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Complications Related to the Administration of Platelet-Rich Plasma in The Treatment Of Rotator Cuff Lesions: A Critical Review of The Literature

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ABSTRACT

Platelet-rich plasma (PRP) has been used in the conservative treatment of tendinopathies and partial-thickness rotator cuff tears, as well as a biological adjunct during surgical repair. Because it is generally prepared from the patient's own blood, the procedure was initially regarded as low risk, and it was frequently claimed that it did not cause clinically relevant complications. This perception, however, should be interpreted with caution.

Although clinical studies have reported few serious adverse events, exacerbated inflammatory pain, edema, hematoma, reactive bursitis, infection, injuries related to improper needle positioning, structural worsening of the lesion, and shoulder stiffness may occur. Evidence published in 2026 identified an overall incidence of complications similar to that observed with other injections, but a significantly higher frequency of adhesive capsulitis among patients treated with PRP.

PRP should therefore not be considered a risk-free procedure. Its indication should be judicious and accompanied by informed consent, documentation of product composition, a description of the application technique, and post-procedure clinical follow-up.

Keywords: Platelet-rich plasma; PRP, Rotator cuff, Tendinopathy, Injection, Adhesive capsulitis, Complications, Adverse events

INTRODUCTION

As rotator cuff disorders encompass a clinical spectrum ranging from tendinopathic changes without structural disruption to partial-thickness or full-thickness tears. Traditional conservative treatment includes activity modification, physical therapy, therapeutic exercise, analgesia, and, in selected situations, injection procedures.

In this context, platelet-rich plasma has been used to promote tissue repair through the release of growth factors, cytokines, and bioactive proteins contained in platelet granules. Despite its biological plausibility, the clinical efficacy of the procedure remains variable, with outcomes depending on the condition being treated, product composition, injection site, and preparation method.[1-5]

The 2025 American Academy of Orthopaedic Surgeons (AAOS) guideline concluded that routine use of PRP is not

sufficiently supported for the treatment of rotator cuff tendinopathy or partial-thickness tears. Evidence likewise does not support its routine use for conservatively treated full-thickness tears. As an adjunct to surgical repair, platelet-derived products have not consistently improved patient-reported outcomes, although some liquid formulations may reduce the retear rate.[1]

The discussion regarding PRP safety has also evolved. Its autologous origin reduces the risks of immunologic incompatibility and disease transmission, but it does not eliminate risks related to venipuncture, blood handling, centrifugation, product activation, shoulder injection, and the inflammatory response following administration.[2,3]

HETEROGENEITY OF PRP PREPARATIONS

The term 'platelet-rich plasma' does not define a single standardized product. Important variations include:

- final platelet concentration
- presence or absence of leukocytes
- amount of residual red blood cells
- type of anticoagulant used
- use of activating substances
- administered volume
- number of injections
- interval between injections
- anatomic injection site
- use or non-use of ultrasound guidance

The literature describes injections into the glenohumeral joint, subacromial space, subacromial bursa, and directly within or around the affected tendon. There is no definitive consensus regarding the ideal site for partial-thickness rotator cuff tears [5]. This variability directly affects both efficacy and safety. Leukocyte-rich PRP, for example, has a biological profile different from that of leukocyte-poor PRP. Likewise, an intratendinous injection does not necessarily produce the same effects as a subacromial or intra-articular injection.[5,10-12]

Consequently, it is not technically appropriate to consider all PRP preparations equivalent or to assign them a single efficacy and complication profile.

EARLY EVIDENCE SUGGESTING APPARENT SAFETY

Several clinical trials evaluating PRP for rotator cuff disorders did not report serious complications. In a randomized trial comparing PRP with placebo in patients with chronic tendinopathy, the product was not superior in terms of pain, function, quality of life, or range of motion at one-year follow-up.[7]

Another randomized study compared PRP with corticosteroid injection in patients with tendinopathy or partial-thickness

tears. Both treatments produced clinical improvement, and PRP showed an advantage in some short-term outcomes, without a sustained benefit during longer follow-up.[6]

The absence of serious adverse events in these studies contributed to the perception that PRP was highly safe. However, this conclusion must be tempered because many studies had:

- small samples
- limited clinical follow-up
- no uniform definition of adverse events
- a primary focus on efficacy rather than safety
- insufficient reporting of transient inflammatory reactions
- limited power to identify uncommon complications

Thus, the absence of documented complications in a small study does not mean that the intervention is risk-free.

CURRENT EVIDENCE ON COMPLICATIONS

The principal evidence specifically addressing complications was presented by Driscoll et al. in a systematic review and meta-analysis published in 2026.[2]

The authors included 19 randomized clinical trials involving 1,043 patients, of whom 510 received PRP injections. Nine studies reported no complications. In the remaining ten studies, 102 complications were identified, 48 of which occurred in the PRP group.

The overall complication rate was 9.41% in the PRP group and 10.13% in groups receiving other injection treatments, with no statistically significant difference between them. However, patients treated with PRP had a significantly higher frequency of adhesive capsulitis, or frozen shoulder.[2]

The most frequently reported complications were:

- persistent pain
- adhesive capsulitis
- worsening or progression of the rotator cuff lesion
- bursitis
- stiffness and functional loss of the shoulder

No serious adverse events were observed in the included trials. This supports the view that PRP is generally safe, but it does not justify describing it as free of complications. In particular, the higher frequency of adhesive capsulitis should be considered in patient selection, informed consent, and clinical follow-up.[2]

ADHESIVE CAPSULITIS AFTER PRP ADMINISTRATION

Adhesive capsulitis is characterized by progressive pain and limitation of both active and passive shoulder motion, with particularly marked restriction of external rotation. Its course may be prolonged and functionally disabling.

Although it is not a life-threatening complication, it may result in:

- persistent pain
- limitations in activities of daily living
- difficulty with hygiene and dressing
- temporary or prolonged occupational disability
- need for intensive physical therapy
- additional injections
- hydro dilatation
- manipulation under anesthesia
- arthroscopic capsular release in resistant cases

The meta-analysis by Driscoll et al. did not demonstrate an increase in the overall complication rate, but it identified a specific statistical association between PRP used for rotator cuff disorders and a higher frequency of adhesive capsulitis.[2]

This finding should not be confused with studies that investigate PRP as a treatment for patients who already have adhesive capsulitis. These are distinct clinical situations. In one, PRP is evaluated as therapy for established adhesive capsulitis; in the other, adhesive capsulitis is investigated as a complication arising after an injection performed to treat a rotator cuff disorder.

POSSIBLE MECHANISMS OF ADHESIVE CAPSULITIS

Exacerbated inflammatory response

PRP administration is intended to trigger a biological repair response. During the first hours or days after injection, increased pain, edema, and local inflammatory reaction may occur.[3]

In some patients, this response may be more intense or prolonged. Pain causes spontaneous reduction in shoulder movement, resulting in relative immobilization. When this antalgic protection persists, it may favor capsular contracture and progressive stiffness.

A possible pathophysiological cycle is therefore established:
Inflammation -> increased pain -> reduced mobility -> capsular contracture -> greater stiffness and functional limitation.
The association is biologically plausible, although it does not establish that every case of adhesive capsulitis diagnosed after PRP administration was necessarily caused by the procedure.
The following figure illustrates the concepts discussed above.

Salient Visionary Publications

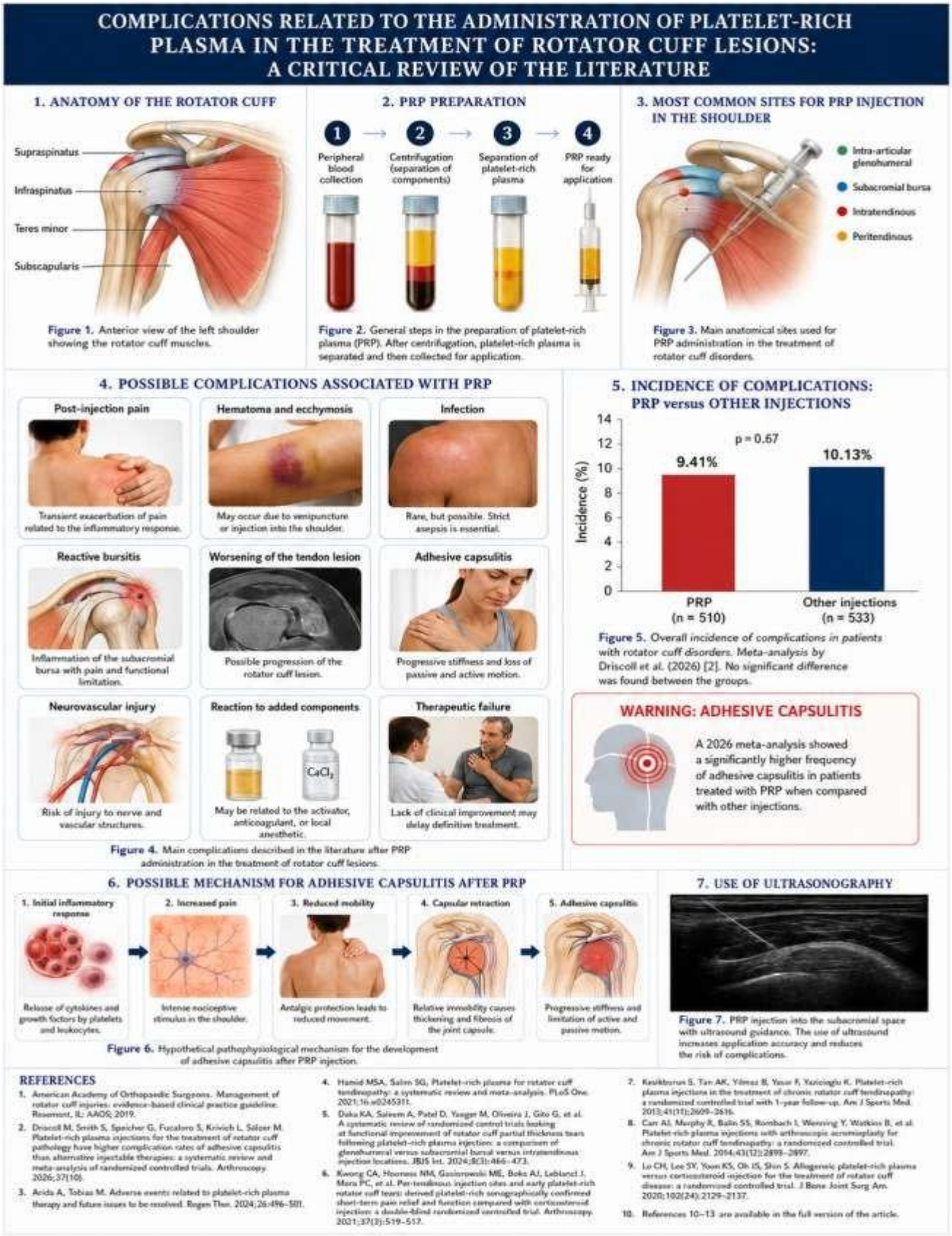

Figure 1 Schematic representation of the possible progression toward adhesive capsulitis after PRP injection in the treatment of rotator cuff disorders.

Presence of leukocytes
Leukocyte-rich PRP contains neutrophils and other cells capable of releasing pro-inflammatory cytokines, metalloproteinases, proteolytic enzymes, and reactive oxygen species.

In an experimental study, Zhang et al. observed that leukocyte-rich PRP could increase catabolic mediators, inflammation, and apoptosis of tendon progenitor cells.[11] Conversely, Lin et al. reported greater proliferative stimulation of human tenocytes exposed to certain leukocyte-rich formulations.[12]

These apparently divergent findings demonstrate that leukocyte effects depend on concentration, lesion stage, the tissue analyzed, and experimental conditions. These laboratory studies do not, by themselves, prove clinical harm, but they support the conclusion that different PRP preparations do not have the same biological behavior.[10-12]

Injection site and technique
Intratendinous injection may produce additional microtrauma, bleeding, and transient increases in local pressure. Subacromial injection may trigger reactive bursitis, whereas intra-articular administration may cause painful synovitis.

Repeated punctures, administration of large volumes, or deposition of the product in an unintended anatomical plane may intensify the inflammatory response. Ultrasound guidance improves procedural accuracy but does not completely eliminate risk.[5]

Individual predisposition
Diabetes mellitus, thyroid dysfunction, previous adhesive capsulitis, preexisting stiffness, severe pain before the procedure, and prolonged periods of immobilization are conditions that may predispose to frozen shoulder.

In these patients, inflammation and pain after injection may act as triggering or contributing factors, even when they are not the sole cause of adhesive capsulitis.

OTHER POSSIBLE COMPLICATIONS

Post-injection pain
Transient exacerbation of pain is among the most commonly expected reactions. It may result from tendon puncture, increased tissue pressure, platelet activation, and the release of inflammatory mediators.[2,3]

It is usually self-limited. However, it becomes clinically relevant when severe, prolonged, or when it prevents early shoulder mobilization.

Edema, ecchymosis, and hematoma
Local edema, ecchymosis, or hematoma may occur as a result of venipuncture or needle introduction into the shoulder. The risk may be increased in patients with coagulopathies or those using anticoagulants or antiplatelet agents.

Infection
The autologous nature of PRP does not prevent contamination. Risk may arise during blood collection, processing, centrifugation, transfer between containers, or administration.

A review of adverse events related to PRP identified post-procedure infection as one of the most relevant complications described in the general literature. Because the product cannot be sterilized in the same manner as an industrially manufactured drug, strict aseptic control throughout all stages is essential.[3]

In the literature specifically addressing the rotator cuff, serious infections are rare and a precise incidence cannot be established. Rarity, however, is not equivalent to impossibility.

Nerve, vascular, or tendon injury
As with any invasive percutaneous procedure, there is a possibility of injury to neural or vascular structures, bleeding, excessive tendon puncture, and injection outside the intended anatomical plane.

Ultrasound guidance reduces the possibility of error but does not replace anatomical knowledge or fully eliminate risk.

Reactions to added components
Autologous PRP has low immunogenicity. Nevertheless, the final product may contain anticoagulants, local anesthetics, calcium chloride, thrombin, or other activating agents.

An adverse reaction may therefore be related to platelets, leukocyte concentration, or substances added during preparation.[3]

Structural worsening or lesion progression
The 2026 meta-analysis identified worsening of the rotator cuff lesion among the reported complications.[2] It is not always possible to determine whether this progression resulted directly from the injection or from the natural history of tendinopathy. Nevertheless, repeated intratendinous punctures, mechanical microtrauma, or premature return to activity may contribute to symptomatic or structural worsening in selected cases.

Therapeutic failure and delay of definitive treatment
Lack of response is not necessarily a biological complication, but it is a clinically relevant outcome. Randomized trials have shown that PRP may not be superior to placebo or other treatment modalities at certain follow-up intervals.[6-8]

Repeated use of PRP in large or full-thickness tears may delay appropriate treatment, allowing tear progression, tendon retraction, muscle atrophy, and fatty infiltration.

For this reason, the AAOS does not recommend routine PRP use for tendinopathy, partial-thickness tears, or conservative treatment of full-thickness rotator cuff tears.[1]

PRP USED DURING SURGICAL REPAIR

In the surgical setting, complications related to PRP must be distinguished from those resulting from the operation itself, anesthesia, immobilization, and rehabilitation.

A randomized study found that adding PRP to acromioplasty did not improve clinical outcomes and produced histological changes characterized by reduced cellularity, decreased vascularity, and increased apoptotic cells in tendon specimens.[8]

Conversely, a more recent randomized study showed that leukocyte-poor PRP applied at the tendon-bone interface reduced the retear rate after arthroscopic repair of tears smaller than 3 cm, although it did not produce clinically relevant improvement in pain or patient-reported functional outcomes.[13]

These findings confirm that PRP may have different effects depending on formulation, timing of administration, and clinical context. A possible reduction in retear rate should not be confused with guaranteed functional recovery or absence of complications.

INFORMED CONSENT AND FOLLOW-UP

Patients should be informed that PRP:

- does not have uniform efficacy for all forms of rotator cuff disease
- is not routinely recommended by current guidelines
- may cause transient pain and inflammation
- may cause hematoma, bursitis, infection, and puncture-related injury
- may be associated with adhesive capsulitis
- does not guarantee tear healing
- may not prevent subsequent surgery

The statement that PRP is autologous is not sufficient to characterize its risks adequately. Whenever possible, the medical record should document:

- type of PRP used
- platelet concentration
- presence or absence of leukocytes
- substances used for activation
- administered volume
- number of injections

- anatomic injection site
- use of ultrasound guidance
- post-procedure instructions

Progressive pain, loss of external rotation, and reduced passive motion after injection should be recognized early as possible signs of adhesive capsulitis.

MEDICO-LEGAL CONSIDERATIONS

When assessing a causal relationship between PRP administration and a subsequent complication, the following should be considered:

- functional status of the shoulder before the procedure
- presence of previous stiffness or passive-motion restriction
- diabetes, thyroid disorders, or previous adhesive capsulitis
- diagnosis and extent of the rotator cuff lesion
- composition of the PRP product
- site, volume, and number of injections
- use or non-use of ultrasound guidance
- interval between injection and symptom onset
- intensity and duration of the inflammatory response
- measures adopted after clinical deterioration
- evolution of imaging findings
- possibility of natural disease progression

Temporal sequence alone does not automatically establish causation. Conversely, it is also scientifically inappropriate to exclude a causal relationship merely on the assumption that PRP is absolutely safe.

Available evidence demonstrates that the procedure may be associated with adhesive capsulitis and other complications. In individual cases, PRP may act as a direct cause, trigger, or contributing factor, particularly when intense inflammatory pain begins soon after injection and is followed by progressive loss of active and passive shoulder motion.

CONCLUSION

The scientific literature supports the conclusion that platelet-rich plasma administration should not be considered free of complications.

Although serious events are rare and the overall complication rate is similar to that observed with other injection treatments, persistent pain, exacerbated inflammation, bursitis, hematoma, infection, worsening of the tendon lesion, and shoulder stiffness may occur.

The principal complication specifically highlighted by recent evidence is adhesive capsulitis. The meta-analysis published in 2026 demonstrated a higher frequency of frozen shoulder among patients who received PRP for rotator cuff disorders, despite finding no significant difference in the overall incidence of complications.

The association is biologically plausible because the procedure may cause inflammation, pain, and reduced mobility. Nevertheless, causation must be assessed individually, taking into account preexisting conditions, product composition, technique, and temporal evolution.

Given the heterogeneity of preparations and the lack of uniform benefit, PRP administration should be preceded by careful indication, specific informed consent, and adequate technical documentation.

Persistent pain and progressive loss of motion after the procedure should be promptly investigated to allow early diagnosis and treatment of possible adhesive capsulitis.

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