All patients of both groups underwent repair of both tendons with the core suture of modified Kessler using 4-0 prolene suture materials and 6-0 prolene sutures for the running epitendinous suture.

Then, a volume of activated PRP was injected, this volume ranges from 50µL-80µL. In group I, single PRP injection was done intraoperatively using a 22-gauge needle. This small needle should be used to access the lesion without causing injury of a relatively healthy tendon tissue. It was used to inject a volume of activated PRP enough to fill the defect, completely covering the suture line and extending 1cm proximally and distally, without creating potential injury to the fibers or any separation. Following the injection, excursion of the tendon was passively tested to make sure that the pulley system is working with no triggering within.

In group II, injection of saline as a placebo was done in the repair site and with the same volume as in group I. Postoperative antibiotic was used for 3-5 days.

To ensure blindness of the study all patients were sent to the physiotherapist who subjected the patients to a rehabilitation program of 8 weeks following the repair, then evaluation of the results was done.

The rehabilitation program was divided into three phases: Phase 1: In the first 3 weeks, early active rehabilitation protocol was used; a place and hold flexion along with active extension within a dorsal blocking sprint was started. So, contracture of the interphalangeal joints was avoided. Meanwhile, passive flexion and extension exercises of the interphalangeal joints were meticulously overseen by the physiotherapist. Phase 2: In the 4^{th} and 5^{th} weeks, the splint was removed, and the place-and-hold flexion and active extension exercises started without resistance. Phase 3: In the 6^{th} to 8^{th} weeks, active flexion of the finger with applied resistance started.

Patients' results from both groups were evaluated at the end of the physiotherapy program 8 weeks and then after 6 and 12 months postoperatively as regards:

1. "Range Of Motion" of the operated fingers MP and IP joints following assessment of Buck-Gramcko et al., **[14]**, as shown in Table (1), by using a 180-degree short arm goniometer.
2- Grip and Pinch Strength Measurements; according to the "American Society of hand therapist". The patient's suggested position to get accurate grip strength measurement was with the adducted and neutrally rotated shoulder, along with flexed elbow at 90 degrees, neutral position of the forearm, dorsiflexion of the wrist at 0-30 degrees and 0-15 degrees ulnar deviation **[15]**.

Table (1): Shows Buck-Gramcko II evaluation criteria for flexor tendon repair.

Buck-Gramcko II criteria	Units	Points
Free nail palm crease distance:	0.0-0.5 cm	6
- (Measured from the free nail	0.6-1.5 cm	5
margin to the distal palmer crease)	1.6-2.5 cm	4
	2.6-4.0 cm	3
	4.1-6.0 cm	2
	>6.0 cm	1
Total extension deficit:	20º-30º	3
- (MPJ+PIP+DIP)	31º-50º	2
	51º-70º	1
	>70º	0
Modified total active motion:	>400	8
- (MPJ+2XPIP+3XDIP)	320	6
	280	4
	240	2
	240	0
Classification:		
- Excellent		16-17
- Very good		14-15
- Good		11-13
- Fair		7-9
- Poor		0-9

- Metacarpophalangeal Joint (MPJ), Proximal Interphalangeal Joint (PIP), and distal interphalangeal joint (DIP).

Measurement of "Grip Strength" was done by sphygmomanometer. The cuff of blood pressure is rolled to a diameter of 5cm and inflated to 50mm Hg. The cuff is then pressed and the fluctuation in millimeters over 50mmHg is recorded as the power of grip. Then "Finger Pinch strength" was measured by pinch-meter.

All the resulting measurements obtained from all patients were collected, analyzed, and statistically evaluated. Then all the collected data was interpreted to detect which group had favorable results.

RESULTS

All patients had been followed up for an average period of 6 months to one year. Details of patients and results are presented as shown in Table (2).

Table (2): Shows information data of the patients in the research groups.

Characteristic	Group I	Group II	*p*-value
Number of patients	20	20	
Mean age ± SD	33.2	34.1	0.632 (NS)
Sex (M/F)	17/3	19/1	0.745 (NS)
Injured hand (R/L)	9/11	7/13	0.213 (NS)

Male to Female ratio (M/F).
NS: Non-significant difference.

As regards mode of trauma, Knife wounds represents 65% and glass injuries represent 35% of tendon injuries. It was found that no significant statistical difference between the two studied groups concerning age, sex, laterality and causative agents.

Concerning the injected volume in all patients, it was subjective, ranged from 50µL-80 µL. For the FDS tendon, the volume injected was 50µL in 13 patients, 55µL in 5 patients and 60µL in 2 patients. On the other hand, for the FDP tendon 70µL was injected in 15 patients and 80µL in 5 patients.

Based on Buck-Gramcko II score criteria, the overall score of ROM for flexor tendons of the fingers after repair was 11-17 in group I and 8-16 in group II. In group I, the range of movement of twelve (60%) of the digits was rated excellent, four (20%) was very good, four (20%) was good and none was rated fair or poor. In group II, the range of movement of nine (45%) of the digits was rated excellent, two (10%) was very good, six (30%) was good, 3 (15%) was fair and none was rated poor according to Buck-Gramcko II criteria as shown in Table (3) and Fig. (1).

Table (3): Shows the range of movement of flexor tendons after repair in each group based on Buck Gramcko II.

Range of Excellent movement	Group I	Group II	*p*-value
Excellent	12	9	0.012*
Very good	4	2	0.229
Good	4	6	0.290
Fair	0	3	–
Poor	0	0	–

* Significant statistical difference.

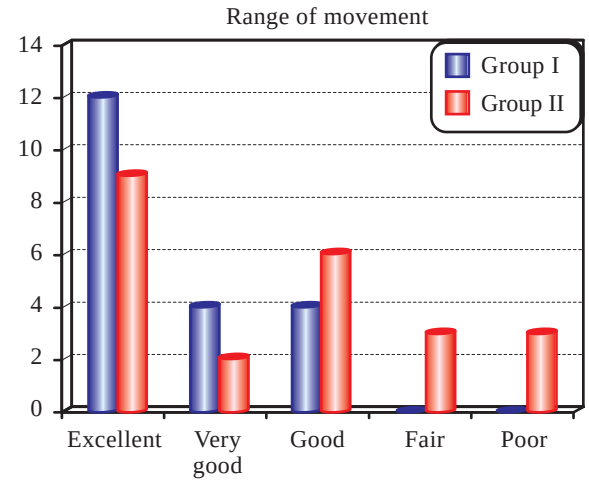

Fig. (1): Range of movement of flexor tendons after repair in both groups based on Buck Gramcko II classification.

Measurements of the "Mean Grip Strength" of the injured hand in comparison to that of the non-injured hand were assessed and analyzed. It was found to be 87% in the injured hand (i.e., 13% grip strength deficit) in group I and the "Mean Finger Pinch Strength" was 86.3%. While in group II, the "Mean Grip Strength" of the injured hand was 74.5% (i.e., 25.5% grip strength deficit) and the "Mean Finger Pinch Strength" was 74.7% as shown in Table (4) and Fig. (2).

Table (4): Functional outcome results of the Mean grip strength, deficit of grip strength and finger pinch strength in both groups.

	Group I	Group II	*p*-value
Grip strength	87%	74.5%	0.0001*
Finger pinch strength	86.3%	74.7%	0.0001*
Deficit	13%	25.5%	0.0001*

* Significant statistical difference.

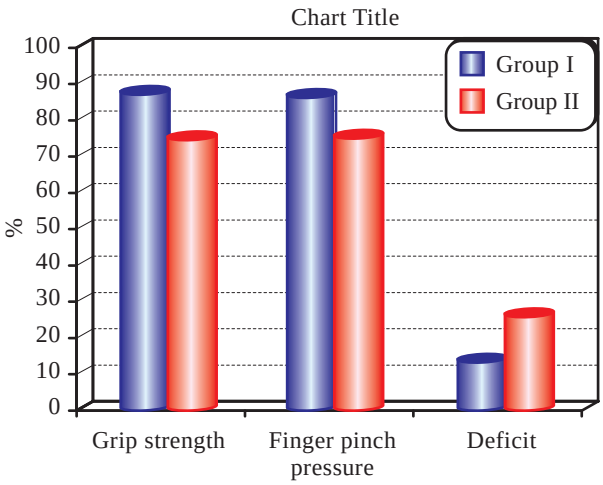

Fig. (2): Functional outcome results of the Mean grip strength, deficit of grip strength and finger pinch strength in both groups.

DISCUSSION

It was noticed that acceleration of flexor tendon healing and prevention of adhesion formation were based on early mobilization following repair of flexor tendons. However, excessively forceful early mobilization puts the repair at risk of disruption **[16]**. Therefore, enhancing the quality of repaired tendon is mandatory, which depends on the biologic adjuvants of tendon healing **[17]**.

PRP has been presented as a likely novel treatment for tendon injuries. Many laboratory studies had elaborated on the useful effects of PRP on gene expression that controls matrix-degrading enzymes and endogenous GFs. So, that it has been successfully used in maxillo-facial surgery to speed up the process of soft tissue and bone healing **[18]**. Also, PRP has been used in hand surgery for its promising role in tendon regeneration **[4,6]**.

There are several reported clinical randomized trials that tested the efficiency of PRP in enhancement of tendon healing or in the treatment of medical conditions. Schepull **[19]** proposed that PRP has no role in the healing of ruptures involving Achilles tendon. Whereas the use of PRP in patients suffering from chronic lateral epicondylitis was found to be helpful in pain reduction and significant improvement of function, surpassing the effect of corticosteroid injection as described by Peerbooms **[20]**. Also, Filardo **[21]** stated that "PRP injections have the ability to stimulate the fulfilment of a satisfactory clinical outcomes, especially in cases with chronic resistant tendinopathy".

Also, PRP treatment in a retrospective study was found to improve muscle healing injuries in humans by almost one week faster than other studied group **[22]**.

PRP treatment of tendon injuries in animal models showed reliable outcomes concerning cellular and molecular responses contrasting results from clinical trials which are still not consistent. Many variables affected the results of previous studies whether PRP associated, as composition, platelet concentration, being activated or not, number and delivery methods or patients associated, as age, type of injury and post-operative rehabilitation plan **[23]**.

In this clinical study, the influence of intralesional injection of activated PRP on flexor tendon healing and functions was assessed and compared in both groups. Also, many variables in this study were avoided by standardization of the technique used and managing the inclusion and exclusion

criteria to efficiently assess the role of PRP in enhancing the process of healing and gliding of injured flexor tendons zone II.

Injection of PRP gel is usually thought to enhance the healing process and produce better treatment consequences as it remains in place without the possibility of potential diffusion from the treated area **[7]**. Not only spreading of the platelet gel film over the suture line was done, but also intralesional injection was applied. As this ensures accurate placement of the PRP within the cut edges to fill the suture lines minimal defects, thus we can get the maximum benefits.

The proper timing for PRP treatment and the number of injections are still controversial. In the present study, the results of intra-operative, single intralesional therapy showed improved functional outcome after both flexor tendons repair zone II. This correlates well with a placebo-controlled experimental trials that proved that a single intratendinous PRP injection improved tissue properties of surgically created lesions that includes biomechanical, biochemical, and histological properties in the superficial flexor tendons of the digits of both front limbs **[24,25]**.

The volume to be injected was subjective, adjusted to the defect without creating additional damage to the tissues. This might be considered as a limitation of the present study and future studies should standardize the amount of injected volume.

In the current study, the activated form of PRP was used, as it is theoretically believed to be more effective due to the release of "Platelet-Derived Growth Factors", for example TGF-β and VEGF from alpha granules of platelets and those GFs are responsible for the valuable effects of the PRP to enhance healing **[26]**.

At the end of the rehabilitation program, based on Buck-Gramcko II criteria, the score of flexor tendons of the fingers was considerably better in group I than in group II and this validates the suggestion of de Mos et al., **[5]** in that, in vivo PRP application may enhance the repair of post-traumatic tendon injuries.

The current study showed that patients in group I had statistically improved "modified total active motion" of MCP, PIP and DIP than those of group II. This is to some extent resembles results from a randomized controlled experimental study **[27]** that was done to evaluate the possible benefits of PRP injection in zone II after repair of the flexor tendons, as it was found that the total range of motion tended to be higher in Group I, but without reaching significance.

Group I showed a better "Mean Grip Strength" of the injured hand than in Group II and this links with the results from other studies that observed significant increase in the biomechanical properties of injured tendons **[25,28,29]**.

Previously, preservation of the whole A2 and A4 pulleys should be attempted to prevent flexor tendons bowstringing; nevertheless, biomechanical studies have shown that 25% of A2 and the whole A4 may be incised with a minimal functional deficit **[30]**. In this study, more care about giving a good space for the repaired two tendons was considered on the expense of pulleys. Just leaving small parts of both pulleys to keep tendons well positioned, however we consider this a limitation of the study, and more studies are needed concerning the dynamics of pulley and tendon gliding with PRP usage.

Other limitations are the small sample size of patients recruited and the short follow-up time. Aside from these limitations, in conclusion, the present study shows that activated PRP injection improves the functional outcome after both flexor tendons repair zone II.

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