PRP and Orthobiologics

Brian Chilelli MD
Disclosures

• Paid speaker for Vericel
What are orthobiologics?

• Biologic cells and growth factors that
  – help mitigate degenerative conditions through anabolic and anti-catabolic pathways
  – Have potential to stimulate a healing/repair process

• Autologous blood
  – Platelet rich plasma (PRP)
  – Autologous conditioned serum (ACS)

• Placental tissue
  – Amniotic membrane
  – Umbilical cord

• Cell based
  – Bone marrow
  – Synovial
  – Adipose tissue
  – Peripheral blood
NIH definition of “Stem Cell”

• **Stem cells**—Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells.

• Stem cells are distinguished from other cell types by **two important characteristics**
  – unspecialized cells **capable of renewing themselves** through cell division, sometimes after long periods of inactivity.
  – under certain physiologic or experimental conditions, they **can be induced to become tissue- or organ-specific cells with special functions**. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues.
STEM CELLS CAN

REPLICATE ITSELF  OR  CHANGE INTO MANY CELL TYPES

- NERVE CELL
- BLOOD CELLS
- INTESTINAL CELLS
- MUSCLE CELLS
- LIVER CELLS
- CARDIAC CELLS
Stem cells can be confusing....?

- **Definitions**
  - **Stem cell**: homogeneous cell population obtained through culture expansion
  - **Cell concentrate**: heterogeneous cell population containing a small fraction of stem cells
  - **Stem cell therapy**: cells have been isolated from a pellet of cell concentrate, followed by culture expansion, and then characterized for the following parameters: self renewal, expression of specific cell surface markers, and multilineage differentiation capacity
    - Homogeneous cell population can then be referred to as mesenchymcal stem cells (MSC) used for stem cell therapy
  - **Cell source aspirate concentrate**: Stem cells derived by cell concentrate
Mesenchymal Stem Cells*

Arnold I. Caplan

The Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, Ohio, U.S.A.

Arnold Caplan, a biologist at Case Western Reserve University, popularized the term MSC in 1991 to describe cells isolated from bone marrow stroma that could give rise to bone and cartilage.
Mesenchymal Stem Cells: Time to Change the Name!

ARNOLD I. CAPLAN

Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, Ohio, USA

Key Words. Medicinal signaling cells • Mesenchymal stem cells • MSCs • Regenerative medicine

SUMMARY

Mesenchymal stem cells (MSCs) were officially named more than 25 years ago to represent a class of cells from human and mammalian bone marrow and periosteum that could be isolated and expanded in culture while maintaining their in vitro capacity to be induced to form a variety of mesodermal phenotypes and tissues. The in vitro capacity to form bone, cartilage, fat, etc., became an assay for identifying this class of multipotent cells and around which several companies were formed in the 1990s to medically exploit the regenerative capabilities of MSCs. Today, there are hundreds of clinics and hundreds of clinical trials using human MSCs with very few, if any, focusing on the in vitro multipotential capacities of these cells. Unfortunately, the fact that MSCs are called “stem cells” is being used to infer that patients will receive direct medical benefit, because they imagine that these cells will differentiate into regenerating tissue-producing cells. Such a stem cell treatment will presumably cure the patient of their medically relevant difficulties ranging from osteoarthritis (bone-on-bone) knees to various neurological maladies including dementia. I now urge that we change the name of MSCs to Medicinal Signaling Cells to more accurately reflect the fact that these cells home in on sites of injury or disease and secrete bioactive factors that are immunomodulatory and trophic (regenerative) meaning that these cells make therapeutic drugs in situ that are medicinal. It is, indeed, the patient’s own site-specific and tissue-specific resident stem cells that construct the new tissue as stimulated by the bioactive factors secreted by the exogenously supplied MSCs. STEM CELLS TRANSLATIONAL MEDICINE 2017;6:1445–1451
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CURING DISEASES WITHOUT SURGERY...

HERE'S TO YOU, STEM CELLS
As Lee Corso would say….Not so fast, my friend

- Many studies claiming to treat knee conditions with “stem cells”
- Unclear and inconsistent with defining “stem cells”
- Most current studies are underpowered, uncontrolled trials and heterogeneous
- Most review articles are based on author conclusions/summaries
What is allowed in the United States?

- FDA’s requirements for HCT/P (human cells, tissues, and cellular or tissue-based products) are set forth in *Title 21 of the Code of Federal Regulations (CFR) Part 1271*
  - 1. Minimal manipulation (centrifugation)
  - 2. Homologous use only (Same tissue function)
  - 3. No adding of cells (growth factors, enzymes, etc)
  - 4. Does not have systemic effect or is not dependent upon the metabolic activity of living cells for its primary function
- Unless its: for autologous use, allogenic use in first or second degree relative, or for reproductive use
Nomenclature Inconsistency and Selective Outcome Reporting Hinder Understanding of Stem Cell Therapy for the Knee

Ian A. Jones, BA, Xiao Chen, BA, Denis Evseenko, MD, PhD, and C. Thomas Vangsness Jr., MD

Investigation performed at the Department of Orthopaedic Surgery, Keck School of Medicine of USC, Los Angeles, California

Tissue Procurement and Processing

Common Point-of-Care Cell Therapies

Stromal Vascular Fraction (SVF)
- A heterogeneous cell population (15-30% stromal cells) isolated from enzymatically digested autologous adipose tissue using differential centrifugation [29].

Adipose-Derived Stromal Cells (ASCs)
- A heterogeneous cell population (15-30% stromal cells) that is isolated from enzymatically digested autologous adipose tissue using differential centrifugation [29].

Fat Grafts (Tissue Transplants)
- Liposaprate that has been washed and mechanically emulsified. Officially administered for their “structural properties”, but are often promoted as “stem cell” or regenerative therapies [45, 46], despite containing fewer stromal cells than SVF [47,48].

Prospective isolation by phenotype

Mesenchymal Stem Cells (MSCs)
- Single progenitors that, when explanted in vivo, exhibit multipotency and self-renewal.

Bone Marrow Aspirate (BMAC)
- Bone marrow that has undergone density gradient centrifugation. A source of potentially beneficial anabolic and anti-inflammatory mediators, but stromal cells only represent 0.001% to 0.01% of the final preparation [51].

Plate BMAC at high-density

Mesenchymal Stromal Cells (MSCs)
- Plastic-adherent stromal populations that have been separated from non-adherent cells.

Plate BMAC at low-density

Jones et al. JBJS 2019
Nomenclature Inconsistency and Selective Outcome Reporting Hinder Understanding of Stem Cell Therapy for the Knee

Ian A. Jones, BA, Xiao Chen, BA, Denis Evseenko, MD, PhD, and C. Thomas Vangness Jr., MD

Investigation performed at the Department of Orthopaedic Surgery, Keck School of Medicine of USC, Los Angeles, California
Results: There was extensive variation among the treatments, adjuvant therapies, and outcome measures. Treatments did not coincide with terminology. Significant differences in clinical outcomes were reported infrequently, and intra-group improvements or inter-group subscore differences were consistently highlighted, particularly when inter-group comparisons were left unreported.

Jones et al. JBJS 2019
Conclusions: Overall, there are isolated cases in which positive efficacy results have been published, but our results suggest that the generally positive efficacy conclusions concerning stem cell therapy for knee cartilage pathology may be overstated. Nevertheless, it is important to understand that the efficacy of stem cell therapies should not be considered in aggregate. Cells that are procured or processed differently produce entirely different drugs. When evaluating the efficacy of “stem cell” therapies, clinicians must consider the methodological quality, nomenclature, and inherent distinctness of each treatment.
Stem Cell Therapy for Articular Cartilage Repair

Review of the Entity of Cell Populations Used and the Result of the Clinical Application of Each Entity

Yong-Beom Park,* MD, PhD, Chul-Won Ha,†‡§ MD, PhD, Ji Heon Rhim, † PhD, and Han-Jun Lee,* MD, PhD

Investigation performed at Samsung Medical Center and Chung-Ang University Hospital, Seoul, Republic of Korea

Background: Following successful preclinical studies, stem cell therapy is emerging as a candidate for the treatment of articular cartilage lesions. Because stem cell therapy for cartilage repair in humans is at an early phase, confusion and errors are found in the literature regarding use of the term stem cell therapy in this field.

Purpose: To provide an overview of the outcomes of cartilage repair, elucidating the various cell populations used, and thus reduce confusion with regard to using the term stem cell therapy.

Study Design: Systematic review.

Methods: The authors systematically reviewed any studies on clinical application of mesenchymal stem cells (MSCs) in human subjects. A comprehensive search was performed in MEDLINE, EMBASE, the Cochrane Library, CINAHL, Web of Science, and Scopus for human studies that evaluated articular cartilage repair with cell populations containing MSCs. These studies were classified as using bone marrow–derived MSCs, adipose tissue–derived MSCs, peripheral blood–derived MSCs, synovium–derived MSCs, and umbilical cord blood–derived MSCs according to the entity of cell population used.

Results: Forty-six clinical studies were identified to focus on cartilage repair with MSCs: 20 studies with bone marrow–derived MSCs, 21 studies with adipose tissue–derived MSCs, 3 studies with peripheral blood–derived MSCs, 1 study with synovium–derived MSCs, and 1 study with umbilical cord blood–derived MSCs. All clinical studies reported that cartilage treated with MSCs showed favorable clinical outcomes in terms of clinical scores or cartilage repair evaluated by MRI. However, most studies were limited to case reports and case series. Among these 46 clinical studies, 18 studies erroneously referred to adipose tissue–derived stromal vascular fractions as “adipose-derived MSCs,” 2 studies referred to peripheral blood–derived progenitor cells as “peripheral blood–derived MSCs,” and 1 study referred to bone marrow aspirate concentrate as “bone marrow–derived MSCs.”

Conclusion: Limited evidence is available regarding clinical benefit of stem cell therapy for articular cartilage repair. Because the literature contains substantial errors in describing the therapeutic cells used, researchers need to be alert and observant of proper terms, especially regarding whether the cells used were stem cells or cell populations containing a small portion of stem cells, to prevent confusion in understanding the results of a given stem cell–based therapy.
Among 46 clinical studies

- 18 studies erroneously referred to adipose tissue–derived stromal vascular fractions as “adipose-derived MSCs”
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Bone Marrow Aspirate Concentrate (BMAC)

- Bone marrow aspirate can be harvested from multiple sites
  - Iliac crest, proximal tibia, distal femur, calcaneous, proximal humerus
- Processed via centrifuge to produce a heterogeneous cell population containing a small fraction of mesenchymal stem cells (MSC)
- One stage implantation
- Minimal manipulation of cells
Bone Marrow Aspirate Concentrate (BMAC)
Bone Marrow Aspirate Concentrate (BMAC)
Bone Marrow Aspirate Concentrate (BMAC)

Aspirate
Small Volume

Concentrate
Automatic Process

Apply to Injury
Ready in 15 Minutes
Bone Marrow Aspirate Concentrate (BMAC)

• Can then be used to treat cartilage defects in isolation or be used as an adjunct procedure.

• Contains high concentrations of
  – vascular endothelial growth factor (VEGF)
  – transforming growth factor-beta (TGF-B)
  – platelet derived growth factor (PDGF)
  – bone morphogenetic proteins (BMP) -2 and -7

• This unique composition has been demonstrated to promote
  – wound healing
  – collagen synthesis
  – MSC differentiation
  – chondrocyte proliferation
  – while suppressing proinflammatory cytokines
Concentrated Bone Marrow Aspirate for the Treatment of Chondral Injuries and Osteoarthritis of the Knee

A Systematic Review of Outcomes

Chahla et al. AJSM 2016

- Systematic Review
- BMAC for treatment of chondral defects and OA of knee
- 11 studies included
  - 5 prospective, 1 retrospective, 2 case series, 3 case reports
  - 3 for OA and 8 for focal chondral defects
- All studies reported good to excellent overall outcomes

- We like good to excellent results but.....We need well conducted randomized controlled trials!
Only RCT

25 patients with bilateral knee pain from bilateral OA

Randomized to BMAC into one knee and saline placebo into the other

Safety outcomes, pain relief, and function measured by OARSI (Osteoarthritis Research Society International) measures and VAS (Visual Analog Scale) tracked initially, 1 week, 3 months, and 6 months

No difference in outcomes between BMAC and saline treatments
Systematic Review

The Role of Bone Marrow Aspirate Concentrate for the Treatment of Focal Chondral Lesions of the Knee: A Systematic Review and Critical Analysis of Animal and Clinical Studies

Leonardo Cavinatto, M.D., Ph.D., Betina B. Hinckel, M.D., Ph.D., Ryan E. Tomlinson, Ph.D., Sunny Gupta, M.D., Jack Farr, M.D., and Arthur R. Bartolozzi, M.D.

- 23 studies: 10 animal models and 13 human studies

...low levels of evidence on average. Conclusions: Although clinical success in short-term and midterm applications has been suggested for the application of BMAC for the restoration of cartilage defects in lesions of the knee, current study designs are generally of low scientific rigor. In addition, clinical applications of this technology in animal model investigations have shown inconsistent outcomes. Thus, clinicians should apply this technology cautiously. Level of Evidence: Level IV, systematic review of Level II, III, and IV evidence studies.

Cavinatto et al. Arthroscopy 2019
Intra-articular injection of culture-expanded mesenchymal stem cells with or without addition of platelet-rich plasma is effective in decreasing pain and symptoms in knee osteoarthritis: a controlled, double-blind clinical trial

Ricardo Bastos\textsuperscript{1,2,3,4,5,15} · Marcelo Mathias\textsuperscript{2} · Renato Andrade\textsuperscript{1,3,6} · Ronaldo J. F. C. Amaral\textsuperscript{7,8,9} · Vinicius Schott\textsuperscript{2} · Alex Balduino\textsuperscript{10} · Raquel Bastos\textsuperscript{11} · J. Miguel Oliveira\textsuperscript{4,5,12} · Rui L. Reis\textsuperscript{4,5,12} · Scott Rodeo\textsuperscript{13} · João Espregueira-Mendes\textsuperscript{1,3,5,14,15}

- Compare injections of culture-expanded bone-derived mesenchymal stem cells (MSCs) with or without PRP to corticosteroid injection for knee OA
- 47 patients: 16 (MSCs), 14 (MSCs + PRP), 17 (corticosteroid)
- Outcomes: KOOS and Range of motion at 1,2,3,6,9, and 12 months and intra-articular cytokines at baseline, 6 months, 12 months
- All 3 groups showed significant improvement in all KOOS domains and global score at 12 months
- MSCs and MSCs + PRP had highest percentage of improvement in most KOOS domains and global score compared to corticosteroid group
Adipose Tissue–Derived Mesenchymal Stem Cells (AD-MSCs)

- Adipose tissue–derived MSCs (AD-MSCs) - adipose tissue can be easily and repeatedly obtained as lipoaspirate via liposuction.
- The amount of MSCs from adipose tissue is approximately 500-fold greater than that from BM when isolated from an equivalent amount of aspirate.
- AD-MSCs have been shown to have inferior chondrogenic potential compared with BM-MSCs in vitro, although the chondrogenic differentiation of Ad-MSCs can be enhanced by modulation with in vitro added factors.
• 38 patients with knee OA
• Treated with arthroscopy and injection of autologous and micro-fragmented adipose tissue
• Clinical outcomes obtained at 1, 3, 6, and 12 months (Knee Injury and Osteoarthritis Outcome Score questionnaire)
• Results
  – Statistically significant improvement of all clinical scores from preop to 1, 3, 6, and 12 months
  – 92% clinically improved
  – 100% satisfied with the treatment
• Compare clinical, radiological, and second-look arthroscopic outcomes of HTO with vs without AD-MSC

• 50 patients HTO vs 50 patients HTO with AD-MSC injection

• Clinical outcomes: International Knee Documentation Committee (IKDC) score and Lysholm score

• Radiologic outcomes: femorotibial angle and posterior tibial slope

• Second-look arthroscopy: Cartilage regeneration using International Cartilage Repair Society (ICRS) grade

• HTO with AD-MSC injection group had better patient reported outcomes and improved ICRS grades
25 patients treated with AD- culture-expanded MSC for a symptomatic cartilage defect and followed for 3 years

- Median Age = 30.5
- Average lesion size = 3.5 cm$^2$
- Objective and subjective scores at preop, 6, 12, 24, and 36 months (KOOS, IKDC, VAS)
- MRI evaluation using MOCART score at 12 ands 24 months

Results:
- Clinical outcomes recorded significant improvement at final follow-up compared to baseline
- Favorable MRI findings in 65% of patients and two post-op biopsies with hyaline-like tissue

Kyriakidis et al. KSSTA 2019
Amniotic-derived treatments

• Specimens recovered from fluid and placental tissues that would normally be discarded at birth from healthy donors
• Allogenic
• Contains
  – Human Amniotic Membrane
  – Human Amniotic Fluid Derived Cells
• Anabolic growth factors include:
  – TGF-a, TGF-B, basic fibroblast factor, IL-4, IL-6, IL-8, IL-10, tissue inhibitors of metalloproteinases 1 (TIMP-1), TIMP-2, TIMP-4, epidermal growth factor, PDGF, FGF-18
Cryopreserved Amniotic Suspension for the Treatment of Knee Osteoarthritis

Jeremy B. Vines, MS1,2  Antonios O. Aliprantis, MD, PhD3  Andreas H. Gomoll, MD, PhD4  Jack Farr, MD5

- Initial pilot study
- 6 pts with knee OA (KL grade 3) and followed for 12 months
- Single injection of 4ml (2ml of amniotic suspension with saline)
- No adverse events
- Improvement in KOOS, IKDC and SANE scores
- Larger RCT against NS and HA
200 patients randomized to amniotic suspension allograft (ASA), hyaluronic acid (HA), or saline

**PRO:** EQ-5D-5L, KOOS, VAS, Tegner, and Single Assessment Numerical Evaluation (SANE) outcome scores were obtained *(baseline, 3 months, 6 months)*

Treatment failure = unacceptable pain at 3 months and withdrawn from study
- ASA (13.2%)
- HA (68.8%)
- Saline (75%)

ASA patients with significantly greater improvements from baseline for VAS, KOOS pain, and KOOS-ADL compared with HA (3 months) and both groups (6 months)

ASA patients with significantly greater improvements from baseline for KOOS symptom scores compared with HA and saline (3 and 6 months)
• 3 Amniotic fluid preparation (AFP) company products compared to unprocessed amniotic fluid and 2 samples of human bone marrow aspirate (BMA) samples

• MSCs could not be identified in the commercial AFPs or the unprocessed amniotic fluid

• MSCs could be cultured from the BMA but most of the cells were dead and the few living cells did not exhibit established characteristics of MSCs
Conclusions:

- The AFPs studied should not be considered "stem cell" therapies, and researchers should use caution when evaluating commercial claims that products contain stem cells. Given their growth factor content, however, AFPs may still represent a promising tool for orthopaedic treatment.
Platelet-Rich Plasma (PRP)

- Whole blood drawn from a patient and centrifuged to separate platelet-poor plasma, PRP, and red blood cells
- Concentrated autologous platelets suspended in a small amount of plasma after centrifugation
- PRP is a natural source of growth factors
  - platelet derived growth factor (PDGF)
  - insulin like growth factor (IGF)
  - vascular endothelial growth factor (VEGF)
  - platelet derived angiogenic factor (PDAF)
  - transforming growth factor beta (TGF-β).
Platelet-Rich Plasma (PRP)

- Can treat various muscle and or tendon conditions
  - Epicondylitis of elbow, patellar tendinopathy, hamstring strain/proximal tendinopathy, plantar fasciitis, gluteal tendinopathy
- Efficacious in treating osteoarthritis of the knee
- Meniscus repair – Newer studies suggest a role for PRP augmentation following isolated meniscus repair
- Cartilage restoration - can be utilized as an adjunct to micronized allograft cartilage and marrow stimulation.
What about the leukocyte content...???
Current Clinical Recommendations for Use of Platelet-Rich Plasma

Adrian D. K. Le¹² • Lawrence Enweze¹ • Malcolm R. DeBaun¹ • Jason L. Dragoo¹

• Abundant high-quality evidence supports the use of LR-PRP injection for lateral epicondylitis and LP-PRP for osteoarthritis of the knee.

• Moderate high-quality evidence supports the use of LR-PRP injection for patellar tendinopathy and of PRP injection for plantar fasciitis
LR-PRP induces a greater inflammatory response than LP-PRP is supported by in vivo studies.

Due to the importance of leukocytes, contributing to both the inflammation and signaling for other cells types, prompt they are crucial for regeneration. Neutrophils secrete cytokines for the chemotaxis of macrophages. Macrophages present plasticity properties which are important in promoting the inflammatory process required to then initiate the healing process.
A rabbit Achilles tendinopathy model was induced by a collagenase injection. A week later, treatments were applied randomly on local Achilles tendon lesions: (1) 200 mL of Lr-PRP (16 legs), (2) 200 mL of Lp-PRP (16 legs), and (3) 200 mL of saline (16 legs). At 3 and 6 weeks after the collagenase injection, outcomes were evaluated by histology, magnetic resonance imaging (MRI), real-time polymerase chain reaction analysis, immunohistochemistry, and transmission electron microscopy (TEM). Conclusion: Lr-PRP had more beneficial effects than Lp-PRP when delivered at an early stage during tendon repair.
Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials

Wen-Li Dai, M.Sc., Ai-Guo Zhou, M.D., Hua Zhang, M.D., and Jian Zhang, M.D.

- 10 RCT with 1069 patients
- 6 months: PRP and HA had similar effects on pain relief (WOMAC) and functional improvement (WOMAC function, IKDC, Lequesne)
- 12 months: PRP with significantly better pain relief and functional improvement compared to HA
- PRP with significantly better pain relief and functional improvement compared to saline at 6 and 12 months
A total of 18 studies (all level 1)

811 patients: PRP (mean age, 57.6 years)

797 patients: HA (mean age, 59.3 years)

Mean follow-up: 11.1 months

Mean improvement was significantly higher in the PRP group (44.7%) than the HA group (12.6%) for WOMAC total scores

Conclusion: Patients undergoing treatment for knee OA with PRP can be expected to experience improved clinical outcomes when compared with HA. Additionally, leukocyte-poor PRP may be a superior line of treatment for knee OA over leukocyte-rich PRP
Platelet-Rich Plasma Reduces Failure Risk for Isolated Meniscal Repairs but Provides No Benefit for Meniscal Repairs With Anterior Cruciate Ligament Reconstruction

Joshua S. Everhart, MD, MPH, Parker A. Cavendish, BS, Alex Eikenberry, BS, Robert A. Magnussen, MD, MPH, Christopher C. Kaeding, MD, and David C. Flanigan, MD
Investigation performed at Sports Medicine Research Institute, The Ohio State University, Columbus, Ohio, USA

- 550 patients
- Isolated meniscus repair with and without PRP
- Meniscus repair at time of ACL reconstruction with and without PRP

Results:
- Failure within 3 years: 17% without PRP and 14.6% with PRP
- Isolated meniscus repair failure at 3 years: 20.3% and PRP was independently associated with lower risk of failure
Complete radial tear of lateral meniscus in Division I football player
Complete radial tear of lateral meniscus in Division I football player
Conclusion:

- Despite some promising early results for PRP, BMSC, ADSC, and AMSC therapies, the majority of level-of-evidence I studies have multiple problems: small sample sizes, potentially inappropriate control cohorts, short-term follow-up, and so on. Despite the limitations, there still appears to be evidence justifying their use for knee osteoarthritis management. More high-level, larger human studies utilizing standardized protocols are needed.
To investigate the functional improvement and pain reduction of different nonsurgical treatments for patellar tendinopathy

Eleven studies with 430 affected patellar tendon

The network meta-analysis demonstrated that LR-PRP has the greatest functional improvement and pain reduction compared with other treatment options.
10 studies

207 hamstring injuries treated with PRP vs 149 in the control group

Statistically nonsignificant evidence to suggest that PRP injection + PT reduced mean time to RTP or reinjury rates compared to no treatment or PT alone for hamstring injuries in a short-term follow-up
NFL players from a single team who sustained acute grade 2 hamstring injuries, as diagnosed on magnetic resonance imaging (MRI) were retrospectively reviewed.

A total of 108 NFL players had MRI evidence of a hamstring injury, and of those, 69 athletes sustained grade 2 injuries.


PRP: Average time missed was 22.5 days, 18.2 practices, and 1.3 games.

No PRP: time missed was 25.7 days (P < .05), 22.8 practices (P < .05), and 2.9 games (P < .05).

Conclusion: no significant difference in days missed or time to return to practice but did allow for faster return to play, with a 1 game overall difference.
Platelet-Rich Plasma Versus Corticosteroids for Plantar Fasciitis

A Systematic Review of Randomized Controlled Trials

Eoghan T. Hurley, MB, BCh, MCh, Yoshiharu Shimozono, MD, Charles P. Hannon, MD, Niall A. Smyth, MD, Christopher D. Murawski, MD, and John G. Kennedy, MD, MCh, MMSc, FFSEM, FRCS(Orth)

Investigation performed at NYU Langone Health, New York, New York, USA

• A total of 9 RCTs
• 239 patients with PRP with 240 patients with CS injection
• At the follow-up time points 1-1.5, 3, 6, and 12 months, there were statistically significant differences in VAS scores in favor of PRP
• 6 and 12 months: there was a difference in AOFAS scores in favor of PRP
Retrospective review of 33 patients with ME and minimum clinical follow-up of 1 year

15 patients: series of 2 leukocyte-rich PRP injections

18 patients: surgery.

Outcome measures included time to pain-free status, time to full range of motion (ROM), the Mayo Elbow Performance Score (MEPS), and the Oxford Elbow Score (OES)

Statistically significant improvement was noted in both time to full ROM (42.3 days for PRP vs 96.1 days for surgery; P < .01) and time to pain-free status (56.2 days for PRP vs 108.0 days for surgery; P < .01).

PRP showed clinically similar outcomes to those of surgery in recalcitrant type 1 ME. PRP can be considered as an alternative to surgery in the treatment of recurrent ME, with an earlier time to full ROM and time to pain-free status compared with surgery.
The Efficacy of Platelet-Rich Plasma on Tendon and Ligament Healing

A Systematic Review and Meta-analysis With Bias Assessment

Xiao Chen,* BA, Ian A. Jones,* BA, Caron Park,† PhD, and C. Thomas Vangsness Jr,**† MD
Investigation performed at Keck School of Medicine of USC, Los Angeles, California, USA

- Systematic review and meta-analysis.
- 37 articles were included in this review, 21 (1031 participants) of which could be included in the quantitative analysis
- PRP may reduce pain associated with lateral epicondylitis and rotator cuff injuries.
There are only rigorous data to support the use of PRP for (1) symptoms of osteoarthritis of the knee and (2) chronic tendinitis of the patellar tendon and elbow extensor tendons.

The major limitation of PRP: significant unpredictability in its effect because of the wide variability in different PRP formulations and lack of information about the optimal PRP formulation for different conditions.
Systematic Review

A total of 78 randomized controlled trials (5308 patients) were included

Conclusion: PRP leads to a reduction in pain; however, evidence for clinically significant efficacy is limited. Available evidence supports the use of PRP in the management of lateral epicondylitis as well as knee osteoarthritis.
Blood from 39 healthy patients was collected at a standardized time and processed into leukocyte-poor PRP within 1 hour of collection using the same laboratory centrifuge protocol and frozen for later analysis.

11 female and 10 male patients were “young” (aged 18-30 years), while 8 male and 10 female patients were “older” (aged 45-60 years).

Male patients had higher cytokine and growth factor levels in PRP compared with female patients for interleukin–1 beta, tumor necrosis factor–alpha (TNF-a), the anti-inflammatory IL-1 receptor antagonist protein (IRAP) and growth factors such as fibroblast growth factor–basic (FGF-basic), platelet-derived growth factor (PDGF-BB) and transforming growth factor-beta 1 (TGF-b1).

Conclusion: There are differences in the composition of PRP between men and women, with sex being a greater factor than age. There was also proteomic variability within the groups.
Thanks!