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CRITICALLY APPRAISED TOPIC

The effect of intra-articular platelet-rich plasma injection on pain and lameness in dogs with osteoarthritis

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Osteoarthritis (OA) is a prevalent and progressive degenerative joint disease in dogs, leading to chronic pain, reduced mobility, and diminished quality of life. Conventional management strategies primarily aim to alleviate and palliate clinical signs of pain and reduced mobility. Platelet-rich plasma (PRP) is an emerging regenerative therapy that has gained interest for its potential disease modifying effects, through modulating inflammation and promoting tissue repair. This paper provides a critical appraisal of current literature on the effectiveness of intra-articular injection of PRP compared to a placebo on the clinical outcomes of lameness and pain in dogs with OA. Findings from 7 studies indicate that current evidence supporting the effectiveness of PRP in reducing pain and lameness is weak. Further research in the form of large, randomised, blinded controlled clinical trials is required to further assess the efficacy of PRP.

Keywords lameness; osteoarthritis; pain; platelet-rich plasma; regenerative therapy

List of abbreviations B-PRP, Biophysically activated platelet-rich plasma; CBPI, Canine Brief Pain Inventory; HVAS, Hudson Visual Analogue Scale; MMP, matrix metalloproteinase; MSC, mesenchymal stem cell; NaCl, sodium chloride; OA, osteoarthritis; PBS, phosphate-buffered saline; PRP, platelet-rich plasma; VAS, visual analogue scale

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Clinical scenario

You are presented with an 8-year-old male neutered Golden Retriever with osteoarthritis (OA) who you have seen previously for a reluctance to move and difficulty sitting and rising from a lying position. You have prescribed nonsteroidal anti-inflammatory drugs and have explained to the owner that this medication can have potential side effects and is used as a form of supportive therapy to treat the clinical signs. The owner wants to know whether there are other treatment options available for their dog that target the joint to repair or halt worsening of the disease.

Question

Does intra-articular injection of platelet-rich plasma (PRP) reduce clinical signs of lameness and pain compared to a placebo in dogs with osteoarthritis?

Methods

Primary research papers were identified through targeted search strategies using the Web of Science Core Collection and PubMed databases (Table 1). The search results were screened for relevance to the clinical question based on predefined inclusion and exclusion criteria (Table 2). After removing duplicates, seven studies met the eligibility criteria and were summarised and presented in tabular format (Tables 3 and 4).

Table 1. Database search strategy

Databases searched and dates covered	1. Web of science core collection (1900–Present) 2. PubMed (1900–Present)
Search terms	**Database**: Web of science **Search terms**: (osteoarthritis OR arthritis OR "degenerative joint disease") AND ("platelet-rich plasma") AND (canine OR dog) **Database**: *PubMed* **Search terms**: (osteoarthritis OR arthritis OR "degenerative joint disease") AND ("platelet-rich plasma") AND (canine OR dog)
Date searches performed	First search: 15 January 2022, five papers Second search: 20 September 2022, five papers Third search: 24 January 2023, seven papers Fourth search: 24 July 2024, seven papers

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Table 2. Inclusion and exclusion criteria applied to database search results

Inclusion	• Primary research paper relevant to all the components of the population, intervention, comparison and outcome (PICO) framework • Compares the intra-articular injection of platelet-rich plasma with a placebo • Reports outcome measures of pain and lameness • Articles published in English
Exclusion	• Case reports or case series • Book chapters • Conference proceedings • Narrative reviews

Table 3. Search outcomes by database and total number of relevant studies

Database	Number of results	Number excluded based on inclusion/ exclusion criteria	Total relevant papers
Web of Science	77	70	7
PubMed	36	33	3
Total relevant papers when duplicates removed			7

Results and Discussion

Critical appraisal of the evidence

Osteoarthritis (OA) is a chronic joint disease characterised by synovial joint abnormalities that involve structural and compositional changes to bone, cartilage, meniscus, synovium and other soft tissues.[1] It is the most commonly diagnosed joint disease in canines,[2] posing a significant threat to their welfare. Currently, this chronic joint disease is incurable, and its complex etiology, individual variation in disease burden and ongoing progressive nature make management challenging.[2,3] Pharmacological and nonpharmacological treatment strategies are directed mainly towards alleviation and palliation of clinical signs, which include pain and reduced mobility.[2–4]

PRP therapy is a recent development in regenerative medicine for OA treatment with anti-inflammatory properties and potential to enhance tissue healing. PRP is an autogenous fluid composed of a supraphysiologic concentration of platelets.[5] Platelets contain growth factors in α-granules such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-b), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF) and insulin-like growth factor 1 (IGF-1).[6] These growth factors have been demonstrated to stimulate cartilage regeneration, angiogenesis and diminish the catabolic effects of proinflammatory cytokines.[7] PRP has been shown to have disease modifying effects

Table 4. Overview of relevant papers retrieved from the database search addressing the clinical question

Author and year	Alves et al. (2021)
Population	• 20 police working dogs • Sex: 12 males and 8 females • Age (>2 years): 8.4 ± 2.4 years • Weight (>20 kg): 31.5 ± 5.7 kg • Body condition score: 4/9 (n = 14) and 5/9 (n = 6) • Breeds: German Shepherd Dogs (n = 10), Belgian Malinois Shepherd Dogs (n = 3), Labrador Retriever (n = 3), Dutch Shepherd Dog (n = 2) • Orthopedic Foundation for Animals hip grading: moderate (n = 13), severe (n = 7) • Recruited based on trainer complaints (difficulty rising, jumping and maintaining obedience positions, stiffness and decreased overall performance), physical examination (pain during joint mobilisation, stiffness and reduced range of motion) and radiographic findings consistent with bilateral hip osteoarthritis (OA). • Excluded animals who had received medication or nutritional supplements less than 6 weeks prior, or those who had confirmed orthopaedic, neurologic or concomitant disease through a physical examination, complete blood count and serum chemistry profile.
Intervention studied	Patients were randomly assigned to two groups using a statistical analysis software – 10 in control group (receiving 0.9% sodium chloride [NaCl]) and 10 in treatment group (receiving platelet-rich plasma [PRP]) **Production of PRP** • 50 ml of whole blood was collected from the jugular vein of each treatment group patient. • PRP produced using a PurePRP kit according to manufacturer's instructions, which had a mean platelet concentration of 1564.28 × 10^3/mm^3 (standard deviation [SD] = 447.98 × 10^3/mm^3). **Intra-articular administration** • Sedation: Intravenous medetomidine (0.01 mg/kg) and butorphanol (0.1 mg/kg) • Synovial fluid aspiration using 21-gauge and 2.5″ length needle (maximum volume withdrawn) • Control: Intra-articular administration of 2-ml 0.9% NaCl per hip jointTreatment: Intra-articular administration of 2 ml of PRP per hip joint • Second intra-articular administration was repeated day 14. • Animals were rested for three days after treatment and then resumed normal activity. All patients followed up to day 180 after treatment.
Outcome studied	• Pain: Canine Brief Pain Inventory (CBPI) – Pain interference score (interference domain – Effect on daily functions), pain severity score (severity domain – Severity of pain)

Table 4. Continued

	• Lameness: Hudson Visual Analogue Scale (HVAS) • Mobility: Liverpool osteoarthritis in dogs Stiffness, function, gait, quality of life outcome: Canine orthopaedic index
Design and sample size	Randomised, prospective, double-blinded placebo-controlled clinical trial • n = 10 control (0.9% NaCl) • n = 10 treatment (PRP)
Main findings	• HVAS score was significantly lower in PRP treatment group versus control group from 60 days up to 150 days post-treatment ($P \leq 0.03$). • CBPI pain interference score was significantly lower in PRP treatment group versus control group from 30 days up to 120 days post-treatment ($P \leq 0.03$). • CBPI pain severity score was significantly higher in PRP treatment group versus control group from 15 days up to 180 days post-treatment ($P \leq 0.04$).
Adverse events and side effects	Postinjection lameness was observed in five patients in PRP treatment group and 3 in control group. This self-resolved within 2–3 days.
Limitations	• Sample-size determined through convenience sampling – Less significant representation of the population. • Activity after treatment of PRP not detailed – Uncontrolled environmental conditions post-treatment. • Not mentioned if any participants were lost at each follow-up or whether all participants were included.
Author and year	Arican et al. (2022)
Population	• 36 medium to large dog breed • Weight: 25–50 kg (mean: 32.1 kg) • Age: 4–8 years (mean: 5.1 years) • Clinical and radiographic evidence of unilateral stifle OA – They had unilateral pain and lameness associated with single joint, and all their OA scores on radiography ranged from moderate to severe. • Did not undergo any surgical procedure or intra-articular injection in the last 3 months. Have not used any treatments or nutritional supplements. • Systemically well
Intervention studied	Patients were divided into six treatment groups: PRP, mesenchymal stem cells (MSCs), PRP with MSCs, biophysically activated platelet-rich plasma (B-PRP), B-PRP with MSCs and control (0.9% NaCl). **Production of PRP and B-PRP** • 27 ml of blood was collected from jugular vein of each patient. • PRP was produced using genesis autologous cell system 2. B-PRP was produced by injecting PRP into a bio-physical activator 30 times. • The injected PRP for each dog had an average platelet count between 1,200,000 and 1,500,000 platelets. **Production of MSCs** • Adipose tissue was taken from three dogs in the study. MSCs were isolated from the allogeneic origin of the adipose tissue and reproduced. • The injected MSCs for each dog had a cell count between 1,000,000 and 1,300,000 cells. **Intra-articular injection:** • **Treatment group (PRP and B-PRP):** PRP and B-PRP was injected until resistance felt on the syringe plunger (mean injection of 4–5 ml). • **Control group**: 0.9% NaCl was injected until resistance felt on the syringe plunger. Patients were assessed on days 1, 3, 5, 7 and 15 and weeks 4, 8 and 12 after intra-articular injections.
Outcome studied	• Lameness: HVAS • Pain: CBPI • Synovial fluid concentration of matrix metalloproteinase (MMP): MMP-1, MMP-2, MMP-8, MMP-9 and MMP-13
Design and sample size	Randomised, blinded, placebo-controlled clinical trial • n = 6 treatment (PRP injection) • n = 6 treatment (MSCs injection) • n = 6 treatment (PRP and MSCs injection) • n = 6 treatment (B-PRP injection) • n = 6 treatment (B-PRP and MSCs injection) • n = 6 control group (0.9% NaCl)
Main findings	Provides no evidence that the injection of PRP plasma reduces lameness and pain more than saline injections.
Adverse events and side effects	No adverse effects were reported in treatment and control groups.
Limitations	• Appropriate sample size calculation for the study was not conducted – difficult to determine whether a clinically relevant effect of treatment can be derived.

- Dogs of different breeds, ages, weights and OA severity levels were included with no indication that the treatment and control groups were matched – This can result in selection bias.
- No result data for CBPI and HVAS of control groups were published.
- Intra-articular injection site and volume injected of PRP and saline was not stated.

Author and year	Arican et al. (2018)
Population	• 20 mixed medium to large breed • Weight: 25–50 kg (mean weight of 38 kg) • Age: 8–10 years (mean age of 8.6 years) • Clinical and radiographic evidence of unilateral stifle OA – They had unilateral lameness associated with single joint, and all their OA scores on radiography ranged from moderate to severe. • Excluded animals with meniscal damage. • Received no previous treatment and nutritional supplements.
Intervention studied	Patients were assigned to two groups – 14 in treatment group (received PRP) and 6 in control group (received 0.9% NaCl) **Production of PRP** • Dogs in the treatment group were sedated with propofol (4–7 mg, IV) • 20 ml of blood sample from each dog was collected from the jugular vein • PRP produced using double centrifuge method with mean platelet count of 1,420,000 platelets/μL **Intra-articular injection:** • Solution for PRP treatment group and control group was injected until resistance was felt on the syringe plunger (mean injection of 4–5 ml). Patients were assessed on days 1, 3, 5, 7, 15 and weeks 4, 8 and 12 after intra-articular injections.
Outcome studied	• Lameness: HVAS • Pain: CBPI • Synovial fluid concentration of MMP-2 and MMP-9
Design and sample size	Randomised, blinded, placebo-controlled clinical trial • n = 6 control (0.9% NaCl) • n = 14 treatment (PRP)
Main findings	Provides no evidence that the injection of PRP plasma reduces lameness and pain more than saline injections.
Adverse events and side effects	No adverse effects were reported in treatment and control groups.
Limitations	• Appropriate sample size calculation for the study was not conducted – Difficult to determine whether a clinically relevant effect of treatment can be derived. • Imbalance of sample sizes between the treatment and control group – This can introduce selection bias and affect statistical comparability. • Specific joint where PRP or saline was injected was not detailed. • Superscripts ([a, b]) in Tables 1-4 are not labelled, making its significance ambiguous. • Inconsistency in units between the "days" used in all tables and the "weeks" indicated in text, for example, weeks 4, 8, 12 was replaced with days 30, 60 and 90 in Tables 1–4. • Although pretreatment HVAS and CBPI scores (on day 0) are presented in the results tables and used for comparison with post-treatment outcomes, their collection is not described in the methods section.

Author and year	Cook et al. (2015)
Population	• 12 adult purpose-bred research hounds that underwent partial transection of the anterior cruciate ligament (ACL) and meniscal release • Age: 2–5 years • Weight: 20–27 kg
Intervention studied	All patients underwent partial transection of ACL and meniscal release in right knee via arthroscopy. • Patients were premedicated and anaesthetised. • Standard craniolateral and anteromedial portals were established in the right knee. • Partial ACL transection: Anteromedial bundle of ACL was transected at the midpoint. • Meniscal release: Complete radial transection of caudal horn of the medial meniscus at its junction with the posterior menisco-tibial ligament. • Postoperative analgesia – Morphine (0.5 mg/kg IM) at the time of anaesthetic recovery, tramadol (2–4 mg/kg PO) every 12 hours for 3 days given 6 hours after last morphine dose. **Production of leucoreduced PRP** • 15 ml of whole blood was collected from jugular vein. PRP was produced using ACP syringes and centrifuge. At weeks 1, 2, 3, 6 and 8 after surgery, dogs were sedated for aseptic intra-articular injection of the right knee. They were randomly assigned to two groups: six in treatment group (receiving PRP) and six in control (receiving saline).

	• **Treatment**: 2 ml of leucoreduced PRP was injected after aspiration of synovial fluid. • **Control**: 2 ml of sterile 0.9% saline was injected after aspiration of synovial fluid.
Outcome studied	Patients were assessed pre-operatively, before first treatment and at 1, 2, 6, 12, 18 and 24 weeks after the first treatment. • Stifle comfortable range of motion (CROM) • Lameness: Clinical lameness score using a 10 cm visual analogue scale (VAS) for function • Knee pain and effusion: VAS • Gait analysis kinetics
Design and sample size	Randomised, blinded, placebo-controlled, animal model study • n = 6 control (saline) • n = 6 treatment (PRP)
Main findings	• VAS pain score was significantly higher in control group compared to PRP treatment group from 1-week post-treatment and at each assessment time point throughout the 6-month post-treatment study period ($P < 0.01$). • VAS lameness score was significantly higher in control group compared to PRP treatment group at 5, 12 and 18 weeks after treatment ($P < 0.05$).
Adverse events and side effects	One dog in the saline group developed marked swelling in the stifle and severe lameness after the second injection. The dog was treated with joint lavage and oral antibiotics. The swelling and lameness improved within 3 days and the dog completed the remainder of the study.
Limitations	• Appropriate sample size calculation for the study was not conducted – difficult to determine whether a clinically relevant effect of treatment can be derived. • Sedation protocol before the intra-articular injection was not detailed. • Didn't mentioned whether animals have any underlying conditions or had any treatments conducted previously. • Treatment was administered one week following ACL transection and meniscal release; however, given the short interval, the intervention appears to serve more as a preventative measure rather than a therapeutic one, as osteoarthritis is a chronic condition that develops over time. • No evidence that the animals had osteoarthritis before the treatment. All animals had a reported OA score of less than 9, however, only animals over the score of 9 were classified as having OA.

Author and year	Parlak et al. (2020)
Population	• 36 mixed breed dogs • Sex: 30 males and 6 females • Mean weight 30 ± 1 kg • Mean age 5 ± 1 years • Radiographic evidence (with Kellgren–Lawrence scoring) of unilateral stifle OA • Did not undergo any surgical procedure in the last 6 months, any intra-articular injection in the last 3 months and no parenteral steroid anti-inflammatory drugs in the last month.
Intervention studied	Patients were randomly divided into three treatment groups: PRP, B-PRP, control (0.9% isotonic saline). These three groups were further divided into two subgroups – One received one injection, and the other received two. **Production of PRP** • 27 ml of blood was collected from jugular vein of each patient. • PRP and bio-physically activated PRP was produced using genesis autologous cell system 2. • The injected PRP had an average platelet count between 1,200,000 and 1,500,000/μL. **Intra-articular injection** • **Treatment group (PRP)**: PRP injected until resistance felt on the syringe plunger • **Treatment (B-PRP)**: B-PRP injected until resistance felt on the syringe plunger • **Control**: 0.9% isotonic saline injected until resistance felt on the syringe plunger • The three treatment groups receiving double intra-articular administrations (of PRP, B-PRP or 0.9% isotonic saline) then received a second injection.
Outcome studied	Patients were assessed on days 0, 15, 30, 60 and 90 after intra-articular injections. • Pain: CBPI • Lameness: HVAS • Inflammatory mediators (tumour necrosis factor alpha, interleukin-1 beta, interleukin-6, interleukin-10) in joint fluid • Radiographic examination: Standing lateromedial, craniocaudal, tibial compression lateromedial • Ultrasonographic examination: Synovial fluid, intra-articular tissue reaction, subchondral cartilage line
Design and sample size	Randomised, placebo-controlled clinical trial • n = 12 treatment (PRP): n = 6 single intra-articular injection, n = 6 double intra-articular injection • n = 12 treatment (B-PRP): n = 6 single intra-articular injection, n = 6 double intra-articular injection • n = 12 control (0.9% isotonic saline): n = 6 single intra-articular injection, n = 6 double intra-articular injection
Main findings	Provides no evidence that the injection of PRP plasma reduces lameness and pain more than saline injections

Adverse events and side effects	No adverse effects were reported in treatment and control groups.
Limitations	• Appropriate sample size calculation for the study was not conducted – difficult to determine whether a clinically relevant effect of treatment can be derived. • The specific interval between the first and second intra-articular injection is not explicitly stated in the three treatment groups receiving double intra-articular injections. • Intra-articular injection site and volume administered for treatment and control groups were not stated. • No result data for CBPI and HVAS of the treatment and control groups were published. • No indication that the veterinarian making clinical evaluations on pain and lameness were blinded to group allocations. • CBPI and HVAS comparisons were only made between single and double PRP administration groups. These results were not compared with the control group in the study.

Author and year	Parlak et al. (2022)
Population	• 36 mixed breed dogs • Weight: 25–50 kg • Age: mean of 5.1 years • Radiographic evidence (with Kellgren–Lawrence scoring) of unilateral stifle OA • Did not undergo any surgical procedure in the last 6 months, intra-articular injection in the last 3 months, parenteral steroid anti-inflammatory drugs in the last month and nutritional supplements in the last month.
Intervention studied	Patients were divided into six treatment groups: PRP, MSCs, PRP with MSCs, B-PRP, B-PRP with MSCs and control (0.9% isotonic saline). **Production of PRP and B-PRP** • 27 ml of blood was collected from jugular vein of each patient • PRP was produced using genesis autologous cell system 2. B-PRP was produced by injecting PRP into a biophysical activator 30 times. • The injected PRP had an average platelet count between 1,000,000 and 1,200,000 platelets. **Production of MSCs** • Adipose tissue was taken from three dogs in the study. MSCs were isolated from the allogeneic origin of the adipose tissue and reproduced. • The injected MSCs for each dog had a cell count between 1,000,000 and 1,300,000 cells. **Intra-articular injection:** Solution for each treatment group (PRP, MSCs, PRP and MSC, B-PRP, B-PRP and MSCs) and control group (0.9% isotonic saline) was injected until resistance was felt on the syringe plunger. Patients were assessed on day 0, 15, 30, 60 and 90 after intra-articular injections.
Outcome studied	• Pain: CBPI • Lameness: HVAS • Clinical: Tibial compression and cranial drawer signs • Inflammatory mediators (tumour necrosis factor alpha, prostaglandin E2, interleukin-1 beta, interleukin-6, interleukin-10) in joint fluid • Radiographic examination: Standing lateromedial, craniocaudal, tibial compression lateromedial • Force plate analysis
Design and sample size	Randomised, placebo-controlled clinical trial • n = 6 treatment (PRP injection) • n = 6 treatment (MSCs injection) • n = 6 treatment (PRP and MSCs injection) • n = 6 treatment (B-PRP injection) • n = 6 treatment (B-PRP and MSCs injection) • n = 6 control group (0.9% isotonic saline)
Main findings	Provides no evidence that the injection of PRP plasma reduces lameness and pain more than saline injections.
Adverse events and side effects	No adverse effects were reported in treatment and control groups.
Limitations	• Appropriate sample size calculation for the study was not conducted – difficult to determine whether a clinically relevant effect of treatment can be derived. • No indication that the veterinarian making clinical evaluations on pain and lameness were blinded to group allocations. • No result data for CBPI and HVAS of the treatment and control groups were published. • Intra-articular injection site and volume administered for treatment and control groups were not stated.

Author and year	Yun et al. (2016)
Population	• 24 beagle dogs that had undergone cranial cruciate ligament transection of their right hind limb • Weight: 7.7 ± 1.1 kg

	• Age: 2–3 years old • Inclusion criteria: Physically healthy
Intervention studied	Patients were divided into four treatment groups: PRP, MSCs rinsed with phosphate-buffered saline (PBS), MSC and PRP cotreatment, control (PBS). **Cranial cruciate ligament transection surgery** • Cranial cruciate ligament of right hind limb was excised with no. 11 scalpel blade. • Postoperative analgesics: Tramadol 8 mg/kg twice daily, given subcutaneously for 3 days • Postoperative antibiotics: Enrofloxacin 5 mg/kg once daily, given subcutaneously for 3 days Each dog was walked for 10 minutes per day for 2 months beginning the week after surgery. Intra-articular injections commenced after these 2 months. **Production of PRP and MSC** • 50 ml of fresh blood from each dog was used to produce autologous PRP. The injected PRP had over 1,000,000 platelets/μL. • 15 g of fat tissue aseptically collected from the flank of a dog was used to produce MSC. **Intra-articular injection in right hind limb stifle every week for 1 month**. • Control group: 1 ml of PBS • PRP group: 1 ml of PRP • MSC group: 1.0×10^7 MSCs in 1 ml of PBS • MSC and PRP cotreatment group: 1.0×10^7 MSCs in 1 ml of PRP
Outcome studied	Patients were assessed before surgery and then every month for 3 months after surgery. • Lameness (5-point rating scale) • Focal compressive strength of the femoral and tibial articular surfaces • Histological profile of the articular cartilages of central region of the lateral femoral and tibial condyle • Characterisation of extracellular matrix composition of cartilage on femoral and tibial articular surfaces
Design and sample size	Blinded, placebo-controlled animal model study • n = 6 PRP group • n = 6 mesenchymal stem cell (MSC) group • n = 6 MSC and PRP group • n = 6 control group (PBS)
Main findings	Lameness score of the PRP group significantly decreased after 2 months post-treatment. In comparison, the lameness score of the control group did not significantly decrease.
Adverse events and side effects	No adverse effects were reported in treatment and control groups.
Limitations	• Appropriate sample size calculation for the study was not conducted – difficult to determine whether a clinically relevant effect of treatment can be derived. • The conditions under which the patients were classified as physically healthy were not explicitly stated. • No assessment of whether the animals have osteoarthritis before commencement of treatment. • No mention of randomisation when patients were divided into four study groups. • Anaesthetic protocol for cranial cruciate ligament transection not stated. • Exercise regime for the beagles were not explicitly detailed apart from the time duration. The use of different terrains to walk dogs can have varying effects on healing after surgery. Similarly, there was little detail of whether the housing of the animal's postsurgery was standardised. • 3 veterinarians blindly assessed the grade of lameness. However, the method of study did not detail what lameness score would be taken if the veterinarians had conflicting scores.

both in vitro, on chondrocytes and synovial cells[8] and in animal models of OA.[9] For clinical application of this treatment, evidence of clinical benefits needs to be established. The therapeutic benefits of PRP treatment in dogs with OA are currently inconclusive. The treatment effect of PRP on lameness and pain were investigated in this critical appraisal due to the significance of these clinical outcomes as the primary reason for dog owners to pursue veterinary intervention. PRP is an invasive and costly therapy that requires a reasonable level of expertise to administer and is not without potential complications. Thus strong justification is required for its introduction into small animal practice as a routine treatment option.

This critical appraisal evaluates published studies reporting the effect of PRP treatment compared to a placebo on the clinical outcomes of lameness and pain in dogs with OA. Seven relevant studies were identified and included in the appraisal: five randomised placebo-controlled clinical trials, three of which were blinded studies and two animal model studies, one of which was randomised.

Two randomised controlled studies by Alves[2] and Cook[10] demonstrated a significant reduction in pain and lameness levels in dogs that received intra-articular PRP therapy, as compared to those that received a placebo injection. Both studies scored relatively high on the Jadad scoring system (Table 5), which infers a high methodology quality. Alves[2] used the Hudson Visual Analogue Scale (HVAS) and the Canine Brief Pain Inventory (CBPI) to demonstrate a reduction in lameness and pain respectively following two intra-articular injections of PRP compared to saline injections. Similarly, Cook[10] used

Table 5. Quality of study reporting based on Jadad Scale[11]

Study	Jadad scale score
Alves et al.[2]	4
Cook et al.[10]	4
Yun et al.[12]	1
Arican et al.[13]	2
Arican et al.[14]	2
Parlak & Arican[15]	1
Parlak et al.[16]	1

the HVAS to demonstrate lower pain scores following five intra-articular injections of leukoreduced PRP compared to saline injections, and a lower clinical lameness score using a 10-cm visual analogue scale (VAS) for function. In both studies, the beneficial effects of PRP on pain had a quicker onset than lameness. Cook[10] demonstrated significant changes in pain score from 1 week following intra-articular injections and in contrast, positive effects on lameness were not seen until 5 weeks after treatment. Similarly, Alves[2] found significantly lower pain levels 15 days after intra-articular injection in contrast to improvements in lameness which were only realised 60 days after initial treatment.

The findings by Yun[12] lent weak evidence towards the efficacy of PRP. This study did not compare lameness outcomes between treatment and control groups directly, but rather analysed changes from baseline within each group over time. The efficacy of PRP can only be inferred based on a significant decrease in lameness score 2 months after injection compared to pre-treatment, compared to no significant change in the control group. Yun[12] utilised a five-point rating scale to assess lameness in dogs in contrast to a VAS that was used in the six other randomised controlled studies.[2,10,13–16] VAS has been shown to be a repeatable and valid measurement tool for lameness.[17] However, the five-point rating scale is less sensitive to increases and decreases of the assessed parameter.[17] Consequently, the reduced number of categories in which to quantify the degree of lameness can result in misclassification bias.

The four randomised controlled studies by Arican[13,14] and Parlak[15,16] reported no evidence of changes to lameness or pain levels in canine patients treated with PRP injection compared to a placebo. All four studies scored low on the Jadad scale (Table 1) suggesting a poor methodology quality. Potential selection bias was present in these four studies, as none provided adequate detail on the methods used for randomisation. Furthermore, the studies by Arican[13] and Parlak[16] did not stratify control and treatment groups by key variables such as age, weight, or breed — factors known to influence the onset and progression of OA.[18] The absence of explicitly reported blinding procedures in three studies[14–16] can introduce detection bias into observational measurements of pain and lameness. These limitations raise concerns about the internal validity and generalisability of their findings on PRP efficacy compared to a placebo.

The two studies by Cook[10] and Yun[12] conducted in surgically induced canine models of OA did not verify that OA was established before performing the knee injections. Given that OA is a slow progressive disease[19] it is unlikely to develop within the time frame that the studies were conducted. The protocols adopted in these papers are more aligned with a prophylactic use of PRP injection to prevent OA development.

The composition profile of platelets and leukocytes in PRP products has been demonstrated to strongly influence its biologic effects.[6,20,21] Platelet concentrations positively correlate with an upregulation of anabolic growth factors and gene expression, which enhances tissue regeneration on a cellular level.[6,20] Five of these studies[2,14–16] used platelet concentrations exceeding 1×10^6/uL, which is the appropriate minimum concentration associated with the enhancement of healing.[22] The use of total volume platelets by Arican[10] and the absence of platelet units by Cook[8] made it difficult to discern whether their results were affected by the platelet concentrations. High leukocyte concentrations in PRP have been shown to increase the expression of catabolic cytokines and inflammatory markers.[23,24] Leukocyte-rich PRP injections have been associated with lower functional outcome scores in human knee OA.[24] Five studies[12–16] did not report the leukocyte concentration of their PRP preparation; hence, the significance of PRP leukocyte concentration on the clinical outcomes of pain and lameness cannot be sufficiently appraised. Due to the heterogeneity of cellular compositions in PRP preparations used across these studies, this complicates the ability to establish consistent treatment recommendations.

The frequency and PRP injection schedule in the appraised studies is also a confounding factor on pain and lameness outcomes. The number of intra-articular injections administered ranged from a single injection to five injections per patient throughout the course of these seven studies. In studies that used multiple injections,[2,10,12,15] the time interval ranged from one to three weeks. There is currently no standardised frequency and interval of injection in PRP therapy for OA treatment in canines or humans[25,26] which is an area of ongoing research. It is important to consider the regularity of PRP injections, which has practical implications in a clinical setting for canine patients due to the requirement of sedation before injection. The incidence of OA is positively correlated to increasing age in canines[18]; hence, the relieving of OA symptoms would be largely targeted towards the older canine population. These patients often have a higher incidence of comorbidities, placing them at higher risk of complications associated with sedation. Thus, the PRP therapy may be associated with increased risks due to the frequency of sedation.

All seven papers used small sample sizes, and a power analysis was not done for any of the studies to determine the optimal population size. An insufficient number of test subjects means that findings will be invariably inconclusive and cannot be confidently extrapolated for the wider population.

Intra-articular injection of PRP was consistently demonstrated to be safe in canines across all seven studies. Self-limiting lameness lasting 2–3 days was documented by Alves[2] after PRP injection; however, no significant or persistent adverse events were reported.

More research investigating the long-term efficacy of PRP in relieving the signs of OA is needed. Due to the chronic nature of canine OA, management of clinical signs is required over a significant length of time throughout the patient's life. Patient outcomes in

these studies were evaluated over a duration of 12 to 24 weeks following PRP injection; hence, its long-term efficacy beyond a few months cannot be extrapolated.

Conclusion

There is currently weak evidence supporting the routine use of intra-articular PRP therapy to reduce pain and lameness in OA dogs. Well-designed, double-blinded, randomised, placebo-controlled clinical trials which have an adequate sample size (justified by a power analysis) are required to provide more conclusive evidence. Further studies evaluating the optimal composition of intra-articular PRP preparations and dosing regimens specifically for treating OA pain and the long-term effects of PRP are required to increase its potential application in a clinical setting.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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