ABSTRACT

RETURN-TO-PLAY OUTCOMES FOR OVERHEAD THROWING ATHLETES WITH ULNAR COLLATERAL LIGAMENT INJURIES TREATED WITH PLATELET RICH PLASMA INJECTIONS AND CONSERVATIVE THERAPY VS. CONSERVATIVE THERAPY ALONE

Background: The number of ulnar collateral ligament (UCL) reconstruction surgeries has increased by 343% from 2003 to 2014. Athletes undergoing UCL reconstruction risk an 83% return to play (RTP) rate and average rehabilitation time of 20.5 months. The use of platelet rich plasma (PRP) injections to improve conservative outcomes and avoid invasive surgery has become a topic of interest for rehabilitating these injuries. The purpose of this meta-analysis is to synthesize the current literature and compare non-operative alternatives of PRP injections and conservative therapy (CT) on the RTP outcomes for overhead throwing athletes with partial UCL tears. ***Methods:*** The included studies examined the return to play outcomes of overhead throwing athletes with partial UCL injuries treated with either PRP injections followed by CT or CT alone. Data were analyzed to determine the grand odds ratio as well as homogeneity across the studies. ***Results:*** Treatment with PRP injection and CT interventions are shown to yield an improved likelihood that the athlete will be able to RTP compared to CT alone with a grand odds ratio of 10.80. ***Conclusion:*** This meta-analysis demonstrates superior RTP outcomes for athletes with partial UCL injuries treated with PRP injections and CT when compared to CT alone.

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BACKGROUND

Ulnar collateral ligament (UCL) injuries of the elbow are common injuries that can prevent overhead athletes from competing in sport. This injury affects athletes of all levels including high school through professional level athletics and the number of UCL reconstructions performed has increased by 343% from 2003 to 2014. It is noted that the highest incidence is between the ages of 15 to 24 years old.[1]

Although baseball pitchers are the most common athletes to experience a UCL injury, it is also associated with other overhead sports such as javelin throwing, volleyball, tennis, gymnastics, wrestling, and water polo.[2-7] The mechanism of injury occurs as a result of repetitive valgus stress on the UCL during overhead throwing which increases tensile strength on the ligament. This causes microtrauma to the ligament and leads to degeneration or eventual tearing of the UCL.[8] It is unknown why there is a significant rise in UCL injury incidence however, this disabling impairment for overhead throwing athletes is well documented.[7] While surgical intervention is the primary treatment for full thickness tears, there is less definitive evidence to suggest consensus for treating partial tears.[3,9]

Functional Anatomy and Biomechanics

The UCL attaches proximally to the central two-thirds of the anteroinferior surface of the medial epicondyle of the humerus and distally to the proximal medial ulna.[10] The UCL is the primary stabilizer responsible for resisting valgus stress between 20-130° of elbow flexion.[11] During full elbow extension, the UCL, joint capsule, and bony articulation primarily resist valgus stress.[12]

Athletes that perform overhead throwing during sport perform a similar motion but the specific demands of each sport place different amounts of stress on the elbow joint. The average maximum acceleration velocity of elbow extension is 2,400°/s for baseball, 1,900°/s for javelin, 1,760°/s for football, 982°/s for tennis, and 570°/s for softball.[13] Baseball is the most researched sport in terms of the effect of overhead throwing on the elbow. During the arm cocking phase of throwing a baseball, a varus torque of 52 to 76 nm (average of 64 nm) is required to counteract the valgus torque placed on the elbow.[13]

The UCL is responsible for resisting 54% of valgus stress placed on the elbow, which results in about 34.5 nm of torque.[14] Studies performed on cadavers reveal the UCL fails under 32 nm of torque.[15] This demonstrates the importance of other dynamic stabilizers during the throw due to the near-failure stress placed on the ligament during overhead throwing.[16] Dynamic stabilizers of the elbow during overhead throwing include the pronator teres, flexor carpi radialis, palmaris longus, flexor carpi ulnaris, and flexor digitorum superficialis.[17] These muscles originate at the medial epicondyle of the elbow and contract to resist valgus stress.[17] Studies have shown that weakness in these dynamic stabilizing muscles correlate to an increased risk of UCL injury.[18]

Ligament Pathophysiology

Although there is extensive knowledge regarding the structure and function of normal ligaments, there is a lack of understanding regarding the structural changes and behavior of injured ligaments and this is most likely due to the unpredictability of ligament healing.[19] The unpredictable healing of ligaments is most likely due to changes in structure such as increased mass, stiffness and load failure when exposed to loading over time.[19,20] When a ligament is overloaded, the tissue will fail, resulting in a partial or complete ligament tear.[21] The healing of the injured ligament occurs by complex cellular processes that create alterations in the biology and biomechanics of the ligament.[19] The biological changes can produce inadequate healing and tissue formation, which leads to persistent ligament laxity and increased risk of further injury.[19]

Injured ligament tissue responds to injury by healing in 3 phases: the acute/inflammatory phase, the proliferative/regenerative phase, and the tissue remodeling phase.[21] During the inflammatory phase, a platelet-rich fibrin clot releases growth factors to promote healing. Platelet-Derived Growth Factor (PDGF), Transforming Growth Factor-B (TGF-β), Vascular Endothelial Growth Factor (VEGF), and Fibroblast Growth Factor (FGF), all have a role in the process of all ligament healing. PDGF and TGF-β attract immune system cells and stimulate proliferation.[21] VEGF increases new blood vessel formation. FGF increases the growth of collagen and cartilage formation.[21] Growth factors also stimulate immune cells to migrate to the region of injury and remove damaged cells and debris.[21]

Immune cells release growth factors and cytokines to initiate the proliferative phase.[21] Ligamentous tissue initially forms in a disorganized scar tissue, with an increased composition of blood vessels, fat cells, fibroblasts, and inflammatory cells compared to healthy ligamentous tissue.[22,23] Over the next several weeks of healing, collagen is created and aligned with the ligament during the proliferative and remodeling phases.[22] However, the newly formed collagen is abnormal and thinner than non-injured ligamentous tissue.[21]

The remodeling phase begins after a few weeks and can last for months or even years after the injury.[21] During this phase, the ligament tissue will begin to resemble non-injured tissue.[21] The ligament structure still resembles scar tissue histologically, biomechanically, and biochemically.[24-26] Even when tissue has been fully remodeled, it still remains functionally different from normal tissue.[24] The dysfunctional ligament causes joint instability, chronic pain, and diminished function which can impair the performance of overhead throwing athletes.[19]

Surgical Treatment

Due to the increased prevalence of UCL injuries in throwing athletes and persistent impairment following ligament healing, trends have been rising for the use of surgical treatment for patients with UCL injuries. Evidence shows that the number of UCL surgical procedures has increased by 6 times over the past 30 years and continues to rise.[7,27] There are 2 different surgical techniques currently being used to treat UCL injuries: the UCL repair and UCL reconstruction. UCL repair can be used when there is sufficient healthy tissue remaining.[9] In the population of high level throwers, surgical reconstruction of the UCL is usually indicated due to chronic damage of the mid-substance of the ligament.[28]

Surgical reconstruction is indicated in all of the following cases: acute ruptures of the UCL in high-level throwers, significant chronic instability, insufficient UCL tissue remaining after debridement for calcifications, and when there is recurrent pain and valgus instability after conservative treatment.[10,14,29-31] UCL reconstruction is performed using a tendon graft and tensioning it between the medial humeral epicondyle and the sublime tubercle of the ulna using bony tunnels.[4] More recently, in the past ten years surgical technique modifications have occurred in efforts to improve patient outcomes.[32]

Even with improvements in surgical techniques, athletes are still experiencing lengthy rehabilitation processes and mixed results for RTP[27,33] A systematic review revealed an 83% RTP rate and average length of rehabilitation of 20.5 months for overhead athletes that have undergone UCL reconstruction.[27,33] Although the surgical procedure has been shown to be effective for return to play, the amount of time necessary to fully recover from surgery can be detrimental to an athletes career.[34]

Conservative Treatment

Conservative management is often the first course of treatment following UCL injury, rather than more invasive alternatives. Conservative treatment involves rest, anti-inflammatory medications, bracing, and physical therapy.[28] In phase I of physical therapy the plan of care is focused on reduction of pain and inflammation.[28] Phase II of physical therapy emphasizes progression of mobility and strength at the elbow, as well as other impairments in the kinetic chain that could place increased stress on the elbow.[28] Phase III includes sport specific therapeutic activities with overhead throwing progression until the athlete is ready for full RTP.[28] Overall the literature suggests a low RTP rate following conservative treatment and the likelihood a patient will respond well to conservative treatment is largely based on the severity of the UCL injury.[28,35] In contrast, throwing athletes with complete tears are likely to be treated with early surgical intervention.[28,35]

Platelet Rich Plasma Injections

Although surgical options are successful, the amount of time required to rehabilitate athletes following surgery is the biggest limiting factor for this form of treatment. The use of platelet rich plasma (PRP) injections to stimulate healing of ligaments has become a topic of interest for surgeons and physical therapists involved in rehabilitating these injuries. One reason rehab professionals are interested in this intervention is because platelets contain bioactive factors such as proteins and cytokines that promote aspects of wound healing.[36] Normal blood values for platelets are 150,000 to 350,000/μL.[36] Plasma contains clotting factors, dissolved proteins, glucose, electrolytes, hormones and oxygen, all of which are precursors to promoting optimal healing effects.[36] Platelet-rich plasma has a platelet concentration of 1,000,000/μL and with these substrates being present in higher concentrations, there is associated enhanced healing ability compared to non-supplemented plasma.[37]

Platelet-rich plasma improves healing by facilitating the delivery of growth factors and cytokines. Growth factor–β (TGF-β), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I, IGF-II), fibroblast growth factor (FGF), epidermal growth factor, vascular endothelial growth factor (VEGF), and endothelial cell growth factor are all cytokines that are present in platelets.[36] These cytokines have responsibilities in proliferation, cell differentiation, and angiogenesis.[36] Platelets also contain serotonin, histamine, dopamine, calcium and adenosine and these elements effect wound healing.[36] Histamine and serotonin allow greater access to the site of injury and activate macrophages.[36,38,39] Adenosine helps modulate inflammation during the healing process.[36] Platelets in PRP are delivered in a clot consisting of cell adhesion molecules.[36] The adhesion molecules also improve healing by acting as a conductive matrix upon which cells can adhere to and start the healing process.[36]

Platelet Rich Plasma Injections are categorized based on the concentration of different cellular components in the concentrate. Type 1 and 2 both have an increased number of white blood cells in the concentrate and are referred to as leukocyte-rich.[40] Type 3 and 4 both have minimal or no white blood cells in the concentrate and are referred to as leukocyte-poor.[40] Type 2 and 4 are activated while Type 1 and 3 are not.[40] Activation refers to using thrombin or calcium chloride for platelet activation prior to injection.[41] Further classification into A or B is based on the amount of increase in platelet concentration.[40] Type A has platelets increased by greater than 5x the baseline and Type B has increased platelets but less than 5x the baseline amount.[40,42]

Overall, PRP has been shown to be effective in the healing of musculoskeletal soft tissues such as tendons, ligaments, and muscles.[36] Further research is needed to solidify what specific tears would be a good candidate for treatment with PRP injections as opposed to surgical intervention.

Purpose

The purpose of this study is to investigate the effectiveness of platelet rich plasma injections in conjunction with conservative physical therapy for treating partial UCL injuries in overhead throwing athletes and optimize return to play rate. Therefore, the null hypothesis for this meta-analysis is that there will be no significant difference in return to play rate for athletes that received PRP injections with conservative physical therapy versus athletes that received conservative physical therapy alone. The alternative hypothesis will demonstrate a significant improvement in return to play rate for athletes that received PRP injections with conservative physical therapy versus athletes that received conservative physical therapy alone. This study will assist in filling the gap in literature regarding non-surgical interventions for treatment of UCL injuries in overhead throwing athletes.

METHODS

Search Strategy

The primary literature search was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. From August 2018 to September 2018, a comprehensive electronic search was conducted systematically using the following databases: PubMed, Elsevier, and SAGE Research. The search was limited to full text, peer-reviewed journals published from 2000 to 2018 in the English language. Search terms used were combined with “AND” or “OR” and found within the title or abstract. Search terms included: Ulnar Collateral Ligament (UCL), Platelet Rich Plasma (PRP), Conservative Treatment/Therapy, Non-Operative Treatment, Non-Surgical, Elbow, Baseball, Throwing Athlete, and Return to Play. A comprehensive list of search terms is included in Table 1. Secondary studies were found by reviewing references of appropriate studies. An independent reviewer screened and excluded articles systematically according to titles, relevance, and abstract and outlined by the consort map in Figure 1.

Eligibility Criteria

Inclusion criteria for the studies required the subjects to be overhead throwing athletes between the ages of 12-35 years old. The studies needed to include subjects with confirmed diagnosis of UCL of grade I, or II with evidence on imaging or physical examination. Exclusion criteria included athletes with grade III ligament tears or previous history of surgical repair or reconstruction of the UCL. Randomized control trials, cohort studies, case series studies, and retrospective studies were all considered. After thorough review of abstracts of pertinent studies in the literature, the studies needed to include the return to play

(RTP) rate as the outcome measure to assess successful treatment intervention. It was decided to exclude literature review articles, case reports, and conference abstracts from the search.

Operational Definitions

For the purpose of this meta-analysis, overhead athletes were defined as "one who uses their upper arm and shoulder in an arc over head to propel a ball".[43] Based on the inclusion criteria for this meta-analysis, the athletes included baseball, softball, volleyball, tennis, javelin throwers, or football quarterbacks.

Conservative physical therapy was defined as any physical therapy interventions including: period of rest, immobilization, ice, cryotherapy, whirlpool, ultrasound, soft tissue mobilization, laser therapy, electrical stimulation, range of motion (ROM) exercises, strengthening exercises (local or whole body), and a progressive throwing program.

PRP treatment was defined as receiving 1-3 PRP injections followed by a period of conservative physical therapy. PRP injections were prepared as either leukocyte rich or leukocyte poor. Patients receiving PRP injections were prescribed relative rest following injections and to hold NSAIDs for 2 weeks before beginning further physical therapy interventions.

Return to Play was defined as the athlete's ability to return to sport without symptoms of elbow pain. There was no specific follow up time frame used in the definition of RTP for this meta-analysis.

Outcome Measures

The Conway-Jobe scale is a return to play scoring system to assess overhead athlete's ability to return to sport following an ulnar collateral ligament reconstruction, but can also be used to assess other more conservative treatments.[3]

The Conway-Jobe scale has not yet been validated for outcomes for elbow injuries in overhead throwing athletes but is still a good measure of the athlete's ability to RTP.[44] The scale scores outcomes from poor to excellent: excellent outcome is RTP at same level or higher, good outcome is RTP at lower level, fair outcome is RTP at a recreational level, and poor outcome is unable to RTP.[44] For purposes of this meta-analysis, a score of excellent or good on the Conway-Jobe scale was rated as the ability to RTP. The only outcome consistent between all studies was the ability of the athletes to RTP. Even though RTP, is not a validated measure, it is a good indicator of healing and improved function in overhead athletes following UCL injuries.

Assessment of Study Quality

A single assessor reviewed titles, abstracts and an in-depth review of studies to determine eligibility in the meta-analysis. Articles that fulfilled inclusion criteria were further analyzed using the Downs and Black Checklist to determine the quality of the study (see Appendix).[45] The Downs and Black Checklist contains 27 items to assess the quality of the study involving categories of reporting, external validity, internal validity, and selection bias.[45] Quality levels were based on the following scores: excellent (≥26); good (20-25); fair (15-19); and poor (≤14). The Downs and Black Checklist is a valid and reliable tool for assessing health care intervention studies.[45] The results for each article can been seen in Table 2.

Data Extraction

The number of athletes that were able to RTP and the number of athletes that were unable to RTP were collected from each study. The values for the studies were reported in percentages of athletes that were able to RTP, so these were converted to number of athletes. In the study by Podesta et al., inclusion criteria stated patients had already failed at least 2 months of conservative treatment.[46] In the study by Dines et al., inclusion criteria stated patients had failed a trial of conservative treatment prior to the study.[47] For purposes of the meta-analysis, the failure of conservative physical therapy in those 2 studies was used as a control group for the conservative physical therapy in which all patients were unable to RTP.

Statistical Analysis

The odds ratio was calculated using the number of athletes able to RTP and unable to RTP following PRP injections with conservative physical therapy compared to. conservative physical therapy alone. Studies were grouped together and analyzed using a combined odds ratio model to obtain confidence intervals (CI), Grand Odds Ratios, and Homogeneity. Statistical significance was determined with an alpha level of less than 0.05 with a 95% confidence interval. Q-values greater than the degrees of freedom and a p-value less than 0.05 was indicative of heterogeneity. Sub-analyses were performed for subjects with distal UCL tears, proximal UCL tears, and grade II UCL tears using the same method. For any group that had 0 subjects, the Haldane-Anscombe correction was used to replace the 0 with 0.5 for purposes of calculation.[48] Forest plots were generated using the data from each analysis for visual representation (see Figures 2-5).

RESULTS

Study Selection

Database search conducted through the National Library of Medicine National Institutes of Health (Pubmed), Elsevier, and Sage Research, yielded a total of 67 articles after duplicates were removed (see consort, Figure 1). Following a review of title and abstract, 37 articles were removed based on relevancy to the PICO components. An additional 17 articles were excluded because they were non-experimental. After an in-depth review, 4 studies were eliminated because they were not conducted on overhead throwing athletes. Two case reports were eliminated due to low level of evidence and small sample. The final 7 studies included in this meta-analysis were published between 2001 and 2017.

Study Characteristics

The 7 studies in this meta-analysis were assessed using the Downs and Blacks Checklist by a single evaluator and scored in a range of 16 to 20 out of a possible 28 points. The most commonly unfulfilled criteria were blinding of subjects or therapist. For physical therapy interventions and platelet rich plasma injections, the patients, therapists, or injection administrators were not blinded. The studies also had no control groups so random allocation of subjects into groups, homogeneity of populations between groups, and recruitment time of individual groups were unfulfilled criteria. Studies lacked random variability for the main outcome measure of return to play because there is no standard deviation for a qualitative measure, therefore standard deviations and effect size of treatment was unable to be performed. A detailed report of the Downs and Blacklist scoring can be found in Table 2.

The PRP treatment studies, Deal et al.[49], Dines et al.[47], and Podesta et al.[46], contained multiple differences including the number of PRP injections administered (1-3 injections), the amount of PRP injected to the site, the type of PRP injection, and the post-injection protocols. Complete PRP injection protocols for each study can be found in Table 3. The conservative physical therapy studies, Dodson et al.[50], Ford et al.[51], Frangiamore et al.[52], and Rettig et al.[53], had differences in the specific rehabilitation protocol implemented. Complete rehabilitation protocols for both PRP and conservative physical therapy studies can be found in Table 4.

Athlete subjects across the 7 studies included in this meta-analysis were included if they had a diagnosis of grade I or grade II UCL tear. Deal et al.[49] contained subjects with only grade II UCL tears. Dines et al.[47], Dodson et al.[50], and Ford et al.[51] contained different saturations of grade I and II UCL tears. Frangiamore et al.,[52] Podesta et al.,[46] and Rettig et al.[53] did not specify grading of partial tears. See Table 5 for specific grades of tears for subjects in each study. Subjects in the studies also differed in level of athletic play. Ford et al.[51] and Frangiamore et al.[52] contained only professional athletes while the other 4 studies had a mixture of professional, college, and high school athletes (see Table 6). All athletes in the study participated in overhead sports, but not all played the same sport. Sports included baseball pitchers, baseball position players, softball players, javelin throwers, and football quarterbacks (see Table 7). Lastly, the studies differed in the average rehabilitation time for the athlete to RTP. Measures for rehabilitation time were not given for Frangiamore et al.[52] or Ford et al.[51]. The other 4 studies provided mean rehabilitation time and ranges of specific subject rehabilitation time. The mean rehabilitation time for the 3 PRP intervention studies was 84.3 days. The mean rehabilitation time for the 2 conservative physical therapy studies was 89.5 days. See Table 8 for full outline of rehabilitation time for each study.

Statistical Analysis

Primary data analysis was completed for the ratio of odds of an athlete to RTP when treated with PRP injections and conservative physical therapy versus conservative physical therapy alone. Studies included in this meta-analysis did not utilize a control group, therefore separate studies were grouped together for purposes of creating forest plots for comparison. Data were analyzed using a combined odds ratio to generate grand odds ratio, confidence intervals, and homogeneity. For the purpose of this meta-analysis, an odds ratio >1.0 favors PRP treatment, an odds ratio of <1.0 favors conservative physical therapy alone, and an odds ratio = 1.0 indicates no difference between treatments. The grand odds ratio (OR), standard error of OR, and confidence intervals were calculated and included in Table 9.

This analysis demonstrated a grand combined OR of 10.80 favoring PRP treatment with a total variance (Q) of 1.21 with 2 degrees of freedom (p-value 0.5457) indicating homogeneity. A forest plot of the data can be found in Figure 2. Additional analyses were performed to demonstrate the importance of the data from different populations included in the PICO. Combined Odds Ratios were performed for proximal tears, distal tears, and grade II tears only. Proximal tears produced a grand combined OR of 17.56 favoring PRP with a total variance (Q) of 8.92 with 1 degree of freedom (p-value 0.0028) indicating heterogeneity. Distal tears produced a grand combined OR of 3.98 with a Q of 1.85 with 1 degree of freedom (p-value 0.17) indicating homogeneity. Lastly, grade II tears produced a combined grand OR of 11.35 with a Q of 9.08 (p-value 0.0026) indicating homogeneity. All results can be found in numeric form in Table 10 or in forest plot form in Figures 2-5.

DISCUSSION

The purpose of this meta-analysis was to determine the effects of PRP injections combined with conservative physical therapy on RTP rate in overhead throwing athletes with partial UCL tears versus conservative physical therapy alone. The alternative hypothesis was accepted because the meta-analysis demonstrated statistically significant improvements in odds of RTP following PRP injections with conservative physical therapy versus conservative physical therapy alone. The null hypothesis can be rejected due to an odds ratio of 10.80 favoring PRP injections over conservative physical therapy alone. This discussion will further examine the results of the meta-analysis, discuss limitations of the studies, and propose clinical implications and suggestions for further research to provide improved insight on the effects of PRP injections with conservative physical therapy on RTP rate for overhead throwing athletes with partial UCL tears.

Review of Meta-Analysis Results

This meta-analysis demonstrated that treating overhead athletes with partial UCL tears with PRP injections combined with conservative physical therapy improves the likelihood they will be able to RTP. Based on the analysis, The odds ratio favored RTP rate for those athletes that received PRP injections with conservative physical therapy. Homogeneity was confirmed with a Q value of 1.21, p-value 0.5457 indicating a correlation across the 6 studies included in this meta-analysis. Sub-analysis for grade II partial UCL injuries had an OR=11.35, CI= 1.95-66.02, and p-value of 0.0026. The results suggested an increase in probability of RTP for athletes with grade II UCL tears treated with PRP injections combined with conservative physical therapy, but also identified significant heterogeneity. Sub-analysis for distal partial UCL tears revealed an

OR=3.98, CI= 0.31-51.73, and p-value of 0.17. The results demonstrate an increased probability of RTP for athletes with a distal UCL tear treated with PRP injections combined with conservative physical therapy and had homogeneity across studies. The final sub-analysis on proximal partial UCL tears demonstrated an OR=17.56, CI=1.81-170.72, and p-value of 0.0028. The results suggested an increase in probability of RTP for athletes with proximal UCL tears treated with PRP injections combined with conservative physical therapy, but also identified significant heterogeneity. The positive odds ratio on RTP outcomes for athletes with a distal UCL tear or grade II UCL tear may not be precise due to heterogeneity found between studies. Therefore, the sources of heterogeneity between studies will be discussed.

Explanation of Forest Plots

Results for the primary meta-analysis can be viewed graphically in a forest plot (see Figure 2). When analyzing the primary forest plot for all 7 studies collectively, Podesta et al. paired with Ford et al. and Dines et al. paired with Ford et al. favored PRP injections over conservative physical therapy with the odds ratio and both upper and lower confidence intervals to the right of the y-axis. The group of Deal et al., Frangiamore et al., and Dodson et al., favors PRP injections with the odds ratio and upper confidence interval to the right, but the lower confidence interval deviates to favor conservative physical therapy alone. The grand odds ratio for all studies indicates a true clinical effect in favor of PRP injections due to a narrow CI that does not cross the y-axis.

The forest plot for proximal partial UCL tears (see Figure 3) demonstrates the pairing of Deal et al. and Frangiamore et al. as favoring PRP injections with the OR, upper CI, and lower CI all to the right of the y-axis. The pairing of Dines et al. and Ford et al. has a OR and upper CI to the right of the no effect line, but a lower CI to the left. Both groups display large CI, which indicates the sample size was too small. There was a total of 60 patients with proximal tears in the studies with 29 patients in the PRP treatment groups and 31 patients in the conservative physical therapy group. The grand OR, Upper CI, and lower CI favor PRP injections. The Q statistic of 8.92 and p-value of 0.0028 indicate significant heterogeneity, therefore no conclusion can be drawn from the results of this sub-analysis.

The forest plot for distal partial UCL tears (see Figure 4) displays the group of Deal et al and Frangiamore et al. as favoring PRP injections with the OR and upper CI to the right of the y-axis and lower CI to the left. The group of Dines et al demonstrates no effect with the OR on the y-axis, upper CI to the right and lower CI to the left. The grand OR and Upper CI favor PRP injections, while the lower CI favors conservative physical therapy. The Q statistic of 1.85 and p-value of 0.17 indicate homogeneity between the studies. Although there is homogeneity between the studies, there is still large confidence intervals that make it difficult to draw conclusions based on small sample sizes. There was a total of 25 patients with distal tears in the studies with 12 in the PRP treatment group and 13 in the conservative physical therapy group.

The last forest plot displays the sub-analysis for grade II UCL tears only (see Figure 5). The of group Deal et al., Frangiamore et al., and Dodson et al., favors PRP injections with the OR and upper CI to the right of the y-axis and lower CI to the left. The group Dines et al. and Ford et al. favors PRP injections with the OR, upper CI, and lower CI to the right of the y-axis. The grand OR, upper CI, and lower CI favor PRP injections. The Q statistic of 9.08 and p-value of 0.0026 indicate significant heterogeneity between the studies, therefore no conclusion can be drawn from the results of this sub-analysis. There was a total of 102 patients with grade II tears in the studies with 48 in the PRP treatment group and 54 in the conservative physical therapy group.

Limitations of Studies Leading to Heterogeneity

The 7 studies included in this meta-analysis were examined for the outcome of RTP. The studies were assessed for internal and external validity threats and limitations. Major validity limitations include low Downs and Black checklist scores, differences in treatment protocols for both the PRP injection and conservative physical therapy groups, and differences in sample subject characteristics.

The first source of possible heterogeneity is the variation in Downs and Black Checklist scores between the 7 studies. For the studies that utilized PRP injections as treatment,[46,47,49] the Downs and Black checklist scores ranged from 16 to 18, indicating fair study quality. For the studies that utilized conservative physical therapy as treatment,[50-53] the Downs and Black checklist scores ranged from 14 to 20, indicating poor to good study quality. All 7 studies lacked blinding of the participants and assessors. The lack of blinding can influence patient performance and assessor evaluation following intervention. Five of the studies did not report random variability for the main outcome because there was no numerical value for the outcomes. Lack of variability statistics such as standard deviations, affects the ability to assess how diverse the outcomes were across an individual study. Low scores on the Downs and Black Checklist affect the extent of a true relationship between the independent and dependent variables, thus creating an internal validity threat and complicating interpretation of results.

The differences amongst PRP injection treatment study protocols may lead to another source of heterogeneity. The number of PRP injections performed ranged from 1 to 3 injections and from 3 to 8mL of PRP per injection across the 3 studies. This must be taken into consideration as a potential source of heterogeneity due to different dosages that may have an effect on ligament healing. There has been shown to be an ideal dosage of 1-3 PRP injections, but only if performed at the optimal stage.[54] Several clinical studies have suggested that weekly, repeated PRP injections demonstrate improved clinical outcomes in tendon injuries. [54-56] Patients were also treated with different types of PRP preparations. Two of the studies used leukocyte-rich preparations and the other study utilized leukocyte poor preparations. Leukocytes may play a positive role in the inhibition of bacterial growth and improvement of soft tissue healing which has been complicated by infection.[57] Contrarily, leukocytes have been proposed to cause exaggerated inflammatory responses and stimulate the production of reactive oxygen species that can provoke further muscle damage and inflammation.[57] Given the cellular differences between leukocyte rich and leukocyte poor PRP injections, it is possible that athletes receiving one preparation may have been at a disadvantage.

Another consideration is the differences amongst post-injection rehabilitation protocols of PRP treatment studies. Following injection, the studies prescribed a range of no rest to 2 weeks of complete rest prior to initiating therapy. The period of rehabilitation prior to beginning a return to throw program ranged from 4 weeks to 10 weeks between studies. Although evidence has shown that periods of prolonged rest may be detrimental to the recovery of ligaments, this still seems to be the first-line of treatment for ligament injuries.[21] Immobilization of a joint with a ligament injury can cause increased collagen degradation with decreasing collagen synthesis and a greater percentage of disorganized collagen fibrils.[19,58,59] Utilizing early, controlled activity after injury, including repetitive loading of ligaments produces enhanced cellular synthetic and proliferative effects, increased strength, size, matrix organization and collagen content of ligaments.[19,21,60] Interestingly, Deal et al.[49] utilized a hinged elbow brace that allowed full elbow range of motion, but provided a varus force to offload the UCL and prevent harmful stress on the ligament during the initial phases of rehabilitation.[61] Athletes in this study began a return to throwing progression at 4 weeks, which was the earliest of the rehabilitation protocols. Utilization of the hinged elbow brace allowed the athlete to perform early, protected overhead throwing without the risk of damaging the weakened ligament. The early loading of the ligament may have increased strength of the ligament, while also preventing muscle atrophy, adhesions, and joint stiffness.[21,62,63] This component of the rehabilitation protocol should be considered when assessing the positive outcomes demonstrated of a RTP rate of 96% in the study by Deal et al.[49]

The variations in therapeutic exercise protocols for the PRP treatment studies is another factor that should be considered. The studies by Deal et al and Podesta et al utilized programs that trained the upper extremity, scapula, and core. The study conducted by Dines et al did not describe the specifics of their protocol aside from stretching and strengthening. Evidence has shown, weakness in the core may be a contributing factor in the development of an overuse upper extremity injury.[64,65] The role of the core is to generate and transfer forces from the lower extremities to the upper extremities, therefore dysfunction within the kinetic chain may lead to overuse of the upper extremity.[64,65] The lack of integration of core training may have disadvantaged athletes in the study by Dines et al. in comparison to the other 2 studies.

The conservative physical therapy treatment studies had large differences in protocols utilized for the treatment of UCL injuries. Dodson et al. was the biggest outlier between studies because they only utilized passive modalities such as ice, ultrasound, electrical stimulation, and whirlpool therapy, along with rest and immobilization for treatment with no therapeutic exercise protocol. Ice and whirlpool therapy have been shown to reduce metabolism and prevent secondary hypoxic injury and minimize tissue damage.[66] Electrical stimulation has been shown to assist with pain modulation, prevent or reduce edema, increase circulation, and promote tissue healing.[67,68]Although these modalities can promote healing, they would be combined with early mobilization and therapeutic exercise for the optimal result.[66,67] Frangiamore et al. and Ford et al. initiated rehabilitation immediately with no period of prescribed rest or immobilization. In contrast, Rettig et al. prescribed 2 months of complete rest before initiating treatment. As mentioned previously, rest and immobilization are poor forms of treatment for ligament injuries and may have had detrimental effects on healing in this study.[19,54,59] Protocol for Frangiamore et al. began a throwing progression at 6 weeks after the start of the rehabilitation program, Rettig et al. began at 3 months, while Ford et al. utilized asymptomatic subjective and object measures to determine when the patient could begin throwing. Due to the factors affecting healing, such as age, nutrition, degree of ligament damage, the appropriate time to begin a throwing progression may be different for each individual athlete.[21,69,70] Frangiamore et al., Ford et al., and Rettig et al. utilized therapeutic exercise protocols that focused on periscapular and upper extremity strengthening but had no mention of core training. As mentioned previously, the implementation of core training is imperative for throwing athletes with upper extremity injuries.

Exclusion of this area of strengthening may have influenced the overall poor outcomes for patients receiving conservative physical therapy.

Ford et al. described use of modalities such as laser therapy, electrical stimulation, and ultrasound in conjunction with scraping, soft tissue mobilization, and therapeutic exercise program. Instrument assisted soft tissue mobilization (IASTM) has been shown to improve healing time, collagen alignment and decreased scar tissue formation.[71,72] IASTM also improves the vascular response in injured tissues by increasing perfusion and the number of arteriole-sized blood vessels.[72,73] Laser therapy is another modality that has gained interest for its ability to improve healing. Laser therapy uses specific wavelengths of light to stimulate mitochondrial chromophores, which increase respiratory chain activity, enhance adenosine triphosphate (ATP) synthesis, contribute to cellular repair and reproduction, and increase production of messenger RNA that codes for pro-collagen.[74,75] Infrared laser also decreases inflammation by increasing vasodilation due to increased histamine and nitric oxide levels, which results in decreased tissue ischemia, increased perfusion, transport of nutrients, and removal of cellular debris.[75,76] The usage of these modalities may have put the athletes in Ford et al. at an advantage for returning to sport due to their healing affects and must be taken into consideration as a potential source of heterogeneity.

As a whole, studies of both treatment groups had differences in samples of grading of tears, level of competition, and types of athletes. The ratio of grade II ligament tears across studies ranged from 33-100%. The ratio of grade I ligament tears across studies ranged from 0-67%. Three of the studies did not specify the specific grading of tears for individual patients, but it was stated the patients had either a grade I or II tear. A grade I ligament tear, involves a few fibers in localized tenderness, but no instability. Grade II ligament tears involve the disruption of more fibers but less than 50% of fibers are involved.[69,77] Due to structural differences and anticipated healing ability and time between grade I and II injuries, we must consider the possibility the studies with higher percentages of grade II tears were at a disadvantage.

Baseball pitchers are the athletes that undergo the highest amount of stress on the UCL due to torque on the elbow, acceleration velocity, and volume of throws.[13] Sample populations in the studies ranged from 0-100% baseball pitchers. Dodson et. al[50] was the biggest outlier containing no baseball pitchers and 100% football quarterbacks in their small study. Football quarterbacks perform maximum elbow extension velocity of 1760°/s while baseball pitchers perform at 2400°/s.[13] Additionally, baseball players undergo higher compressive forces and torque at the elbow in comparison to football quarterbacks.[78,79] The number of times a baseball pitcher's elbow undergoes high levels of stress is much higher than the number of maximum velocity throws a quarterback makes during a game. According to MLB data, the typical number of pitches thrown per inning is 15-20, with about 5 warm up pitches per inning (8 pitches before the first inning).[80] For example, if a starting pitcher pitched 5 innings in a game, he would make approximately 103-128 maximum effort throws per game.[80,81] According to NFL data, the typical number of passes thrown per game is 34.6 and average length of pass is 7.4 yards.[82] Aside from quarterbacks making only about 35 throws per game, rarely are they throwing for top velocity or distance.[79] Another differentiating factor is the weight of ball, a football is approximately 3 times heavier than a baseball, resulting in differences in arm velocities and the position of the trunk and arm during the throwing motion.[78,79] All of these factors demonstrate the fundamental differences between football quarterbacks and baseball pitchers, which makes it difficult to compare the ability of each to RTP following a UCL injury.

Another consideration is the wide range of ages and level of play of athletes between studies. The level of play ranged from high school to professional athletes and age of athlete was not reported for all studies, but the youngest reported participant was 12 years old and oldest was 33 years old. Age related changes in ligaments include collagen fiber disorientation, decreased cell proliferation and migration, and decreased biomechanical response to healing, possibly due to decreased number of growth factor receptors with age.[83-87] Studies performed on anterior cruciate ligaments of the knee have demonstrated a decreased response to PRP, decreased metabolic activity, decreased collagen production and increased cell apoptosis.[87,88] Athletes of increased age may have been at a disadvantage to RTP in comparison to those of younger ages. In contrast, the athletes at higher levels of play may have better access to the best rehabilitation providers and equipment, as well as higher motivation to RTP. Regardless, the studies did not separate athletes by age or level of play and this should be considered a source of heterogeneity between studies.

Limitations of this Meta-Analysis

Major limitations in this meta-analysis include variable types of athletes at various levels of play and ages. There was variability across athlete's age, type of sport played, and grading of tear. Also, many of the studies were level IV retrospective or a case-control studies with no control group. Most of the studies included in this meta-analysis did were not of high quality according to the Downs and Blacks checklists, therefore results may need to be interpreted with caution due to internal and external validity threats.

Clinical Implications

Treatment of UCL injuries has been an area of interest due to the increasing incidence in the population of professional baseball players, as well as little league players. Surgical technique for management of this injury has improved but still yields a RTP rate of 83% followed by an average rehabilitation time of 20.5 months for MLB pitchers.[27] Orthobiologics have been a treatment of interest in hopes of avoiding invasive surgery with lengthy rehabilitation periods. This meta-analysis supports the use of PRP injections for overhead athletes with partial UCL tears to improve their probability to RTP.[46,47,49]

In the overall meta-analysis, the use of PRP injections was shown to be effective with homogeneity amongst studies. The sub-analyses also favored PRP treatment but demonstrated significant heterogeneity between the studies for the analysis on proximal tears only and grade II tears only. In the clinic, the utilization of PRP injections in combination with conservative physical therapy to optimize the athlete's ability to RTP.

Future Directions

Future studies should focus on including participants of similar age and level of play to decrease internal validity threats and improve the ability to apply results to specific patients. Studies should also include baseball players or specifically pitchers due to their specific sport demands on the elbow in order to provide more homogenous samples for UCL injury research. Additional research should have more descriptive rehabilitation protocols, including initiation of rehabilitation immediately following injection, full body targeted therapeutic exercises, and additional modalities such as laser therapy and IASTM to optimize healing. Lastly, future studies should include more objective measures, aside from RTP, such as MRI or ultrasound images, valgus stress testing, or pain scales with throwing, in order to perform more in-depth statistics to evaluate the effectiveness of the treatment.

CONCLUSION

To conclude, PRP injections combined with conservative physical therapy greatly improved the likelihood that overhead throwing athletes with UCL ligament tears will RTP when compared to conservative physical therapy alone. Physical therapy interventions still play an important role in post-injection rehabilitation and can optimize healing by promoting early, protected movement, strengthening the entire kinetic chain, and facilitate timely return to a throwing progression.

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TABLES

Table 1. Search Terms

Platelet Rich Plasma
Platelet Rich Plasma PRP injection
Ulnar Collateral Ligament
Ulnar Collateral Ligament UCL
Conservative Treatment
Non-surgical treatment Non-operative treatment Conservative Therapy Physical Therapy
Overhead Throwing Athlete
Return to Play Throwing Athlete Overhead Athlete
Terms combined with “AND” or “OR” and searched within [Title] or [Abstract]

Table 2. Quality Assessment of Studies using the Downs and Black Checklist

	Deal et al., 2017	Dines et al., 2016	Podesta et al., 2013	Dodson et al., 2010	Ford et al., 2016	Frangiamore et al., 2017	Rettig et al., 2001
Q1: Aim clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q2: Outcomes clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q3: Patients characteristics clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q4: Interventions clearly described?	Yes	Yes	Yes	No	Yes	Yes	Yes
Q5: Principal confounders clearly described?	No	No	No	No	No	Yes	No
Q6: Main findings clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q7: Random variability for main outcome provided?	No	No	Yes	No	No	Yes	No
Q8: Adverse events reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q9: Loss-to-follow up reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q10: Actual p-value reported?	No	No	Yes	No	No	Yes	No
Q11: Sample asked to participate representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q12: Sample agreed to participate representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q13: Staff participating representative of the patients' environment?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q14: Attempt to blind participants?	No	No	No	No	No	No	No
Q15: Attempt to blind assessors?	No	No	No	No	No	No	No
Q16: Data dredging results stated clearly?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q17: Analysis adjusted for length of follow up?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q18: Appropriate statistics?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q19: Reliable compliance?	Yes	Yes	Yes	Unknown	Yes	Yes	Yes
Q20: Accurate outcome measures?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q21: Same population?	No	No	No	No	No	No	No
Q22: Participants recruited at the same time?	No	No	No	No	No	No	No
Q23: Randomised?	No	No	No	No	No	No	No
Q24: Adequate allocation concealment?	No	No	No	No	No	No	No

	Deal et al., 2017	Dines et al., 2016	Podesta et al., 2013	Dodson et al., 2010	Ford et al., 2016	Frangiamore et al., 2017	Rettig et al., 2001
Q25: Adequate adjustment for confounders?	No	No	No	No	No	No	No
Q26: Loss of follow up reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q27: Power calculation?	No	No	No	No	No	No	No
Total	**16**	**16**	**18**	**14**	**16**	**20**	**16**

Table 3. PRP Injection Protocol

	# of PRP injections	Type of Injection	Ultrasound Guided	Volume of PRP	Injection Protocol
Deal et al. 2017	2 injections	Leukocyte Rich	Yes	5-8 mL	• The patients received 2 injections of autologous PRP (Harvest Technologies Corp) spaced 2 weeks apart
Dines et al. 2016	1-3 injections	Leukocyte Poor	No	3 mL	• Patients were injected using the Autologous Conditioned Plasma system (Arthrex). PRP solutions were prepared according to manufacturer guidelines. • After the elbow was prepared sterilely, the UCL was injected at the location of the tear.
Podesta et al. 2013	1 injection	Leukocyte Rich	Yes	5 mL	• Patients were injected using the Arteriocyte PRP system. • Post-injection instructions were discussed with the patient including the application of moist heat packs every 3 hours for 15 minutes' duration over the first 24 hours after injection, use of analgesic pain medications for postprocedural pain, and active-assisted and active range of motion exercises of the treated area. • The patient was also instructed not to take any NSAIDs after the procedure.

Table 4. Rehab Protocols for PRP and Conservative Therapy Groups

	Type of Study	Sample Size	Post-Injection Rehab
Deal et al. 2017	Case Series; Level IV Evidence	23	• Patients were placed in a hinged elbow brace that provided varus force to offload the MUCL. • 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. This regimen included hip, core, scapula, shoulder, elbow, and wrist exercises. • Four weeks after initiation of the treatment protocol, a new MRI 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.
Dines et al. 2016	Retrospective Case Series; Level IV Evidence	44	• After injection, patients used acetaminophen and ice for pain control. Anti-inflammatory medications were avoided for a minimum of 2 weeks after injection. • Typical post-injection therapy protocol consisted of rest followed by progressive stretching and strengthening for about 4 to 6 weeks before the start of an interval throwing program. Although there is no well-defined post-injection recovery protocol, as a general rule rest was prescribed for the first 2 weeks • followed by a progressive stretching and strengthening program for the next month. • Patients who were asymptomatic subjectively and clinically—negative moving valgus stress test, negative milking maneuver, no pain with valgus stress—were started on an interval throwing program.
Podesta et al. 2013	Case Series; Level IV Evidence	34	• Week 1-2: no strengthening, no activity, gentle PROM only. • Week 2: Begin AROM exercises for elbow and wrist within pain-free range. • Week 3: initiate elbow, wrist and hand resisted exercises. Avoid valgus loading or ligament stretching. Shoulder strengthening, PNF for shoulder only. • Week 4: Add functional diagonal PNF patterns, more scapular strengthening (Kibler), and Closed Chain Scapular wall push-ups. • Week 5-6: initiate light stretching and valgus loading of elbow (if no pain with moving valgus, milking stress tests) • Week 6-8: Progress to fast twitch and dynamic exercises (non-throwing med ball and tubing) • Week 8-10: Pending repeated US finding progress to controlled overhand return to sport activities • Week 10-12 progress to 50-75% of activity effort (short toss to long toss) Begin interval return to sport program. • Week 12+ Progress from 75-90% in controlled setting

	Type of Study	Sample Size	Conservative PT Rehab
Dodson et al. 2010	Retrospective Case Series; Level IV Evidence	6	• Rest, ice, anti-inflammatory medications, other forms of local modalities, and immobilization. • Local modalities consist of cryotherapy, stimulation therapy, ultrasound therapy, and whirlpool therapy
Ford et al. 2016	Case Series; Level IV Evidence	31	• Modalities utilized included electrical stimulation, STM, massage, scraping, ultrasound, and laser therapy. • First priority was to reduce pain and regain full ROM, followed by regaining strength back to the baseline level or better. • Strength training consisted of a focused RC and periscapular program. • An interval throwing program was initiated once the player was asymptomatic and demonstrating good strength.
Frangiamore et al. 2017	Case-Control Study; Level III Evidence	24	• A period of throwing rest and range of motion exercises in the first week. • Followed by protected rotator cuff strengthening in the second week. • The third week consisted of advanced rotator cuff and forearm strengthening. • Two-hand and 1-hand plyometric exercises were begun in weeks 4 and 5, respectively. • Patients began a progressive return to a throwing program beginning in week 6.
Rettig et al. 2001	Case Series; Level IV Evidence	31	• Phase I: rest from throwing for 2-3 months, anti-inflammatory medication, Ice elbow for 10 minutes 4 times daily, Long-arm splint or improved ROM brace at 90 degrees at night, wear as needed during the day, AROM and PROM exercises for flexors and pronators. • Phase II: If pain free: discontinue splint or brace, progress UE strengthening program to all muscle groups, begin throwing progression at 3 months, elbow hyperextension brace may be used for throwing and lifting.

Table 5. Grading of Partial

	Dines et al. 2016	Deal et al. 2017	Podesta et al. 2013	Dodson et al. 2010	Rettig et al. 2001	Ford et al. 2016	Frangiamore et al. 2017
Grade I	19	0	-	4	-	4	-
Grade II	25	23	-	2	-	27	-
Unknown	-	-	34	-	31	-	18

Table 6. Level of Play of Athletes

	Dines et al. 2016	Deal et al. 2017	Podesta et al. 2013	Dodson et al. 2010	Rettig et al. 2001	Ford et al. 2016	Frangiamore et al. 2017
Professional	6	-	2	6	3	31	24
College	14	9	12	-	23	-	-
High School	24	14	10	-	5	-	-
Little League	-	-	1	-	-	-	-
Recreational	-	-	2	-	-	-	-

Table 7. Type of Athletes

	Dines et al. 2016	Deal et al. 2017	Podesta et al. 2013	Dodson et al. 2010	Rettig et al. 2001	Ford et al. 2016	Frangi-amore et al. 2017
Baseball Pitcher	36	22	16	-	20	21	24
Baseball Position	8	-	11	-	9	10	-
Softball Player	-	1	3	-	-	-	-
Javelin	-	-	-	-	2	-	-
Football Quarterback	-	-	-	6	-	-	-
Other	-	-	4	-	-	-	-

Table 8. Mean Rehabilitation Duration (Days)

	Dines et al. 2016	Deal et al. 2017	Podesta et al. 2013	Dodson et al. 2010	Rettig et al. 2001	Ford et al. 2016	Frangi-amore et al. 2017
Mean Time to Return to Competition	84	82	84	7.5	171.5	-	-
Range Low	35	21	70	1	91	-	-
Range High	168	175	105	23	378	-	-

Table 9. Combined Odds Ratio for PRP vs. Conservative PT Interventions on Return to Play Outcomes

	Primary Analyses, All partial UCL injuries
OR Combined	10.8
SE Combined	0.35
CI Lower	5.47
CI Upper	21.32
Q-Value	1.21
Degrees of Freedom	2
p-value	0.55

Table 10. Sub-Analyses

	Proximal UCL Injuries	Distal UCL Injuries	Grade II UCL injuries
OR Combined	17.56	3.98	11.35
SE Combined	1.16	1.31	0.9
CI Lower	1.81	0.31	1.95
CI Upper	170.72	51.73	66.02
Q-Value	8.92	1.85	9.08
Degrees of Freedom	1	1	1
p-value	0.0028	0.17	0.0026

FIGURES

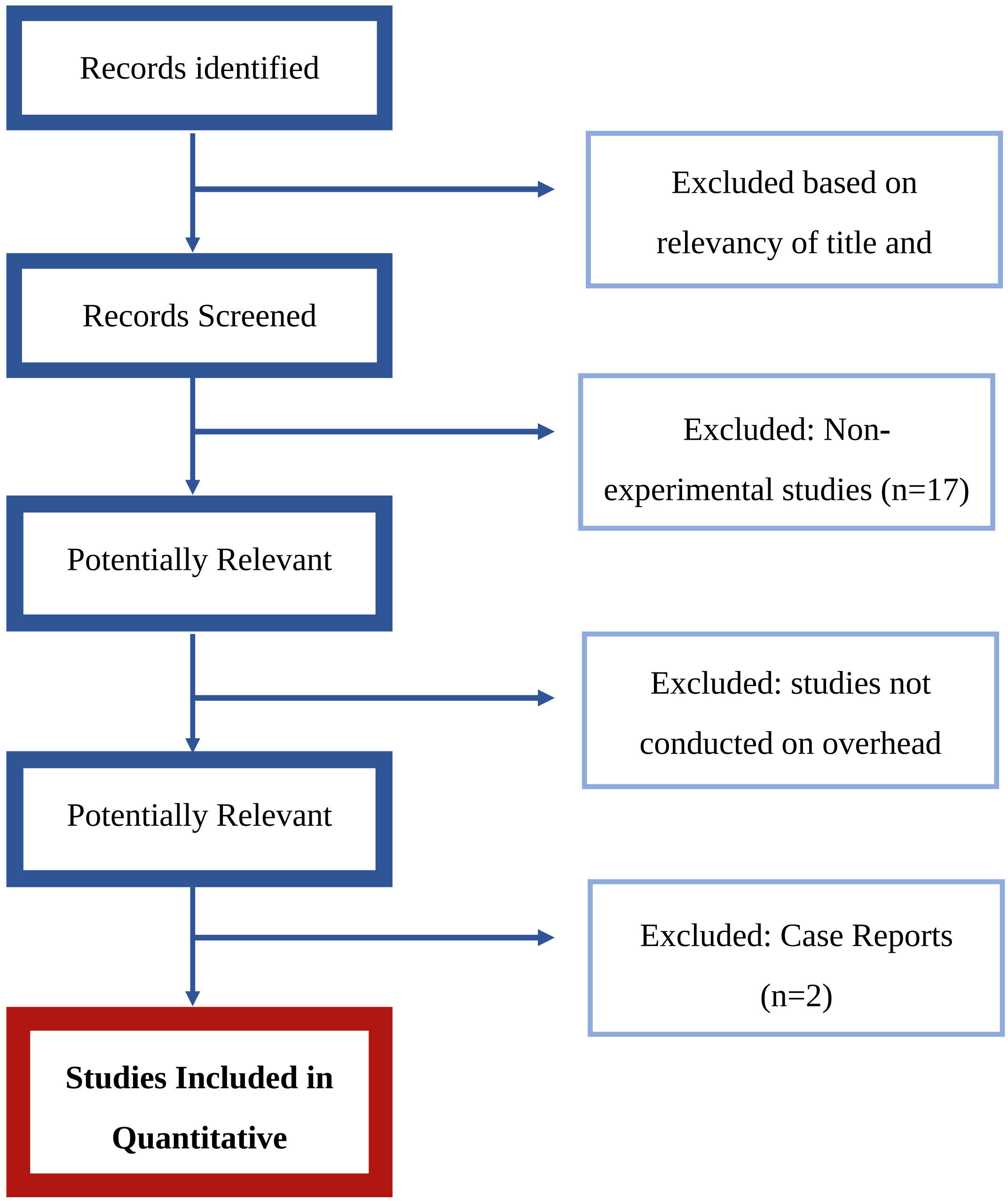

Figure 1. Consort

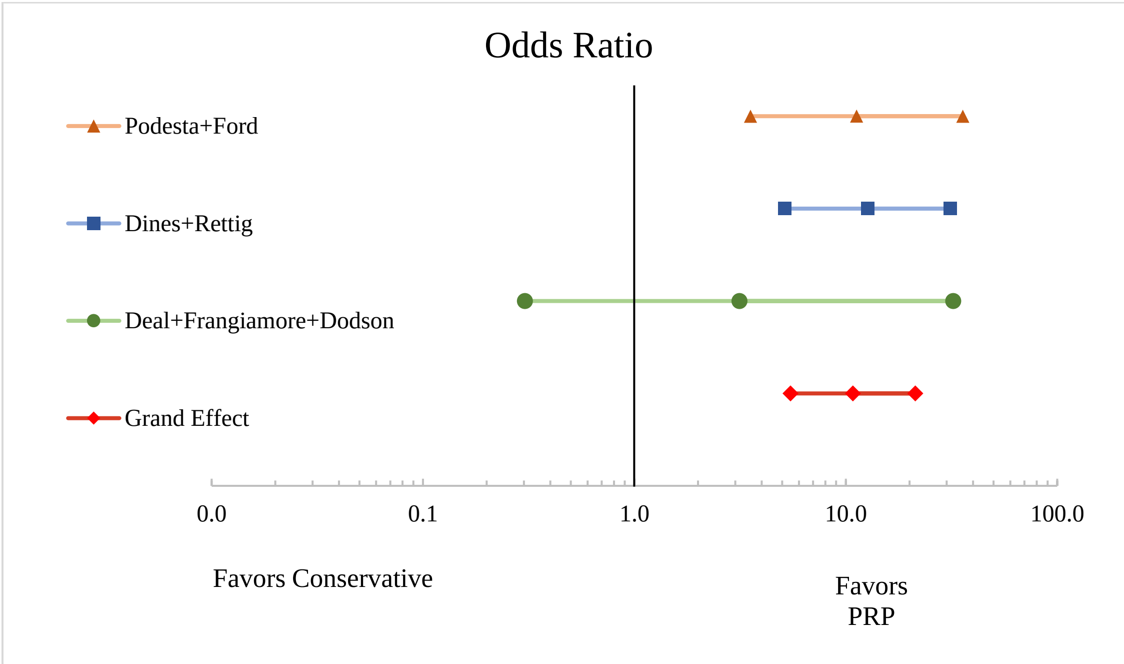

Figure 2. Combined odds ratio for PRP treatment vs. conservative PT for all partial UCL injuries

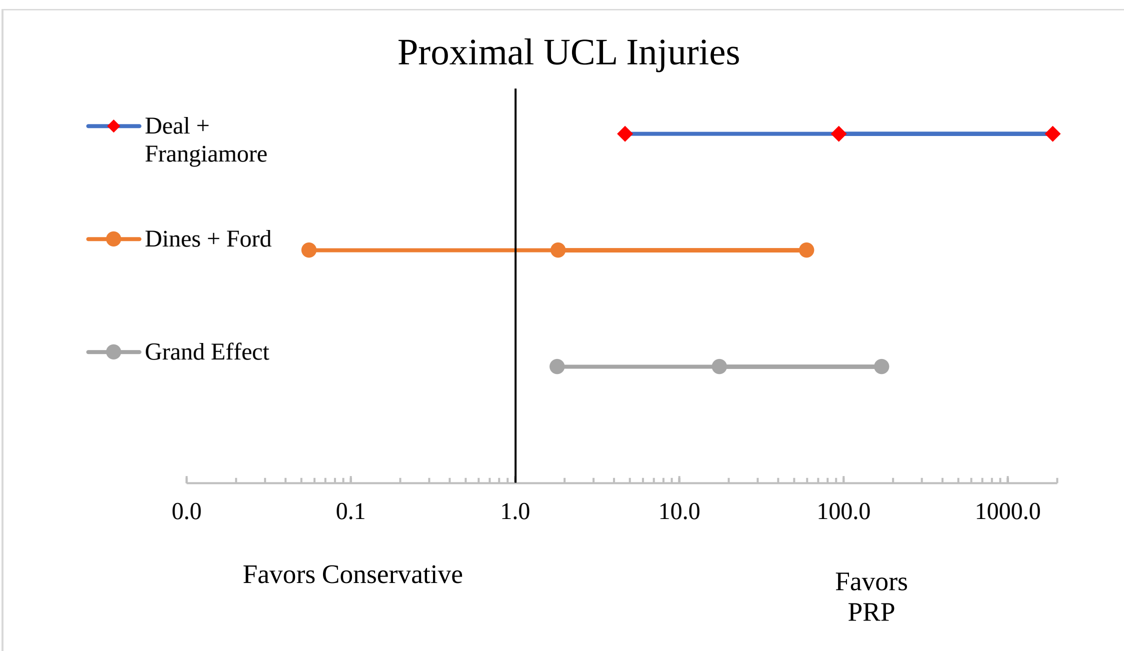

Figure 3. Combined odds ratio for PRP treatment vs. conservative PT for proximal UCL injuries

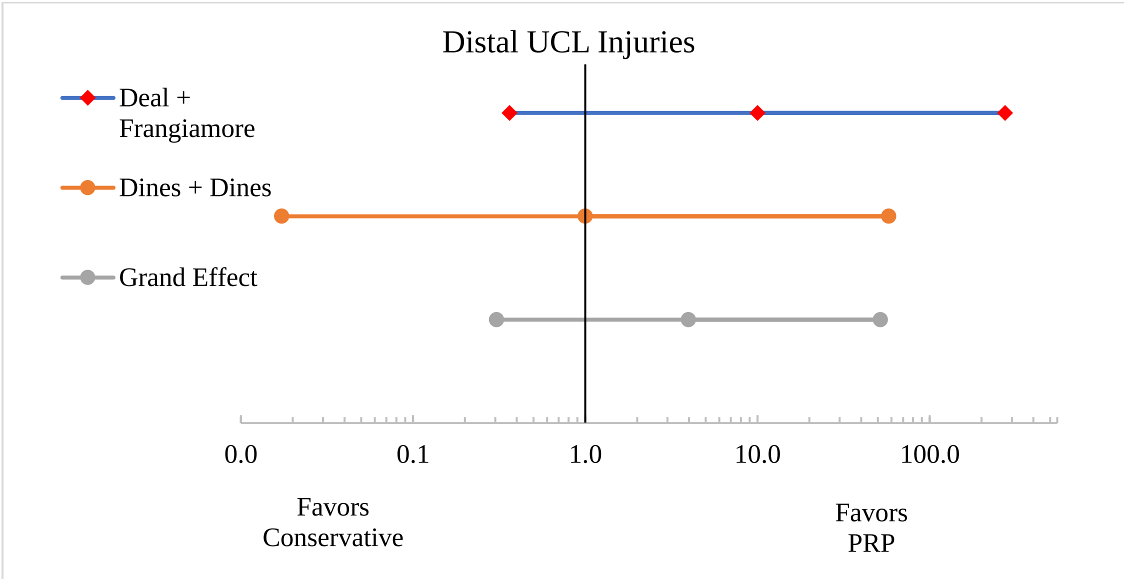

Figure 4. Combined odds ratio for PRP treatment vs. conservative PT for distal UCL injuries

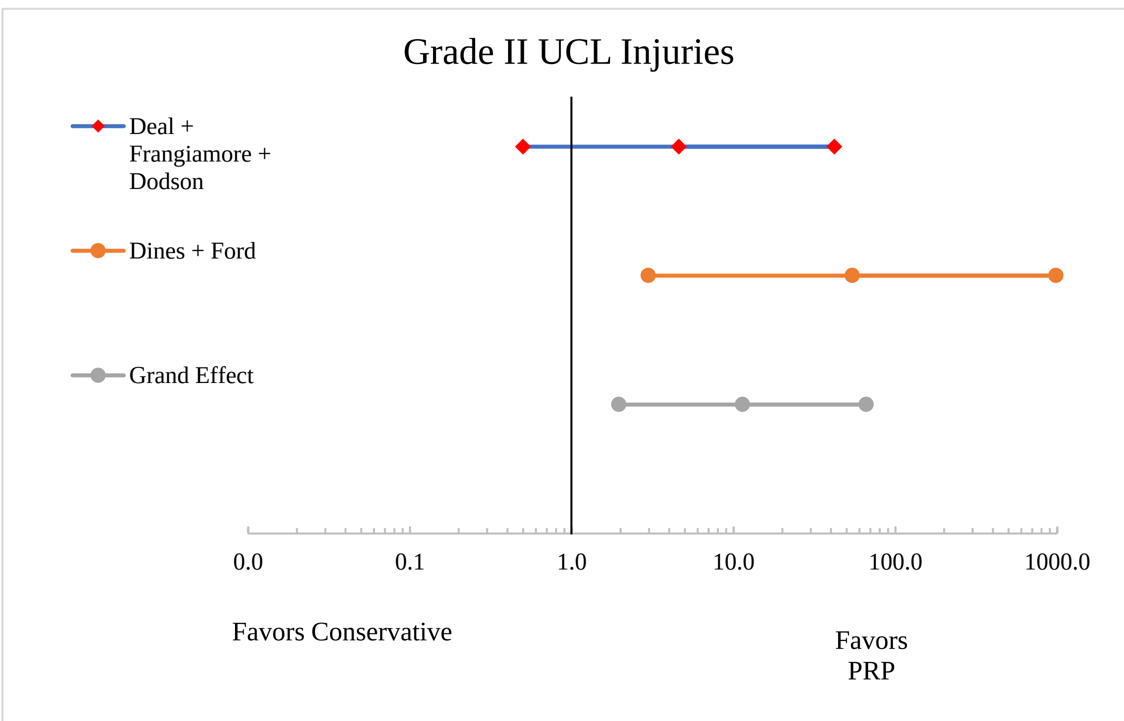

Figure 5. Combined odds ratio for PRP treatment vs. conservative PT for Grade II UCL injuries

APPENDIX: DOWNS AND BLACK CHECKLIST

Aspects	Check list term
Reporting	
1	Is the hypothesis/aim/objective of the study clearly described?
2	Are the main outcomes to be measured clearly described in the introduction or methods section?
3	Are the characteristics of the patients included in the study clearly described?
4	Are the interventions of interest clearly described?
5	Are the distributions of principal confounders in each group of subjects to be compared clearly described?
6	Are the main findings of the study clearly described?
7	Does the study provide estimates of the random variability in the data for the main outcomes?
8	Have all important adverse events that may be a consequence of the intervention been reported?
9	Have the characteristics of patients lost to followup been described?
10	Have actual probability values been reported (e.g., 0.035 rather than <0.05) for the main outcomes except where the probability value is <0.001?
External validity-bias	
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?
13	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?
Internal validity-bias	
14	Was an attempt made to blind study subjects to the intervention they have received?
15	Was an attempt made to blind those measuring the main outcomes of the intervention?
16	If any of the results of the study were based on "data dredging", was this made clear?
17	In trials and cohort studies, do the analyses adjust for different lengths of followup of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?
18	Were the statistical tests used to assess the main outcomes appropriate?
19	Was compliance with the intervention/s reliable?
20	Were the main outcome measures used accurate (valid and reliable)?
Internal validity-confounding	
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?
22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?
23	Were study subjects randomized to intervention groups?
24	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?
26	Were losses of patients to followup taken into account?
Power	
27	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is <5%?
	Amount

Yes=1, No=0, Unable to determine=0