MiKS
Medical Innovation
Knowledge Sharing

CONSENSUS STATEMENT OF THE GRIIP ON INTRA-ARTICULAR PLATELET-RICH PLASMA INJECTIONS FOR THE TREATMENT OF SYMPTOMATIC KNEE OSTEOARTHRITIS

Florent Eymard, Paul Ornetti, Jérémy Maillet, Éric Noel, Philippe Adam, Virginie Legré Boyer, Thierry Boyer, Fadoua Allali, Vincent Gremeaux-Bader, **Jean-François Kaux**, Karine Louati, Martin Lamontagne, Fabrice Michel, Pascal Richette, Hervé Bard

Groupe de Recherche International sur les Injections de PRP

1st MIKS International Congress on Biological Therapies

Prof Jean-François KAUX, MD PhD

Vice-president of the GRIIP

University and University Hospital of Liège (Belgium)

I have **N0** competing commercial or financial interests related to this topic

Le GRIIP

Groupe de Recherche International sur les Injections de Plaquettes

Aims of the GRIIP

- **To promote**, among all audiences, **the progress of knowledge on good practices and uses of Platelet Rich Plasma (PRP) in musculoskeletal pathology** in the context of other available treatments (hyaluronic acid, stem cells...) and more globally on regenerative medicine treatments

- To define with the medical profession and the regulatory authorities a framework for the use of PRP in humans

- This will be implemented :
  - by supporting research programmes and clinical studies of good methodology
  - through publications
  - by organizing training for healthcare teams and the public through all means of communication

The GRIIP Ethic

- **To be independent from the industry**
- To fight against commercial abuses and misuse of PRP in MSK pathology
- **To maintain a scientific and rigorous approach**
- To be a recognized interlocutor of the public authorities
- To work with the various learned societies in a transparent manner

Website & social medias

- www.griip.org

RATIONNEL

- The use of autologous PRP in KOA has risen drastically in recent years
- The use of PRP in the management of knee osteoarthritis remains debated
- The lack of standardization is a limitation of the current literature
- Heterogeneity of preparation and injection protocols
- Objective: To formulate the first clinical practice recommendations on PRP injections in knee osteoarthritis via expert consensus

MATERIALS AND METHODS

2021

15 French-speaking doctors:

- 10 Rheumatologists
- 4 PRM / Sports medicine physicians
- 1 Radiologist

5 countries

- Belgium, Canada, France, Morocco and Switzerland

Comprehensive literature review

Delphi Method / Formalized Consensus

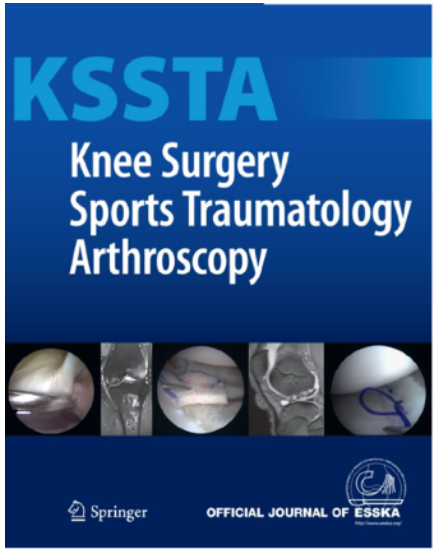
Knee Surgery, Sports Traumatology, Arthroscopy
https://doi.org/10.1007/s00167-020-06102-5

KNEE

Check for updates

Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: a consensus statement from French-speaking experts

Florent Eymard[1] · Paul Ornetti[2] · Jérémy Maillet[3] · Éric Noel[4] · Philippe Adam[5] · Virginie Legré-Boyer[6] · Thierry Boyer[7] · Fadoua Allali[8] · Vincent Gremeaux[9] · Jean-François Kaux[10] · Karine Louati[11] · Martin Lamontagne[12] · Fabrice Michel[13] · Pascal Richette[14] · Hervé Bard[15] on behalf of the GRIP (Groupe de Recherche sur les Injections de PRP, PRP Injection Research Group)



MATERIALS AND METHODS

2021

25 RECOMMENDATIONS

- Effectiveness of PRP
- General recommendations
- Characteristics of PRP
- Contraindications and interactions
- Rules of good practice and adverse effects

Knee Surgery, Sports Traumatology, Arthroscopy
https://doi.org/10.1007/s00167-020-06102-5

KNEE

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Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: a consensus statement from French-speaking experts

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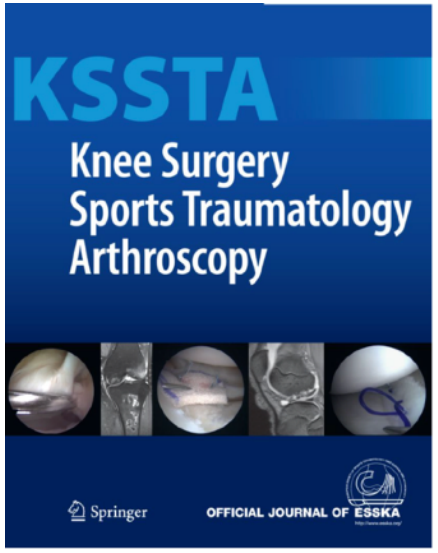
CLASSIFIED (between 1 and 9) **AS :**

- Appropriate (≥ 7) or
- Not appropriate(≤ 3.5)
- with strong agreement (distribution of ratings in the (1–3) range) or
- relative agreement (distribution of ratings in the (1–5) range
- LEVEL OF EVIDENCE : 1 to 5



EFFECTIVENESS OF PRP IN KNEE OA

Recommandations	Expert opinion	Median	Distribution			Level
			≤ 3	4-6	≥ 7	Evidence
IA injections of PRP in the knee are an effective symptomatic treatment for early to moderate osteoarthritis	Appropriate with relative agreement	8	0	1	14	1A
IA injections of PRP into the knee joint may be useful in severe osteoarthritis (Kellgren and Lawrence stage IV)	Appropriate with relative agreement	7	0	5	10	2B
Age, weight and physical activity can influence the indication and the outcome of IA injections of PRP in knee OA	Appropriate with relative agreement	8	0	1	14	4
The location of knee osteoarthritis influences the outcome of knee osteoarthritis treatment with PRP	Uncertain, Lack of consensus	7	0	4	11	4

4 RECOMMENDATIONS

- **Indication according to radiographic severity**
- **Response predictors**

EFFECTIVENESS OF PRP IN KNEE OA

RECOMMENDATION 1

Recommandations	Expert opinion	Median	Distribution		
			≤ 3	4-6	≥ 7
IA injections of PRP in the knee are an effective symptomatic treatment for early to moderate osteoarthritis	Appropriate with relative agreement	8	0	1	14

>75 published clinical studies (pubmed)
13 RCT vs. placebo

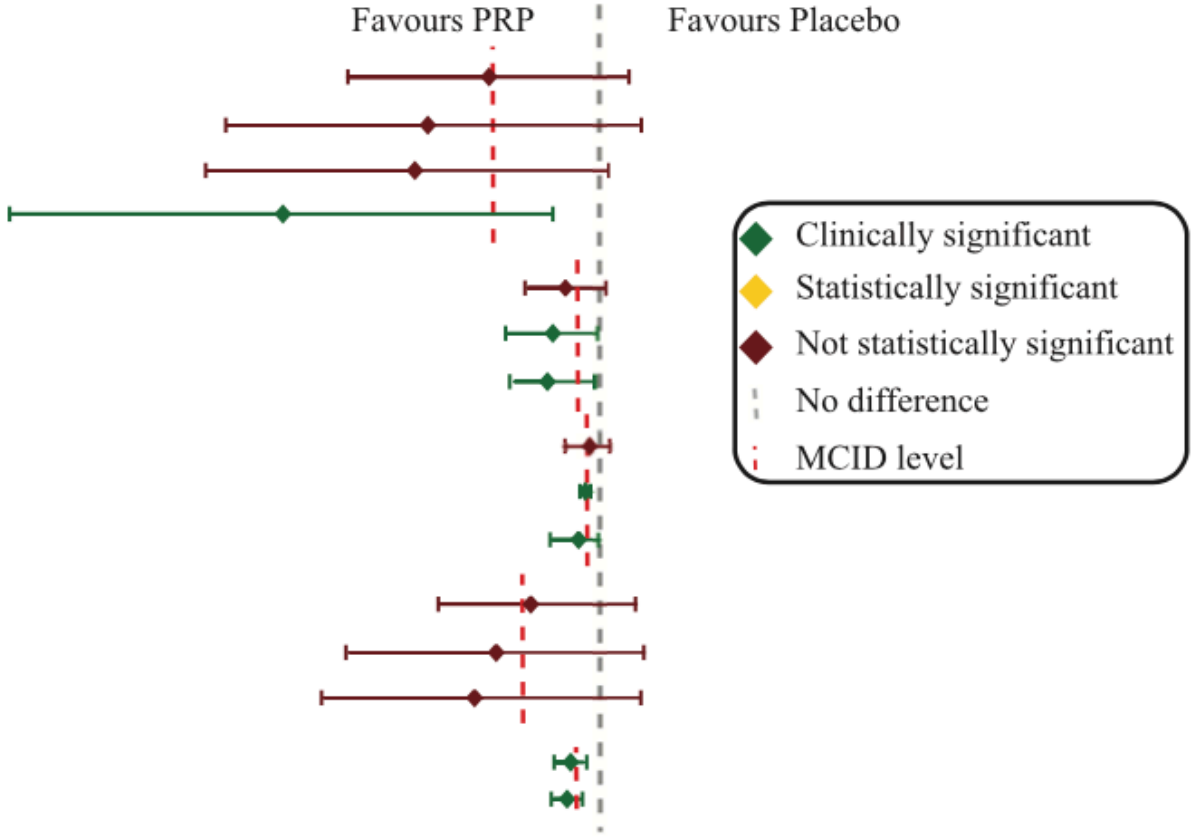
Level of evidence 1A

Chang et al. Arch Phys Med Rehabil. 2014
Laudy et al. Br J Sports Med. 2015
Xu et al. Am J Phys Med Rehabil. 2017
Shen et al. J Orthop Surg. 2017
Dai et al. Arthroscopy. 2017
Zhang et al. Drug Des Devel Ther. 2018
Sadabad et al. Electron Physician. 2016
Han et al. Pain Med. 2019
Kanchanatawan et al. Knee Surg Sports Traumatol Arthrosc. 2016

META-ANALYSIS PRP vs. PLACEBO

Compared treatment	Outcome	Follow-up	No. of trials	No. of pts	Mean difference [95% C.I.]
Placebo	WOMAC overall	1 month	6	266	-6.47 [-14.39, 1.45]
		3 months	4	153	-10.71 [-23.71, 2.29]
		6 months	6	266	-12.50 [-25.69, 0.69]
		12 months	3	129	-19.38 [-36.04, -2.72]
	WOMAC pain	1 month	5	210	-1.66 [-3.87, 0.55]
		3 months	4	153	-3.03 [-5.74,-0.32]
		6 months	5	210	-3.08 [-5.51, -0.65]
	WOMAC stiffness	1 month	5	210	-0.55[-1.77, 0.66]
		3 months	4	153	-0.89 [-1.26, -0.52]
		6 months	5	210	-1.32 [-2.59,-0.05]
	WOMAC function	1 month	5	210	-4.43 [-11.45, 2.58]
		3 months	4	153	-6.78 [-16.89, 3.33]
		6 months	5	210	-8.03 [-18.57, 2.51]
	VAS	1 month	3	140	-1.47 [-2.12,-0.82]
		6 months	4	238	-1.91 [-2.71, -1.10]

Results of the meta-analysis



- PRP injections provide better results than other injectable options.
- This benefit increases over time, being not significant at earlier follow-ups but becoming clinically significant after 6 to 12 months

Filardo. Cartilage. 2021

PRP vs. PLACEBO

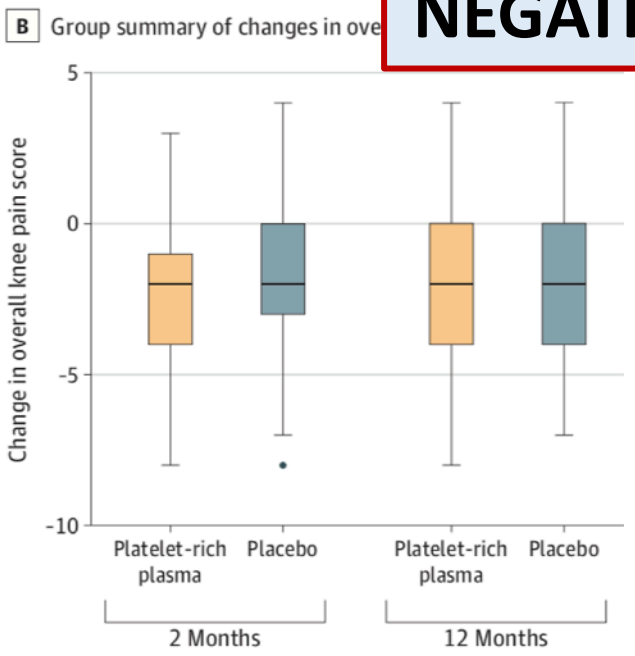
RECOMMENDATION 1

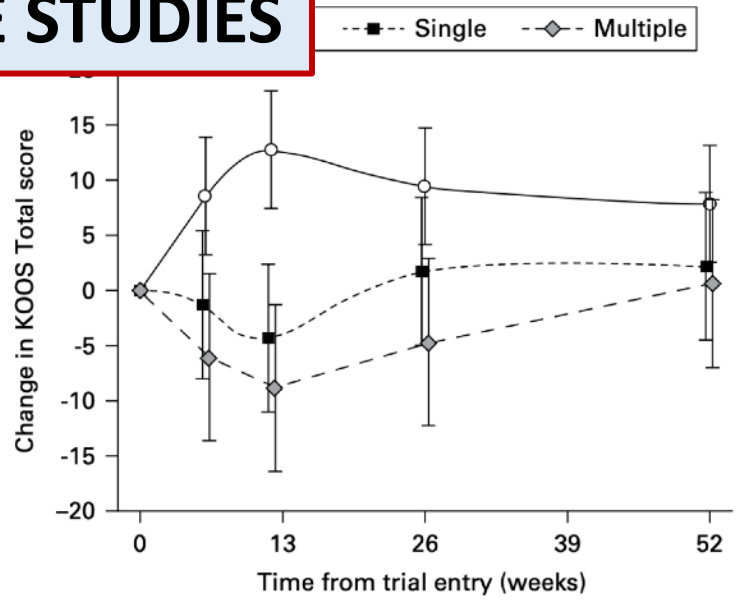
288 patients
Knee OA KL 2-3
PRP (3B) vs. Placebo
3 weekly injections (5mL)
12 month follow-up
Primary endpoint: ENS/MRI 12 months

102 patients
Low grade of knee OA (KL 0-2)
P-PRP (3B) (x1 or x3) vs. Placebo 3 weekly injections (5mL)
12 month follow-up
Main criterion: KOOS and EQ5DL

610 patients
Symptomatic knee osteoarthritis (KL 1-3)
P-PRP (3B) vs. Placebo
3 weekly injections (5mL)
60 month follow-up
Main criterion: WOMAC

NEGATIVE STUDIES



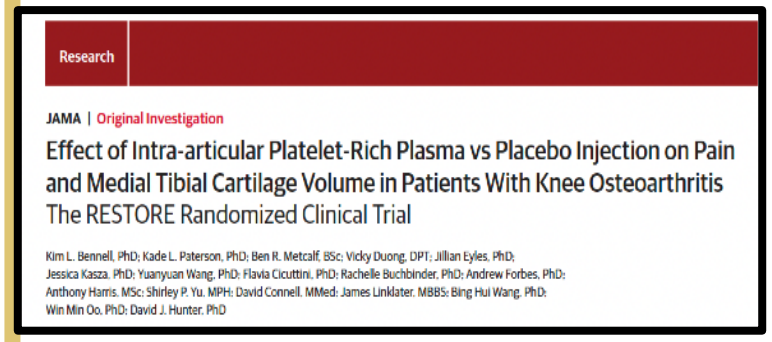


POSITIVE STUDY

Variable				*P* value
WOMAC				
3	5.4 (2.7, 5.1 to 5.7)	8.3 (2.7, 8.0 to 8.6)	− 2.9 (− 3.3 to − 2.4)	<0.001
6	3.8 (2.4, 3.5 to 4.0)	9.5 (2.5, 9.2 to 9.8)	− 5.7 (− 6.1 to − 5.3)	<0.001
12	3.6 (2.7, 3.3 to 3.9)	10.2 (2.6, 9.9 to 10.5)	− 6.6 (− 7.1 to − 6.2)	<0.001
24	4.7 (3.2, 4.3 to 5.0)	11.5 (2.6, 11.2 to 11.7)	− 6.8 (− 7.2 to − 6.3)	<0.001
60	12.3 (2.9, 11.9 to 12.6)	13.7 (2.4, 13.4 to 13.9)	− 1.4 (− 1.8 to − 1.0)	<0.001
WOMAC score, physical function, mean (SD, 95% CI), months				
3	29.0 (10.1, 27.8 to 30.1)	32.5 (10.9, 31.3 to 33.8)	− 3.6 (− 5.2 to − 1.9)	<0.001
6	23.6 (9.0, 22.6 to 24.6)	35.4 (10.8, 34.2 to 36.6)	− 11.8 (− 13.4 to − 10.2)	<0.001
12	22.3 (8.7, 21.4 to 23.3)	38.9 (11.0, 37.7 to 40.2)	− 16.6 (− 18.2 to − 15.0)	<0.001
24	24.0 (9.4, 23.0 to 25.1)	41.9 (10.9, 40.7 to 43.2)	− 17.9 (− 19.5 to − 16.3)	<0.001
60	37.5 (11.27, 36.20 to 38.73)	49.8 (9.6, 48.8 to 50.9)	− 12.4 (− 14.0 to − 10.7)	<0.001
Visual analogue scale score, mean (SD, 95% CI), months				
3	2.2 (1.5, 2.0 to 2.4)	3.4 (1.3, 3 to 3.6)	− 1.25 (− 1.5 to − 1.0)	<0.001
6	1.3 (1.1, 1.2 to 1.4)	4.3 (1.1, 4.1 to 4.4)	− 2.9 (− 3.1 to − 2.8)	<0.001
12	1.2 (1.2, 1.1 to 1.4)	4.6 (1.1, 4.5 to 4.7)	− 3.4 (− 3.5 to − 3.2)	<0.001
24	1.6 (1.5, 1.4 to 1.8)	5.1 (1.0, 5.0 to 5.2)	− 3.5 (− 3.7 to − 3.3)	<0.001
60	4.9 (1.7, 4.7 to 5.1)	6.2 (0.9, 6.1 to 6.4)	− 1.4 (− 1.6 to − 1.2)	<0.001

Bennell. JAMA. 2021
Lewis. Bone Joint J. 2022
Chu. Knee Surg Sports Traumatol Arthrosc. 2022

HOW TO EXPLAIN THESE CONTRADICTORY RESULTS??

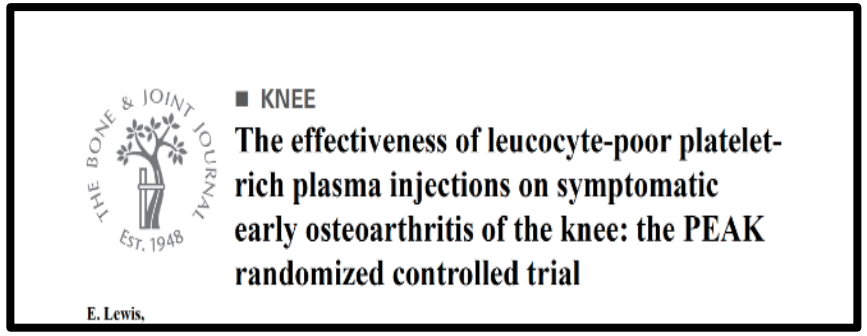


Research

JAMA | Original Investigation

Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis
The RESTORE Randomized Clinical Trial

Kim L. Bennell, PhD; Kade L. Paterson, PhD; Ben R. Metcalf, BSc; Vicky Duong, DPT; Jillian Eyles, PhD; Jessica Kasza, PhD; Yuanyuan Wang, PhD; Flavia Cicuttini, PhD; Rachelle Buchbinder, PhD; Andrew Forbes, PhD; Anthony Harris, MSc; Shirley P. Yu, MPH; David Connell, MMed; James Linklater, MBBS; Bing Hui Wang, PhD; Win Min Oo, PhD; David J. Hunter, PhD

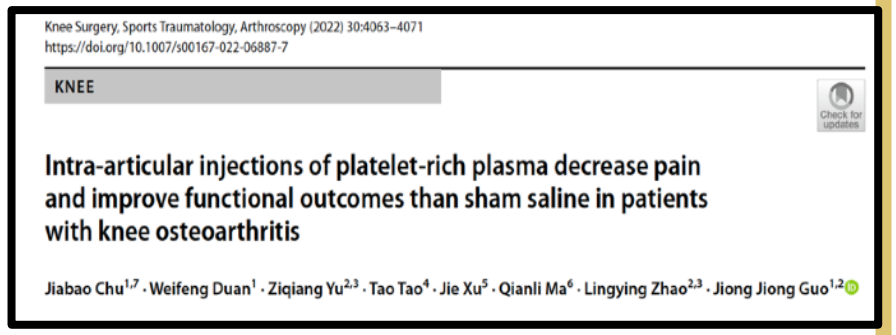


THE BONE & JOINT JOURNAL EST. 1948

■ KNEE

The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial

E. Lewis,



Knee Surgery, Sports Traumatology, Arthroscopy (2022) 30:4063–4071
https://doi.org/10.1007/s00167-022-06887-7

KNEE

Check for updates

Intra-articular injections of platelet-rich plasma decrease pain and improve functional outcomes than sham saline in patients with knee osteoarthritis

Jiabao Chu[1,7] · Weifeng Duan[1] · Ziqiang Yu[2,3] · Tao Tao[4] · Jie Xu[5] · Qianli Ma[6] · Lingying Zhao[2,3] · Jiong Jiong Guo[1,2]

BENNELL	LEWIS	CHU
Platelet concentration: 1.6 x Volume: 5ml Absolute platelets count: 1.6 billion	Platelet concentration: 1.3 x Volume: 4-6 ml Absolute platelets count: 1.3 to 1.9 billion	Platelet concentration: 4,3 x Volume: 5ml Absolute platelets count: 5,3 billion

EFFECTIVENESS OF PRP IN KNEE OA

RECOMMENDATION 2

Recommandations	Expert opinion	Median	Distribution		
			≤ 3	4-6	≥ 7
Injections of PRP into the knee joint may be useful in severe osteoarthritis (Kellgren and Lawrence IV)	Appropriate with relative agreement	7	0	5	10

Evidence level 2B

Görmeli et al. Knee Surg Sports Traumatol Arthrosc. 2017
Chang et al. Arch Phys Med Rehabil. 2014
Joshi Jubert et al. Orthop J Sports Med. 2017
Filardo et al. Knee Surg Sports Traumatol Arthrosc. 2012
Kon et al. Arthroscopy. 2011

PREDICTIVE RESPONSE FACTORS

Radiographic severity

RECO 2

260 patients
6 injections, monthly LR-PRP injections (2.4ml)
Double centrifugation
24 month follow-up

Journal of Orthopaedics 29 (2022) 31–37
Contents lists available at ScienceDirect
Journal of Orthopaedics
journal homepage: www.elsevier.com/locate/jor

Consecutive injections of leukocyte-rich platelet-rich plasma are effective in not only mild but also severe knee degeneration

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Characteristics	Total	K-L grade I	K-L grade II	K-L grade III	K-L grade IV
Cases, n	260	33	67	106	54
Injections, n	1295	129	307	554	305
Age, years	67.1 ± 11.1	59.2 ± 10.9	63.4 ± 9.8	69.6 ± 11.3	71.6 ± 7.6
BMI	25.5 ± 4.2	23.7	25.2	25.3	27.1
Mean FTA	180.9	178	178.3	181.0	185.5
PLT CR	5.6	5.1	5.3	5.4	5.5
WBC CR	2.9	2.6	2.9	2.9	2.9

CR = ratio PRP/WB

K-L	I				II				III				IV				P-value (comparison)					
Time	mean	95% CI		P-value vs. Pre	mean	95% CI		P-value vs. Pre	mean	95% CI		P-value vs. Pre	mean	95% CI		P-value vs. Pre	P-value Time * group	I vs II	I vs III	I vs IV	II vs III	II vs IV	III vs IV
VAS																	0.015						
Pre	51.9	43.6	60.2		62.7	57.5	68.0		59.9	55.8	64.1		69.8	63.9	75.6			0.026	0.089	0.001	0.386	0.074	0.004
3 M	23.7	15.2	32.1	0.000	31.4	26.1	36.7	0.000	38.4	34.1	42.6	0.000	50.1	44.2	56.0	0.000		0.114	0.002	0.000	0.032	0.000	0.001
6 M	24.3	15.6	33.0	0.000	33.0	27.3	38.8	0.000	35.3	30.7	39.9	0.000	44.3	38.1	50.5	0.000		0.091	0.028	0.000	0.521	0.008	0.015
1Y	21.3	12.2	30.4	0.000	29.0	22.7	35.2	0.000	34.8	29.9	39.7	0.000	49.4	42.2	56.6	0.000		0.155	0.010	0.000	0.134	0.000	0.001
2Y	15.0	2.7	27.4	0.000	27.5	19.0	35.9	0.000	43.7	37.1	50.4	0.000	44.8	34.7	54.8	0.000		0.100	0.000	0.000	0.002	0.009	0.862
KOOS (pain)																	0.230						
Pre	64.9	58.2	71.6		57.0	52.8	61.2		54.0	50.6	57.3		44.4	39.7	49.1			0.040	0.004	0.000	0.238	0.000	0.000
3 M	81.0	74.3	87.7	0.000	71.3	67.0	75.5	0.000	64.3	60.9	67.7	0.000	57.6	52.9	62.3	0.000		0.012	0.000	0.000	0.007	0.000	0.015
6 M	80.1	73.1	87.0	0.000	70.7	66.2	75.3	0.000	68.4	64.7	72.1	0.000	62.4	57.4	67.3	0.000		0.022	0.003	0.000	0.404	0.013	0.039
1Y	82.4	75.2	89.6	0.000	75.8	70.8	80.7	0.000	67.8	63.9	71.7	0.000	60.3	54.6	66.0	0.000		0.118	0.000	0.000	0.009	0.000	0.024
2Y	86.2	76.5	95.9	0.000	76.9	70.3	83.5	0.000	66.3	61.1	71.5	0.000	53.9	46.5	61.3	0.012		0.115	0.000	0.000	0.010	0.000	0.005

Kemmochi. J Orthopaedics. 2022

Indian Journal of Orthopaedics (2022) 56:1722–1728
https://doi.org/10.1007/s43465-022-00730-4

ORIGINAL ARTICLE

Serial Platelet-Rich Plasma Intra-articular Injections in Kellgren and Lawrence Grade IV Knee Joint Osteoarthritis: A Prospective Blinded Placebo-Controlled Interventional Study

Amit Saraf[1] · Altaf Hussain[1,2] · Sandeep Bishnoi[1] · Goushul Azam[1] · Hamza Habib[1]

RCT
84 patients
All KL grade 4
PRP vs NACL
Outcomes : VAS and WOMAC
3 injections, monthly PRP injections (3ml)
Platelets concentration ?
Double centrifugation
6 months follow-up

Table 3 Comparison of WOMAC score at different intervals among the groups

WOMAC score	NS group		PRP group		*t* test	*P* value
	Mean	SD	Mean	SD		
Baseline	78.49	6.69	81.54	7.43	4.89	0.052
3 months	70.22	10.51	61	7.64	21.28	<0.01*
6 months	70.73	10.27	60.37	8.95	24.35	<0.01*

*Statistically significant

Table 5 Comparison of VAS at different intervals among the groups

VAS	NS group		PRP group		*t* test	*P* value
	Mean	SD	Mean	SD		
Baseline	7.90	1.04	8.02	1.12	0.26	0.61
3 Months	6.37	1.58	5.79	0.94	4.17	0.044*
6 Months	6.61	1.39	5.74	1.03	10.57	0.002*

*Statistically significant

CONCLUSION:
Serial Intra-articular Injections of autologous PRP mildly improve short-term pain and knee function scores in **patients of Grade IV KOA** without any major complications.

Archives of Orthopaedic and Trauma Surgery (2023) 143:1393–1408
https://doi.org/10.1007/s00402-021-04304-1

ORTHOPAEDIC SURGERY

The use of platelet-rich plasma in studies with early knee osteoarthritis versus advanced stages of the disease: a systematic review and meta-analysis of 31 randomized clinical trials

Félix Vilchez-Cavazos[1] · Jaime Blázquez-Saldaña[1] · Augusto Andrés Gamboa-Alonso[2] · Víctor Manuel Peña-Martínez[1] · Carlos Alberto Acosta-Olivo[1] · Adriana Sánchez-García[3] · Mario Simental-Mendía[1]

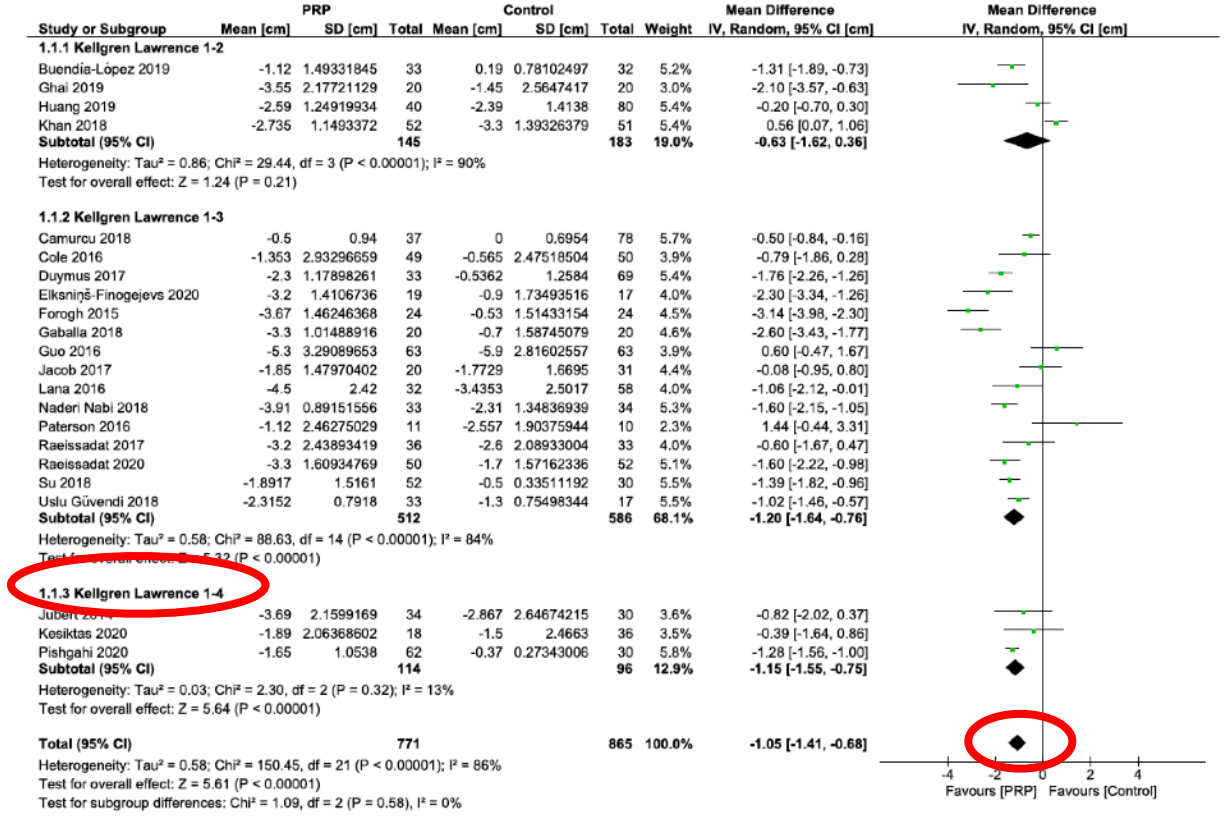


Fig. 3 Forest plot displaying the mean difference and 95% CI for the effect of PRP on pain (visual analog scale) as compared to a control group at different stages of knee osteoarthritis

CONCLUSION:

Our results indicate that including patients **with advanced knee OA** does not seem to affect the outcomes of clinical trials in which the effectiveness of the PRP in knee OA is assessed.

GENERAL RECOMMENDATIONS

Recommandations	Expert opinion	Median	Distribution			Level
			≤ 3	4-6	≥ 7	Evidence
PRP treatment should be offered as a second-line treatment, after failure of oral or non-pharmacological treatment of knee OA	Appropriate with relative agreement	9	0	1	14	5
PRP treatment should not be used during a flare up of knee OA	Appropriate with relative agreement	7	0	6	9	5
A sequence of PRP treatment in knee osteoarthritis may include 1 to 3 injections	Appropriate with strong agreement	9	0	0	15	1A
PRP injections in knee osteoarthritis should be performed under ultrasound or scopic guidance	Lack of consensus	8	1	1	13	5
A joint effusion should be systematically drained before the injection of PRP	Appropriate with strong agreement	9	0	0	15	5
Symptomatic bilateral knee osteoarthritis can be treated at the same time	Lack of consensus	8	2	0	13	5
After injection of PRP, resting the knee for 48 hours is recommended	Lack of consensus	9	1	0	14	5

7 RECOMMENDATIONS

- **Place of PRP in the management of knee osteoarthritis**
- **Therapeutic protocol**

GENERAL RECOMMENDATIONS

Recommandations	Expert opinion	Median	Distribution		
			≤ 3	4-6	≥ 7
A sequence of PRP treatment in knee osteoarthritis can include 1 to 3 injections	Appropriate with strong agreement	9	0	0	15

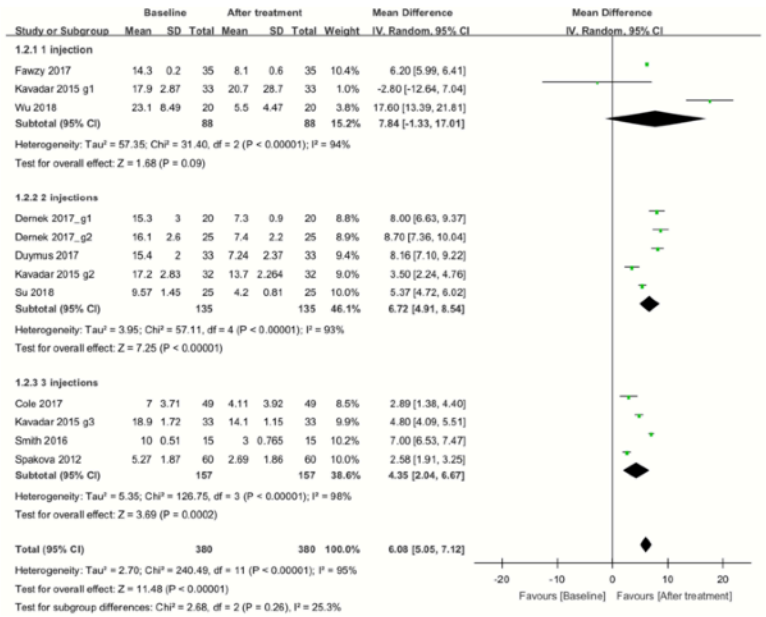
Evidence level 1A

Chou. Int J Clinical Practice. 2021
Kavadar et al. J Phys Ther Sci. 2015
Huang et al. Int J Surg Lond Engl. 2017
Patel et al. Am J Sports Med. 2013
Görmeli et al. Knee Surg Sports Traumatol Arthrosc. 2017

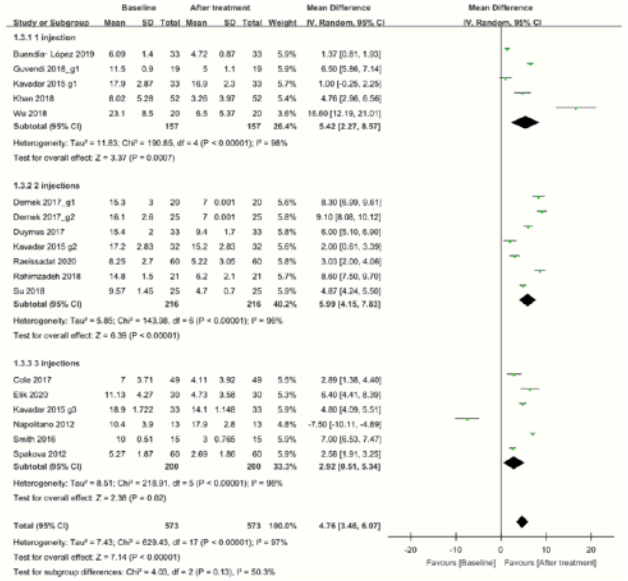
NUMBER OF PRP INJECTIONS

Meta-analysis knee osteoarthritis KL2-3

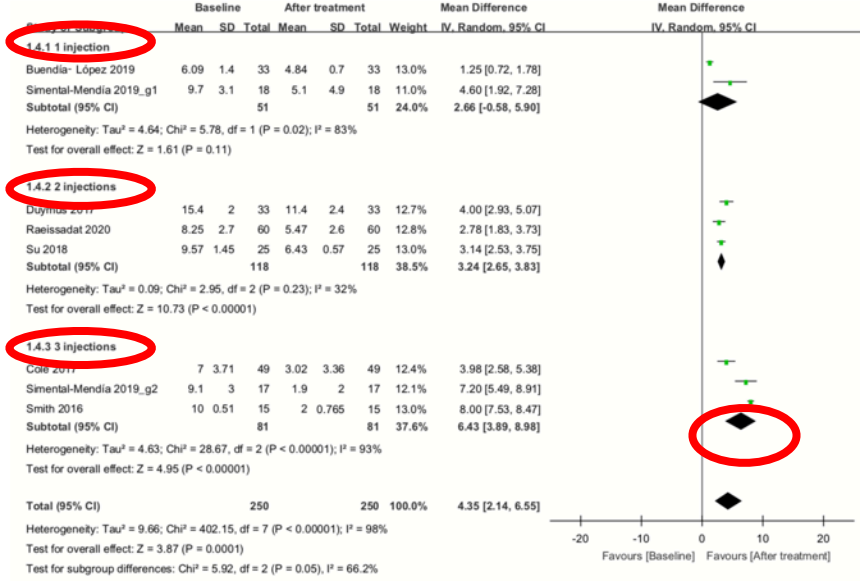
RECOMMENDATION 7



WOMAC P at M3



WOMAC P at M6



WOMAC P at M12

- **VAS PAIN: No differences between the groups at M3, M6 and M12**
- **WOMAC Pain: 3 inj > 2 inj +/- 1 inj at 12 months**
- **WOMAC Function: 3 inj > 1 or 2 inj at 12 months**

Chou. Int J Clinical Practice. 2021

TLAR 1947

Arch Rheumatol 2021;36(3):326-334
doi: 10.46497/ArchRheumatol.2021.8408

ORIGINAL ARTICLE

Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: A single-blind, randomized, superiority trial

Koushik Subramanyam, Rajkumar Alguvelly, Abhishek Mundargi, Prakash Khanchandani

Department of Orthopaedics, Sri Sathya Sai Institute of Higher Medical Sciences - Prashanthigram, Puttaparthi, Andhra Pradesh, India

RCT
90 patients
All KL grade 1 or 2
3 groups : 1, 2 or 3 injections
Outcome : VAS and functionnal scales
12 month follow-up

Table 2. Comparison of outcome measures across time points within each group and between groups at each time point

	1-dose group	2-dose group	3-dose group	
	Mean±SD	Mean±SD	Mean±SD	p†
Visual Analog Scale				
Pre-intervention	7.7±1.0	7.4±1.0	7.6±1.0	0.58
6 weeks	5.1±1.1	5.0±1.0	5.0±1.0	0.85
3 months	3.0±1.2	2.8±1.2	2.7±1.0	0.45
6 months	1.1±0.8	1.0±0.8	1.0±0.8	0.65
1 year	3.7±1.0	3.4±1.3	1.5±1.3	<0.001*
p value‡	<0.001*	<0.001*	<0.001*	
IKDC Score				
Pre-intervention	48.8±8.6	50.3±7.4	51.4±7.1	0.42
6 weeks	57.4±8.0	58.5±6.9	59.9±6.5	0.4
3 months	62.7±7.9	63.7±6.4	65.2±6.3	0.37
6 months	68.9±8.2	69.8±6.9	71.5±6.4	0.38
1 year	60.6±8.3	61.8±6.9	71.7±6.4	<0.001*
p value	<0.001*	<0.001*	<0.001*	
KOOS				
Pre-intervention	49.0±7.5	49.9±6.8	50.8±7.0	0.61
6 weeks	55.6±7.7	56.4±6.7	57.0±6.9	0.73
3 months	62.1±7.0	62.9±6.2	63.6±6.4	0.69
6 months	68.2±7.4	69.4±6.4	71.1±7.1	0.53
1 year	59.1±7.3	59.9±6.3	69.3±6.7	<0.001*
p value	<0.001*	<0.001*	<0.001*	
Tegner Lysholm knee score				
Pre-intervention	59.8±8.3	60.7±6.7	61.4±7.1	0.69
6 weeks	67.0±8.3	67.2±7.3	67.9±7.1	0.89
3 months	73.7±8.1	74.7±7.3	75.7±7.2	0.61
6 months	79.5±8.9	80.8±7.9	81.5±8.2	0.68
1 year	71.9±8.4	72.3±7.9	80.5±7.9	<0.001*
p value	<0.001*	<0.001*	<0.001*	

IKDC: International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score; † One-way ANOVA; ‡ Repeated measures ANOVA; * Statistically significant.

3 INJECTIONS BETTER THAN ONE OR TWO INJECTIONS AT 1 YEAR

CHARACTERISTICS OF PRP

Recommandations	Experts opinion	Median	Distribution			Level
			≤ 3	4-6	≥ 7	Evidence
The characteristics of the injected PRP influence the outcome in knee osteoarthritis	Appropriate with relative agreement	8	0	2	13	4
Leukocyte-poor PRPs should be preferred in knee osteoarthritis	Appropriate with relative agreement	8	0	1	14	5
The effectiveness of PRP in knee osteoarthritis depends on the number of platelets injected	Appropriate with relative agreement	8	0	1	14	5
The volume of a PRP injection in knee osteoarthritis should be 4-8 ml	Appropriate with strong agreement	8	0	0	15	4

4 RECOMMENDATIONS

- **Role of cell composition**
- **Impact of injected volume**

CHARACTERISTICS OF PRP

Recommandations	Experts opinion	Mediane	Distribution		
			≤ 3	4-6	≥ 7
Leukocyte-poor PRPs should be preferred in knee osteoarthritis	Appropriate with relative agreement	8	0	1	14

Evidence level 5

Filardo et al. Knee Surg Sports Traumatol Arthrosc. 2012
Riboh et al. Am J Sports Med. 2016

EFFECTIVENESS OF PRP DEPENDING ON THE PROTOCOL
LR vs LP PRP

RECO 13

Meta-analysis
- 32 studies

- WOMAC: No difference at 3, 6 and 12 months
- IKDC: No difference at 3, 6 and 12 months

Adverse Reactions and Clinical Outcomes for Leukocyte-Poor Versus Leukocyte-Rich Platelet-Rich Plasma in Knee Osteoarthritis

A Systematic Review and Meta-analysis

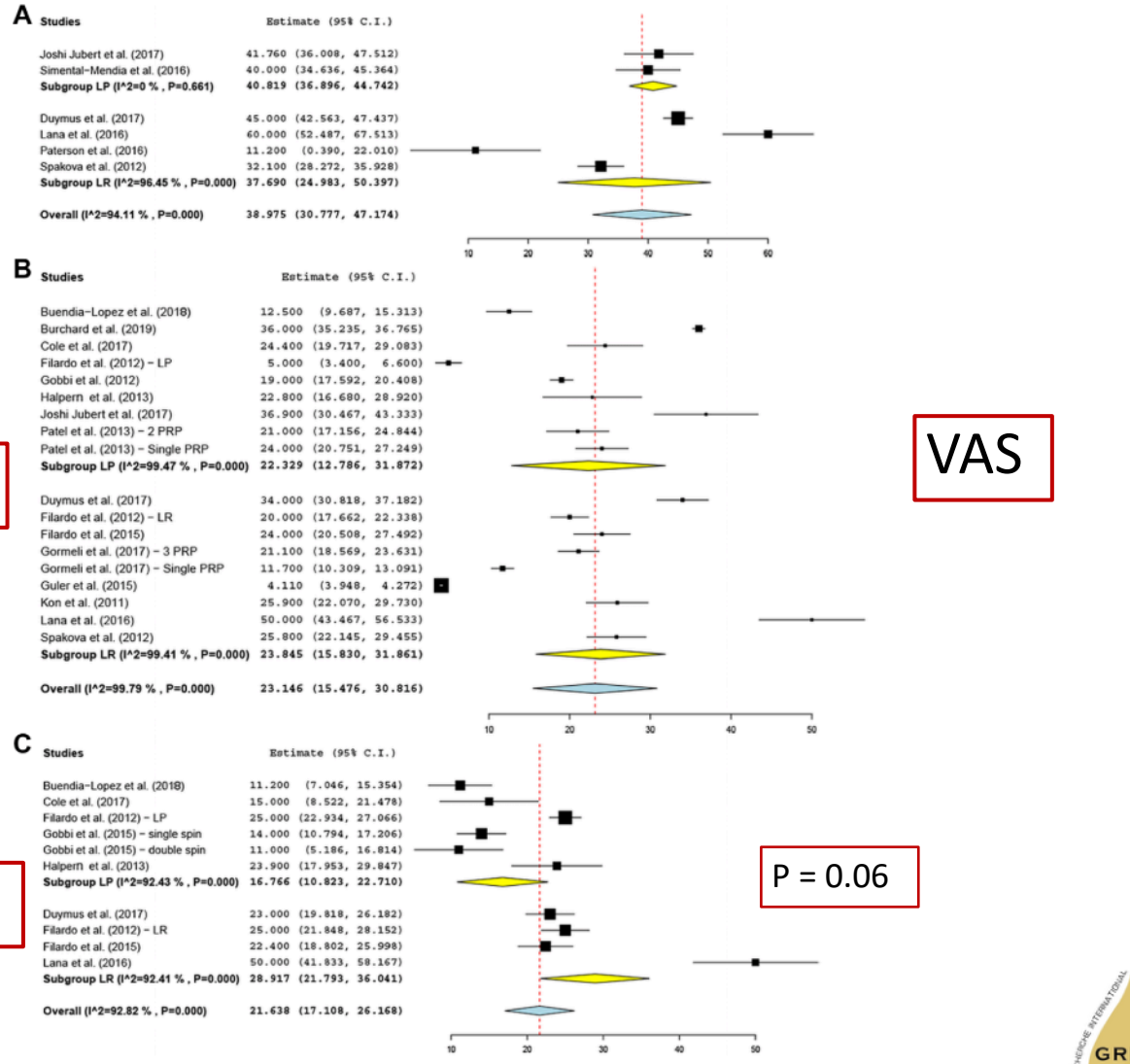
Jun-Ho Kim,* MD, PhD, Yong-Beom Park,†‡ MD, PhD, Chul-Won Ha,§ MD, PhD, Young Ju Roh,|| MD, and Jung-Gwan Park,¶ MD

Investigation performed at Chung-Ang University Hospital, Chung-Ang University, Seoul, Republic of Korea

3 month

6 month

12 month

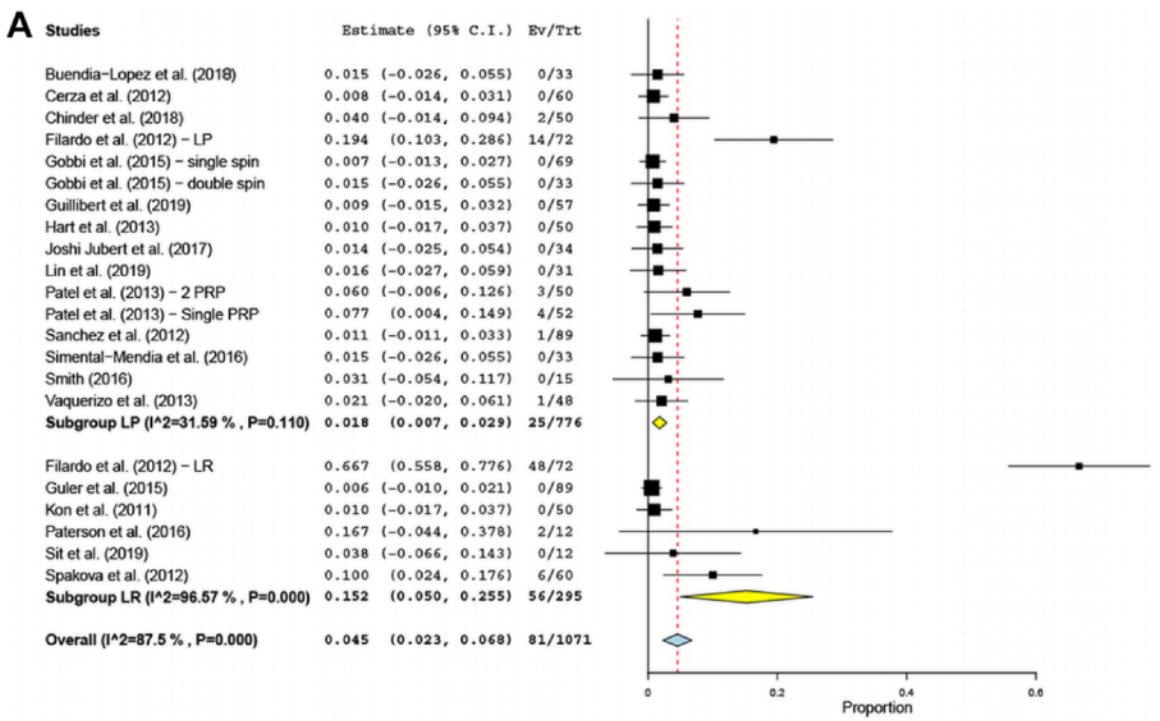


VAS

P = 0.06

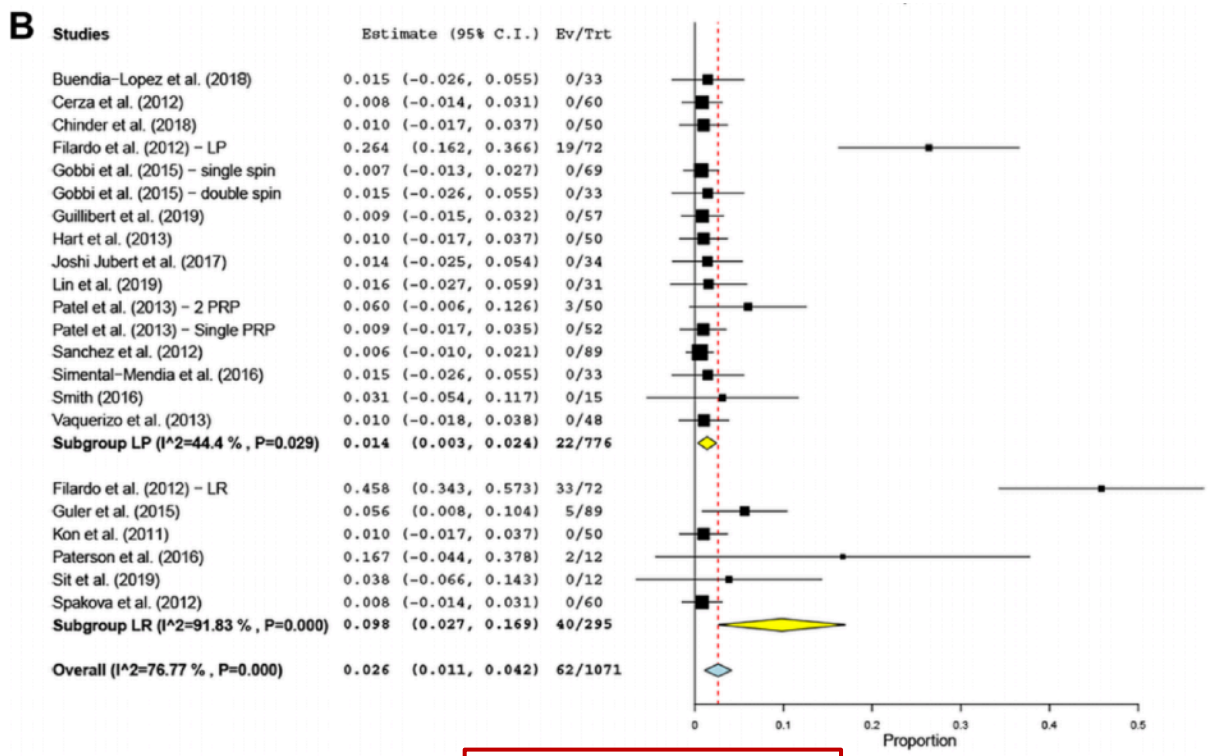
EFFECTIVENESS OF PRP DEPENDING ON THE PROTOCOL
LR vs LP PRP

RECO 13



PAIN

OR LR vs. LP = 1.64; p<0.05



Swelling

OR LR vs. LP = 1.56; p<0.05

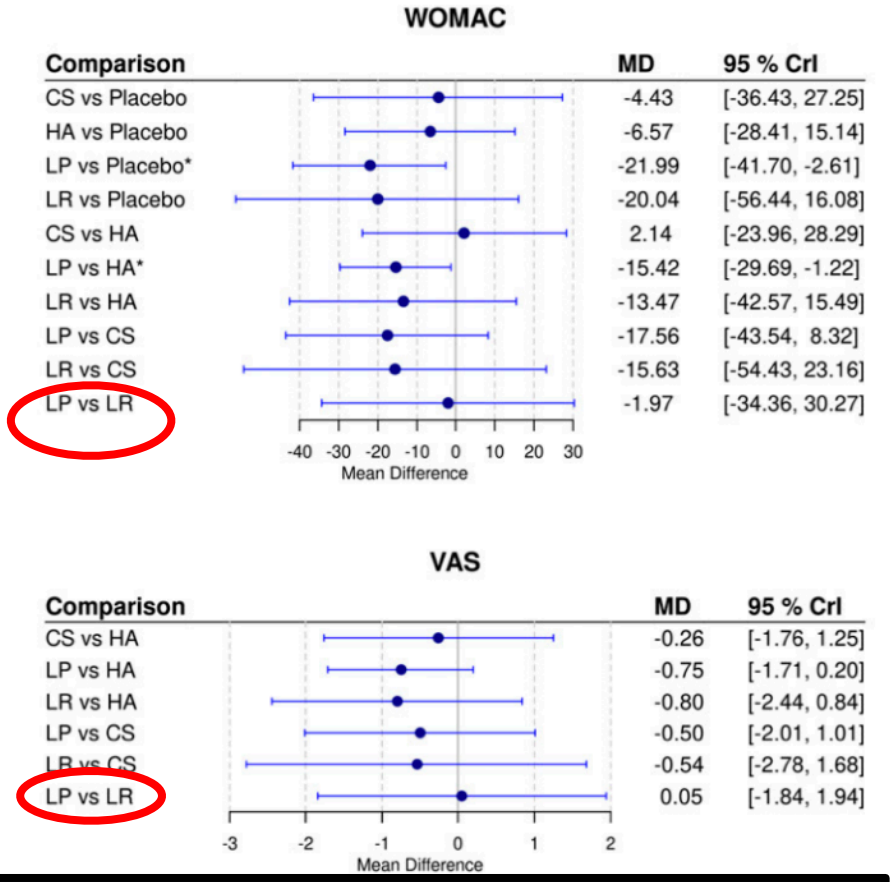
Kim. Orthopaedic Journal of Sports Medicine. 2021

The Effect of Leukocyte Concentration on Platelet-Rich Plasma Injections for Knee Osteoarthritis

A Network Meta-Analysis

Aazad Abbas, HBSc, Jin Tong Du, BMSc, and Herman S. Dhotar, MD, MPH, FRCSC

b) 12 months follow-up



CONCLUSIONS:

- **Leukocyte concentration of PRP does not play a significant role** in patient-reported outcome measures for knee OA.

- LP-PRP is preferred to LR-PRP according to SUCRA rankings, but this preference may not be important in clinical practice

CONTRAINDICATIONS AND INTERACTIONS

RecommandationsL	Experts opinion	Median	Distribution			Level
			≤ 3	4-6	≥ 7	Evidence
PRPs should not be mixed with anesthetic or CS IA	Appropriate with relative agreement	9	0	1	14	5
Treatment of knee osteoarthritis with PRP should not be done soon after an IA injection of cortisone	Appropriate with relative agreement	8	0	1	14	5
Anti-inflammatory treatment should be avoided in the days preceding and following PRP treatment	Appropriate with strong agreement	9	0	0	15	5
Antiplatelet treatment is not a contraindication to PRP injections, but could alter the result by preventing platelet activation	Appropriate with strong agreement	9	0	0	15	5
A recent neoplasia (malignant tumours, hemopathies) can be a contraindication to PRP injections in gonarthrosis	Appropriate with relative agreement	7	0	6	9	5
The presence of radiographic articular chondrocalcinosis is not a contraindication to IA injections of PRP	Appropriate with strong agreement	8	0	0	15	5

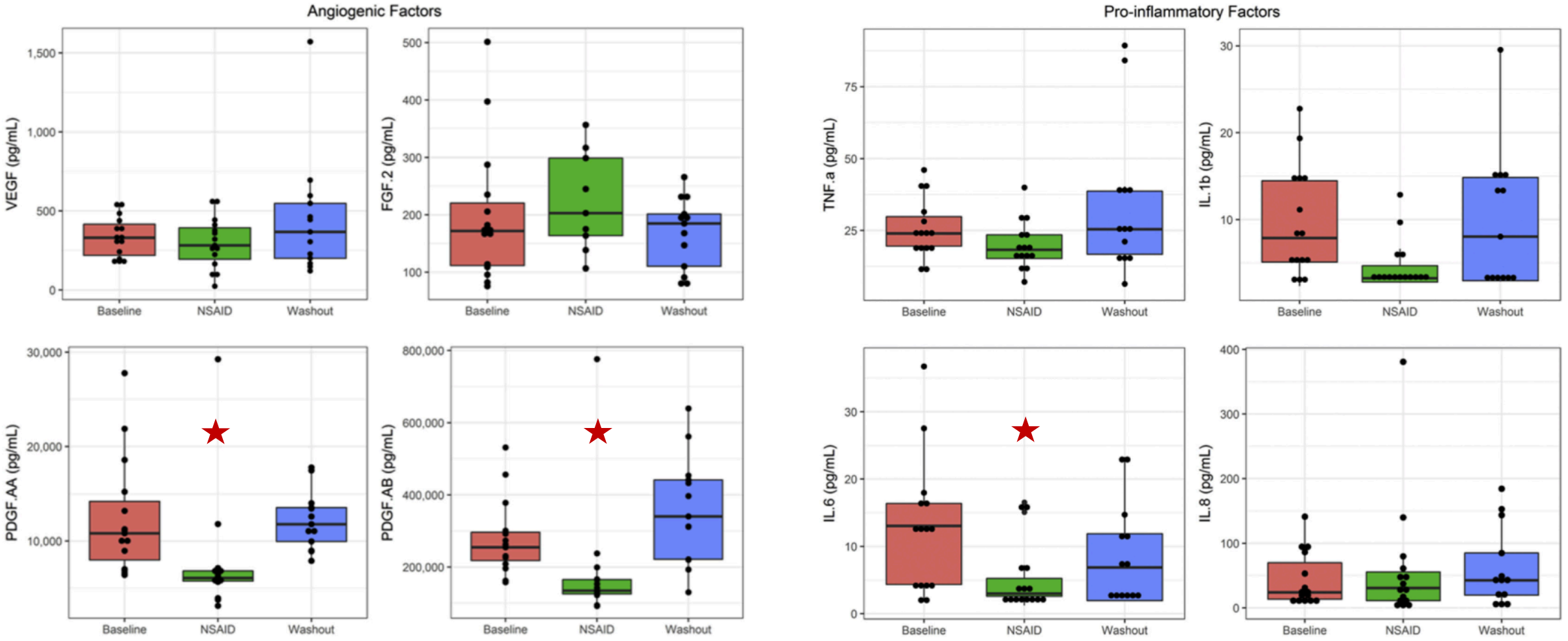
6 RECOMMENDATIONS

- **Combination with other injectable products**
- **Drug co-prescriptions**
- **Associated pathologies**

RECO 18

EFFECT of NSAIDs on PRP

16 healthy subjects
Naproxène 1w
Washout 1w



Mannava et al. Arthroscopy 2018

RULES OF GOOD PRACTICE AND ADVERSE EFFECTS

Recommandations	Experts opinion	Median	Distribution			Level
			≤ 3	4-6	≥ 7	Evidence
A blood count less than 3 months old is recommended before PRP treatment	Appropriate with relative agreement	8	0	2	13	
PRP injections should be subject to the same traceability rules as other injectable therapeutic devices	Appropriate with strong agreement	9	0	0	15	
PRP injections in knee osteoarthritis are a locally well tolerated treatment	Appropriate with strong agreement	8	0	0	15	1A
PRP injections in knee osteoarthritis are a generally well-tolerated treatment	Appropriate with relative agreement	9	0	1	14	1A

4 RECOMMENDATIONS

- **Pre-therapy assessment**
- **Traceability**
- **Tolerance**

RULES OF GOOD PRACTICE AND ADVERSE EFFECTS

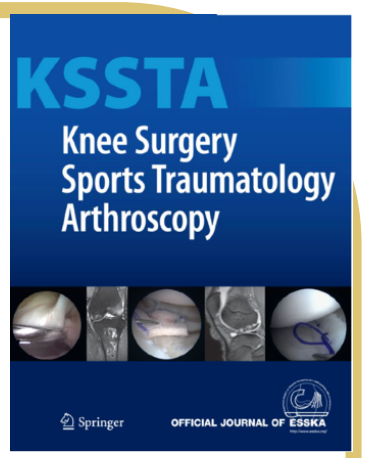
Recommandations	Experts opinion	Median	Distribution		
			≤ 3	4-6	≥ 7
PRP injections in knee osteoarthritis are a locally well tolerated treatment	Appropriate with strong agreement	8	0	0	15
PRP injections in knee osteoarthritis are a generally well-tolerated treatment	Appropriate with relative agreement	9	0	1	14

Evidence level 1A

A case of septic arthritis due to Streptococcus Mitis

Beatty, Regen Med. 2019
Toraman. Turk J Phys Med Rehab 2022

CONCLUSION: PRP and KNEE OA



25 recommendations based on "evidence-based medicine" and clinical experience

- Harmonizing the use of IA injections of PRP in knee osteoarthritis
- Draw guidelines for the design of future clinical research
- **THE UPDATING OF THE LITERATURE DOES NOT JUSTIFY SUBSTANTIAL MODIFICATIONS OF THESE RECOMMENDATIONS.**

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