Dear Reviewers,

Thank you for your time and thoughtful review of our manuscript "**The role of platelet-rich plasma in the treatment of rotator cuff tendinopathy".**

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Manuscript NO: 83526
Provenance and peer review: Invited Manuscript; Externally peer reviewed

The reviewer's comments are included in standard font, while the authors' responses are italicized. Again, thank you for your time and consideration.

Reviewer 1.

General Comments

very good narrative review

Thank you for your comment. No changes were made to the text.

Reviewer 2.

Authors The review displays the role of platelet-rich plasma in treating rotator cuff tendinopathy suggesting its future potential role in patients with contraindications to corticosteroids or with an inadequate healing process.

Thank you for your comment. No changes were made to the text.

It provides useful and updated information on the matter. It is well-written and requires minor revisions. I recommend also considering the following remarks:

1. R63: Please correct the quoting numbers

Thank you for your comment. We have modified the text accordingly.Aging can promote the development of many tendinopathic and avascular changes in RC, altering its intrinsic healing capacity and increasing failure rates after surgical or non-surgical treatment[2]. RC lesions include a wide range of pathological states, …]

2. R68-69 rephrase

   Thank you for your comment. We have modified the text accordingly.

   Full-thickness RC tears represent the end stage of RC pathology and have an incidence of approximately 20% in adults. The prevalence of these tears increases to over 50% after the age of 60 years[4–6].

   To ensure accurate management and effective communication among clinicians, it is necessary to establish a clear definition for tendinitis and tendinosis[7,8].

3. R78: The verb should be "include"

   Thank you for your comment. We have modified the text accordingly.

   "New biological therapies aim to improve tendon healing as part of the ongoing development for the treatment of RC tendinopathy. These therapies include platelet-rich plasma (PRP) injections, growth factors, mesenchymal stem cells, adipose-derived, and bone marrow aspirate concentrate.

4. R103: rephrase

   Thank you for your comment. We have modified the text accordingly.

   Furthermore, sleep disturbances may be characterized by discomfort in the mid-lateral region of the humerus or the anterolateral aspect of the acromion[7,8]. Indeed, partial tears are usually more painful than full-thickness[17].

5. R108: I suggest replacing the word "repair" from the syntax "tendon repair" with another one

   Thank you for your comment. We have modified the text accordingly.

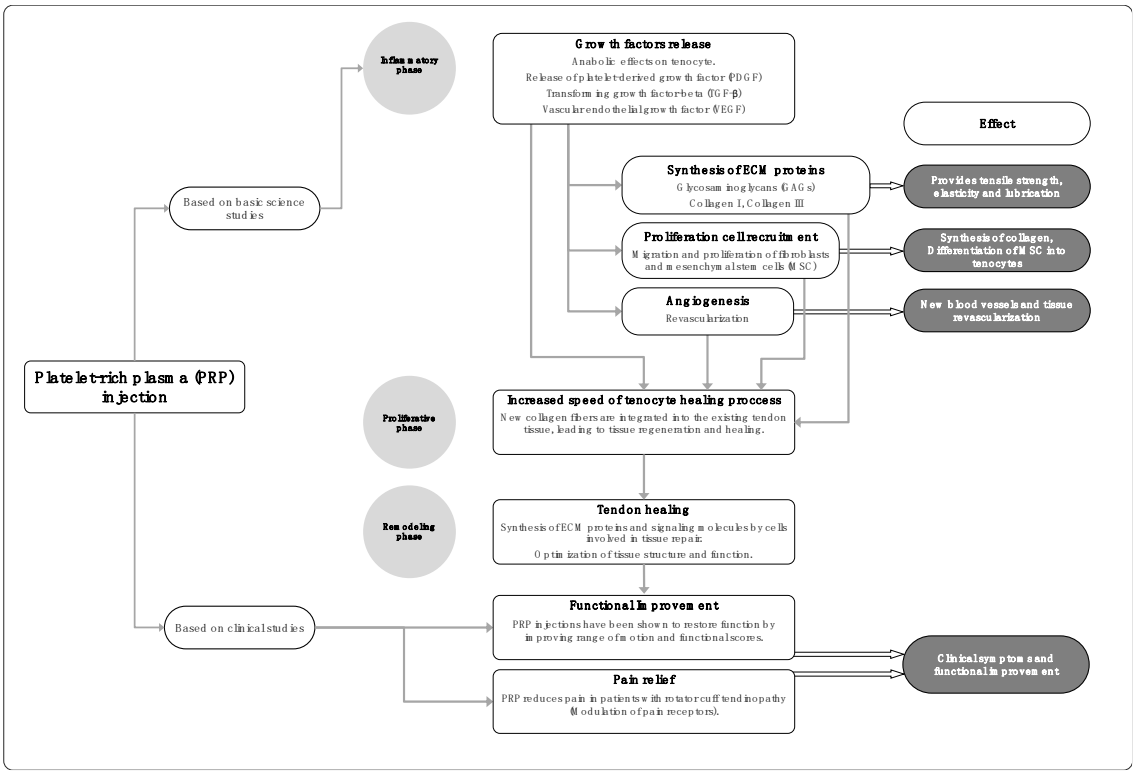
Regardless of the type of treatment applied, tendon healing occurs in three overlapping phases: inflammatory, proliferative, and remodeling[18].

6. R115: rephrase

   Thank you for your comment. We have modified the text accordingly.
   During the proliferative phase, mesenchymal stem cells (MSCs) migrate and differentiate, influenced by platelet-derived growth factors[18]. The cells involved in tissue repair, such as fibroblasts and MSCs, proliferate and synthesize extracellular matrix (ECM) proteins[19–23]. Fibroblasts that migrate during this phase generate type III collagen and glycosaminoglycans (GAGs), which enhances the tissue's tensile strength, elasticity, and lubrication[24,25].

7. R117: I suggest explaining a bit about the role of "tenocyte" • I recommend explaining more about the PRP mechanism - a scheme could help to clarify the information and the way it attenuates the symptoms

   Thank you for your comment. We have modified the text accordingly.
   Tenocytes become the primary cell type responsible for producing and maintaining the ECM proteins that provide the necessary structure and mechanical properties to form new tissue[19].
   Collagen cross-linking increases during the remodeling phase, and collagen type III is reabsorbed and replaced, resulting in an improved organization[25]. During this stage, tenocytes produce ECM proteins and other signaling molecules that amplify the upregulation of collagen type I gene expression and optimize the structure and function of the newly formed tissue[19,20,22,23].



8. R231- rephrase

   Thank you for your comment. We have modified the text accordingly.

   The study showed that patients who underwent PRP injections reported considerable improvements in pain and disability[58].

9. R354- rephrase

   Thank you for your comment. We have modified the text accordingly.

   High-quality evidence supports the use of PRP after RC repair[76]. However, the clinical evidence on the benefits of PRP in the nonoperative treatment of RC disorders is inconsistent

10. R659 - please correct the description of table 2 specifying the studies that were compared to PRP studies

    Thank you for your comment. We have modified the text accordingly.

TABLE 2. Randomized controlled trials comparing platelet-rich plasma versus corticosteroid injections for rotator cuff tendinopathy.

References	Level of evidence	Design	Groups (n)	Dosis/Quantity	Outcomes measure	Follow-up	Conclusions
Barreto et al. 2019[81]	I	Subacromial PRP injections versus CI	51 patients. (26) PRP, (25) CI	1 / ~ 3 mL	DASH, UCLA-SRS, CMS	3months, 6 months	No statistically significant differences
Dadgostar et al. 2021[65]	I	Ultrasound guided PRP injections versus CI	58 patients (30) PRP, (28) CI	1 / 3 ml intra-articular, 3 mL intratendinoeus.	VAS, ROM, WORC, DASH, US supraspinatus thickness	3 months	PRP with similar results to CI
Kwong et al. 2021[72]	I	Ultrasound-guided Leokocyte-poor PRP injection versus CI	99 patients (47) PRP, (52) CI	1 / 3 – 5 mL intratendineous (non-specific) and the rest at the subacromial space.	VAS, ASES score, and WORC	6, 12, 48 weeks.	The PRP group showed superior improvement in pain and function at short-term follow-up, without benefit at long-term follow-up.
Ibrahim et al. 2018[82]	I	Ultrasound guided subacromial PRP vs CI	30 patients (15 PRP), (15) CI	1/ 2 mL	VAS, SDQ, ROM Clnical tests, US findings.	8 weeks	Both groups showed significant improvement. PRP is safe and can be used for PRCT.
Jo et al. 2019[83]	I	Ultrasound guided allogenic PRP vs CI	60 patients (30 PRP), (30) CI	1/ 4 ml.	VAS, CMS, ASES, DASH, RC strength, ROM.	1, 4, 12, 24 weeks.	PRP reduced pain and improved overall function at 6 months. DASH score, overall function, and external rotation were significantly better in the PRP group.
Pasin et al. 2019[84]	I	PRP vs CI vs Exercise	60 patients (30 PRP), (30) CI	1/ 4 mL	VAS,QuickDASH, UCLA SRS, SF-36	3, 8 weeks.	PRP had better scores than CI and Physical Therapy even in a long time.
Sabaah et al. 2020[85]	I	Prolotherapy versus CI and PRP.	40 patients (20) PRP, (20) CI	2/ 5 mL	VAS, WORC-Index, ROM and US findings	12 weeks	Prolotherapy was superior. PRP improve tendon healing.
Sari et al. 2019[86]	I	Ultrasound guided PRP versus CI, Prolotherapy and Lidocaine.	60 patients (30 PRP), (30) CI	1/ 5 mL	VAS, ASES and WORC	3, 12, 24 weeks	CI were better at 3 weeks. NO difference at 12 weeks. PRP had better ooutcomes at 24 months.