Platelet-Rich Plasma for Primary Treatment of Partial Ulnar Collateral Ligament Tears

MRI Correlation With Results

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Background: Jobe revolutionized the treatment of medial ulnar collateral ligament (MUCL) tears with his reconstruction technique. However, not all MUCL injuries require operative management; Rettig showed that 42% of MUCL injuries respond to conservative management. This was improved by Podesta, who showed that augmentation of nonoperative management with platelet-rich plasma (PRP) and magnetic resonance imaging (MRI) for detecting partial MUCL tears resulted in significantly higher success rates. Their series used a single injection of leukocyte-rich PRP. However, to our knowledge, no study has established optimal dosing and composition of PRP for augmentation of soft tissue healing. We present a series of patients with partial MUCL tears of the elbow treated with a series of 2 leukocyte-rich PRP injections, bracing, physical therapy, and a structured return-to-throwing protocol.

Hypothesis: Nonoperative management of acute or subacute partial MUCL tears of the elbow with a formal treatment protocol will allow the injured ligament to heal without surgery and will permit a rapid return to sport.

Study Design: Case series; Level of evidence, 4.

Methods: Patients with symptomatic MUCL instability and magnetic resonance arthrography demonstrating grade 2 MUCL tears at the proximal or distal aspect were treated with varus-loading elbow bracing, activity restriction, and physical therapy, supplemented by 2 injections of PRP. The injections were separated by 2 weeks. Two weeks after the second injection, a repeat examination and magnetic resonance arthrogram were obtained to evaluate the response to treatment.

Results: A total of 25 athletes (23 baseball athletes, 2 softball athletes [1 participant also danced]) underwent PRP injections and guided rehabilitation. Of these patients, 23 were diagnosed with primary grade 2 injuries of the MUCL; 22 patients with primary injuries (96%) demonstrated stability of the MUCL after treatment and returned to play at the same or higher level of competition without further intervention. Repeat MRI demonstrated reconstitution of the ligament in all patients, although 2 patients demonstrated only partial reconstitution. Patients were released to play at 6 weeks; due to vagaries of sports seasons, the mean time to return to competitive play was 82 days. Two of the 25 patients had undergone prior surgery (1 MUCL reconstruction and 1 repair). These patients remained unstable and symptomatic on examination after this treatment regimen, did not show complete reconstitution of the ligament on subsequent MRI, and required MUCL reconstruction.

Conclusion: Ouf of 23 primary injury patients who received PRP injections and nonoperative measures, 22 (96%) were able to return to play and demonstrated reconstitution of the MUCL on MRI. Two of the 3 patients for whom PRP therapy failed had undergone previous MUCL surgery. We conclude that a 2-injection regimen of leukocyte-rich PRP is a safe and effective treatment for partial MUCL tears, but it appears to be less effective in patients with previous surgery for MUCL repair or reconstruction.

Keywords: elbow; medial ulnar collateral ligament; magnetic resonance imaging; platelet-rich plasma; biologic healing enhancement

Injury to the medial ulnar collateral ligament (MUCL) of the elbow is common in overhead-throwing athletes at the high school, collegiate, and professional levels. In the late cocking and early acceleration phases of the throwing motion, up to 64 N of valgus force and 300 N of shear force is experienced across the structures of the medial elbow.[22] Repetitive valgus stress on the elbow joint can lead to insufficiency of the anterior band of the MUCL, with either an acute or insidious onset. Analysis of statistics from professional baseball players have shown statistically significant changes in earned run average (ERA), walks plus hits per innings pitched, innings thrown, and win percentage in the

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games preceding recognition and treatment of their MUCL injuries.[17]

Since Jobe et al[15] published their original paper describing MUCL reconstruction in 1986, many surgical techniques for repairing and reconstructing the MUCL have been described.[26,27] In professional baseball, an estimated one-third of pitchers have had surgical reconstruction of the MUCL.[17] Recent years have seen a dramatic increase in the number of MUCL injuries in the collegiate and high school ranks. With modern surgical treatment, up to 95% of athletes can return to play at their previous level of competition or higher with a low rate of complications, but it is a season-ending procedure requiring a prolonged period of rehabilitation.[2,3,31] Additionally, although professional pitchers who undergo MUCL reconstruction demonstrate lower ERAs, they have been shown to experience progressive decrease in pitch velocity and an average career length of only 3.9 ± 2.84 years.[7,14]

Treatment regimens that return these athletes to play reliably, quickly, and without resorting to season-ending reconstruction are a topic of ongoing interest. Rettig et al[24] provided the first large series of patients treated with nonoperative management for MUCL injuries. In their cohort, only 42% of patients returned to play at an average of 24.5 weeks of rehabilitation. However, this study did not discriminate between complete and partial disruptions of the MUCL. We can now consistently differentiate between complete and partial tears on magnetic resonance (MR) arthrogram.[20,28] Podesta et al[23] described a grading system for MUCL injuries based on magnetic resonance imaging (MRI), wherein grade 1 injuries consist of edema in and around the ligament without structural disruption, grade 2 injuries consist of partial ligamentous disruption, and grade 3 injuries are complete ligamentous disruptions.

It is thought that improved diagnosis of partial tears, which may have a higher chance of recovery with nonoperative management, may increase the success of nonoperative management for MUCL tears. In addition to improving patient selection, improving the biological characteristics of the injured site may further increase success. To that end, the use of platelet-rich plasma (PRP) has been explored. PRP is a solution rich in platelets and growth factors derived from the patient's own serum. The solution is concentrated and then injected into the site of injury to promote healing. It is easily obtained with little risk to the patient and has been studied in a variety of musculoskeletal injuries.[1,5,9,13,21,32] PRP has been shown in vitro to increase proliferation and differentiation of ligament cells, their collagen synthesis, and intracellular adhesion.[10,16,30] In a leporine model of knee medial collateral ligament injuries, platelet-derived growth factor β (a key product found in PRP) increased load to failure.[11]

Podesta et al[23] showed that a single leukocyte-rich PRP injection was a safe adjunct to nonsurgical management in partial MUCL tears, with 88% of patients returning to their prior level of competition after an average rehabilitation course of 20 weeks. In that protocol, patients were given the PRP injection after 8 weeks of nonoperative management.

Figure 1. Pretreatment magnetic resonance arthrogram showing a proximal medial ulnar collateral ligament tear.

Based on the initial work of Rettig and Podesta, we changed our practice to include a 2-injection series of leukocyte-rich PRP injections, bracing, and physical therapy. In this initial series of patients, we additionally obtained follow-up MRI to visualize the ligament after treatment and prior to return to sport. We hypothesized that partial MUCL tears treated with 2 leukocyte-rich PRP injections, MUCL offloading bracing, and whole-body physical therapy would result in return to play and reconstitution of the ligament on subsequent imaging.

METHODS

After institutional review board approval was granted, a retrospective chart review was performed for patients with MUCL injuries. A consecutive series of 25 patients with grade 2 MUCL injuries were identified. All patients had documented positive moving valgus stress test and/or milking maneuver. All patients had an MR arthrogram demonstrating a partial tear of the MUCL (Podesta grade 2) (Figure 1). A 1.5-T scanner was used for all studies. Arthrogram contrast consisting of 20 mL of normal saline and 1 mL of gadolinium dye (Magnevist; Bayer Healthcare Pharmaceuticals) was injected by the treating surgeon. MRIs were performed at presentation and after treatment at a 6-week interval. The treating surgeon and radiologist reviewed the studies; there was no attempt at blinding.

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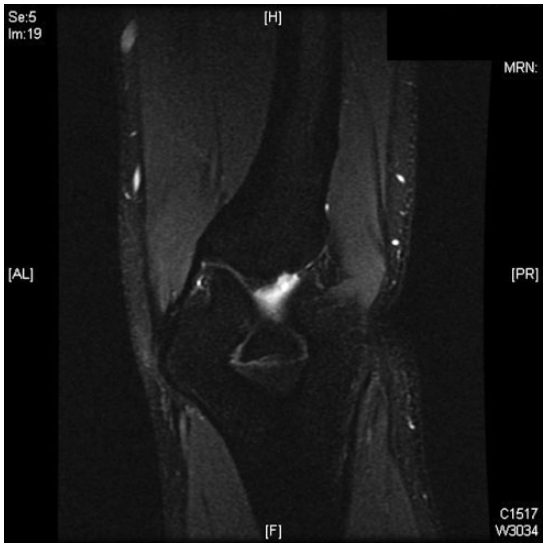

Figure 2. Posttreatment magnetic resonance image revealing reconstitution of the ligament.

Indications for treatment were a grade 2 MUCL injury, a desire to return to sport, the ability to undergo consecutive PRP injections, and a postinjection MRI. Exclusion criteria included grade 1 or 3 injuries, concomitant injuries to that extremity, lack of desire to return to play, and/or inability or unwillingness to comply with the bracing and rehabilitation program.

Immediately upon diagnosis, the patients were placed in a hinged elbow brace that provided varus force to offload the MUCL. The patients received 2 injections of autologous PRP (Harvest Technologies Corp) spaced 2 weeks apart; 5 to 8 mL was injected into the tear in the MUCL. The preparation is a nonactivated, leukocyte-rich and platelet-rich (type IB) preparation with a platelet concentration of 1228 $\pm$ 312 $\times$ $10^3/\mu L$ (ratio to donor whole blood, 4.44:1), capture efficiency of 63.4% $\pm$ 7.9%, leukocyte concentration of 19 $\pm$ 8 $\times$ $10^3/\mu L$, and high concentrations of platelet-derived growth factor (208 $\pm$ 85.2 ng/mL), tendonlike growth factor β1 (77.2 $\pm$ 54.8 ng/mL), and insulinlike growth factor (91.4 $\pm$ 21.3 ng/mL).[33] The injections were performed under ultrasonographic guidance to confirm accuracy of placement of the PRP into the area of tearing. After injections, nonsteroidal anti-inflammatory drugs were held for a 2-week period. Immediate physical therapy was instituted in the brace, consisting of Kibler-integrated rehabilitation.[18,19] This regimen included hip, core, scapula, shoulder, elbow, and wrist exercises. Four weeks after initiation of the treatment protocol, a new MRI (Figure 2) was obtained to evaluate for reconstitution of the MUCL.

A return-to-throw program was initiated in the brace and progressed as tolerated, with the brace being gradually eliminated over the ensuing 2 weeks. Athletes were allowed to return to unrestricted activity once they were nontender on examination and could demonstrate good throwing mechanics.

RESULTS

Of the 25 patients in the study, 23 were male and 2 were female, with an average age of 18 years (range, 15-22 years). All 23 males played baseball (21 pitchers, 2 position players). All of the injuries, save one, were acute on chronic throwing injuries, meaning that the patients had baseline pain that acutely worsened, prompting cessation of throwing and presentation for evaluation. Six patients were referrals who had tried varied regimens of rest and physical therapy between 1 and 6 months' duration; all met criteria for inclusion and were treated identically. Both female patients played softball, and one also competed in dance. Ten patients were athletes at the collegiate level, while 15 were high school athletes (Table 1).

Twenty-three patients were diagnosed with primary grade 2 injuries to the MUCL. Of these, 22 (96%) patients demonstrated stability of the MUCL after treatment and returned to play at the same or higher level of competition. Patients were released to play at 6 weeks; due to vagaries of sports seasons, the mean time to return to play was 82 days. The posttreatment MRI showed full reconstitution in 20 of 22 (91%) patients who successfully returned to sport. The 2 patients who returned to sport with partial reconstitution of the ligament were nontender to the moving valgus stress examination and to the milking test. The 1 patient in the primary injury group for whom treatment failed was able to return to play at the same level at 6 weeks but within that season incurred a midsubstance MUCL ligament tear, requiring reconstruction. He went on to return to play at 243 days from initial presentation.

Two patients with a history of operative intervention for MUCL instability (1 repair, 1 reconstruction) were treated in the same fashion. At follow-up, these patients demonstrated continued pain with moving valgus stress examinations and the milking movement. They required MUCL reconstruction and returned to sport at an average of 261 days (range, 180-320 days).

No complications occurred after the PRP injection aside from localized soft tissue swelling that resolved within 24 hours. No systemic reactions, nerve palsies, or infections were noted.

DISCUSSION

The initial study on nonoperative treatment was that of Rettig et al.[24] Although only 42% success was reported, the main treatment was rest and rehabilitation. Our study differed from that of Rettig et al[24] not only in the PRP injections but also in the use of an offloading brace and advanced integrated rehabilitation of the throwing athlete. These added treatments most likely had positive effect on the success of the nonoperative management.

Injection of PRP for the management of MUCL tears was first reported by Podesta et al,[23] and the present study is based on their excellent work. A tremendous variety of PRP treatment regimens are used in sports medicine, and no gold standard has been established.[25] Questions exist regarding the optimum regimen, including the number and

TABLE 1
Patient Descriptions[a]

Age, y	Sex	Position	Mechanism	Location of Tear	Posttreatment Examination	Posttreatment MRI
15	F	Softball 3B	Acute on chronic	Proximal	Normal	Reconstituted
21	M	College RHP	Acute on chronic	Distal, proximal	Normal	Reconstituted
15	M	High school RHP	Acute on chronic	Proximal	Normal	70%
18	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
19	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
16	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
17	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
18	M	High school RHP	Acute on chronic	Proximal, slight distal edema	Normal	Reconstituted
17	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
18	M	High school RHP	Acute on chronic	Distal	Normal	Reconstituted
17	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
18	M	College RHP	Acute on chronic	Distal	Normal	Reconstituted
21	M	High school LHP	Acute on chronic	Proximal	Normal	Reconstituted
21	M	College RHP	Acute on chronic	Proximal	Normal	50%
20	M	College RHP	Acute on chronic	Proximal, distal thinning	Normal	Reconstituted
17	M	High school RHP	Acute on chronic	Proximal	Normal	Reconstituted
18	M	High school RHP	Acute on chronic	Distal	Normal	Reconstituted
20	M	College RHP	Acute on chronic	Distal	Normal	Reconstituted
18	M	College RHP	Acute on chronic	Distal	Normal	Reconstituted
20	M	College RHP	Acute on chronic	Proximal	Normal	Reconstituted
20	M	College RHP	Acute on chronic	Proximal	Normal	Reconstituted
21	M	College RHP	Acute on chronic	Proximal	Normal	Reconstituted
16	M	High school LHP	Acute on chronic	Proximal, distal	Abnormal	Minimal change
15	F	Dancer, softball pitcher	Handstand	Proximal	Abnormal	Minimal change
21	M	College LHP	Acute on chronic	Proximal, middle	Abnormal	Minimal change

[a]All acute-on-chronic injuries occurred in overhead throwing injuries. For the tears with multiple involved areas, the areas are listed in order of severity. F, female; LHP, left-hand pitcher; M, male; MRI, magnetic resonance imaging; RHP, right-hand pitcher; 3B, third baseman.

timing of doses, use of leukocyte-rich or leukocyte-poor preparations, volume of injection, and others. Previously reported protocols include single and multiple injections and varying intervals, and some have convincingly demonstrated improved efficacy with multiple injections.[4,8,34] We elected to use 2 consecutive leukocyte-rich PRP injections, spaced 2 weeks apart, to augment our bracing and rehabilitation regimen. This strategy is based on unpublished data from our research group showing an advantage of 2 injections over a single injection but no further benefit with 3 injections. Repeat MRI obtained 4 weeks after initiation of this protocol demonstrated reconstitution of the ligament, although 2 patients returned to play without total reconstitution of the ligament. Clearly the use of leucocyte-rich PRP seems to stimulate ligament healing, as noted on the repeat MRI scan. We believe the potentiation of the inflammatory response by the added PRP increases the body's healing mechanism, as noted in other studies.[4,8,19,21,29] The repeat MRI was conducted for the purpose of the study; now we routinely allow return to play at 6 weeks when patients are stable and nontender.

In both the present study and the work by Podesta et al,[23] no significant complications were observed with PRP injection into the MUCL. For patients with primary grade 2 MUCL injuries, our results are comparable (88% return to sport in Podesta's work vs 96% in our study), although differences in treatment strategy and relatively small sample size cloud attempts to determine whether these contributed to differing outcomes. Important differences include our use of a varus-producing brace to offload the MUCL during rehabilitation, the whole-body Kibler rehabilitation protocol, and a second injection of PRP. Podesta et al[23] used ultrasonographic guidance for injections, collected serial dynamic ultrasonographic measurements, and obtained subjective patient outcome scores (Kerlan-Jobe Orthopaedic Clinic [KJOC] and Disabilities of the Arm, Shoulder and Hand [DASH]). The PRP injections used in both studies were comparable, and although the system used by Podesta et al[23] has reported platelet concentrations around two-thirds as high as the system we used, both qualify as type 1B under the Mishra scheme.[4,19,33] These two studies address similar patients with partial tears confirmed on MRI, and this patient selection largely accounts for the differences seen with the study by Rettig et al,[24] where MRI was not available to differentiate complete and partial tears.

Treatment of the 2 patients with prior MUCL surgery was not successful with this protocol. It may be that partial disruption of repaired or reconstructed ligaments is equivalent to complete disruption of native structures with regard to capacity for healing; however, this group is too small to draw definitive conclusions.

This study is limited by its retrospective nature, lack of validated patient outcome scores, and lack of a control group. All patients were seen by the same treating staff surgeon and a small group of therapists, lending this cohort

good homogeneity. Further research is required to determine the optimal concentration, frequency, and dosing of PRP for soft tissue injuries in orthopaedics and to ascertain whether PRP improves results over MUCL offloading bracing and whole-body physical therapy. Additionally, to our knowledge, no one has yet published a cohort of MRI-confirmed partial MUCL tears managed without PRP injection. Future studies, including a randomized controlled trial, should be performed and would benefit from both validated scoring systems (KJOC, DASH) and dynamic ultrasonography.[6,12]

CONCLUSION

Treatment of grade 2 MUCL injuries with 2 leukocyte-rich PRP injections, along with a bracing and physical therapy program, was a safe and effective protocol that returned throwing athletes to competition without surgery. This treatment regimen was successful in reconstituting the MUCL in partial tears, as determined by the postinjection MRI. The reconstitution occurred in a rapid time frame and allowed a high rate of return to play in throwing athletes who had not undergone prior surgery. This treatment protocol may not be as effective in athletes with prior surgery for MUCL repair or reconstruction.

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