Indications on appropriate clinical use of blood components for topical use

Second Edition
June 2021

INDICATIONS ON APPROPRIATE CLINICAL USE OF BLOOD COMPONENTS FOR TOPICAL USE

INTRODUCTION

THE WORKING GROUP AND ITS AIMS

Pursuant to Ministry of Health Decree (MHD) of 2nd November, 2015 (Ordinary Supplement N. 300 of Official Journal of 28th December, 2015) "Provisions relative to quality and safety standards of blood and blood components", the Italian National Blood Centre (CNS) set up and coordinated a multidisciplinary working group (MWG) the aims of which was to provide and periodically update the list of clinical conditions and grade of recommendations regarding appropriate clinical use of blood components for topical use based on the published scientific evidence regarding different clinical, medical and surgical settings.

The MWG, formed with Decree of the Director General of the CNS Prot. n. 0848.CNS.2016 of 13/04/2016, has recently changed its composition, and in addition to the scientific societies already signatories of this technical document, now includes the Italian Ophthalmological Society - SOI.

As part of its mandate, the MWG performs:

- the systematic review of scientific literature with the aim of verifying the grade of appropriateness of already known clinical conditions as well as new ones;
- the identification, through surveys, of those areas of application which, not falling under the conditions regulated by the transfusion regulations currently in force, need to be consolidated by clinical studies;
- the establishment of a multidisciplinary network of professionals with specific expertise in the production and clinical use of blood components for topical use, in order to timely update the list of clinical conditions based on the respective grades of recommendation/evidence.

The examination of the scientific literature produced up to 31/12/2020, with particular reference to the most recent meta-analyses and systematic reviews, showed that studies conducted in certain settings on the topical use of blood components had a high level of risk bias. In particular, many clinical studies appear to be neither well designed nor comparable, with insufficient statistical power also due to differences in the choice of criteria for the inclusion of patients and in the timing of treatment. On the other hand, many indications are already part of currently used clinical practices, for which scientific evidence suggests that the topical use of these products as alternative or supportive therapies in certain settings is not only efficacious but also cost-effective.

BLOOD COMPONENTS FOR TOPICAL USE

CLINICAL USE

Blood components for topical use are being increasingly utilised in different specialized medical and surgical fields with the following methods:

- application on skin or mucous surfaces - topical use
- intra-tissue or intra-articular infiltration - infiltrative use
- local application in surgical fields - surgical use.

TYPES OF PRODUCTS

The blood components for topical use utilised for the clinical conditions mentioned in this document, are those specified in the MoH Decree of 1st August 2019 - Amendment of the MoH Decree of 2nd November 2015 "Provisions relative to quality and safety standards of blood and blood components" – in which a distinction is made between platelet-derived products, plasma-derived products and serum-based products.

For the production and utilisation of blood components for topical use, authorised medical devices of Class IIa or higher must be used pursuant to current legislation on medical devices.

LAWS IN FORCE

Thanks to their regenerative propriety and the capacity to regenerate tissues and to facilitate the healing of skin and mucous lesions, blood components for topical use are widely utilised in various clinical settings in both private and public health facilities.
Patients can be treated while hospitalised (ordinary hospitalisation, day-hospital) or as outpatients or in day-surgery. They can be treated in public health facilities, both accredited and non-accredited private facilities, and in medical and dental surgeries.
Allogeneic and autologous blood components for topical use are prepared within Blood Establishments (BEs) and their peripheral organisational sites in compliance with the current legislation regarding their collection, preparation, biological qualification (when foreseen), storage, and distribution.
Autologous blood components for topical use can be prepared in accredited and non-accredited private health care facilities within the framework of a specific agreement between the aforementioned health care facilities and the local public health care facility where the BE is located, in compliance with Annex X, Point E of MoH Decree of 1st August 2019.
The BEs ensure the traceability of the processes and products and are responsible for all haemovigilance activities regarding blood components for topical use whether prepared and used directly by the BEs or prepared and used by public health facilities or both accredited and non-accredited private facilities under the provisions of an agreement with the BE in question.

Pursuant to paragraph 3, Art. 3 of MoH Decree of 1st August 2019, for those recommendations still not consolidated by the available scientific evidence either due to the type of production or the utilisation of blood components for topical use not specified in the laws in force, specific clinical trials must be conducted in accordance with best clinical practices and the involvement of BEs and all health facilities that will use the products. The RBCCs shall inform the CNS when the trials start and shall update on the results obtained.

As regards providing therapeutic treatments that foresee the utilisation of blood components for topical use, in Annex 4D of the Decree of the Prime Minister *"Definition and updating of the essential levels of care, referred to in Article 1, paragraph 7, of Legislative Decree of 30th December 1992, N. 502"* of 12th January, 2017 regarding specialised outpatient services, the following codes were introduced:

- 99.07.2 - APPLICATION ON SKIN OR MUCOUS SURFACES;
- 99.07.3 - INTRA-TISSUE, INTRA-ARTICULAR INFILTRATION OR LOCAL APPLICATION IN SURGICAL FIELDS.

For the application of the above-mentioned codes, the Decree of the Prime Minister of 12th January, 2017 refers to note n. 89 (Annex 4D of the Decree of the Prime Minister of 12th January, 2017) that reads: Deliverability conditions as specified in the Decree through the implementation of Articles 3 and 21 of Law 219/2005.

CLASSIFICATION OF CLINICAL CONDITION

The classification of clinical conditions for the utilisation of blood components for topical use stems from the systematic evaluation of available scientific literature, conducted according to the methods described in Appendix 1.

For the purposes of this document, the term appropriateness is intended as the proper or correct utilisation of blood components for topical use in specific clinical and health settings, as well as criteria of efficacy, safety and effectiveness based on supporting scientific evidence.

After closely examining the available scientific literature three groups of clinical conditions were identified:

1. Clinical conditions for the use of blood components for topical use based on **strong recommendations.**
   - ✓ Clinical conditions with **grade of recommendation 1B** (Table I, Appendix 1): strong recommendations, likely to apply to most patients.

2. Clinical conditions for the use of blood components for topical use based on **weak recommendations**.
   - ✓ Clinical conditions with **grade of recommendation 2B** (Table I, Appendix 1): Weak recommendation; alternative approaches likely to be better for some patients under certain circumstances.

3. Clinical conditions for the use of blood components for topical use based on **very weak recommendations**.
   - ✓ Clinical conditions with **grade of recommendation 2C** (Table I, Appendix 1): Very weak recommendations; other alternatives may be equally reasonable.

TABLE OF CLINICAL CONDITIONS AND GRADE OF RECOMMENDATION

CLINICAL CONDITIONS	GRADE OF RECOMMENDATION
DIABETIC FOOT ULCERS (for cycles of 12 applications)	**1B**
CHRONIC ULCERS AND WOUNDS (for cycles of 12 applications)	**1B**
BURN INJURIES	**1B**
GRADE 1-3 KNEE AND HIP OSTEOARTHRITIS ACCORDING TO THE KELLGREN-LAURENCE SCALE (for cycles of 3 applications)	**1B**
TEMPOROMANDIBULAR JOINT OSTEOARTHRITIS (for cycles of 3 applications)	**2B**
ANKLE OSTEOARTHRITIS (for cycles of 3 applications)	**2B**
TREATMENT OF PSEUDOARTHRITIS	**2B**
RECONSTRUCTION OF ANTERIOR CRUCIATED TENDON	**2B**
TREATMENT OF ANTERIOR CRUCIATE LIGAMENT LESIONS	**2B**
TREATMENT OF ROTULAR TENDONS DISORDERS	**2B**
INFILTRATION TREATMENT OF EPICONDYLITIS	**2B**
TREATMENT OF ACHILLES TENDON LESIONS	**2B**
ROTATOR CUFF REPAIR	**2B**
OTHER BONE, MUSCLE, AND TENDON DISORDERS (e.g. PLANTAR FASCIITIS)	**2B**
MAXILLARY SINUS LIFT	**2B**
PERIDONTAL REGENERATION	**2B**
COADJUVANT TREATMENT IN POST-EXTRACTIVE ALVEOLAR REGENERATION	**2B**
COADJUVANT HEALING TREATMENT FOLLOWING POST-EXTRACTIVE AND IMPLANT SURGERY IN PATIENTS WITH SYSTEMIC DISEASES	**2B**
ORAL SURGERY (IMPACTED TEETH REMOVAL, EXERESIS OF CYSTIC LESIONS) TO ENHANCE THE EPITHELISATION OF WOUND AND TO ACCELERATE THE FORMATION OF THE MUCOSAL SEAL	**2B**
ORAL SURGERY IN PATIENTS IN IV BISPHOSPHONATES AND ANTI-ANGIOGENIC THERAPY	**2B**
SURGICAL EXERESIS OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ)	**2B**
IMPLANT OPERATIONS	**2B**
BONE GRAFT AND REGENERATION OPERATIONS TO ENHANCE THE HEALING OF SOFT TISSUES AND COADJUVANT OF GRAFT MATERIALS	**2B**
DRY EYE SYNDROME	**2B**
OCULAR SURFACE BURNS	**2B**
LESIONS AND ULCERS OF THE CORNEAL SURFACE	**2B**
TREATMENT OF EARLY ANDROGENETIC ALOPECIA	**2B**
TREATMENT OF EARLY ALOPECIA AREATA	**2B**
TREATMENT OF SCARRING DISEASES	**2B**
GRADE 4 KNEE AND HIP OSTEOARTHRITIS ACCORDING TO THE KELLGREN-LAURENCE SCALE (for cycles of 3 applications)	**2B**
REGENERATION OF INTERVERTEBRAL DISCS	**2C**
ANTI-AGEING PLASTIC SURGERY	**2C**
TREATMENT OF MALE AND FEMALE GENITAL LICHEN	**2C**
TREATMENT OF ORAL LICHEN	**2C**

CONCLUSIONS

This document is the result of a shared, organic and systematic evaluation of the available scientific literature with the aim of updating therapeutic indications on the clinical use of blood components for topical use in various clinical, medical and surgical settings.

Both the list of clinical conditions and the grade of evidence will be periodically updated and revised taking into account new available scientific evidence on the subject.

The evaluation of the scientific evidence currently available shows that several clinical trials provided inadequate data for comparison and were statistically weak due to the differences in the choice of patient inclusion criteria, in the timing of the treatment, and in the clinical outcomes taken into account.

Therefore, it is desirable that more and better production of scientific evidence be encouraged based on well-designed and adequately powered randomized clinical trials with a low risk bias, also through the close collaboration between blood establishments and the health facilities that utilise blood components for topical with the active support of the scientific societies in question.

APPENDIX 1 - APPROACH TO GRADES OF RECOMMENDATIONS

For the definition of the grade of recommendation and the scientific evidence in the clinical conditions reported in literature, the Consensus Conference of the American College of Chest Physicians of 2004[1] was adopted. The grade of recommendation is expressed in Arab numbers (1, 2), depending on the strength, and in letters (A, B, C), according to the evidence examined and the type of studies conducted (Table 1).

Table 1 - Grade of recommendation

GRADE OF RECOMMENDATION	CLARITY OF RISK/BENEFIT	METHODOLOGICAL STRENGTH OF SUPPORTING EVIDENCE	IMPLICATIONS
1A	*Clear*	*RCTs without important limitations.*	*Strong recommendation; can apply to most patients in most circumstances without reservation.*
1C+	*Clear*	*No RCTs but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies.*	*Strong recommendation; can apply to most patients in most circumstances.*
1B	*Clear*	*RCTs with important limitations (inconsistent results, methodological flaws).*	*Strong recommendations; likely to apply to most patients.*
1C	*Clear*	*Observational studies.*	*Intermediate-strength recommendation; may change when stronger evidence is available.*
2A	*Unclear*	*RCTs without important limitations.*	*Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values.*
2C+	*Unclear*	*No RCTs but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies.*	*Weak recommendation; best action may differ depending on circumstances or patients' or societal values.*
2B	*Unclear*	*RCTs with important limitations (inconsistent results, methodological flaws).*	*Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.*
2C	*Unclear*	*Observational studies.*	*Very weak recommendations; other alternatives may be equally reasonable.*

[1] Guyatt G, Schünemann HJ, Cook D, et al. Applying the grades of recommendation for antithrombotic and thrombolytic therapy. Chest 2004; 126: S179-87.

Literature published up until 30th December 2020, was analysed.

The evaluation of the scientific literature was conducted starting with the articles supplied by scientific societies with representatives who participated in the MWG as well as articles from PubMed/Medline, Cochrane and Call Detail Recording (CDR) databases. The research was conducted with the use of additional restrictions in order to exclude those which did not meet the inclusion criteria.

In particular, the following types of scientific articles were examined:

- Cochrane Systematic Reviews;
- Systematic Reviews, meta-analysis and reviews;
- Controlled clinical trials, randomized clinical trials and observational studies published after the last systematic review/ meta-analysis, when available.

The examined articles were divided according to the clinical condition or the medical/surgical setting.

After the analysis of each single article, the relative level of evidence regarding the therapeutic efficacy of blood components for topical use was extracted; subsequently, where sufficient evaluation elements were available the grade of recommendation resulting from the aforementioned levels of evidence was formulated.
When discrepancies in the conclusions of the studies examined were found, the grade of recommendation was formulated taking into account methodology, and the limitations and date of publication of each article analysed.
At present, for certain clinical conditions, there are no clinical studies meeting the criteria adopted for the purpose of this document.
However, the authors acknowledge that when it comes to the clinical utilisation of blood components for topical use, strong recommendation may not always apply to all patients in all circumstances, and that certain weaker recommendations could be affective in some patients and some circumstances, for example where alternative therapies do not exist.

2020

Ali M, Benjamin B, Jain N, Malviya A. Does Platelet-rich Plasma Augmentation Following Hip Arthroscopy Improve Outcomes: A Systematic Review. Hip Pelvis. 2020 Jun;32(2):70-77. doi: 10.5371/hp.2020.32.2.70.

Alkhatib N, Salameh M, Ahmed AF, Alkaramany E, Ahmed G, Mekhaimar MM, Alsaei J. Platelet-Rich Plasma Versus Corticosteroids in the Treatment of Chronic Plantar Fasciitis: A Systematic Review and Meta-analysis of Prospective Comparative Studies. J Foot Ankle Surg. 2020 May-Jun;59(3):546-552. doi: 10.1053/j.jfas.2019.10.003.

Belk JW, Kraeutler MJ, Thon SG, Littlefield CP, Smith JH, McCarty EC. Augmentation of Meniscal Repair With Platelet-Rich Plasma: A Systematic Review of Comparative Studies. Orthop J Sports Med. 2020 Jun 17;8(6):2325967120926145. doi: 10.1177/2325967120926145.

Brewer CF, Smith A, Miranda BH. The use of platelet-rich products for skin graft donor site healing: a systematic review and meta-analysis. J Plast Surg Hand Surg. 2020 Nov 15:1-8. doi: 10.1080/2000656X.2020.1846544.

Catapano M, Catapano J, Borschel G, Alavinia SM, Robinson LR, Mittal N. Effectiveness of Platelet-Rich Plasma Injections for Nonsurgical Management of Carpal Tunnel Syndrome: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Arch Phys Med Rehabil. 2020 May;101(5):897-906. doi: 10.1016/j.apmr.2019.10.193.

Cavendish PA, Everhart JS, DiBartola AC, Eikenberry AD, Cvetanovich GL, Flanigan DC. The effect of perioperative platelet-rich plasma injections on postoperative failure rates following rotator cuff repair: a systematic review with meta-analysis. J Shoulder Elbow Surg. 2020 May;29(5):1059-1070. doi: 10.1016/j.jse.2020.01.084.

Chen Z, Wang C, You D, Zhao S, Zhu Z, Xu M. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: A meta-analysis. Medicine (Baltimore). 2020 Mar;99(11):e19388. doi: 10.1097/MD.0000000000019388.

Davey MS, Hurley ET, Withers D, Moran R, Moran CJ. Anterior Cruciate Ligament Reconstruction with Platelet-Rich Plasma: A Systematic Review of Randomized Control Trials. Arthroscopy. 2020 Apr;36(4):1204-1210. doi: 10.1016/j.arthro.2019.11.004.

de Andrade ALL, Sardeli AV, Garcia TA, Livani B, Belangero WD. PRP does not improve the objective outcomes of anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2020 Nov 9. doi: 10.1007/s00167-020-06348-z.

Evans A, Ibrahim M, Pope R, Mwangi J, Botros M, Johnson SP, Al Kassis S. Treating hand and foot osteoarthritis using a patient's own blood: A systematic review and meta-analysis of platelet-rich plasma. J Orthop. 2020 Jan 28;18:226-236. doi: 10.1016/j.jor.2020.01.037.

Evans AG, Mwangi JM, Pope RW, Ivanic MG, Botros MA, Glassman GE, Pearce FB Jr, Kassis S. Platelet-rich plasma as a therapy for androgenic alopecia: a systematic review and meta-analysis. J Dermatolog Treat. 2020 May 26:1-14. doi: 10.1080/09546634.2020.1770171.

Garcia FL, Williams BT, Polce EM, Heller DB, Aman ZS, Nwachukwu BU, Nho SJ, Chahla J. Preparation Methods and Clinical Outcomes of Platelet-Rich Plasma for Intra-articular Hip Disorders: A Systematic Review and Meta-analysis of Randomized Clinical Trials. Orthop J Sports Med. 2020 Oct 29;8(10):2325967120960414. doi: 10.1177/2325967120960414.

Gazendam A, Ekhtiari S, Bozzo A, Phillips M, Bhandari M. Intra-articular saline injection is as effective as corticosteroids, platelet-rich plasma and hyaluronic acid for hip osteoarthritis pain: a systematic review and network meta-analysis of randomised controlled trials. Br J Sports Med. 2021 Mar;55(5):256-261. doi: 10.1136/bjsports-2020-102179.

Gentile P, Garcovich S. Systematic Review of Platelet-Rich Plasma Use in Androgenetic Alopecia Compared with Minoxidil®, Finasteride®, and Adult Stem Cell-Based Therapy. Int J Mol Sci. 2020 Apr 13;21(8):2702. doi: 10.3390/ijms21082702.

Giovannetti de Sanctis E, Franceschetti E, De Dona F, Palumbo A, Paciotti M, Franceschi F. The Efficacy of Injections for Partial Rotator Cuff Tears: A Systematic Review. J Clin Med. 2020 Dec 25;10(1):51. doi: 10.3390/jcm10010051.

Gupta AK, Bamimore MA, Foley KA. Efficacy of non-surgical treatments for androgenetic alopecia in men and women: a systematic review with network meta-analyses, and an assessment of evidence quality. J Dermatolog Treat. 2020 Apr 13:1-11. doi: 10.1080/09546634.2020.1749547.

Han J, Gao F, Li Y, Ma J, Sun W, Shi L, Wu X, Li T. The Use of Platelet-Rich Plasma for the Treatment of Osteonecrosis of the Femoral Head: A Systematic Review. Biomed Res Int. 2020 Mar 7;2020:2642439. doi: 10.1155/2020/2642439.

Hohmann E, Tetsworth K, Glatt V. Is platelet-rich plasma effective for the treatment of knee osteoarthritis? A systematic review and meta-analysis of level 1 and 2 randomized controlled trials. Eur J Orthop Surg Traumatol. 2020 Aug;30(6):955-967. doi: 10.1007/s00590-020-02623-4.

Hohmann E, Tetsworth K, Glatt V. Platelet-Rich Plasma Versus Corticosteroids for the Treatment of Plantar Fasciitis: A Systematic Review and Meta-analysis. Am J Sports Med. 2020 Aug 21:363546520937293. doi: 10.1177/0363546520937293.

Hurley ET, Shimozono Y, Hannon CP, Smyth NA, Murawski CD, Kennedy JG. Platelet-Rich Plasma Versus Corticosteroids for Plantar Fasciitis: A Systematic Review of Randomized Controlled Trials. Orthop J Sports Med. 2020 Apr 27;8(4):2325967120915704. doi: 10.1177/2325967120915704.

Irby A, Gutierrez J, Chamberlin C, Thomas SJ, Rosen AB. Clinical management of tendinopathy: A systematic review of systematic reviews evaluating the effectiveness of tendinopathy treatments. Scand J Med Sci Sports. 2020 Oct;30(10):1810-1826. doi: 10.1111/sms.13734.

Karasavvidis T, Totlis T, Gilat R, Cole BJ. Platelet-Rich Plasma Combined With Hyaluronic Acid Improves Pain and Function Compared With Hyaluronic Acid Alone in Knee Osteoarthritis: A Systematic Review and Meta-analysis. Arthroscopy. 2020 Dec 3:S0749-8063(20)31053-7. doi: 10.1016/j.arthro.2020.11.052.

Li F, Wu C, Sun H, Zhou Q. Effect of Platelet-Rich Plasma Injections on Pain Reduction in Patients with Temporomandibular Joint Osteoarthrosis: A Meta-Analysis of Randomized Controlled Trials. J Oral Facial Pain Headache. 2020 Spring;34(2):149-156. doi: 10.11607/ofph.2470.

Lin MT, Wei KC, Wu CH. Effectiveness of Platelet-Rich Plasma Injection in Rotator Cuff Tendinopathy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Diagnostics (Basel). 2020 Mar 28;10(4):189. doi: 10.3390/diagnostics10040189.

Long T, Gupta A, Ma S, Hsu S. Platelet-rich plasma in noninvasive procedures for atrophic acne scars: A systematic review and meta-analysis. J Cosmet Dermatol. 2020 Apr;19(4):836-844. doi: 10.1111/jocd.13331

López-Royo MP, Ortiz-Lucas M, Gómez-Trullén EM, Herrero P. The Effectiveness of Minimally Invasive Techniques in the Treatment of Patellar Tendinopathy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Evid Based Complement Alternat Med. 2020 Sep 5;2020:8706283. doi: 10.1155/2020/8706283.

Lui M, Shih W, Yim N, Brandstater M, Ashfaq M, Tran D. Systematic Review and Meta-Analysis of Nonoperative Platelet-Rich Plasma Shoulder Injections for Rotator Cuff Pathology. PM R. 2020 Nov 1. doi: 10.1002/pmrj.12516.

Madhi MI, Yausep OE, Khamdan K, Trigkilidas D. The use of PRP in treatment of Achilles Tendinopathy: A systematic review of literature. Study design: Systematic review of literature. Ann Med Surg (Lond). 2020 Jun 1;55:320-326. doi: 10.1016/j.amsu.2020.04.042.

Medina-Porqueres I, Ortega-Castillo M, Muriel-Garcia A. Effectiveness of platelet-rich plasma in the management of hip osteoarthritis: a systematic review and meta-analysis. Clin Rheumatol. 2021 Jan;40(1):53-64. doi: 10.1007/s10067-020-05241-x.

Mohammed W, Farah S, Nassiri M, McKenna J. Therapeutic efficacy of platelet-rich plasma injection compared to corticosteroid injection in plantar fasciitis: A systematic review and meta-analysis. J Orthop. 2020 Apr 3;22:124-134. doi: 10.1016/j.jor.2020.03.053.

Nauwelaers AK, Van Oost L, Peers K. Evidence for the use of PRP in chronic midsubstance Achilles tendinopathy: A systematic review with meta-analysis. Foot Ankle Surg. 2020 Jul 30:S1268-7731(20)30163-6. doi: 10.1016/j.fas.2020.07.009.

Ortega-Mejia H, Estrugo-Devesa A, Saka-Herrán C, Ayuso-Montero R, López-López J, Velasco-Ortega E. Platelet-Rich Plasma in Maxillary Sinus Augmentation: Systematic Review. Materials (Basel). 2020 Jan 30;13(3):622. doi: 10.3390/ma13030622.

Simental-Mendía M, Vilchez-Cavazos F, Álvarez-Villalobos N, Blázquez-Saldaña J, Peña-Martínez V, Villarreal-Villarreal G, Acosta-Olivo C. Clinical efficacy of platelet-rich plasma in the treatment of lateral epicondylitis: a systematic review and meta-analysis of randomized placebo-controlled clinical trials. Clin Rheumatol. 2020 Aug;39(8):2255-2265. doi: 10.1007/s10067-020-05000-y.

Sochacki KR, Safran MR, Abrams GD, Donahue J, Chu C, Sherman SL. Platelet-Rich Plasma Augmentation for Isolated Arthroscopic Meniscal Repairs Leads to Significantly Lower Failure Rates: A Systematic Review of Comparative Studies. Orthop J Sports Med. 2020 Nov 20;8(11):2325967120964534. doi: 10.1177/2325967120964534.

Torabi P, Behrangi E, Goodarzi A, Rohaninasab M. A systematic review of the effect of platelet-rich plasma on androgenetic alopecia of women. Dermatol Ther. 2020 Nov;33(6):e13835. doi: 10.1111/dth.13835.

Trams E, Kulinski K, Kozar-Kaminska K, Pomianowski S, Kaminski R. The Clinical Use of Platelet-Rich Plasma in Knee Disorders and Surgery-A Systematic Review and Meta-Analysis. Life (Basel). 2020 Jun 25;10(6):94. doi: 10.3390/life10060094.

Vilchez-Cavazos F, Millán-Alanís JM, Blázquez-Saldaña J, Álvarez-Villalobos N, Peña-Martínez VM, Acosta-Olivo CA, Simental-Mendía M. Comparison of the Clinical Effectiveness of Single Versus Multiple Injections of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Systematic Review and Meta-analysis. Orthop J Sports Med. 2019 Dec 16;7(12):2325967119887116. doi: 10.1177/2325967119887116.

Wu N, Sun H, Sun Q, Cong L, Liu C, Zheng Y, Ma L, Cong X. A meta-analysis of fractional CO_2 laser combined with PRP in the treatment of acne scar. Lasers Med Sci. 2021 Feb;36(1):1-12. doi: 10.1007/s10103-020-03105-z.

Wu Q, Luo X, Xiong Y, Liu G, Wang J, Chen X, Mi B. Platelet-rich plasma versus hyaluronic acid in knee osteoarthritis: A meta-analysis with the consistent ratio of injection. J Orthop Surg (Hong Kong). 2020 Jan-Apr;28(1):2309499019887660. doi: 10.1177/2309499019887660.

Yang FA, Liao CD, Wu CW, Shih YC, Wu LC, Chen HC. Effects of applying platelet-rich plasma during arthroscopic rotator cuff repair: a systematic review and meta-analysis of randomised controlled trials. Sci Rep. 2020 Oct 14;10(1):17171. doi: 10.1038/s41598-020-74341-0.

You J, Hodge C, Hoque M, Petsoglou C, Sutton G. Human Platelets and Derived Products in Treating Ocular Surface Diseases - A Systematic Review. Clin Ophthalmol. 2020 Oct 12;14:3195-3210. doi: 10.2147/OPTH.S265701.

Zhao J, Huang H, Liang G, Zeng LF, Yang W, Liu J. Effects and safety of the combination of platelet-rich plasma (PRP) and hyaluronic acid (HA) in the treatment of knee osteoarthritis: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2020 Apr 11;21(1):224. doi: 10.1186/s12891-020-03262-w.

Zhao Z, Ma JX, Ma XL. Different Intra-articular Injections as Therapy for Hip Osteoarthritis: A Systematic Review and Network Meta-analysis. Arthroscopy. 2020 May;36(5):1452-1464.e2. doi: 10.1016/j.arthro.2019.09.043.

Zheng W, Zhao DL, Zhao YQ, Li ZY. Effectiveness of platelet rich plasma in burn wound healing: a systematic review and meta-analysis. J Dermatolog Treat. 2020 Feb 21:1-7. doi: 10.1080/09546634.2020.1729949.

2019

Chang HC, Sung CW, Lin MH. Combination Therapy With Microneedling and Platelet-Rich Plasma for Acne Scarring: A Systematic Review and Meta-analysis. Dermatol Surg. 2020 Aug;46(8):1118-1122. doi: 10.1097/DSS.0000000000002033.

Chang HC, Sung CW, Lin MH. Efficacy of Autologous Platelet-Rich Plasma Combined With Ablative Fractional Carbon Dioxide Laser for Acne Scars: A Systematic Review and Meta-Analysis. Aesthet Surg J. 2019 Jun 21;39(7):NP279-NP287. doi: 10.1093/asj/sjz048.

Charlesworth J, Fitzpatrick J, Perera NKP, Orchard J. Osteoarthritis- a systematic review of long-term safety implications for osteoarthritis of the knee. BMC Musculoskelet Disord. 2019 Apr 9;20(1):151. doi: 10.1186/s12891-019-2525-0.

Cruciani M, Franchini M, Mengoli C, Marano G, Pati I, Masiello F, Profili S, Veropalumbo E, Pupella S, Vaglio S, Liumbruno GM. Platelet-rich plasma for sports-related muscle, tendon and ligament injuries: an umbrella review. Blood Transfus. 2019 Nov;17(6):465-478. doi: 10.2450/2019.0274-19.

Dervishi G, Liu H, Peternel S, Labeit A, Peinemann F. Autologous platelet-rich plasma therapy for pattern hair loss: A systematic review. J Cosmet Dermatol. 2020 Apr;19(4):827-835. doi: 10.1111/jocd.13113.

El-Rabbany M, Duchnay M, Raziee HR, Zych M, Tenenbaum H, Shah PS, Azarpazhooh A. Interventions for preventing osteoradionecrosis of the jaws in adults receiving head and neck radiotherapy. Cochrane Database Syst Rev. 2019 Nov 20;2019(11):CD011559. doi: 10.1002/14651858.CD011559.

Fice MP, Miller JC, Christian R, Hannon CP, Smyth N, Murawski CD, Cole BJ, Kennedy JG. The Role of Platelet-Rich Plasma in Cartilage Pathology: An Updated Systematic Review of the Basic Science Evidence. Arthroscopy. 2019 Mar;35(3):961-976.e3. doi: 10.1016/j.arthro.2018.10.125.

Franchini M, Cruciani M, Mengoli C, Masiello F, Marano G, D'Aloja E, Dell'Aringa C, Pati I, Veropalumbo E, Pupella S, Vaglio S, Liumbruno GM. The use of platelet-rich plasma in oral surgery: a systematic review and meta-analysis. Blood Transfus. 2019 Sep;17(5):357-367. doi: 10.2450/2019.0177-19.

Gupta AK, Cole J, Deutsch DP, Everts PA, Niedbalski RP, Panchaprateep R, Rinaldi F, Rose PT, Sinclair R, Vogel JE, Welter RJ, Zufelt MD, Puig CJ. Platelet-Rich Plasma as a Treatment for Androgenetic Alopecia. Dermatol Surg. 2019 Oct;45(10):1262-1273. doi: 10.1097/DSS.0000000000001894.

Han Y, Huang H, Pan J, Lin J, Zeng L, Liang G, Yang W, Liu J. Meta-analysis Comparing Platelet-Rich Plasma vs Hyaluronic Acid Injection in Patients with Knee Osteoarthritis. Pain Med. 2019 Jul 1;20(7):1418-1429. doi: 10.1093/pm/pnz011.

Hesseler MJ, Shyam N. Platelet-rich plasma and its utility in medical dermatology: A systematic review. J Am Acad Dermatol. 2019 Sep;81(3):834-846. doi: 10.1016/j.jaad.2019.04.037.

Hesseler MJ, Shyam N. Platelet-rich plasma and its utility in the treatment of acne scars: A systematic review. J Am Acad Dermatol. 2019 Jun;80(6):1730-1745. doi: 10.1016/j.jaad.2018.11.029.

Houck DA, Kraeutler MJ, Thornton LB, McCarty EC, Bravman JT. Treatment of Lateral Epicondylitis With Autologous Blood, Platelet-Rich Plasma, or Corticosteroid Injections: A Systematic Review of Overlapping Meta-analyses. Orthop J Sports Med. 2019 Mar 14;7(3):2325967119831052. doi: 10.1177/2325967119831052.

Hsieh TS, Chiu WK, Yang TF, Wang HJ, Chen C. A Meta-analysis of the Evidence for Assisted Therapy with Platelet-Rich Plasma for Atrophic Acne Scars. Aesthetic Plast Surg. 2019 Dec;43(6):1615-1623. doi: 10.1007/s00266-019-01471-w.

Hu Z, Qu S, Zhang J, Cao X, Wang P, Huang S, Shi F, Dong Y, Wu J, Tang B, Zhu J. Efficacy and Safety of Platelet-Rich Plasma for Patients with Diabetic Ulcers: A Systematic Review and Meta-analysis. Adv Wound Care (New Rochelle). 2019 Jul 1;8(7):298-308. doi: 10.1089/wound.2018.0842.

Hurley ET, Hannon CP, Pauzenberger L, Fat DL, Moran CJ, Mullett H. Nonoperative Treatment of Rotator Cuff Disease With Platelet-Rich Plasma: A Systematic Review of Randomized Controlled Trials. Arthroscopy. 2019 May;35(5):1584-1591. doi: 10.1016/j.arthro.2018.10.115.

Johal H, Khan M, Yung SP, Dhillon MS, Fu FH, Bedi A, Bhandari M. Impact of Platelet-Rich Plasma Use on Pain in Orthopaedic Surgery: A Systematic Review and Meta-analysis. Sports Health. 2019 Jul/Aug;11(4):355-366. doi: 10.1177/1941738119834972.

Kunze KN, Hannon CP, Fialkoff JD, Frank RM, Cole BJ. Platelet-rich plasma for muscle injuries: A systematic review of the basic science literature. World J Orthop. 2019 Jul 18;10(7):278-291. doi: 10.5312/wjo.v10.i7.278.

Li A, Wang H, Yu Z, Zhang G, Feng S, Liu L, Gao Y. Platelet-rich plasma vs corticosteroids for elbow epicondylitis: A systematic review and meta-analysis. Medicine (Baltimore). 2019 Dec;98(51):e18358. doi: 10.1097/MD.0000000000018358.

Liu CJ, Yu KL, Bai JB, Tian DH, Liu GL. Platelet-rich plasma injection for the treatment of chronic Achilles tendinopathy: A meta-analysis. Medicine (Baltimore). 2019 Apr;98(16):e15278. doi: 10.1097/MD.0000000000015278.

Maisel-Campbell AL, Ismail A, Reynolds KA, Poon E, Serrano L, Grushchak S, Farid C, West DP, Alam M. A systematic review of the safety and effectiveness of platelet-rich plasma (PRP) for skin aging. Arch Dermatol Res. 2020 Jul;312(5):301-315. doi: 10.1007/s00403-019-01999-6.

Mao G, Zhang G, Fan W. Platelet-Rich Plasma for Treating Androgenic Alopecia: A Systematic Review. Aesthetic Plast Surg. 2019 Oct;43(5):1326-1336. doi: 10.1007/s00266-019-01391-9.

Marchitto MC, Qureshi A, Marks D, Awosika O, Rengifo-Pardo M, Ehrlich A. Emerging Nonsteroid-Based Procedural Therapies for Alopecia Areata: A Systematic Review. Dermatol Surg. 2019 Dec;45(12):1484-1506. doi: 10.1097/DSS.0000000000002053.

Rosati P, Barone M, Alessandri Bonetti M, Giorgino R, Panasiti V, Coppola R, Tambone V, Persichetti P. A Systematic Review of Outcomes and Patient Satisfaction Following Surgical and Non-surgical Treatments for Hair Loss. Aesthetic Plast Surg. 2019 Dec;43(6):1523-1535. doi: 10.1007/s00266-019-01480-9.

Shen Z, Zheng S, Chen G, Li D, Jiang Z, Li Y, Huang F. Efficacy and safety of platelet-rich plasma in treating cutaneous ulceration: A meta-analysis of randomized controlled trials. J Cosmet Dermatol. 2019 Apr;18(2):495-507. doi: 10.1111/jocd.12853. Epub 2019 Mar 26.

Wang C, Xu M, Guo W, Wang Y, Zhao S, Zhong L. Clinical efficacy and safety of platelet-rich plasma in arthroscopic full-thickness rotator cuff repair: A meta-analysis. PLoS One. 2019 Jul 29;14(7):e0220392. doi: 10.1371/journal.pone.0220392.

Wang Y, Han C, Hao J, Ren Y, Wang J. Efficacy of platelet-rich plasma injections for treating Achilles tendonitis : Systematic review of high-quality randomized controlled trials. Orthopade. 2019 Sep;48(9):784-791. English. doi: 10.1007/s00132-019-03711-y.

Xia Y, Zhao J, Xie J, Lv Y, Cao DS. The Efficacy of Platelet-Rich Plasma Dressing for Chronic Nonhealing Ulcers: A Meta-Analysis of 15 Randomized Controlled Trials. Plast Reconstr Surg. 2019 Dec;144(6):1463-1474. doi: 10.1097/PRS.0000000000006281.

Xu Q, Chen J, Cheng L. Comparison of platelet rich plasma and corticosteroids in the management of lateral epicondylitis: A meta-analysis of randomized controlled trials. Int J Surg. 2019 Jul;67:37-46. doi: 10.1016/j.ijsu.2019.05.003.

2018

Ali M, Mohamed A, Ahmed HE, Malviya A, Atchia I. The use of ultrasound-guided platelet-rich plasma injections in the treatment of hip osteoarthritis: a systematic review of the literature. J Ultrason. 2018;18(75):332-337. doi: 10.15557/JoU.2018.0048.

Bousnaki M, Bakopoulou A, Koidis P. Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review. Int J Oral Maxillofac Surg. 2018 Feb;47(2):188-198. doi: 10.1016/j.ijom.2017.09.014.

Chen JX, Justicz N, Lee LN. Platelet-Rich Plasma for the Treatment of Androgenic Alopecia: A Systematic Review. Facial Plast Surg. 2018 Dec;34(6):631-640. doi: 10.1055/s-0038-1660845.

Chen X, Jones IA, Park C, Vangsness CT Jr. The Efficacy of Platelet-Rich Plasma on Tendon and Ligament Healing: A Systematic Review and Meta-analysis With Bias Assessment. Am J Sports Med. 2018 Jul;46(8):2020-2032. doi: 10.1177/0363546517743746.

Di Y, Han C, Zhao L, Ren Y. Is local platelet-rich plasma injection clinically superior to hyaluronic acid for treatment of knee osteoarthritis? A systematic review of randomized controlled trials. Arthritis Res Ther. 2018 Jun 19;20(1):128. doi: 10.1186/s13075-018-1621-0.

Franchini M, Cruciani M, Mengoli C, Marano G, Pupella S, Veropalumbo E, Masiello F, Pati I, Vaglio S, Liumbruno GM. Efficacy of platelet-rich plasma as conservative treatment in orthopaedics: a systematic review and meta-analysis. Blood Transfus. 2018 Nov;16(6):502-513. doi: 10.2450/2018.0111-18.

Grassi A, Napoli F, Romandini I, Samuelsson K, Zaffagnini S, Candrian C, Filardo G. Is Platelet-Rich Plasma (PRP) Effective in the Treatment of Acute Muscle Injuries? A Systematic Review and Meta-Analysis. Sports Med. 2018 Apr;48(4):971-989. doi: 10.1007/s40279-018-0860-1.

Haigler MC, Abdulrehman E, Siddappa S, Kishore R, Padilla M, Enciso R. Use of platelet-rich plasma, platelet-rich growth factor with arthrocentesis or arthroscopy to treat temporomandibular joint osteoarthritis: Systematic review with meta-analyses. J Am Dent Assoc. 2018 Nov;149(11):940-952.e2. doi: 10.1016/j.adaj.2018.07.025.

Han YH, Huang HT, Pan JK, Lin JT, Zeng LF, Liang GH, Yang WY, Liu J. Comparison of platelet-rich plasma vs hyaluronic acid injections in patients with knee osteoarthritis: A protocol for a systematic review and meta-analysis. Medicine (Baltimore). 2018 Nov;97(44):e13049. doi: 10.1097/MD.0000000000013049.

Hirase T, Ruff E, Surani S, Ratnani I. Topical application of platelet-rich plasma for diabetic foot ulcers: A systematic review. World J Diabetes. 2018 Oct 15;9(10):172-179. doi: 10.4239/wjd.v9.i10.172.

Kramer ME, Keaney TC. Systematic review of platelet-rich plasma (PRP) preparation and composition for the treatment of androgenetic alopecia. J Cosmet Dermatol. 2018 Oct;17(5):666-671. doi: 10.1111/jocd.12679.

Lei X, Xu P, Cheng B. Problems and Solutions for Platelet-Rich Plasma in Facial Rejuvenation: A Systematic Review.

Aesthetic Plast Surg. 2019 Apr;43(2):457-469. doi: 10.1007/s00266-018-1256-1.

Lin MT, Chiang CF, Wu CH, Hsu HH, Tu YK. Meta-analysis Comparing Autologous Blood-Derived Products (Including Platelet-Rich Plasma) Injection Versus Placebo in Patients With Achilles Tendinopathy. Arthroscopy. 2018 Jun;34(6):1966-1975.e5. doi: 10.1016/j.arthro.2018.01.030.

Ling Y, Wang S. Effects of platelet-rich plasma in the treatment of plantar fasciitis: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2018 Sep;97(37):e12110. doi: 10.1097/MD.0000000000012110.

Miller LE, Parrish WR, Roides B, Bhattacharyya S. Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection-controlled trials. BMJ Open Sport Exerc Med. 2017 Nov 6;3(1):e000237. doi: 10.1136/bmjsem-2017-000237.

Motosko CC, Khouri KS, Poudrier G, Sinno S, Hazen A. Evaluating Platelet-Rich Therapy for Facial Aesthetics and Alopecia: A Critical Review of the Literature. Plast Reconstr Surg. 2018 May;141(5):1115-1123. doi: 10.1097/PRS.0000000000004279.

Muchedzi TA, Roberts SB. A systematic review of the effects of platelet rich plasma on outcomes for patients with knee osteoarthritis and following total knee arthroplasty. Surgeon. 2018 Aug;16(4):250-258. doi: 10.1016/j.surge.2017.08.004.

Niu W, Wang P, Ge S, Ji P. Effects of Platelet Concentrates Used in Alveolar Ridge Preservation: A Systematic Review. Implant Dent. 2018 Aug;27(4):498-506. doi: 10.1097/ID.0000000000000797.

Saleem M, Pisani F, Zahid FM, Georgakopoulos I, Pustina-Krasniqi T, Xhajanka E, Almasri M. Adjunctive Platelet-Rich Plasma (PRP) in Infrabony Regenerative Treatment: A Systematic Review and RCT's Meta-Analysis. Stem Cells Int. 2018 Mar 19;2018:9594235. doi: 10.1155/2018/9594235.

Smith OJ, Kanapathy M, Khajuria A, Prokopenko M, Hachach-Haram N, Mann H, Mosahebi A. Systematic review of the efficacy of fat grafting and platelet-rich plasma for wound healing. Int Wound J. 2018 Aug;15(4):519-526. doi: 10.1111/iwj.12892.

Stähli A, Strauss FJ, Gruber R. The use of platelet-rich plasma to enhance the outcomes of implant therapy: A systematic review. Clin Oral Implants Res. 2018 Oct;29 Suppl 18(Suppl Suppl 18):20-36. doi: 10.1111/clr.13296.

Vannabouathong C, Del Fabbro G, Sales B, Smith C, Li CS, Yardley D, Bhandari M, Petrisor BA. Intra-articular Injections in the Treatment of Symptoms from Ankle Arthritis: A Systematic Review. Foot Ankle Int. 2018 Oct;39(10):1141-1150. doi: 10.1177/1071100718779375.

Ye Y, Zhou X, Mao S, Zhang J, Lin B. Platelet rich plasma versus hyaluronic acid in patients with hip osteoarthritis: A meta-analysis of randomized controlled trials. Int J Surg. 2018 May;53:279-287. doi: 10.1016/j.ijsu.2018.03.078.

Zhang HF, Wang CG, Li H, Huang YT, Li ZJ. Intra-articular platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. Drug Des Devel Ther. 2018 Mar 5;12:445-453. doi: 10.2147/DDDT.S156724.

Zhang YJ, Xu SZ, Gu PC, Du JY, Cai YZ, Zhang C, Lin XJ. Is Platelet-rich Plasma Injection Effective for Chronic Achilles Tendinopathy? A Meta-analysis. Clin Orthop Relat Res. 2018 Aug;476(8):1633-1641. doi: 10.1007/s11999.0000000000000258.

2017

Ayatollahi A, Hosseini H, Gholami J, Mirminachi B, Firooz F, Firooz A. Platelet rich plasma for treatment of non-scarring hair loss: systematic review of literature. J Dermatolog Treat. 2017 Nov;28(7):574-581. doi: 10.1080/09546634.2017.1303571.

Casabona F, et al. Autologous platelet-rich plasma (PRP) in chronic penile lichen sclerosus: the impact on tissue repair and patient quality of life. Int Urol Nephrol. 2017; 49(4): 573-580.

Dai WL, Zhou AG, Zhang H, Zhang J. Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials. Arthroscopy. 2017 Mar;33(3):659-670.e1. doi: 10.1016/j.arthro.2016.09.024.

Frautschi RS, Hashem AM, Halasa B, Cakmakoglu C, Zins JE. Current Evidence for Clinical Efficacy of Platelet Rich

Plasma in Aesthetic Surgery: A Systematic Review. Aesthet Surg J. 2017 Mar 1;37(3):353-362. doi: 10.1093/asj/sjw178.

Giordano S, Romeo M, Lankinen P. Platelet-rich plasma for androgenetic alopecia: Does it work? Evidence from meta analysis. J Cosmet Dermatol. 2017 Sep;16(3):374-381. doi: 10.1111/jocd.12331.

Ma J, Sun J, Guo W, Li Z, Wang B, Wang W. The effect of platelet-rich plasma on reducing blood loss after total knee arthroplasty: A systematic review and meta-analysis. Medicine (Baltimore). 2017 Jun;96(26):e7262. doi: 10.1097/MD.0000000000007262.

Miranda I, Sánchez-Alepuz E, Lucas FJ, Carratalá V, González-Jofre CA. Use of platelet-rich plasma in the treatment of rotator cuff pathology. What has been scientifically proven? Rev Esp Cir Ortop Traumatol. 2017 Jul-Aug;61(4):249-258. English, Spanish. doi: 10.1016/j.recot.2017.03.001.

Pan Q, et al. Autologous serum eye drops for dry eye. Cochrane Database Syst Rev 2017**;** 2

Picard F, Hersant B, Niddam J, Meningaud JP. Injections of platelet-rich plasma for androgenic alopecia: A systematic review. J Stomatol Oral Maxillofac Surg. 2017 Oct;118(5):291-297. doi: 10.1016/j.jormas.2017.06.011.

Roffi A, Di Matteo B, Krishnakumar GS, Kon E, Filardo G. Platelet-rich plasma for the treatment of bone defects: from pre-clinical rational to evidence in the clinical practice. A systematic review. Int Orthop. 2017 Feb;41(2):221-237. doi: 10.1007/s00264-016-3342-9.