


# A comprehensive evaluation and meta-analysis of the efficacy of autologous conditioned serum vs platelet-rich plasma in knee osteoarthritis treatment

Piotr Fudalej<sup>1,2,A-E</sup>, Mahdi Al-Jeabory<sup>3,4,E-F</sup>, Michał Pruc<sup>1,B,D,F</sup>, Jarosław Pecold<sup>1,4,E-F</sup>, Łukasz Szarpak<sup>5,1,A-F</sup> 

<sup>1</sup> Department of Clinical Research and Development, LUXMED Group, Warsaw, Poland

<sup>2</sup> ORTHOS Multi-Specialty Hospital Komorowice, LUXMED Group, Wrocław, Poland

<sup>3</sup> Department of Trauma and Orthopaedic Surgery, Silesian Rheumatology Centre, Ustronie, Poland

<sup>4</sup> Department of Trauma and Orthopaedic Surgery, City Hospital, Ruda Śląska, Poland

<sup>5</sup> Henry JN Taub Department of Emergency Medicine, Baylor College of Medicine, Houston, USA

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation,

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## Abstract

**Introduction and Objective.** Knee osteoarthritis (OA) is an advanced, degenerative condition of the joint that impairs movement and quality of life. The pathologic process of OA is multifaceted, and while traditional interventions offer only symptom relief, novel approaches, such as autologous conditioned serum (ACS) and platelet-rich plasma (PRP) therapy, are showing greater promise.

**Materials and Method.** This systematic review and meta-analysis were conducted in accordance with the PRISMA guidelines and Cochrane Handbook for Systematic Reviews of Interventions. The primary outcomes were changes in pain intensity (Visual Analog Scale, VAS) and functional status (Western Ontario and McMaster Universities Osteoarthritis Index – WOMAC).

**Results.** Relief from pain in the long term was greater with ACS than the PRP group, with better VAS score improvements at three months ( $p<0.001$ ), six months ( $p=0.03$ ), and the 24-month mark ( $p<0.001$ ). WOMAC score evaluations demonstrated ACS had significant differences for functional recovery, along with sustained functional improvement at three months ( $p<0.001$ ) and six months ( $p<0.001$ ).

**Conclusions.** The results obtained indicate that some patients with knee OA can obtain sustained relief from pain and improve function more than one year after treatment with anti-inflammatory ACS. Sustained pain relief and functional recovery are also likely due to regulatory mechanisms on inflammation and homeostasis of the joint. This meta-analysis indicates that ACS is more effective than PRP in relieving pain and improving joint function in knee OA. Further studies should be directed towards standardization of protocols, determining the cost, and looking at other outcomes over longer periods to better understand the benefits and refine the clinical use.

## Key words

autologous conditioned serum, platelet-rich plasma, pain reduction, functional improvement, meta-analysis, systematic review, osteoarthritis, Visual Analog Scale, WOMAC score

## INTRODUCTION

Knee osteoarthritis (OA) is a chronic disease characterized by progressive degeneration of articular cartilage, changes in subchondral bone, and inflammatory changes in the synovium [1, 2]. Knee OA, which is a prevalent form of arthritis, is disruptive to physical mobility, and the overall well-being of a person, especially the older population [3, 4]. The global prevalence of knee OA is expected to rise consequent to increased life expectancy and obesity, making it a leading contributor to disability worldwide.

There is no definitive cure for knee OA. Currently, treatments focus on alleviating symptoms and optimizing

joint function. Other treatment approaches, such as non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular steroid injections, physiotherapy, and knee braces, may be beneficial, but they can have unwanted side-effects, or lower effectiveness over time [5]. More drastic measures, such as total knee arthroplasty, are often viewed as a last resort option because of their highly invasive nature and possible accompanying complications. The controversies have led to the exploration of solutions that can biologically and structurally modulate the underlying pathophysiology of knee OA.

Platelet-Rich Plasma (PRP) treatment involves centrifugation of blood to extract and activate platelets, whereby the patient's blood is drawn and treated, and forms part of the patient's regenerative medicine within Autologous Conditioned Serum (ACS), which is stimulated through interleukin-1 receptor antagonists incorporating anti-inflammatory cytokines [6, 7]. The PRP designer claims that

✉ Address for correspondence: Łukasz Szarpak, Henry JN Taub Department of Emergency Medicine, Baylor College of Medicine, 1, Baylor Plaza, Houston (TX) 77030, USA.

E-mail: lukasz.szarpak@gmail.com

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ACS procedure offers further improvement over the primary ACS procedure by making a second incubation for 24 hours; however, it is shown through this research that virtually all existing PRP and ACS techniques are not effective in treating knee OA [8, 9]. It can be hypothesized that the variability of the results stems from the use of currently developed ACS techniques claiming effectiveness without clinically proven results. Most recent research certainly suggest the potential of easily treating knee primary OA through a fully automated ACS (Platelet Rich Plasma + Autologous Conditioned Serum) with a cynomolgus macaques metabolic cage style machine [10].

The aim of the presented meta-analysis is two-fold: 1) to evaluate and synthesize clinical data and biochemical information of PRP vs ACS on knee OA, and 2) to provide meaningful information on the effectiveness of existing studies in alleviating pain, improving range of motion, and controlling inflammation. The findings will help clinicians make better evidence-based decisions and improve the use of biologics in knee OA treatment.

## MATERIALS AND METHOD

The meta-analysis was conducted in accordance with the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions [11] and adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [12]. A detailed research protocol was developed and registered in the International Prospective Register of Systematic Reviews (PROSPERO) database with the ID: CRD42025637420. As this study is a secondary analysis of previously published data, ethical approval from a research Ethics Committee was not required.

**Eligibility and exclusion criteria.** Studies were included which were based on the evidence-based PICOS criteria as follows: (P) Patients – individuals diagnosed with knee osteoarthritis, (I) Intervention – intra-articular injection therapy using autologous conditioned serum; (C) Comparator – intra-articular injection therapy with platelet rich plasma; (O) Outcomes – reporting of pre-defined efficacy and safety endpoints, specifically changes in the Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores; (S) Study design – randomized controlled trials (RCTs) and non-randomized studies (non-RCTs) published in peer-reviewed journals.

The exclusion criteria were: (i) Studies that did not report outcomes of interest; (ii) animal or cell-based studies; (iii) duplicate publications; (iv) non-peer-reviewed materials, such as letters, comments, editorials, and clinical practice guidelines; (v) articles not written in English

**Search strategies.** The search for literature was carried out independently by two authors (PF and MP) in five databases: PubMed, EMBASE, Google Scholar, Cochrane Central Register of Controlled Trials and Scopus, without any date restrictions on publications until 11 January 2025. A detailed approach was used in the search by combining certain key words with the Boolean operators: 'autologous conditioned serum', 'Orthokine', 'ACS', 'PRP', 'platelet rich plasma', 'knee', 'osteoarthritis', 'osteoarthritis', 'osteoarthr\*', 'arthrosis', 'degenerative arthr\*', 'knee OA'. Furthermore, to ensure

all pertinent material was obtained, the reference lists of these articles were searched 'manually'. No restrictions were set for other languages. Lastly, all results from the search were uploaded into Endnote X8.2 (Clarivate Analytics) for reference management and identifying duplicates. With insufficient or missing information, the original authors were approached by email. Gaps in the procedure were filled-in by discussions for a consensus among the authors, or if required, with an experienced reviewer (LS).

**Study selection process.** The research selection method for this systematic review and meta-analysis was carried out in three separate phases. The initial phase entailed the identification and elimination of duplicate records acquired from the preliminary search. During the second phase, titles and abstracts were evaluated to eliminate papers that failed to satisfy the inclusion criteria, or were considered irrelevant. The third and last phase entailed a comprehensive review of the complete texts of the remaining studies, with evaluative decisions made about their eligibility according to established criteria. Furthermore, the reference lists of the included studies and recent systematic reviews were examined to discover any potentially pertinent research that may have been overlooked. Two investigators (PF and MAJ) separately selected the studies, resolving any discrepancies by consensus.

**Data extraction.** Data extraction was performed independently by two authors (PF and MP), concentrating on essential variables including the first author's name, country of origin, study type, clinical characteristics of the patient population (such as gender, age, and Kellgren-Lawrence scores), and the outcomes of interest in both study groups. Any disagreements that arose during the data extraction process were resolved through dialogue. In instances where necessary data were not explicitly available in the research, computations were conducted, or the original authors were consulted to obtain the missing information.

**Risk of bias assessment.** The possibility of bias for every single investigation was investigated independently by two authors (PF and MP). Disagreements were resolved through discussions or arbitration by more members of the research team (LS and MAJ), if necessary. For randomized controlled trials (RCTs), four people worked in parallel and adopted the RoB 2 tool [13]. This tool assesses bias arising from five primary domains: randomization, process, deviations from intended interventions, missing outcome data, and outcome measurement, and selection of reported results. For non-randomized studies (NRSIs) the ROBINS-I Tool was used [14], which assesses bias across several domains, such as: confounding, participant selection, intervention, classification and deviations, missing data, outcome measurement, and selection of reported results. Both tools target bias risk at domain level, and RoB 2 gives concern rating at domain level to either 'low risk', 'some', or 'high concerns', while studies classified with ROBINS-I are low, moderate, serious and critical. Synthesizing domain level assessments into a final judgement gives the benefit of an overall bias categorization for each study, all of which was carried out on Risk-of-Bias Visualization, robvis [15].

**Outcomes.** From various trials, clinical and procedural outcomes were derived to assess pain, functional capacity,

and quality of life in the studied groups. Pain intensity was assessed using the Visual Analog Scale (VAS) [16], where individuals rated their discomfort on a continuum from 0 (no pain) to 10 (the worst conceivable agony). The functional impairment and symptoms of lower limb osteoarthritis were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [17]. The WOMAC scale consists of 24 items divided into three domains: pain – five items, stiffness – 2 items, and physical function – 17 items. Elevated WOMAC ratings indicate more severe symptoms or increased functional limits. These verified criteria provided a thorough and rigorous evaluation of the clinical and procedural impacts on the patient groups.

Subgroup analyses of outcomes were conducted according to predetermined follow-up intervals (1, 3, 6, 12, 24, or 60 months) to mitigate heterogeneity in follow-up durations among trials. This stratified method enabled a comprehensive understanding of the temporal dynamics of the interventions, and their impact on the outcomes.

**Statistical analysis.** Data synthesis was performed using Review Manager 5.4 (Cochrane Collaboration, London, UK) in accordance with Cochrane Collaboration standards [18]. Dichotomous outcomes were expressed as risk ratios (RRs) with 95% confidence intervals (CIs), while continuous outcomes were reported as mean differences (MDs) with 95% CIs. When necessary, continuous data presented as medians and interquartile ranges (IQRs) were converted to means and standard deviations (SDs) using the Hozo formula [19].

In order to calculate percentage changes among scale parameters, the percentage change for each individual was calculated using the following formula:

$$\text{Mean percentage change} = \frac{\text{Follow-up Value} - \text{Baseline Value}}{\text{Baseline value}} \times 100$$

where the baseline value represented the initial measurement, and the follow-up value corresponded to the outcome at a specific follow-up point. The mean percentage change was computed as the arithmetic mean of individual percentage changes, while variability was expressed as the standard deviation (SD), calculated using the formula:

$$SD = \sqrt{\frac{\sum_{i=1}^N (\text{Percentage change} - \text{Mean Percentage Change})^2}{N-1}}$$

Cases with missing or zero baseline values were excluded from the analysis to avoid computational errors.

To account for variability across studies, the DerSimonian-Laird random effects model was applied, regardless of the degree of heterogeneity. Statistical heterogeneity was assessed using the  $I^2$  statistic, interpreted as follows according to the Cochrane Handbook: 0–40%: negligible heterogeneity; 30–60%: moderate heterogeneity; 50–90%: substantial heterogeneity; and 75–100%: considerable heterogeneity [20, 21].

Due to the limited number of studies included in this meta-analysis, formal evaluations of publication bias using funnel plot asymmetry and Egger's regression test were not performed, as these methods require at least 10 studies to yield reliable results [19, 22]. Instead, the likelihood of publication bias based on study parameters were subjectively assessed, such as sample size, reported outcomes, and study quality. Sensitivity analyses were conducted to evaluate

the robustness of the pooled estimates by systematically removing individual studies and examining their influence on the overall results. Statistical significance was set at a  $p$ -value  $<0.05$  for all tests, except for Cochran's Q test, and analyses were conducted using two-tailed tests.

## RESULTS

**Study selection and characteristics.** The primary search method produced 261 studies. Following duplication removal and title/abstract screening, 16 studies were selected for full-text review. After another review by the same two independent coders, four studies [10, 23, 24, 25] that met the criteria were included for analysis and included in the review (Fig. 1).

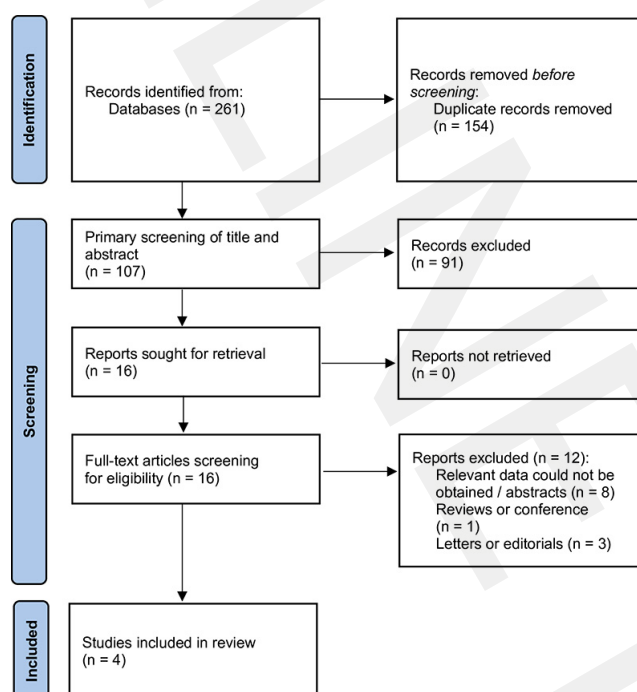


Figure 1. PRISMA flow chart

A total of 315 patients were included for analysis. The sample size of the ACS group ranged from 21 – 65 patients, whereas that of PRP group ranged from 27 – 58. The studies were conducted respectively in Turkey, India, Iran, and Russia. One study consisted of randomized controlled trials; two were prospective control studies, and one was designed as a retrospective trial. Follow-up duration ranged from one month to five years, with all studies reporting at least one interim assessment point (1–6 months). Mean age of patients treated with ACS was 57.93 ( $\pm 8.91$ ) years, compared to 57.05 ( $\pm 8.79$ ) for the PRP group (MD = 0.38; 95%CI: -3.44 to 4.20;  $p=0.85$ ). The characteristics of the patients included in the meta-analysis are presented in Table 1.

Evaluation of the randomized studies with ROB 2 signalled a medium risk of bias, especially with concerns about allocation (D2) and outcome measurement (D4). Other domains predominantly scored low risk. Similarly, the non-randomized studies with ROBINS-I had an evaluation of moderate to serious risk of bias, especially with the outcome measurement (D3), which justified hesitant interpretation of the findings due to methodological shortcomings (Fig. 2).



Table 1. Baseline characteristics of included trials

Study	Country	Study design	Treatment group	No. of patients	Age, years	Gender, male	BMI	Follow-up
Coskun et al., 2022	Turkey	RS	ACS	40	56.68 (8.96)	28 (70.0%)	30.04 (5.30)	1, 6, 12, 24, 60-mo
			PRP	42	50.79 (10.67)	32 (76.2%)	30.05 (4.82)	
Khurana et al., 2021	India	PCS	ACS	21	50.81 (8.93)	7 (33.3%)	30.46 (3.57)	6-mo
			PRP	27	56.33 (4.37)	9 (33.3%)	31.48 (3.91)	
Pishgahi et al., 2020	Iran	RCT	ACS	32	61.28 (1.67)	12 (37.5%)	NS	1-, 6-mo
			PRP	30	58.93 (1.71)	16 (53.3%)	NS	
Shirokova et al., 2019	Russia	PCS	ACS	65	59.36 (9.71)	NS	31.68 (4.97)	1-, 3-mo
			PRP	58	60.94 (8.56)	NS	32.15 (4.76)	

ACS – Autologous Conditioned Serum; BMI – Body mass index; NS – Not specified; PCS – Prospective control study; PRP – Platelet Rich Plasma; RCT: Randomized control trial; RS – Retrospective study.

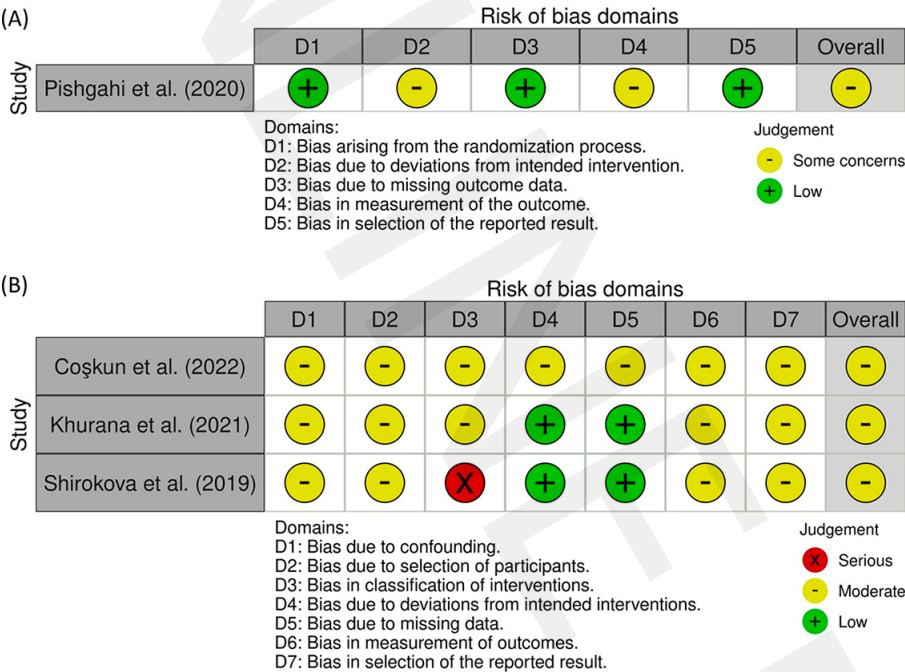


Figure 2. Risk of bias assessment among included trials

**Visual Analog Scale outcomes.** The analysis of Visual Analog Scale (VAS) scores indicated no statistically significant difference in baseline pain levels between the ACS and PRP groups (MD: 0.03, 95% CI: -0.09 to 0.15;  $p = 0.66$ ,  $I^2 = 0\%$ ) (Tab. 2).

However, the percentage change in VAS scores over time demonstrated a more pronounced reduction in pain severity in the ACS group compared to PRP. At one month, the mean percentage reduction was greater in the ACS group ( $-31.81\% \pm 13.62$ ) than in the PRP group ( $-27.29\% \pm 18.21$ ) (Fig. 3), although the difference did not reach statistical significance ( $p = 0.26$ ). By three months, the pain reduction was markedly greater in the ACS group ( $-46.8\% \pm 27.4$ ) compared to PRP ( $-18.86\% \pm 8.57$ ), with a statistically significant difference between groups ( $p < 0.001$ ).

At six months, the ACS group continued to demonstrate superior pain reduction ( $-54.53\% \pm 30.11$ ) compared to the PRP group ( $-37.42\% \pm 29.14$ ), with statistical significance ( $p = 0.03$ ,  $I^2 = 87\%$ ). At 12 months, ACS maintained a greater reduction in pain severity ( $-60.32\% \pm 40.27$ ) relative to PRP ( $-50.49\% \pm 31.33$ ); however, this difference was not statistically significant ( $p = 0.22$ ).

Long-term follow-up assessments further supported the superior efficacy of ACS in pain reduction. At 24 months, the

percentage reduction in VAS scores remained significantly higher in the ACS group ( $-38.67\% \pm 17.75$ ) than in the PRP group ( $-11.59\% \pm 4.29$ ;  $p < 0.001$ ). A similar pattern was observed at 60 months, with ACS demonstrating a greater sustained pain reduction ( $-17.05\% \pm 6.23$ ) compared to PRP ( $-11.59\% \pm 4.29$ ;  $p < 0.001$ ).

**WOMAC score outcomes.** At baseline, the ACS and PRP groups demonstrated comparable functional impairment, with mean WOMAC scores of  $56.81 \pm 14.48$  and  $59.42 \pm 13.86$ , respectively (Tab. 3). The difference between groups was not statistically significant (MD: -3.97, 95% CI: -5.57 to -2.37,  $p = 0.89$ ,  $I^2 = 0\%$ ).

Over time, the ACS group showed a greater improvement in joint function compared to PRP, which was consistent with the observed trend in pain reduction. At one month, the percentage improvement in WOMAC scores was slightly higher in the ACS group ( $-21.14\% \pm 9.96$ ) compared to PRP ( $-17.81\% \pm 5.99$ ) (Fig. 4); however, the difference was not statistically significant ( $p = 0.99$ ). By three months, ACS demonstrated a substantially greater improvement in function ( $-28.74\% \pm 11.57$ ) relative to PRP ( $-13.63\% \pm 5.26$ ), with a statistically significant difference between groups ( $p < 0.001$ ). This superiority of ACS persisted at the six-month

Table 2. Pooled analysis of VAS score

Outcome	No. of studies	MD (SD)		Events		Heterogeneity between Trials		p-Value for Differences across Groups
		ACS	PRP	MD	95%CI	p-Value	I2 statistics	
VAS score								
Baseline	4	6.33 (1.24)	6.26 (1.53)	0.03	-0.09 to 0.15	0.66	0%	0.64
1-mo	3	4.31 (1.31)	4.53 (1.54)	-0.35	-1.11 to 0.40	<0.001	88%	0.36
3-mo	1	3.25 (1.77)	4.69 (1.66)	-1.44	-2.05 to -0.83)	NA	NA	<0.001
6-mo	3	2.90 (1.42)	4.09 (1.91)	-1.36	-2.24 to -0.49	0.004	82%	0.002
12-mo	1	2.75 (1.75)	3.5 (2.0)	-0.75	-1.56 to 0.06	NA	NA	0.07
24-mo	1	4.25 (1.75)	6.25 (1.75)	-2.00	-2.76 to -1.24	NA	NA	<0.001
60-mo	1	5.75 (1.75)	6.25 (1.75)	-0.50	-1.26 to 0.26	NA	NA	0.20
Percentage change of VAS score								
Δ 1-mo	3	-31.81 (13.62)	-27.29 (18.21)	-6.36	-17.36 to 4.65	<0.001	95%	0.26
Δ 3-mo	1	-46.8 (27.4)	-18.86 (8.57)	-27.94	-34.96 to -20.92	NA	NA	<0.001
Δ 6-mo	3	-54.53 (30.11)	-37.42 (29.14)	-19.45	-37.29 to -1.61	<0.001	87%	0.03
Δ 12-mo	1	-60.32 (40.27)	-50.49 (31.33)	-9.83	-25.50 to 5.84	NA	NA	0.22
Δ 24-mo	1	-38.67 (17.75)	-11.59 (4.29)	-27.08	-32.73 to -21.43	NA	NA	<0.001
Δ 60-mo	1	-17.05 (6.23)	-11.59 (4.29)	-5.46	-7.79 to -3.13	NA	NA	<0.001

ACS – Autologous Conditioned Serum; CI – Confidence intervals; MD – Mean difference; NA – Not applicable; PRP – Platelet-Rich Plasma

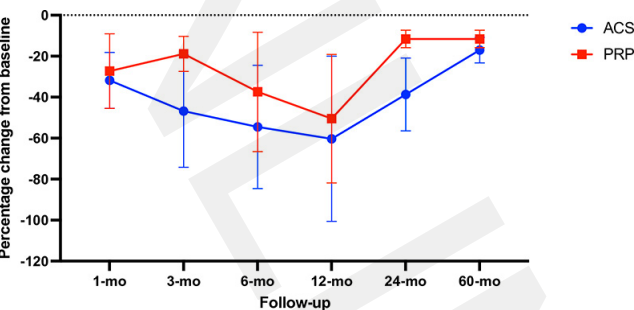


Figure 3. Percentage changes in VAS score during follow-up periods

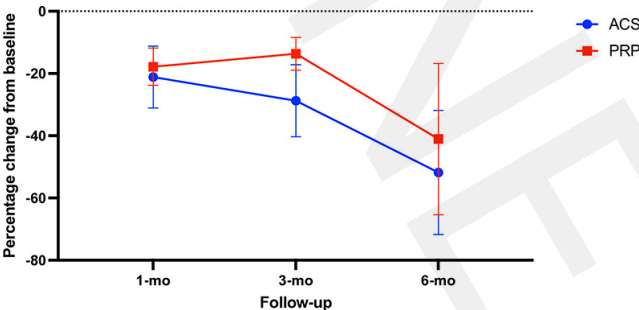


Figure 4. Percentage changes in WOMAC score during follow-up periods

Table 3. Pooled analysis of WOMAC score

Outcome	No. of studies	MD (SD)		Events		Heterogeneity between Trials		p-Value for Differences across Groups
		ACS	PRP	MD	95%CI	p-Value	I2 statistics	
WOMAC score								
Baseline	3	56.81 (14.48)	59.42 (13.86)	-3.97	-5.57 to -2.37	0.89	0%	<0.001
1-mo	2	46.94 (10.48)	51.75 (13.25)	-2.69	-14.02 to 8.64	<0.001	94%	0.64
3-mo	1	43.76 (14.18)	55.45 (16.41)	-11.69	-17.14 to -6.24	NA	NA	<0.001
6-mo	2	25.55 (12.57)	33.77 (16.31)	-10.66	-12.39 to -8.94	0.62	0%	<0.001
Percentage change of WOMAC score								
Δ 1-mo	2	-21.14 (9.96)	-17.81 (5.99)	0.18	-20.30 to 20.66	<0.001	100%	0.99
Δ 3-mo	1	-28.74 (11.57)	-13.63 (5.26)	-15.11	-18.23 to -11.99	NA	NA	<0.001
Δ 6-mo	2	-51.79 (19.93)	-41.06 (24.31)	-15.41	-17.20 to -13.62	0.43	0%	<0.001

ACS – Autologous Conditioned Serum; CI – Confidence intervals; MD – Mean difference; NA – Not applicable; PRP – Platelet-Rich Plasma;

follow-up, with the ACS group achieving a mean reduction of  $-51.79\% \pm 19.93$  in WOMAC scores, compared to  $-41.06\% \pm 24.31$  in the PRP group ( $p < 0.001$ ). The low heterogeneity observed ( $I^2 = 0\%$ ) suggests consistency across studies in favour of ACS.

DISCUSSION

This meta-analysis, together with the studies reviewed, adds important information regarding the efficacy of ACS and PRP in the management of knee OA. The results obtained show that, although both ACS and PRP have a positive effect on pain and function, the long-term outcomes of pain relief and functional improvement with ACS are greater, especially in patients suffering from moderate synovitis.

Shirokova et al. reported that pain worsened and the WOMAC score did not improve significantly in other patients after the three-month mark; these findings correspond with the results obtained in the current study [25]. This meta-analysis reveals that greater pain relief and functional improvement did occur with ACS, compared to PRP, especially in the follow-up periods of more than six months. The patients also used ACS at three months post-treatment, where patients with moderate synovitis were responding much better than those with severe synovitis. The greater efficacy of ACS might be attributed to increased anti-inflammatory cytokines concentration, particularly the interleukin-1 receptor antagonist, which plays a key modulatory role in response to inflammation of OA joints. While PRP shows better outcome in the short term, it is predicted that worse outcomes over time are observed due to dependence on platelet-derived growth factors, which offer limited anti-inflammation and regeneration opportunities.

The different effectiveness of ACS and PRP is due to their various methods of functioning. ACS is particularly rich in IL-1Ra which directly opposes IL-1 $\beta$ , one of the major pro-inflammatory cytokines. This IL-1 $\beta$  is well known for its role in cartilage destruction and inflammation of the synovium in OA [26]. Moreover, ACS has a number of other growth factors, such as Transforming Growth Factor-beta (TGF- $\beta$ ) and Insulin-like growth factor-1 (IGF-1), which are known to enhance cartilage formation and decrease the oxidative insult by lowering the level of reactive oxygen species (ROS) and Nitric oxide (NO) within the synovial fluid [25].

On the other hand, PRP relies mainly on the secretion of various platelet-derived growth factors, e.g. platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and TGF- $\beta$ , which are important in tissue regeneration and angiogenesis. Still, the inflammatory setting typical of OA joints may compromise the effectiveness of PRP since platelets are also capable of releasing pro-inflammatory substances which aggravate the synovitis [27]. Such observations might account for the lower effectiveness of PRP in patients with moderate to severe synovitis, as supported by the current meta-analysis, as well as the observations of Shirokova et al. [25].

The superior long-term efficacy of ACS indicates that it may be better suited as a therapeutic option for uncontrollable moderate-to-severe OA patients, compared to other traditional HA or corticosteroid therapies. This observation is supported by Pishgahi et al., who described more than six-months improvements in pain and associated function after ACS, while noting PRP had only temporary effects [24]. Moreover, lower adverse effects of ACS compared to PRP have been shown, which is in line with Coskun et al. who found more adverse events in patients treated with PRP [23].

The potential of ACS to postpone surgical interventions should also be investigated further. Darabos et al. provided evidence that the use of ACS reduces the widening of bone tunnels which occur commonly after ACL reconstruction, thus leading to other uses in addition to OA of the knee [28]. However, the sophisticated and labour-intensive steps involved in the preparation of ACS are likely to limit its routine use. Subsequent studies should seek to improve the steps taken in ACS preparation to ease and increase its use in actual practice.

**Limitations of the study and future directions.** The key finding of this meta-analysis brings to light important issues, some of which need to be addressed. The first challenge which may be the lack of homogeneity of studies, involves differences in design, patient populations and outcome metrics. For example, Khurana et al. found no substantial difference between ACS and PRP treatment at six months, which could also be a result of differing OA severity, injection technique, or preparation [10]. Secondly, the lack of a follow-up period for the patients constitutes a limitation in understanding the long-term effects of ACS and PRP. In particular, the sustained effects, or any adverse impact arising of these biologic treatments during the 12-to-24-month mark, requires further research. This gap in knowledge can easily be addressed in future studies.

Furthermore, ACS and PRP can be compared to other already existing biologics, such as mesenchymal stem cells (MSCs) and stromal vascular fraction (SVF) for OA as they have a promising regenerative potential, and seems to stem from using ACS. Arjmand et al. argue that it could be the use of ACL tears [29].

Lastly, any analysis involving the cost of ACS and PRP care needs to perceive the two as equally important in consideration. As with all other newer treatments, ACS and PRP have sponsors in clinical research and thus are more expensive than standard pharmacologic measures. Nevertheless, the costs of these treatments may be easily absorbed due to the saving on numerous surgical procedures and long-standing medications. More studies with cost-utility and cost-benefit focus should be conducted to make economic burden sharing easier, with known treatment for clinicians and public health manager alike.

## CONCLUSIONS

In summary, this meta-analysis suggests that ACS is more effective than PRP in pain relief and joint function improvement for patients with knee OA. The superior performance of ACS over PRP may be attributed to its anti-inflammatory properties and its capacity to regulate joint homeostasis. Further research is required to enhance the treatment protocols, establish the cost-benefit ratio, and assess long-term outcomes. ACS is believed to be a reasonable therapeutic option for patients with OA who do not respond well to conventional treatment, and are suffering from moderate to severe OA. No data on interim outcomes is currently available.

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