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Randomized Controlled Trial

Single- and double-dose of platelet-rich plasma *versus* hyaluronic acid for treatment of knee osteoarthritis: A randomized controlled trial

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Abstract

BACKGROUND

Platelet-rich plasma (PRP) and hyaluronic acid have been shown to be useful in the treatment of knee osteoarthritis. However, investigations comparing the efficacy of these two drugs together are insufficient.

AIM

To compare the outcomes of PRP *vs* hyaluronic acid injections in three groups of patients with bilateral knee osteoarthritis.

METHODS

This randomized controlled trial study involved 95 patients. Thirty-one subjects received a single injection of PRP (group PRP-1), 33 subjects received two injections of PRP at an interval of 3 wk (group PRP-2) and 31 subjects received three injections of hyaluronic acid at 1-wk intervals (group hyaluronic acid). The patients were investigated prospectively at the enrollment and at 4-, 8- and 12-wk follow-up with the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale questionnaires.

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RESULTS

Percentages of patients experiencing at least a 30% decrease in the total score for the WOMAC pain subscale from baseline to wk 12 of the intervention were 86%, 100% and 0% in the groups PRP-1, PRP-2 and hyaluronic acid, respectively ($P < 0.001$). The mean total WOMAC scores for groups PRP-1, PRP-2 and hyaluronic acid at baseline were 63.71, 61.57 and 63.11, respectively. The WOMAC scores were significantly improved at final follow-up to 42.5, 35.32 and 57.26, respectively. The highest efficacy of PRP was observed in both groups at wk 4 with about 50% decrease in the symptoms compared with about 25% decrease for hyaluronic acid. Group PRP-2 had higher efficacy than group PRP-1. No major adverse effects were found during the study.

CONCLUSION

PRP is a safe and efficient therapeutic option for treatment of knee osteoarthritis. It was demonstrated to be significantly better than hyaluronic acid. We also found that the efficacy of PRP increases after multiple injections.

Key words: Platelet-rich plasma; Hyaluronic acid; Osteoarthritis; Knee; Pain

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Core tip: Studies comparing the efficacy of platelet-rich plasma (PRP) and hyaluronic acid in treatment of knee osteoarthritis are insufficient. In this randomized controlled trial study, we compared the outcomes of PRP *versus* hyaluronic acid injections in three groups of patients with bilateral knee osteoarthritis. It was observed that PRP is significantly more efficient than hyaluronic acid. We also found that the efficacy of PRP increases after multiple injections. PRP was a safe treatment in our study, and no major adverse effects were found.

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INTRODUCTION

Osteoarthritis is the most common articular disease, and it is an important cause of disability in the elderly^[1,2]. The knee is the most frequent joint affected by osteoarthritis^[3]. Osteoarthritis is a multifactorial chronic disease that starts with breakdown of joint cartilage and leads to decrease in joint space, subchondral sclerosis, synovitis and peripheral osteophytes formation^[4,5]. It was estimated that more than 10% of the people aged ≥ 60 years suffer from this disease, and it is a major expense for all healthcare systems^[6,7]. Clinical manifestations of the disease include functional pain and joint stiffness. Morning stiffness usually lasts less than 30 min followed by gel phenomenon that is a transient joint stiffness due to short-term immobility^[8,9].

Current treatments for osteoarthritis include non-pharmacologic treatment, such as physical activity^[10-12], and pharmacologic treatment, such as non-steroidal anti-inflammatory drugs, glucocorticoids and hyaluronic acid. These treatments aim to decrease pain and inflammation, but these drugs have restricted and short-term effects on control of symptoms and the patient's quality of life^[13,14]. Platelet-rich plasma (PRP) is a plasma that is prepared from each patient's own blood, and it has a higher platelet concentration in comparison to normal plasma. PRP injection is a simple, low cost and minimally invasive procedure that provides concentrated growth factors for use as an intra-articular injection^[15]. These growth factors are said to stimulate the healing of cartilage and thus improve arthritis^[16,17]. Some studies alluded to the potential effect of PRP in treatment of chronic tendonitis, tennis elbow, chronic rotator cuff tendinopathy, jumper's knee, acute Achilles tendon rupture, muscle rupture, osteochondritis and osteoarthritis and meniscus repair^[18-22]. The positive effects of PRP in improvement of knee osteoarthritis have been reported in

some studies^[23-26]. Studies have reported the effects of PRP on the proliferation of mesenchymal root cells and their chondrocyte differentiation in an *in vitro* environment^[27,28], but evidence about the clinical use of PRP in the treatment of knee osteoarthritis is still insufficient.

Hyaluronic acid is a polysaccharide compound that includes glucuronic acid and acetylglucosamine. In osteoarthritis, the concentration and molecular weight of hyaluronic acid are reduced, and this is the basis of hyaluronic acid injection. Hyaluronic acid provides viscoelasticity of synovial fluid and stimulates formation of endogenous hyaluronic acid^[29,30]. In addition to its effects on viscoelasticity, hyaluronic acid may be effective for the treatment of osteoarthritis by biochemical effects, such as stimulation of formation and accumulation of proteoglycan, inhibition of inflammatory mediators and analgesic effect^[29,31,32]. However, because there are inadequate data on the effects of either different doses of PRP or hyaluronic acid in patients with osteoarthritis, we aimed in this study to compare the therapeutic efficacy of intra-articular injection of two different doses of PRP *versus* hyaluronic acid in the management of patients with osteoarthritis of the knee.

MATERIALS AND METHODS

This single-blinded parallel randomized controlled trial study was conducted on patients aged 40- to 80-years-old with knee osteoarthritis who were referred in 2018 to Shahid Beheshti teaching hospital affiliated to Babol University of Medical Sciences, Babol, Northern Iran.

The inclusion criteria were as follows: (1) patients with diagnosis of knee osteoarthritis as defined by the criteria of the American College of Rheumatology^[33]; (2) patients who were staged using the Ahlback radiological grading; (3) patients having bilateral knee osteoarthritis with the same Ahlback grade; and (4) all knees with full range of motion.

The exclusion criteria were as follows: (1) history of diabetes; (2) history of other joint diseases in the knee, such as rheumatoid arthritis or gout; (3) history of knee surgery; (4) history of knee fracture; (5) intra-articular injection of corticosteroids during the previous 2 wk; (6) intra-articular injection of other drugs, such as hyaluronic acid over the previous 1 year; (7) contraindications for intra-articular injection, such as thrombocytopenia, coagulopathy, articular infection of knee, skin infection in the injection site, impairment of immunity (*e.g.*, acquired immune deficiency syndrome or receiving immunosuppressive medication) and severe intra-articular effusion (in this case, intra-articular injection was started after treatment and cure of effusion); and (8) patients with Ahlback grade 3 or more.

All of the patients were examined by the senior orthopedic surgeon, who was blinded to the intervention groups. Plain radiographs were then taken of the knees with anterior-posterior and lateral views. Drug treatments (such as non-steroidal anti-inflammatory drugs, corticosteroids and other anti-inflammatory drugs) and non-drug treatments (knee physiotherapy with modalities, such as transcutaneous electrical nerve stimulation, laser, *etc*) were stopped for the 48 h before study interventions.

Ahlback radiological grading of knee osteoarthritis is classified as follows^[34,35]: I: joint space narrowing < 3 mm; II: joint space obliterated or almost obliterated; III: minor bone attrition (< 5 mm); IV: moderate bone attrition (5-15 mm); and V: severe bone attrition (> 15 mm).

The patients' information was collected by a checklist, including age, gender, weight, height, body mass index and Ahlback grade. All necessary laboratory tests (complete blood count, erythrocyte sedimentation rate, C-reactive protein) were conducted in the laboratory of Shahid Beheshti hospital.

Outcome measures

For the evaluation of function in all patients, the Persian version of the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale (VAS) questionnaires were completed by an interview performed by the resident doctor in orthopedic surgery. The WOMAC index consists of 27 questions about three parameters, including pain (five questions), stiffness (two questions) and physical function (twenty questions). Each question is scored from 0 (none) to 4 (extreme). The sum of scores of subscales is the total WOMAC score (ranging from 0 to 108). Higher scores indicated worse conditions. Validity and reliability of WOMAC for knee osteoarthritis have been documented in Iran^[36,37]. The VAS index also assessed the patients' pain. Its scores range from 0 (no pain) to 10 (worst possible pain)^[38,39].

The primary outcome for this study was defined as the percentage of patients experiencing at least a 30% decrease in the summed score for the WOMAC pain subscale from baseline to wk 12 of the intervention. Generally, clinically meaningful pain relief is defined as $\geq 30\%$ reduction in pain intensity from baseline^[40,41]. The secondary outcomes included change in joint stiffness, physical function and total WOMAC. We also evaluated the patients for pain by VAS score, and this was a secondary outcome. Additionally, we assessed a reduction of $\geq 50\%$ in the scales as another secondary outcome. These data were recorded before injection and at 4 wk, 8 wk and 12 wk after injection.

Sample size calculation

The sample size was estimated as at least 30 patients in each group by a superiority margin of $\delta = -0.15$ that was based on clinical judgement with 80% power, type I error rate of 5% and percentage drop of 10%. The proportion of the primary study outcome in PRP single-dose and hyaluronic acid groups was considered as 35% and 20%.

PRP preparation

The PRP preparation was performed by the Rooyagen kit (Arya Mabna Tashkhis Corporation, Tehran, Iran). For preparation of the PRP, about 40 mL of venous blood was drawn from antecubital vein with an 18-gauge needle. Then 5 mL acid-citrate-dextrose solution was added as an anticoagulant. The blood sample was then centrifuged for 15 min at 1500 rpm, leading to two different layers, including RBC sediment (inferior layer) and plasma (superior layer). The plasma was separated and then centrifuged for 7 min at 3500 rpm, which created two new (superior and inferior) layers with the lower white sediment containing platelets. Then the upper layer was removed, and the remaining 4-6 mL was mixed with the white platelet sediment by shaking. The final product was 4-6 mL of PRP. A laboratory analyzer Sysmex KX 21 (Sysmex Corporation, Kobe, Japan) assessed the quality and quantity of each batch of PRP.

Randomization and intervention

The subjects included in the study were divided by random allocation using computer generated numbers into three groups: (1) group PRP-1 with 31 participants (62 knees) who received a single injection of PRP; (2) group PRP-2 with 33 participants (66 knees) who received two injections of PRP; and (3) group hyaluronic acid with 31 participants (62 knees) who received three injections of hyaluronic acid.

Each patient received the same randomized intra-articular injection into both knees. The injection site on the skin was prepped and draped and under aseptic conditions. PRP was injected using a 22-gauge needle with classic inter-articular approach (through the superolateral corner of patella or mid-portion of patella while the knee is extended). After 15-20 min rest, the patients were asked to flex and extend their knees so that PRP was completely distributed in the joint before becoming a gel. For group PRP-2 (double-dose of PRP), the second injection was performed after an interval of 3 wk. Patients in group hyaluronic acid received three injections of Hyalgan brand hyaluronic acid as a prepared needle, which contains a high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL). Three Hyalgan injections were performed at 1-wk intervals. Before starting each procedure, the patients were evaluated for range of motion on knee joints and also by VAS and WOMAC questionnaires. The patients could use acetaminophen tablets (325 mg) if they experienced pain during the study. They could not use this analgesia for at least 12 h before being examined for follow-up.

Statistical analysis

The collected data were analyzed using SPSS statistical software. The descriptive analysis was used for the determination of the frequency, percentages, mean and standard deviation. Normality of the data was tested using the Kolmogorov-Smirnov test. For comparing the data before and after the treatment with normal distribution, paired *t*-test, independent *t*-test and ANOVA test were applied. To assess the non-parametric data, Wilcoxon signed rank, Mann-Whitney and Kruskal-Wallis were used. Chi-square test was used for qualitative variables. A *P*-value of < 0.05 was considered to be significant in all tests. Linear and box plot charts were prepared to illustrate the results.

Ethical issues

The informed written consent was provided by all participants. The patients' information was kept confidential. This study was approved by the Ethical Research Committee of Babol University of Medical Sciences (code: IR.MUBABOL.HRI.REC.1397.082). This trial was registered in the Iranian Registry of

Clinical Trials with the number IRCT20180129038548N1.

RESULTS

A total of 129 patients were screened initially, of whom 34 were excluded due to failing to meet inclusion criteria or declining to participate. Finally, 95 patients underwent randomization. The flow of subjects from evaluation to participation is shown in the Consolidated Standards of Reporting Trials diagram (Figure 1). Three patients from group PRP-1, five patients from group PRP-2 and four patients from group hyaluronic acid were lost during follow-up. Hence, the final study population for analysis contained 28 patients in groups PRP-1 and PRP-2 and 27 patients in group hyaluronic acid.

The baseline characteristics of the patients are shown in Table 1. There were no significant differences between the groups in age, gender, height, weight, BMI, Ahlback grading, WOMAC score and VAS pain score.

Clinical outcomes

The percentage of patients experiencing at least a 30% and/or 50% decrease in the summed score for VAS pain and all WOMAC subscales from baseline at each follow-up are shown in Table 2. Analysis of the primary outcome showed that the response rate to a single dose of PRP was 85.7% and to hyaluronic acid was 0% over the 12 wk of follow-up ($P < 0.001$). This significant difference was also observed when comparing first and second follow-up between the groups, and the two groups of PRP had a significantly higher response rate compared to the hyaluronic acid group. For group PRP-1, no significant differences were identified in the percentage of patients experiencing at least a 30% and/or 50% decrease in the summed score for the WOMAC pain subscale between knees with Ahlback grade 1 and 2 from baseline at each follow-up. It was observed for group II as well.

The mean scores for all WOMAC and VAS pain parameters decreased significantly in the three groups from baseline at wk 4. However, it started a slightly increasing trend thereafter. There were significant differences in percentage change in the mean scores from baseline to wk 4 between the three groups. Group PRP-2 had the highest decreases in the mean scores from baseline to wk 4, which were significantly higher than group PRP-1 and group hyaluronic acid. Group PRP-1 also had significant decreases in the mean scores in comparison with group hyaluronic acid at wk 4. Percentage change in the mean scores was highest in group PRP-2 compared with groups PRP-1 and hyaluronic acid and was significantly higher in group PRP-1 *versus* group hyaluronic acid at other follow-ups as well. The findings are shown in Table 3 and Figures 2-6.

Among the patients with Ahlback grade 1, the percentage change in scores from baseline for VAS pain score and all WOMAC subscales at each follow-up was significantly higher for group PRP-2 in comparison with group PRP-1. These differences were also found in the patients with Ahlback grade 2.

Over the study period, no major adverse events or complications were observed in the patients, and mild worsening of pain was noted in seven patients in the PRP groups, which was resolved by doses of acetaminophen.

DISCUSSION

In this study, we attempted to compare the clinical outcomes of PRP *versus* hyaluronic acid injections in patients with bilateral knee osteoarthritis. We divided patients with Ahlback grade 1 or 2 osteoarthritis into the three groups of single and double injection of PRP and three injections of hyaluronic acid. All the patients were followed-up for 3 mo. We used WOMAC and VAS pain scores to evaluate the clinical outcomes. We found that the efficacy of PRP (single or double injection) and hyaluronic acid started from intervention and continued until wk 4 and then started to decrease until wk 12. In other words, the highest efficacy of PRP was seen in both groups at wk 4 with about a 50% decrease in the symptoms compared with about a 25% decrease for those who had received hyaluronic acid. The efficacy of PRP treatment was significantly greater than the hyaluronic acid group at all follow-up times. In addition, two injections of PRP were more effective at each follow-up than a single injection. We did not witness any major complications during the follow-up. No similar studies exist from our region. Therefore, these data are beneficial in this point as well.

Few studies have been published comparing these treatments for osteoarthritis of the knee. In a recent systematic review, which collected the data related to the studies

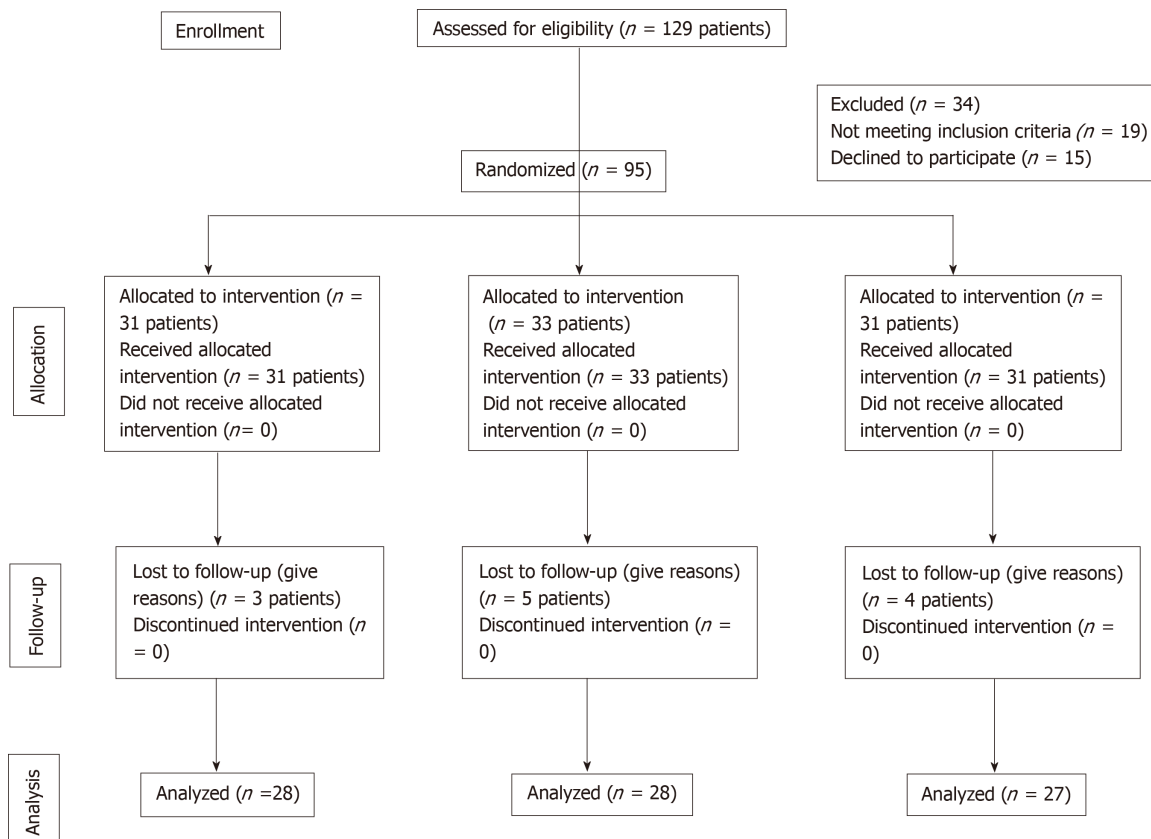


Figure 1 CONSORT flowchart.

comparing outcomes between PRP and hyaluronic acid interventions, the reported studies were mostly in agreement with our research, showing that PRP injection is more effective for the treatment of osteoarthritis of the knee, especially in patients with lower grades of arthritis^[42]. Two articles did not show any superiority of treatment with PRP over hyaluronic acid^[43,44]. In our investigation, the trend of efficacy of PRP was demonstrated to continue until the first month after treatment with a decline thereafter. However, there was still a significant difference in the mean scores between follow-ups and baseline. However, in the study by Cerza *et al*^[45], this benefit continued until the last follow-up at mo 6 without an eventual decline in efficacy. The systematic review by Di *et al*^[42], showed that PRP could improve the WOMAC score at a minimum of 24 wk. However, PRP had no benefit over the control group when assessed by other pain measures, such as the International Knee Documentation Committee, the Knee Injury and Osteoarthritis Outcome Score and VAS^[42]. When reviewing the literature, it becomes clear that there are variations between the individual studies in terms of number of patients, grading of osteoarthritis (Kellgren-Lawrence^[30,43-47] or Ahlback^[48] classification), length of follow-up (variable between 6 mo^[30,45,48] and 12 mo^[43,44,46,47], outcome scores used (WOMAC, Lequesne^[45-49], VAS, the Knee Injury and Osteoarthritis Outcome Score^[15,30,44,48,49] and number of PRP injections (one^[15], two^[46], three^[30,43,44,47,48] or four^[45]). Hence, the results can only be compared with caution.

One of the mechanisms by which PRP could improve the osteoarthritis of the knee is reported to be its anti-inflammatory effect. It has been shown that PRP can decrease the pro-inflammatory cytokines of interleukin-1 beta and tumor necrosis factor-alpha^[50]. Leukocytes in PRP have been thought to have a role in anti-inflammatory activity, immune regulation and promotion of angiogenesis^[51]. However, potential harmful effects of leukocytes on cartilage regeneration through the NF-κB pathway (a major pathway involved in the pathogenesis of osteoarthritis) have also been noted^[52]. Therefore, further experimental and clinical studies are needed to clarify this molecular mechanism of PRP against osteoarthritis. It has been demonstrated that inactivated PRP increased formation of bone and cartilage *in vitro* and *in vivo*. Non-activated PRP was also reported to have an anabolic effect on proliferation of mesenchymal stem cells^[53]. In addition, thrombin activation of PRP has an inhibitory action on chondrogenesis and osteogenesis^[54]. Growth factors in PRP potentially affect tissue repair and growth through immigration and cell proliferation, angiogenesis,

Table 1 Comparison of baseline characteristics of the patients in the three groups

Variables	Group PRP-1 (Single injection; <i>n</i> = 28 patients)	Group PRP-2 (Double injection; <i>n</i> = 28 patients)	Group hyaluronic acid (<i>n</i> = 27 patients)	<i>P</i> value
Gender, M/F, <i>n</i>	5/23	6/22	8/19	0.323
Age, mean \pm SD, yr-old	63.23 \pm 8.03	66.04 \pm 7.58	63.30 \pm 8.87	0.121
Weight, mean \pm SD, kg	73.36 \pm 7.02	76.57 \pm 6.58	75.37 \pm 8.10	0.252
Height, mean \pm SD, cm	160.57 \pm 7.25	160.43 \pm 6.57	159.37 \pm 17.27	0.504
BMI, mean \pm SD, kg/m ²	28.43 \pm 2.11	29.61 \pm 1.64	28.94 \pm 2.26	0.097
Ahlback grade, <i>n</i>	(<i>n</i> = 56 knees)	(<i>n</i> = 56 knees)	(<i>n</i> = 54 knees)	0.509
1	21	17	22	
2	35	39	32	
WOMAC score, mean \pm SD	(<i>n</i> = 56 knees)	(<i>n</i> = 56 knees)	(<i>n</i> = 54 knees)	
Pain	12.03 \pm 2.31	12.11 \pm 2.53	12.07 \pm 2.41	0.958
Stiffness	4.39 \pm 1.53	5.04 \pm 2.01	4.85 \pm 1.84	0.077
Physical function	46.93 \pm 7.59	44.39 \pm 7.82	46.19 \pm 6.32	0.236
Total	63.71 \pm 9.87	61.57 \pm 11.29	63.11 \pm 8.94	0.695
VAS score, mean \pm SD	8.25 \pm 0.92	8.29 \pm 0.80	8.15 \pm 0.81	0.631

BMI: Body mass index; F: Female; M: Male; PRP: Platelet-rich plasma; VAS: Visual analog scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index.

collagen production and stimulation of articular cartilage anabolism. They may slow down the catabolic process and decrease the synovial membrane hyperplasia^[55,56]. It was pointed out that plasma rich in growth factors may also decrease NF- κ B activation^[57]. Additionally, platelet-derived growth factor has been stated to promote chondrocyte proliferation and the maintenance of their hyaline-like phenotype^[47]. Fibrin is another factor that exists in PRP, which is used as a network for the differentiation of root cells and biological glue^[58,59].

One limitation of the present study is the lack of a control group that was treated with corticosteroids for comparison. The second one is the short-time period of study. Future studies with longer follow-up are suggested to evaluate long-term efficacy and potential complications. We also propose that future studies use magnetic resonance imaging to assess and quantify cartilage regeneration, if costs and ethical issues allow.

In conclusion, the results of this study showed that PRP is a safe and efficient therapeutic option for treatment of early stages of knee osteoarthritis by reducing the symptoms and recovering articular function. PRP was indicated to be significantly better than hyaluronic acid. We also found that the efficacy of PRP increases after multiple injections. More studies with longer follow-up and a double-blind comparison of PRP with corticosteroids are suggested for the future.

Table 2 Number of patients having at least a 30% and 50% decrease in the summed score for the Western Ontario and McMaster Universities Arthritis Index and Visual Analog Scale, *n* (%)

Variables	Follow-up								
	1 st (wk 4)	2 nd (wk 8)	3 rd (wk 12)	1 st (wk 4)	2 nd (wk 8)	3 rd (wk 12)	1 st (wk 4)	2 nd (wk 8)	3 rd (wk 12)
	Group PRP-1 (Single injection; <i>n</i> = 28 patients)			Group PRP-2 (Double injection; <i>n</i> = 28 patients)			Group hyaluronic acid (<i>n</i> = 27 patients)		
Patients having at least a 30% decrease in the summed score for the scales									
WOMAC pain score	28 (100)	27 (96.4)	24 (85.7)	28 (100)	28 (100)	28 (100)	6 (22.2)	5 (18.5)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
WOMAC stiffness score	26 (92.9)	25 (89.3)	19 (67.9)	28 (100)	28 (100)	25 (89.3)	16 (59.3)	17 (63)	5 (18.5)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
WOMAC physical function score	26 (92.9)	23 (82.1)	12 (42.9)	28 (100)	26 (92.9)	23 (82.1)	2 (7.4)	0 (0)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
Total WOMAC score	27 (96.4)	26 (92.9)	17 (60.7)	28 (100)	28 (100)	24 (85.7)	2 (7.4)	0 (0)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
Patients having at least a 50% decrease in the summed score for the scales									
WOMAC pain score	14 (50)	11 (39.3)	6 (21.4)	25 (89.3)	23 (82.1)	16 (19.3)	0 (0)	0 (0)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
WOMAC stiffness score	17 (60.7)	16 (57.1)	7 (25)	26 (92.9)	26 (92.9)	16 (57.1)	8 (29.6)	8 (29.6)	1 (3.7)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
WOMAC physical function score	5 (17.9)	5 (17.9)	1 (3.6)	17 (60.7)	11 (39.3)	5 (17.9)	0 (0)	0 (0)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
Total WOMAC score	6 (21.4)	5 (17.9)	0 (0)	19 (67.9)	17 (60.7)	7 (25)	0 (0)	0 (0)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-
VAS pain score	17 (60.7)	11 (39.3)	2 (7.1)	28 (100)	25 (89.3)	17 (60.7)	3 (11.1)	2 (7.4)	0 (0)
<i>P</i> value ¹	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-

¹In comparison with hyaluronic acid group. VAS: Visual analog scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index.**Table 3** Comparison of mean scores and percentage change in each parameter of the Western Ontario and McMaster Universities Arthritis Index and Visual Analog Scale with baseline at each follow-up for the three groups

Variable -s	Follow-up											
	0	Wk 4	Wk 8	Wk 12	0	Wk 4	Wk 8	Wk 12	0	Wk 4	Wk 8	Wk 12
	Group PRP-1 (Single injection; <i>n</i> = 28 patients)				Group PRP-2 (Double injection; <i>n</i> = 28 patients)				Group hyaluronic acid (<i>n</i> = 27 patients)			
WOMAC subscales												
Pain												
Mean	12.03	6.11	6.46	7.32	12.11	5	5.29	6.25	12.07	9.41	9.67	10.63
<i>P</i> value	Mean scores decreased significantly (<i>P</i> < 0.05)				Mean scores decreased significantly (<i>P</i> < 0.05)				Mean scores decreased significantly (<i>P</i> < 0.05)			
% change ¹ (<i>vs</i> baseline)		-49.09	-45.81	-39.09		-59.47	-56.95	-48.61		-22.01	-19.80	-11.34
<i>P</i> value	At each follow-up, the percentage change from baseline was greater in group PRP-2 than in group PRP-1, and greater in group PRP-1 than in group hyaluronic acid (<i>P</i> < 0.001).											
Stiffness												
Mean	4.39	2.14	2.25	2.79	5.04	1.75	1.89	2.57	4.85	3.11	3.07	3.93
<i>P</i> value	Mean scores decreased significantly (<i>P</i> < 0.05)				Mean scores decreased significantly (<i>P</i> < 0.05)				Mean scores decreased significantly (<i>P</i> < 0.05)			
% change ¹ (<i>vs</i> baseline)		-50.64	-47.36	-32.87		-67.96	-65.12	-47.65		-32.50	-33.16	-14.42

<i>P</i> value	At each follow-up, the percentage change from baseline was greater in group PRP-2 than in group PRP-1, and greater in group PRP-1 than in group hyaluronic acid ($P < 0.001$).											
Physical function												
Mean	46.93	28.14	28.04	31.89	44.39	22	23.39	26.54	46.19	37.85	39.41	42.52
<i>P</i> value	Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)			
% change ¹ (vs baseline)		-39.28	-39.30	-30.97		-49.46	-46.31	-38.91		-18.31	-14.53	-7.69
<i>P</i> value	At each follow-up, the percentage change from baseline was greater in group PRP-2 than in group PRP-1, and greater in group PRP-1 than in group hyaluronic acid ($P < 0.001$).											
Total												
Mean	63.71	36.46	37.14	42.5	61.57	28.75	30.61	35.32	63.11	50.44	52.67	57.26
<i>P</i> value	Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)			
% change ¹ (vs baseline)		-42.34	-41.13	-32.66		-52.77	-49.79	-41.75		-20.35	-16.61	-9.12
<i>P</i> value	At each follow-up, the percentage change from baseline was greater in group PRP-2 than in group PRP-1, and greater in group PRP-1 than in group hyaluronic acid ($P < 0.001$).											
VAS												
Mean	8.25	4.32	4.61	5.39	8.29	2.89	3.79	4.46	8.15	5.96	6.37	7.04
<i>P</i> value	Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)				Mean scores decreased significantly ($P < 0.05$)			
% change ¹ (vs baseline)		-47.6	-44.25	-34.44		-65.28	-54.31	-46.25		-26.69	-21.99	-13.71
<i>P</i> value	At each follow-up, the percentage change from baseline was greater in group PRP-2 than in group PRP-1, and greater in group PRP-1 than in group hyaluronic acid ($P < 0.001$).											

¹Negative percent shows improvement from baseline. VAS: Visual analog scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index.

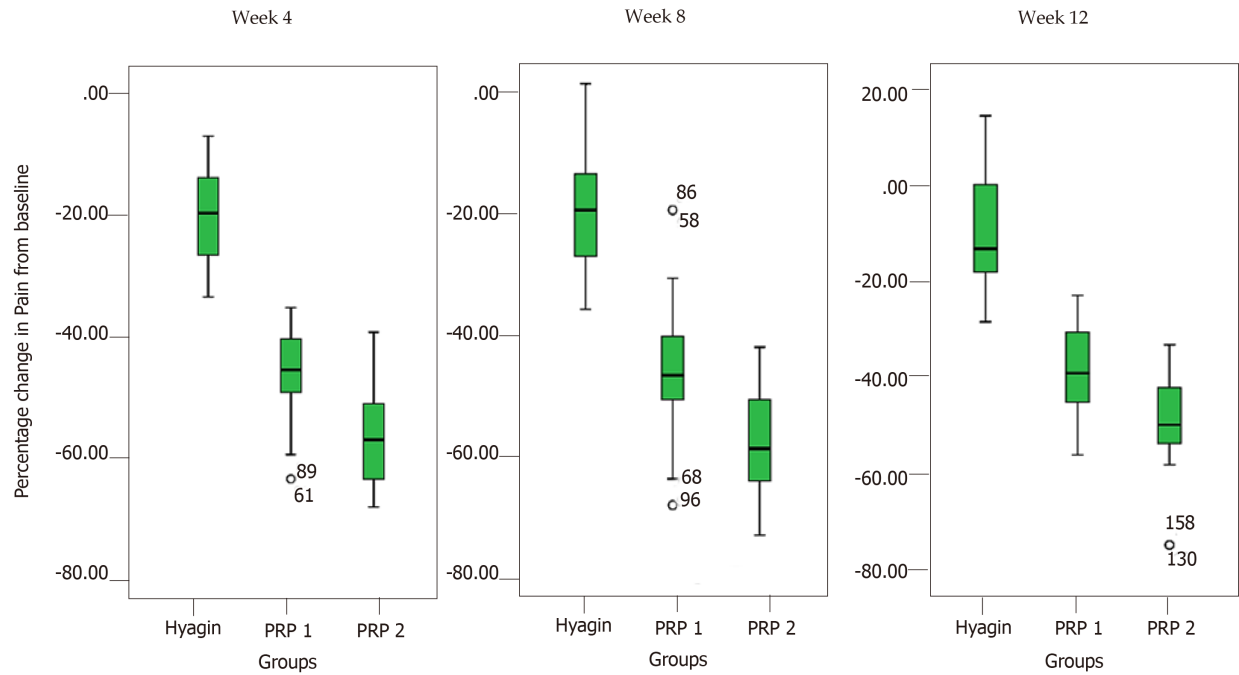
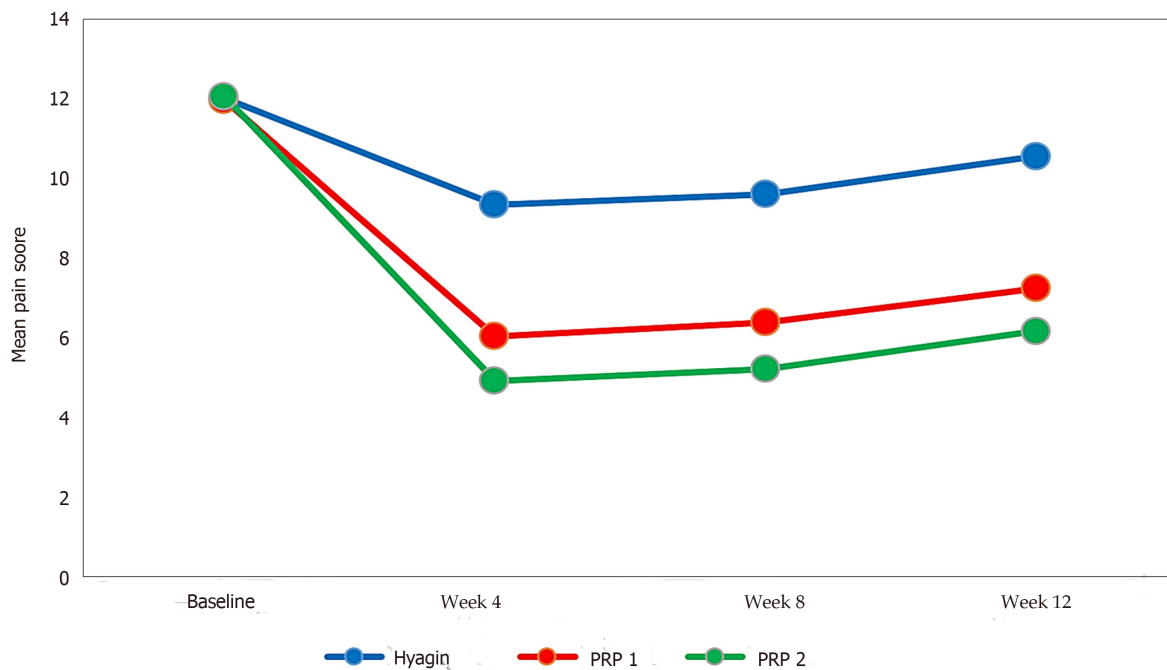
A**B**

Figure 2 Comparison of the pain score indices between the three intervention groups at baseline and subsequent follow-ups. A: Comparison of the percentage change in pain from baseline to wk 4 (1st follow-up), wk 8 (2nd follow-up) and wk 12 (3rd follow-up) between the three groups; B: Comparison of the mean pain scores at baseline and subsequent follow-ups between the three groups. Negative shows a benefit from pre-treatment values.

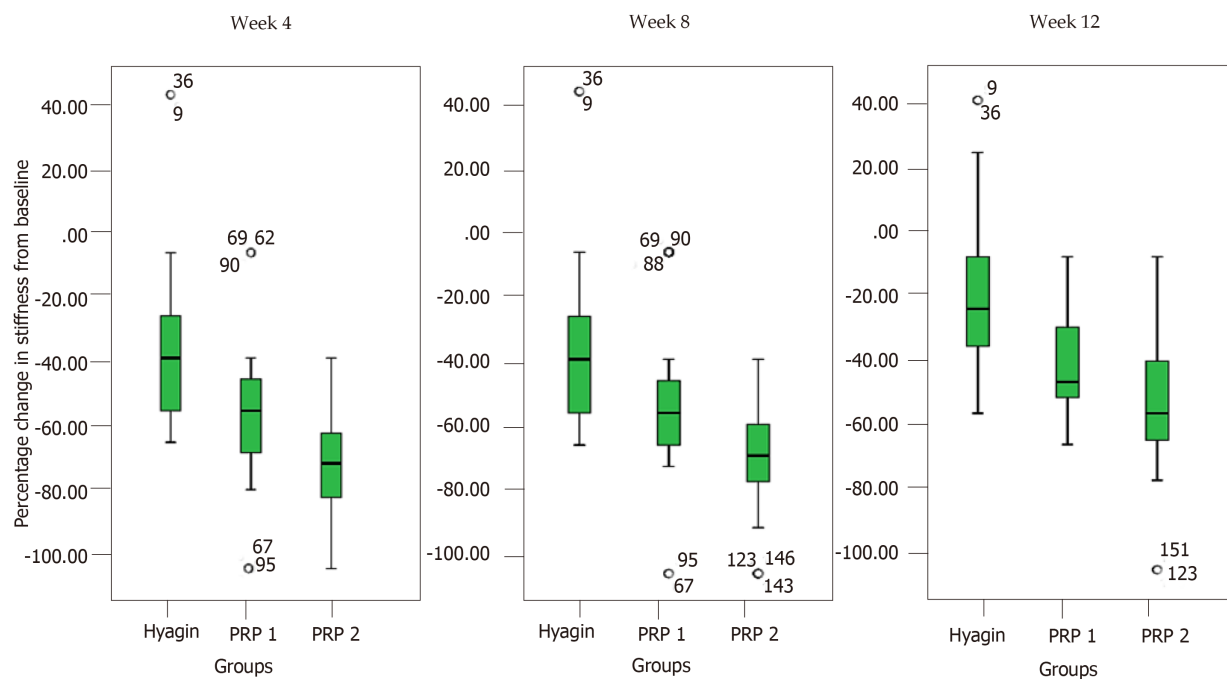
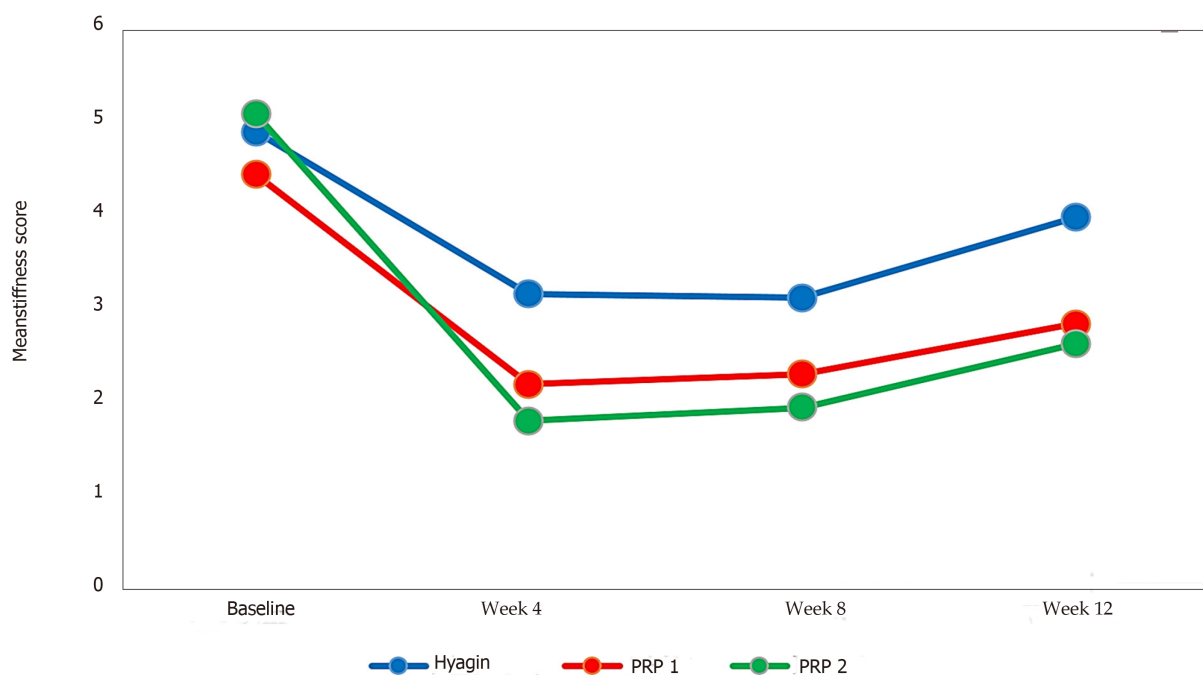
A**B**

Figure 3 Comparison of the stiffness score indices between the three intervention groups at baseline and subsequent follow-ups. A: Comparison of the percentage change in stiffness from baseline to wk 4 (1st follow-up), wk 8 (2nd follow-up), and wk 12 (3rd follow-up) between the three groups; B: Comparison of the mean stiffness scores at baseline and subsequent follow-ups between the three groups. Negative shows a benefit from pre-treatment values.

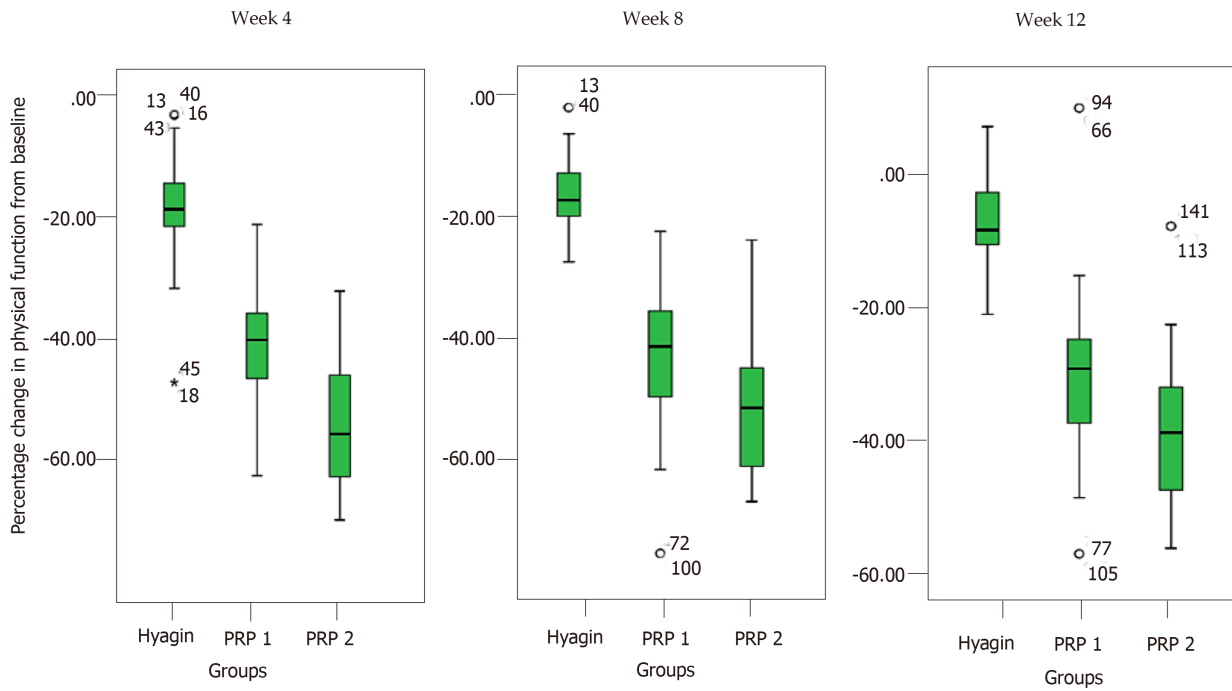
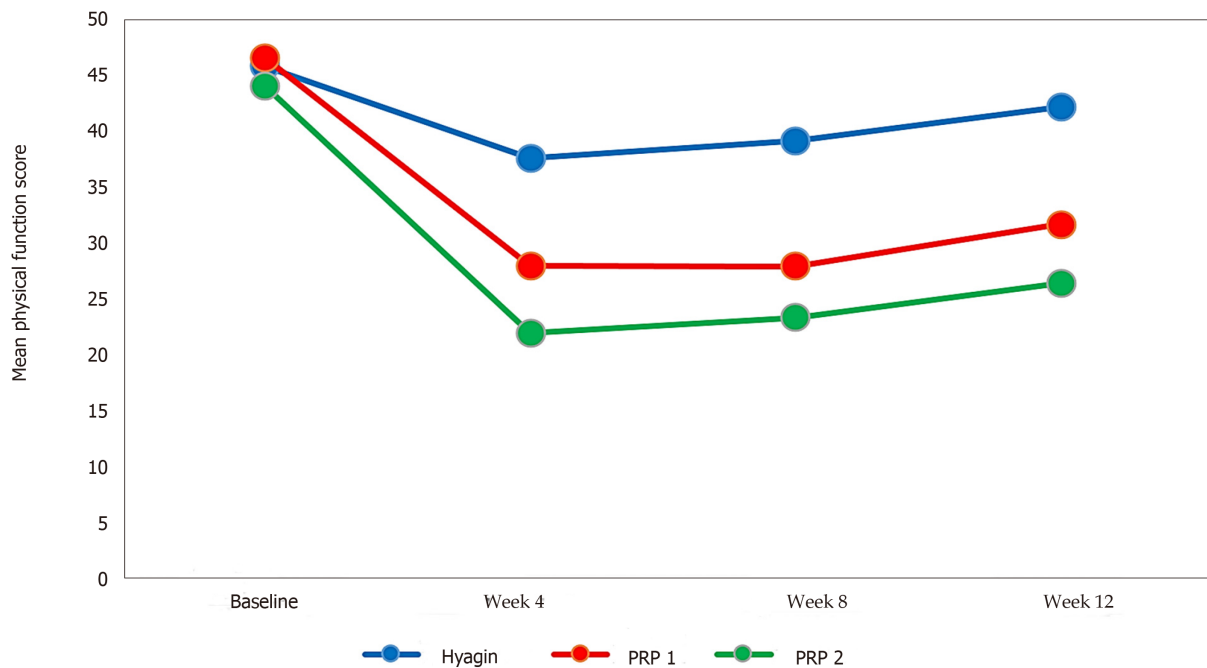
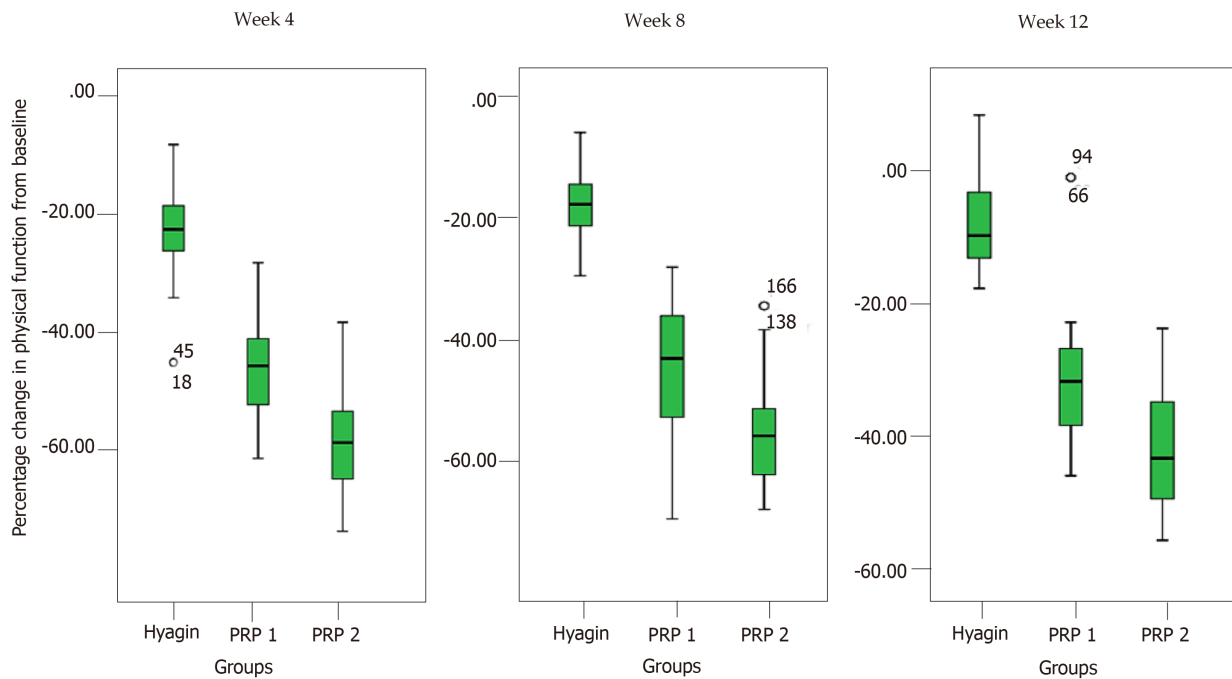
A**B**

Figure 4 Comparison of the physical function score indices between the three intervention groups at baseline and subsequent follow-ups. A: Comparison of the percentage change in physical function from baseline to wk 4 (1st follow-up), wk 8 (2nd follow-up), and wk 12 (3rd follow-up) between the three groups; B: Comparison of the mean physical function scores at baseline and subsequent follow-ups between the three groups. Negative shows a benefit from pre-treatment values.

A



B

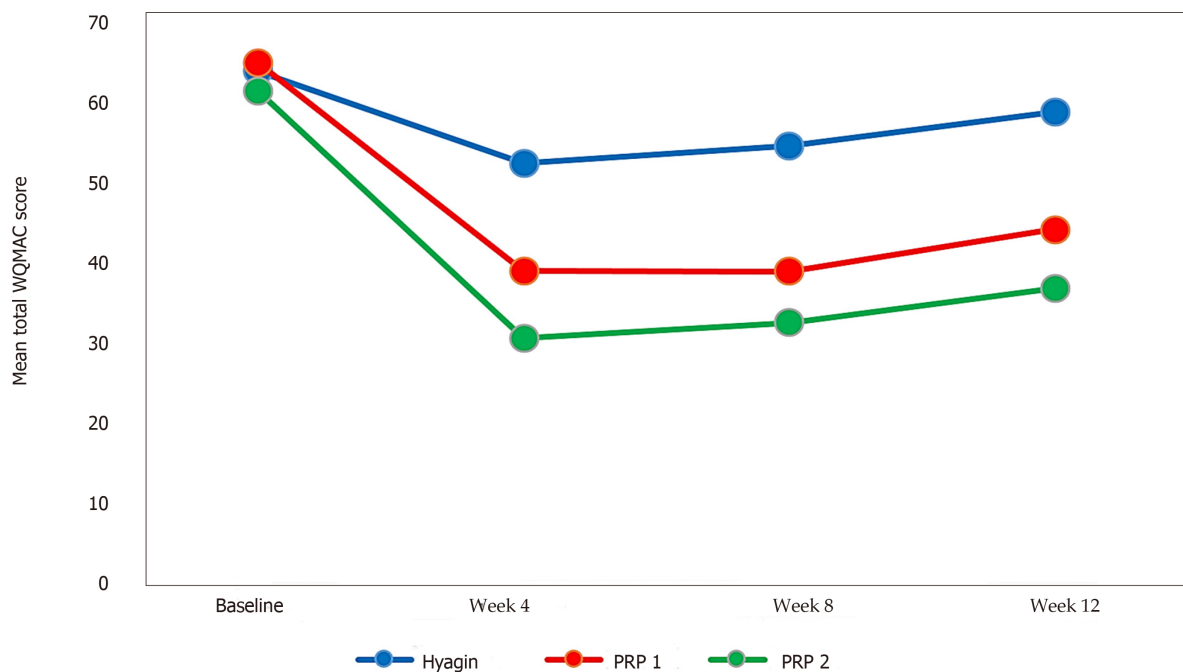


Figure 5 Comparison of the total Western Ontario and McMaster Universities Arthritis Index scores between the three intervention groups at baseline and subsequent follow-ups. A: Comparison of the percentage change in total scores from baseline to wk 4 (1st follow-up), wk 8 (2nd follow-up), and wk 12 (3rd follow-up) between the three groups; B: Comparison of the mean total scores at baseline and subsequent follow-ups between the three groups. Negative shows a benefit from pre-treatment values.

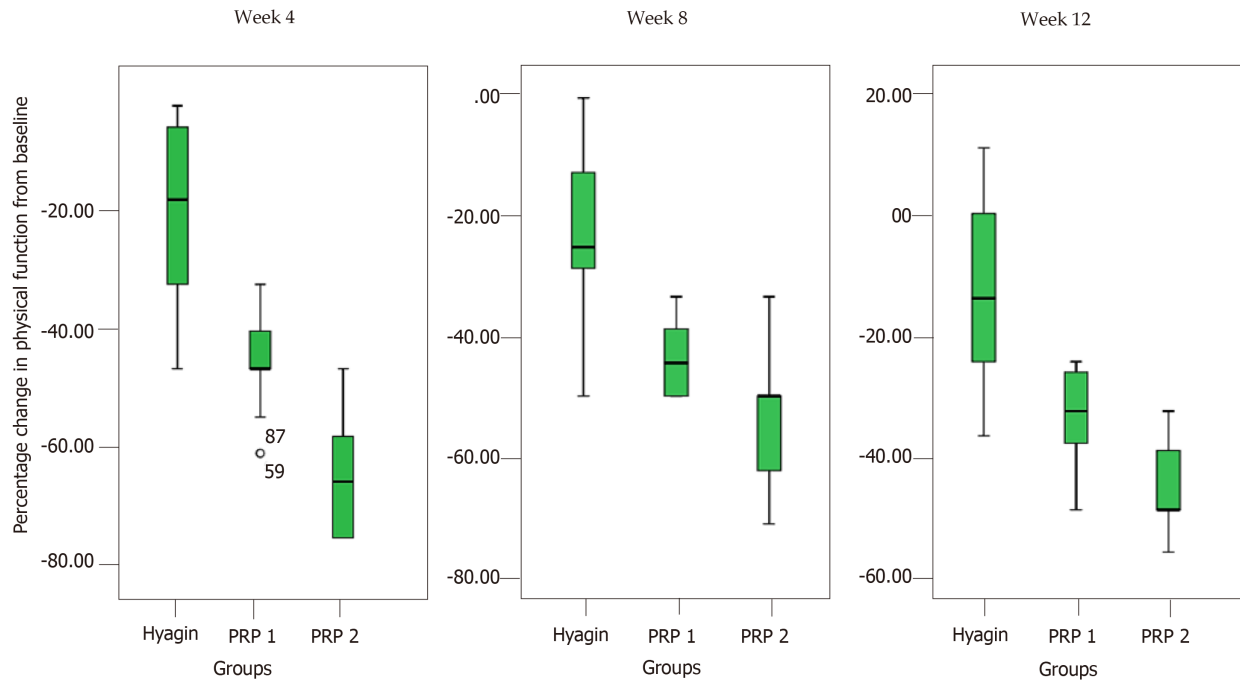
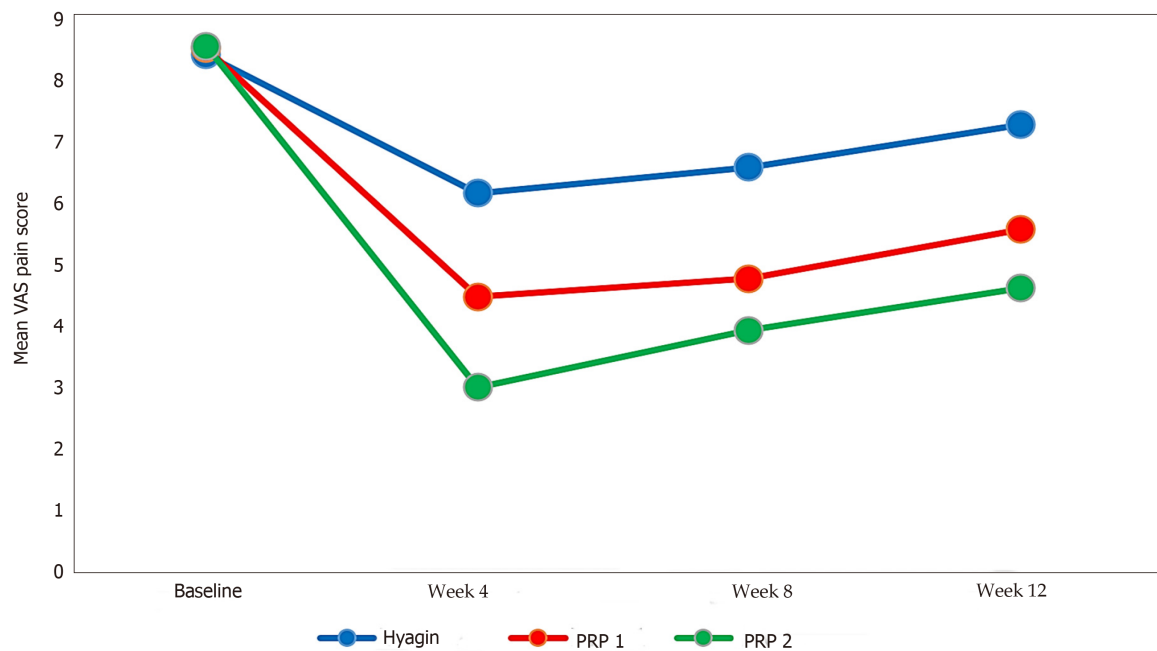
A**B**

Figure 6 Comparison of the Visual Analogue Scale pain scores between the three intervention groups at baseline and subsequent follow-ups. A: Comparison of the percentage change in scores from baseline to wk 4 (1st follow-up), wk 8 (2nd follow-up), and wk 12 (3rd follow-up) between the three groups; **B:** Comparison of the mean scores at baseline and subsequent follow-ups between the three groups. Negative shows a benefit from pre-treatment values.

ARTICLE HIGHLIGHTS

Research background

Knee osteoarthritis is the most common articular disease that manifests as functional pain and joint stiffness, leading to disability in the elderly. More than 10% of the people aged ≥ 60 years suffer from this disease.

Research motivation

Hyaluronic acid is a therapeutic option for knee osteoarthritis. However, it has short-term effects on control of symptoms. Platelet-rich plasma (PRP) is also suggested for treatment of knee osteoarthritis. However, evidence about the clinical use of PRP is still insufficient. Investigations

comparing the efficacy of these two drugs together are also insufficient.

Research objectives

The objective of this study was to compare the therapeutic efficacy of intra-articular injection of two different doses of PRP *versus* hyaluronic acid in three groups of patients with knee osteoarthritis.

Research methods

This single-blinded randomized controlled trial study involved 95 patients with bilateral knee osteoarthritis. Thirty-one subjects received a single injection of PRP (group PRP-1), 33 subjects received two injections of PRP at an interval of 3 wk (group PRP-2) and 31 subjects received three injections of hyaluronic acid at 1-wk intervals (group hyaluronic acid). The patients were investigated prospectively at the enrollment and at 4-, 8- and 12-wk follow-up with the Western Ontario and McMaster Universities Arthritis Index and Visual Analogue Scale questionnaires.

Research results

In the groups PRP-1, PRP-2 and hyaluronic acid, 86%, 100% and 0% of the patients, respectively experienced at least a 30% decrease in the total score for the Western Ontario and McMaster Universities Arthritis Index pain subscale from baseline to wk 12 of the intervention ($P < 0.001$). The mean total Western Ontario and McMaster Universities Arthritis Index scores for groups PRP-1, PRP-2 and hyaluronic acid at baseline were 63.71, 61.57 and 63.11, respectively, which were significantly improved at final follow-up to 42.5, 35.32 and 57.26, respectively. The highest efficacy of PRP was observed in both groups at wk 4 with about a 50% decrease in the symptoms compared with about a 25% decrease for the hyaluronic acid group. Group PRP-2 had higher efficacy than group PRP-1. No major adverse effects were found during the study.

Research conclusions

PRP is a safe and efficient therapeutic option for treatment of knee osteoarthritis (significantly better than hyaluronic acid). The efficacy of PRP increases after multiple injections.

Research perspectives

Future studies with longer follow-up are suggested to evaluate long-term efficacy and potential complications. We also propose that future studies use magnetic resonance imaging to assess and quantify cartilage regeneration if costs and ethical issues allow.

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REFERENCES

- Migliore A, Giovannangeli F, Granata M, Laganà B. Hyaluronate: review of its safety and efficacy in the management of joint pain in osteoarthritis. *Clin Med Insights Arthritis Musculoskelet Disord* 2010; **3**: 55-68 [PMID: 21151854 DOI: 10.1177/117954411000300001]
- Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage* 2013; **21**: 1145-1153 [PMID: 23973124 DOI: 10.1016/j.joca.2013.03.018]
- Wood AM, Brock TM, Heil K, Holmes R, Weusten A. A Review on the Management of Hip and Knee Osteoarthritis. *Int J Chronic Dis* 2013; **2013**: 845015 [PMID: 26464847 DOI: 10.1155/2013/845015]
- Chen D, Shen J, Zhao W, Wang T, Han L, Hamilton JL, Im HJ. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. *Bone Res* 2017; **5**: 16044 [PMID: 28149655 DOI: 10.1038/boneres.2016.44]
- Man GS, Mologhianu G. Osteoarthritis pathogenesis - a complex process that involves the entire joint. *J Med Life* 2014; **7**: 37-41 [PMID: 24653755]
- Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Clin Geriatr Med* 2010; **26**: 355-369 [PMID: 20699159 DOI: 10.1016/j.cger.2010.03.001]
- Bitton R. The economic burden of osteoarthritis. *Am J Manag Care* 2009; **15**: S230-S235 [PMID: 19817509]
- Abhishek A, Doherty M. Diagnosis and clinical presentation of osteoarthritis. *Rheum Dis Clin North Am* 2013; **39**: 45-66 [PMID: 23312410 DOI: 10.1016/j.rdc.2012.10.007]
- Herrero-Beaumont G, Roman-Blas JA, Bruyère O, Cooper C, Kanis J, Maggi S, Rizzoli R, Reginster JY. Clinical settings in knee osteoarthritis: Pathophysiology guides treatment. *Maturitas* 2017; **96**: 54-57 [PMID: 28041596 DOI: 10.1016/j.maturitas.2016.11.013]
- Castrogiovanni P, Di Rosa M, Ravalli S, Castorina A, Guglielmino C, Imbesi R, Vecchio M, Drago F, Szychlinska MA, Musumeci G. Moderate Physical Activity as a Prevention Method for Knee Osteoarthritis and the Role of Synovocytes as Biological Key. *Int J Mol Sci* 2019; **20**, 511 [PMID: 30691048 DOI: 10.3390/ijms20030511]
- Musumeci G, Castrogiovanni P, Trovato FM, Imbesi R, Giunta S, Szychlinska MA, Loreto C, Castorina S, Mobasheri A. Physical activity ameliorates cartilage degeneration in a rat model of aging: a study on lubricin expression. *Scand J Med Sci Sports* 2015; **25**: e222-e230 [PMID: 25039883 DOI: 10.1111/sms.12511]

- 10.1111/sms.12290]
- 12 **Szychlińska MA**, Castrogiovanni P, Trovato FM, Nsir H, Zarrouk M, Lo Furno D, Di Rosa M, Imbesi R, Musumeci G. Physical activity and Mediterranean diet based on olive tree phenolic compounds from two different geographical areas have protective effects on early osteoarthritis, muscle atrophy and hepatic steatosis. *Eur J Nutr* 2019; **58**: 565-581 [PMID: 29450729 DOI: 10.1007/s00394-018-1632-2]
 - 13 **Ringdahl E**, Pandit S. Treatment of knee osteoarthritis. *Am Fam Physician* 2011; **83**: 1287-1292 [PMID: 21661710]
 - 14 **Reid MC**, Shengelia R, Parker SJ. Pharmacologic management of osteoarthritis-related pain in older adults. *Am J Nurs* 2012; **112**: S38-S43 [PMID: 22373746 DOI: 10.1097/01.NAJ.0000412650.02926.e3]
 - 15 **Say F**, Gürlü D, Yener K, Bülbül M, Malkoc M. Platelet-rich plasma injection is more effective than hyaluronic acid in the treatment of knee osteoarthritis. *Acta Chir Orthop Traumatol Cech* 2013; **80**: 278-283 [PMID: 24119476]
 - 16 **Dhillon MS**, Patel S, John R. PRP in OA knee - update, current confusions and future options. *SICOT J* 2017; **3**: 27 [PMID: 28322719 DOI: 10.1051/sicotj/2017004]
 - 17 **Glynn LG**, Mustafa A, Casey M, Krawczyk J, Blom J, Galvin R, Hannigan A, Dunne CP, Murphy AW, Mallen C. Platelet-rich plasma (PRP) therapy for knee arthritis: a feasibility study in primary care. *Pilot Feasibility Stud* 2018; **4**: 93 [PMID: 29997901 DOI: 10.1186/s40814-018-0288-2]
 - 18 **Mishra A**, Woodall J, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. *Clin Sports Med* 2009; **28**: 113-125 [PMID: 19064169 DOI: 10.1016/j.csm.2008.08.007]
 - 19 **Knop E**, Paula LE, Fuller R. Platelet-rich plasma for osteoarthritis treatment. *Rev Bras Reumatol Engl Ed* 2016; **56**: 152-164 [PMID: 27267529 DOI: 10.1016/j.rbre.2015.07.002]
 - 20 **Hamid MS**, Yusof A, Mohamed Ali MR. Platelet-rich plasma (PRP) for acute muscle injury: a systematic review. *PLoS One* 2014; **9**: e90538 [PMID: 24587389 DOI: 10.1371/journal.pone.0090538]
 - 21 **Blanke F**, Vavken P, Haenle M, von Wehren L, Pagenstert G, Majewski M. Percutaneous injections of Platelet rich plasma for treatment of intrasubstance meniscal lesions. *Muscles Ligaments Tendons J* 2015; **5**: 162-166 [PMID: 26605189 DOI: 10.11138/mltj/2015.5.3.162]
 - 22 **Andia I**, Latorre PM, Gomez MC, Burgos-Alonso N, Abate M, Maffulli N. Platelet-rich plasma in the conservative treatment of painful tendinopathy: a systematic review and meta-analysis of controlled studies. *Br Med Bull* 2014; **110**: 99-115 [PMID: 24795364 DOI: 10.1093/bmb/ldu007]
 - 23 **Patel S**, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med* 2013; **41**: 356-364 [PMID: 23299850 DOI: 10.1177/0363546512471299]
 - 24 **Filardo G**, Kon E, Pereira Ruiz MT, Vaccaro F, Guitaldi R, Di Martino A, Cenacchi A, Fornasari PM, Maracchi M. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 2082-2091 [PMID: 22203046 DOI: 10.1007/s00167-011-1837-x]
 - 25 **Meheux CJ**, McCulloch PC, Lintner DM, Varner KE, Harris JD. Efficacy of Intra-articular Platelet-Rich Plasma Injections in Knee Osteoarthritis: A Systematic Review. *Arthroscopy* 2016; **32**: 495-505 [PMID: 26432430 DOI: 10.1016/j.arthro.2015.08.005]
 - 26 **Görmeli G**, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O, Ertem K. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 958-965 [PMID: 26233594 DOI: 10.1007/s00167-015-3705-6]
 - 27 **Rubio-Azpeitia E**, Andia I. Partnership between platelet-rich plasma and mesenchymal stem cells: in vitro experience. *Muscles Ligaments Tendons J* 2014; **4**: 52-62 [DOI: 10.11138/mltj/2014.4.1.052]
 - 28 **Stessuk T**, Puzzi MB, Chaim EA, Alves PC, de Paula EV, Forte A, Izumizawa JM, Oliveira CC, Frei F, Ribeiro-Paes JT. Platelet-rich plasma (PRP) and adipose-derived mesenchymal stem cells: stimulatory effects on proliferation and migration of fibroblasts and keratinocytes in vitro. *Arch Dermatol Res* 2016; **308**: 511-520 [PMID: 27394438 DOI: 10.1007/s00403-016-1676-1]
 - 29 **Altman RD**, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. *BMC Musculoskelet Disord* 2015; **16**: 321 [PMID: 26503103 DOI: 10.1186/s12891-015-0775-z]
 - 30 **Montañez-Heredia E**, Irizar S, Huertas PJ, Otero E, Del Valle M, Prat I, Díaz-Gallardo MS, Perán M, Marchal JA, Hernandez-Lamas Mdel C. Intra-Articular Injections of Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Osteoarthritic Knee Pain: A Randomized Clinical Trial in the Context of the Spanish National Health Care System. *Int J Mol Sci* 2016; **17** [PMID: 27384560 DOI: 10.3390/ijms17071064]
 - 31 **McArthur BA**, Dy CJ, Fabricant PD, Valle AG. Long term safety, efficacy, and patient acceptability of hyaluronic acid injection in patients with painful osteoarthritis of the knee. *Patient Prefer Adherence* 2012; **6**: 905-910 [PMID: 23271899 DOI: 10.2147/PPA.S27783]
 - 32 **Bowman EN**, Hallock JD, Throckmorton TW, Azar FM. Hyaluronic acid injections for osteoarthritis of the knee: predictors of successful treatment. *Int Orthop* 2018; **42**: 733-740 [PMID: 29299652 DOI: 10.1007/s00264-017-3731-8]
 - 33 **Altman R**, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum* 1986; **29**: 1039-1049 [PMID: 3741515 DOI: 10.1002/art.1780290816]
 - 34 **Köse Ö**, Acar B, Çay F, Yılmaz B, Güler F, Yüksel HY. Inter- and Intraobserver Reliabilities of Four Different Radiographic Grading Scales of Osteoarthritis of the Knee Joint. *J Knee Surg* 2018; **31**: 247-253 [PMID: 28460407 DOI: 10.1055/s-0037-1602249]
 - 35 **Ahlbäck S**. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968; **Suppl** 277: 7-72 [PMID: 5706059]
 - 36 **Nadrian H**, Moghimi N, Nadrian E, Moradzadeh R, Bahmanpour K, Iranpour A, Bellamy N. Validity and reliability of the Persian versions of WOMAC Osteoarthritis Index and Lequesne Algofunctional Index. *Clin Rheumatol* 2012; **31**: 1097-1102 [PMID: 22526476 DOI: 10.1007/s10067-012-1983-7]
 - 37 **Ebrahimzadeh MH**, Makhmalbaf H, Birjandinejad A, Keshtan FG, Hoseini HA, Mazloumi SM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in Persian Speaking Patients with Knee Osteoarthritis. *Arch Bone Jt Surg* 2014; **2**: 57-62 [PMID: 25207315]
 - 38 **Hawker GA**, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain

- Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res (Hoboken)* 2011; **63** Suppl 11: S240-S252 [PMID: 22588748 DOI: 10.1002/acr.20543]
- 39 **Fadaizadeh L**, Emami H, Samii K. Comparison of visual analogue scale and faces rating scale in measuring acute postoperative pain. *Arch Iran Med* 2009; **12**: 73-75 [PMID: 19111034]
- 40 **Rowbotham MC**. What is a "clinically meaningful" reduction in pain? *Pain* 2001; **94**: 131-132 [PMID: 11690725 DOI: 10.1016/S0304-3959(01)00371-2]
- 41 **Salaffi F**, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004; **8**: 283-291 [PMID: 15207508 DOI: 10.1016/j.ejpain.2003.09.004]
- 42 **Di Y**, Han C, Zhao L, Ren Y. Is local platelet-rich plasma injection clinically superior to hyaluronic acid for treatment of knee osteoarthritis? A systematic review of randomized controlled trials. *Arthritis Res Ther* 2018; **20**: 128 [PMID: 29921309 DOI: 10.1186/s13075-018-1621-0]
- 43 **Filardo G**, Di Matteo B, Di Martino A, Merli ML, Cenacchi A, Fornasari P, Marcacci M, Kon E. Platelet-Rich Plasma Intra-articular Knee Injections Show No Superiority Versus Viscosupplementation: A Randomized Controlled Trial. *Am J Sports Med* 2015; **43**: 1575-1582 [PMID: 25952818 DOI: 10.1177/0363546515582027]
- 44 **Filardo G**, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, Fornasari PM, Marcacci M. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. *BMC Musculoskelet Disord* 2012; **13**: 229 [PMID: 23176112 DOI: 10.1186/1471-2474-13-229]
- 45 **Cerza F**, Carni S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, De Biasi G, Ciuffreda M. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *Am J Sports Med* 2012; **40**: 2822-2827 [PMID: 23104611 DOI: 10.1177/0363546512461902]
- 46 **Raeesadat SA**, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babaee M, Azma K. Knee Osteoarthritis Injection Choices: Platelet-Rich Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial). *Clin Med Insights Arthritis Musculoskelet Disord* 2015; **8**: 1-8 [PMID: 25624776 DOI: 10.4137/CMAMD.S17894]
- 47 **Vaquero V**, Plasencia MÁ, Arribas I, Seijas R, Padilla S, Orive G, Anitua E. Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. *Arthroscopy* 2013; **29**: 1635-1643 [PMID: 24075613 DOI: 10.1016/j.arthro.2013.07.264]
- 48 **Sánchez M**, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, García Gutierrez A, Albillos J, Gárate R, Aguirre JJ, Padilla S, Orive G, Anitua E. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy* 2012; **28**: 1070-1078 [PMID: 22840987 DOI: 10.1016/j.arthro.2012.05.011]
- 49 **Duymus TM**, Mutlu S, Dernek B, Komur B, Aydogmus S, Kesiktaş FN. Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 485-492 [PMID: 27056686 DOI: 10.1007/s00167-016-4110-5]
- 50 **Cole BJ**, Karas V, Hussey K, Pilz K, Fortier LA. Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis. *Am J Sports Med* 2017; **45**: 339-346 [PMID: 28146403 DOI: 10.1177/0363546516665809]
- 51 **Everts PA**, van Zundert A, Schönberger JP, Devilee RJ, Knappe JT. What do we use: platelet-rich plasma or platelet-leukocyte gel? *J Biomed Mater Res A* 2008; **85**: 1135-1136 [PMID: 17907242 DOI: 10.1002/jbm.a.31570]
- 52 **Xu Z**, Yin W, Zhang Y, Qi X, Chen Y, Xie X, Zhang C. Comparative evaluation of leukocyte- and platelet-rich plasma and pure platelet-rich plasma for cartilage regeneration. *Sci Rep* 2017; **7**: 43301 [PMID: 28265109 DOI: 10.1038/srep43301]
- 53 **Spaková T**, Rosocha J, Lacko M, Harvanová D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil* 2012; **91**: 411-417 [PMID: 22513879 DOI: 10.1097/PHM.0b013e3182aab72]
- 54 **Han B**, Woodell-May J, Ponticelli M, Yang Z, Nimni M. The effect of thrombin activation of platelet-rich plasma on demineralized bone matrix osteoinductivity. *J Bone Joint Surg Am* 2009; **91**: 1459-1470 [PMID: 19487525 DOI: 10.2106/JBJS.H.00246]
- 55 **Kon E**, Mandelbaum B, Buda R, Filardo G, Delcogliano M, Timoncini A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intra-articular injection versus hyaluronic acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy* 2011; **27**: 1490-1501 [PMID: 21831567 DOI: 10.1016/j.arthro.2011.05.011]
- 56 **Leitner GC**, Gruber R, Neumüller J, Wagner A, Kloimstein P, Höcker P, Körmöczy GF, Buchta C. Platelet content and growth factor release in platelet-rich plasma: a comparison of four different systems. *Vox Sang* 2006; **91**: 135-139 [PMID: 16907874 DOI: 10.1111/j.1423-0410.2006.00815.x]
- 57 **van Buul GM**, Koevoet WL, Kops N, Bos PK, Verhaar JA, Weinans H, Bernsen MR, van Osch GJ. Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. *Am J Sports Med* 2011; **39**: 2362-2370 [PMID: 21856929 DOI: 10.1177/0363546511419278]
- 58 **Dohan Ehrenfest DM**, Andia I, Zumstein MA, Zhang CQ, Pinto NR, Bielecki T. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. *Muscles Ligaments Tendons J* 2014; **4**: 3-9 [PMID: 24932440 DOI: 10.11138/mltj/2014.4.1.0013]
- 59 **Borie E**, Olivé DG, Orsi IA, Garlet K, Weber B, Beltrán V, Fuentes R. Platelet-rich fibrin application in dentistry: a literature review. *Int J Clin Exp Med* 2015; **8**: 7922-7929 [PMID: 26221349]



Who should you be following? The top 100 social media influencers in orthopaedic surgery

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Abstract

BACKGROUND

Social media has been credited with the potential to transform medicine, and Twitter was recently named “an essential tool” for the academic surgeon. Despite this, peer-to-peer and educational influence on social media has not been studied within orthopaedic surgery. This knowledge is important to identify who is controlling the conversation about orthopaedics to the public. We hypothesized that the plurality of top influencers would be sports medicine surgeons, that social media influence would not be disconnected from academic productivity, and that some of the top social media influencers in orthopaedic surgery would not be orthopaedic surgeons.

AIM

To identify the top 100 social media influencers within orthopaedics, characterize who they are, and relate their social media influence to academic influence.

METHODS

Twitter influence scores for the topic “orthopaedics” were collected in July 2018 using Right Relevance software. The accounts with the top influence scores were linked to individual names, and the account owners were characterized with respect to specialty, subspecialty, practice setting, location, board certification, and academic Hirsch index (*h*-index).

RESULTS

Seventy-eight percent of top influencers were orthopaedic surgeons. The most common locations included California (13%), Florida (8%), New York (7%), United Kingdom (7%), Colorado (6%), and Minnesota (6%). The mean academic

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h-index of the top influencers ($n = 79$) was 13.67 ± 4.12 (mean \pm 95%CI) and median 7 (range 1-89) (median reported *h*-index of academic orthopaedic faculty is 5 and orthopaedic chairpersons is 13). Of the 78 orthopaedic surgeons, the most common subspecialties were sports medicine (54%), hand and upper extremity (18%), and spine (8%). Most influencers worked in private practice (53%), followed by academics (17%), privademics (14%), and hospital-based (9%). All eligible orthopaedic surgeons with publicly-verifiable board certification statuses were board-certified ($n = 74$).

CONCLUSION

The top orthopaedic social media influencers on Twitter were predominantly board-certified, sports-medicine subspecialists working in private practice in the United States. Social media influence was highly concordant with academic productivity as measured by the academic *h*-index. Though the majority of influencers are orthopaedic surgeons, 22% of top influencers on Twitter are not, which is important to identify given the potential for these individuals to influence patients' perceptions and expectations. This study also provides the top influencer network for other orthopaedic surgeons to engage with on social media to improve their own social media influence.

Key words: Social media; Influence; Impact; Twitter; Orthopaedics; Orthopedics

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Core tip: In this study, we identify and characterize the top 100 social media influencers in orthopaedic surgery. We find that the top influencers were predominantly board-certified, sports-medicine subspecialists working in private practice in the United States (though 22% of top influencers were not orthopaedic surgeons). Social media influence was highly concordant with academic productivity as measured by the academic Hirsch index.

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INTRODUCTION

Social media is comprised of many platforms for real time information sharing between physicians, between patients, and between physicians and patients. Consequently, the use of social media in medicine has skyrocketed with up to 90% of physicians having a social media account and up to 80% of patients turning to the Internet for medical information^[1,2]. Within orthopaedics, social media is a valuable tool for both the academic and private practice surgeon. Academic articles are frequently shared and discussed^[3], and surgeons commonly use social media to promote their practices^[4]. Regardless of practice setting, social media is useful for branding, networking, mentoring, and most importantly, as a direct channel for physicians to share information with their colleagues and patients.

Previous studies have explored the correlation between social media activity and orthopaedic articles' citation counts^[3], as well as examined how patients share information about their orthopaedic injuries online^[5-7]. However, to date, the individuals with the largest social media influence within the orthopaedic community have not been established. A social media *influencer* is a person who carries significant impact within a given circle or topic (e.g., orthopaedics). Social media influence is not just about having "top posts;" rather, it is a complex interplay between engagement (likes and comments), content impact, and interconnectedness with other influencers. In many ways, social media influence is akin to the academic Hirsch index (*h*-index), which calculates a researchers productivity and citation impact^[8]. Influencers are extremely important because they directly drive user behavior. Data analytics firm Annalect (New York, NY, United States) and Twitter (San Francisco, CA, United

States) have shown that influencers rival friends in building trust: 49% of users rely on influencers before buying a product compared to 56% relying on recommendations by friends^[9]. Moreover, while brand advertising exposure alone results in a user to be 2.7 times more likely to purchase a product, the combined influence of brand advertising and social media influencer endorsement nearly doubles this effect to 5.2 times as likely to make the purchase.

Which individuals have the largest social media influence in orthopaedics thus has a number of clinical implications. For example, recent work has highlighted the role of expectation-setting in delivering high-quality, value-based orthopaedic care^[10-12]. Given that nearly 80% of patients read medical information online^[2], influencers serve in a unique position to sway patient expectations in a positive or negative manner. Similarly, in a field with many elective procedures, the propensity for users to act based on influencers highlights the need to know who is sharing and what is being shared (marketed) with patients. Additionally, orthopaedics is a highly multidisciplinary field that encompasses numerous types of providers, including: orthopaedic surgeons, primary care/family practice sports medicine physicians, physiatrists, chiropractors, physical therapist, and athletic trainers, among others. Patients may develop beliefs, questions, or concerns based on the influencers to which they are exposed. From a provider perspective, insights gleaned from characterizing the top influencers in orthopaedic surgery may help inform the average orthopaedic surgeon on how to more effectively use social media, which is particularly relevant in light of recent work by Logghe *et al.*^[13] highlighting Twitter's potential to advance the core values of academic surgery. In response to this work, members of the orthopaedic community have even contemplated whether Twitter is now an essential tool for the orthopaedic surgeon^[14]. Therefore, the purpose of this study is to identify the top 100 Twitter influencers in orthopaedics and characterize them with respect to specialty, subspecialty and board certification status (if orthopaedic surgeon), practice setting, location, website use, and *h*-index. We hypothesized that the plurality of top influencers would be sports medicine surgeons, that social media influence would not be disconnected from academic productivity, and that some of the top social media influencers in orthopaedic surgery would not be orthopaedic surgeons.

MATERIALS AND METHODS

We chose to study social media influence on Twitter given its particular medical relevance^[3,13,15-17] coupled with a recent analysis of orthopaedic social media activity demonstrating that 82% of mentions were on Twitter^[3]. Adapted from the methods of Chandawarkar *et al.*^[18], we queried the Right Relevance API (www.rightrelevance.com, San Francisco, CA, United States) to generate Twitter influence scores for the topic of "orthopaedics." Right Relevance uses sophisticated partitioning techniques to calculate influence based on a variety of factors, including connections (follower/following) to other influencers and engagement (views, likes, retweets). The API was queried on July 5, 2018, and data were placed in a database (Microsoft Excel, Seattle, WA, United States).

We subsequently ranked the accounts according to influence and generated a list of the handles with the highest influence scores. We then excluded handles belonging to groups and organizations to determine the top 100 most influential individuals in orthopaedics. We further characterized these individuals with respect to specialty, subspecialty, practice setting (academic, privademic, private practice, hospital based, trainee, no longer practicing, and anonymous), use of a personal website, and location from their Twitter account biography. In cases where this information was not available on Twitter, we searched several public resources including Dximity (San Francisco, CA, United States), LinkedIn (Sunnyvale, CA, United States), ResearchGate (Berlin, Germany), and practice and institutional websites. All orthopaedic surgeons were then queried for board certification status in their respective country. Finally, *h*-index scores were queried from Scopus (Reed Elsevier, London, United Kingdom) on July 16, 2018 and added to the database. Statistics and graphical representation were performed in Microsoft Excel (Seattle, WA, United States).

RESULTS

The top 100 most influential individuals in orthopaedic surgery on social media are listed in Table 1. Seventy-eight percent of the top influencers were orthopaedic surgeons; 7% were physical therapists; 4% were primary care sports medicine physicians; physical medicine and rehabilitation, general surgery, and interventional

cardiology physicians each composed 1%; and 8% were other non-physician individuals (Figure 1A). Eighty percent of influencers were located in the United States. The most common locations included California (13%), Florida (8%), New York (7%), United Kingdom (7%), Colorado (6%), and Minnesota (6%) (Table 2). We found a strikingly high average *h*-index among the top social media influencers in orthopaedic surgery ($n = 79$) of 13.67 ± 4.12 (mean \pm 95%CI) with a median of 7 (range 1 to 89). This can be benchmarked by the median reported *h*-index for orthopaedic academic faculty which is 5 and the median *h*-index for orthopaedic chairpersons which is 13^[19].

Of the 78 orthopaedic surgeon influencers, the ten most influential individuals were: (1) Brian Cole, MD, MBA; (2) Howard Luks, MD; (3) Steve Mora, MD; (4) David Geier, MD; (5) Robert LaPrade, MD, PhD; (6) Peter Millett, MD; (7) Katherine Burns, MD; (8) James Lubowitz, MD; (9) Sean McMillan, DO; and (10) Thomas Clanton, MD. Fifty-four percent of orthopaedic surgeon influencers primarily specialized in sports medicine, 18% in upper extremity, 8% in spine, 6% in foot and ankle, 4% in trauma, 4% in hip, 3% in arthroplasty, and 4% were unlisted (Figure 1B). Approximately half of the orthopaedic influencers worked primarily in the private practice setting (53%), followed by academics (17%), privademics (14%), and hospital based (9%) (Figure 1C). Three percent of orthopaedic surgeon influencers were no longer practicing, 3% were trainees, and 1% had an anonymous account. Information on the orthopaedic surgeon influencers' board certification is provided in Table 3. Overall, all non-trainee orthopaedic surgeons who were from countries with publicly verifiable boards were board certified (74/78). One hundred percent ($n = 63$) of United States-based allopathic orthopaedic surgeon influencers were board certified by the American Board of Orthopaedic Surgery; twenty-five of these individuals held subspecialty certification in sports medicine; and four held subspecialty certification in hand surgery (with one physician holding subspecialty certification in both sports medicine and hand surgery). Fifty-four percent (42/78) of the top influencers, including all of the top ten influencers, had a professional portfolio website about themselves. For 74% of such influencers (31/42), this website was an entirely separate website from their practice website.

DISCUSSION

Social media has emerged as a critical component of modern medicine^[3,13,14,16,20]. A large body of work has highlighted the increasing use of social media by orthopaedic patients and surgeons^[4,7,21-26]. At academic conferences, including the American Academy of Orthopaedic Surgeons annual meetings, Twitter has been used to increase exposure and engagement^[27,28]. The keynote address at the 2018 annual meeting of the American Orthopaedic Association-by internist and Twitter personality Kevin Pho (@kevinmd)-was about how to "make a difference in health care with social media." Orthopaedic journals, hospitals, patients, and physicians are rapidly adopting Twitter^[5,29]. The current study highlights those individuals that have the largest impact on social media within orthopaedics.

We found that the most influential orthopaedic surgeons were predominantly board-certified, sports-medicine subspecialists working in private practice in the United States. Recent work has emphasized the under-utilization of social media by academicians^[4,25,30], which may be reflected in our study. For example, Lander *et al*^[4] found private practice pediatric orthopaedic surgeons had approximately double the social media utilization of academic physicians, consistent with our finding that the majority of top influencers worked in private practice. One may assume that these private practice users are primarily using social media to promote their practice; however, not only was this not reflected in our review of the accounts, such users would be unlikely to build high influence scores. A high influence score requires both high impact content that users engage with, as well as integration into and interaction with a larger network of experts in the particular field (*e.g.*, orthopaedics). Thus, these surgeons are producing relevant content that is followed by and of interest to others in the field, consistent with our finding that nearly all of the top influencers were board certified and further supported by the high academic *h*-index scores among the top influencers.

Similarly, the high number of sports medicine physicians in our study is consistent with the work of Curry *et al*^[21] who found sports medicine patients were generally the most likely to be social media users (likely due to overlapping demographics). Surgeons tweeting about sports medicine may have the largest potential audience (younger users) fostering the growth of their influence. Prior work by Ramkumar *et al*^[5] identified over 500 Instagram posts a month by patients on anterior cruciate

Table 1 Top 100 most influential individuals

Rank	Twitter Handle	Name	Occupation
1	briancolemd	Brian Cole	Orthopaedic Surgery
2	hjluku	Howard Luks	Orthopaedic Surgery
3	myorthodoc	Steve A. Mora	Orthopaedic Surgery
4	drdavidgeier	David Geier	Orthopaedic Surgery
5	thekneedoc	Robert LaPrade	Orthopaedic Surgery
6	the_jockdoc	Andrew Blecher	Family Medicine Sports Medicine
7	milletmd	Peter Millett	Orthopaedic Surgery
8	cmichaelgibson	C. Michael Gibson	Interventional Cardiology
9	afranklynmiller	Andy Franklyn-Miller	Primary Care Sports Medicine
10	kburnsmd	Katherine Burns	Orthopaedic Surgery
11	orthohead	April Bright	General Manager, Orthoworld
12	jameslubowitzmd	James Lubowitz	Orthopaedic Surgery (Editor-in-Chief, Arthroscopy)
13	sportsdrsean	Sean McMillan	Orthopaedic Surgery
14	tomclantonmd	Thomas Clanton	Orthopaedic Surgery
15	anklefootmd	Lance Silverman	Orthopaedic Surgery
16	drpamortho	Pamela Petrocy	Orthopaedic Surgery
17	stephania_espn	Stephania Bell	Physical Therapy
18	tigerbuford	Tiger Buford	Recruiter
19	thomasleemd	Thomas H. Lee	Orthopaedic Surgery
20	shoulderarth	Frederick Matsen	Orthopaedic Surgery
21	sportscaduceus	Sportscaduceus	Orthopaedic Surgery
22	shouldermd	Jonathan Levy	Orthopaedic Surgery
23	bonedoc95	Ronald Navarro	Orthopaedic Surgery
24	sheldenmartinmd	Shelden Martin	Orthopaedic Surgery
25	anthonyromeomd	Anthony A. Romeo	Orthopaedic Surgery
26	drderekochiai	Derek Ochiai	Orthopaedic Surgery
27	adammeakins	Adam Meakins	CSCS/physiotherapist
28	sinicropispine	Stefano Sinicropi	Orthopaedic Surgery
29	drnikhilverma	Nikhil Verma	Orthopaedic Surgery
30	drroddymcgee	Roddy McGee	Orthopaedic Surgery
31	drcorenman	Donald Corenman	Orthopaedic Surgery
32	zehrcenter	Robert J. Zehr	Orthopaedic Surgery
33	lauramiller19	Laura Dyrda	Editor-in-Chief, Becker's ASC and Spine Review
34	flspinedoc	Jonathan Hyde	Orthopaedic Surgery
35	drellylaroque	Elly LaRoque	Orthopaedic Surgery
36	drkmarberry	Kevin Marberry	Orthopaedic Surgery
37	nashvillehipmds	Tania A. Ferguson and J.W. Thomas Byrd	Orthopaedic Surgery
38	mikereinold	Mike Reinold	Physical Therapy
39	cyclingsurgeon	Chris Oliver	Orthopaedic Surgery (Retired)
40	vegascourse	Raffy Mirzayan	Orthopaedic Surgery
41	drgreghoover	Gregory Hoover	Orthopaedic Surgery
42	samcartermd	Samuel Carter	Orthopaedic Surgery
43	scoliosisdoctor	Neel Anand	Orthopaedic Surgery
44	chrisgearyortho	Christopher Geary	Orthopaedic Surgery
45	traumatologoald	David Maldonado	Orthopaedic Surgery
46	drdecampos	Juliet DeCampos	Orthopaedic Surgery
47	drmartinleland	J. Martin Leland	Orthopaedic Surgery
48	petercoffaro	Peter Coffaro	Medical Device Consultant, Gerson Lehrman Group
49	mizzousportsdoc	Aaron Gray	Family Medicine Sports Medicine
50	stiebermd	Jonathan Stieber	Orthopaedic Surgery
51	krisjonesmd	Kristofer Jones	Orthopaedic Surgery
52	julie_eib	Julie Eibensteiner	Physical Therapy

53	drjustinroe	Justin Roe	Orthopaedic Surgery
54	fixnbones	Dan Fuentes	Orthopaedic Surgery
55	randysportsdoc	Randy Schwartzberg	Orthopaedic Surgery
56	benjamindombmd	Benjamin Domb	Orthopaedic Surgery
57	meierorthopedic	Steven W. Meier	Orthopaedic Surgery
58	richlamourmd	Richard Lamour	Orthopaedic Surgery
59	joshdinesmd	Josh Dines	Orthopaedic Surgery
60	skepticalscalpel	Skeptical Scalpel	General Surgery
61	ashishrawalmd	Ashish M. Rawal	Orthopaedic Surgery
62	ccentenomd	Chris Centeno	Physical Medicine and Rehabilitation
63	drnickusa	Nicholas DiNubile	Orthopaedic Surgery
64	knee_surgeon	Christopher Vertullo	Orthopaedic Surgery
65	drhalbrecht	Jeffrey Halbrecht	Orthopaedic Surgery
66	mikereiman	Mike Reiman	Physical Therapy
67	glenncohenmd	Glenn D. Cohen	Orthopaedic Surgery
68	drpaci	James Paci	Orthopaedic Surgery
69	drjosephkim	Joseph Kim	President, Q Synthesis
70	drpeachy	Chris Peach	Orthopaedic Surgery
71	str8bonesjim	Jim Ficke	Orthopaedic Surgery
72	herschmd	Jonathan Hersch	Orthopaedic Surgery
73	kevinfarmermd	Kevin W. Farmer	Orthopaedic Surgery
74	jocktodoc	Mark Adickes	Orthopaedic Surgery
75	orthopodreg	Simon Fleming	Orthopaedic Surgery
76	drhanyelrashidy	Hany Elrashidy	Orthopaedic Surgery
77	saraedwardsmd	Sara Edwards	Orthopaedic Surgery
78	orthobiohealing	William D Murrell	Orthopaedic Surgery
79	drbadia	Alejandro Badia	Orthopaedic Surgery
80	trentwilsonmd	Trent Wilson	Orthopaedic Surgery
81	angryorthopod	angryorthopod	Orthopaedic Surgery
82	sportzdoc	Brian Shannon	Orthopaedic Surgery
83	drjordanmetzl	Jordan D. Metzl	Pediatric Sports Medicine
84	drmartinsalgado	Martin Salgado	Orthopaedic Surgery
85	nickferran	Nick Ferran	Orthopaedic Surgery
86	kthorborg	Kristian Thorborg	Physical Therapy
87	chrisandersonmd	Chris N Anderson	Orthopaedic Surgery
88	jsanchezsotelo	Joaquin Sanchez-Sotelo	Orthopaedic Surgery
89	mykneedoc	Gareth Stables	Orthopaedic Surgery
90	the_ompt	Erson Religioso	Physical Therapy
91	handwristdr	John T. Knight	Orthopaedic Surgery
92	jenarofv_md	Jenaro Fdez-Valencia	Orthopaedic Surgery
93	hip_arthroscopy	Jon Conroy	Orthopaedic Surgery
94	ricesportsmd	Robert Rice	Orthopaedic Surgery
95	brentmorrismd	Brent J. Morris	Orthopaedic Surgery
96	rayravenmd	Ray Raven	Orthopaedic Surgery
97	hewett1tim	Tim Hewett	Researcher - Biomechanics
98	bill_vicenzino	Bill Vicenzino	Physical Therapy
99	medtronicceo	Omar Ishrak	Chairman and CEO, Medtronic
100	drpedrojdelgado	Pedro J. Delgado	Orthopaedic Surgery

ligament surgery alone, highlighting the use of social media by sports medicine patients. Interestingly, National Football League team physicians were chosen as a convenience sample of potential high-influence orthopaedic surgeons in that study; however, only 16% of these individuals had Twitter accounts with an average of 94 posts. One possible explanation for this difference would be these individuals typically working at top orthopaedic hospitals (96% of which were found to have social media accounts^[5]) and thus relying on hospital accounts, rather having their

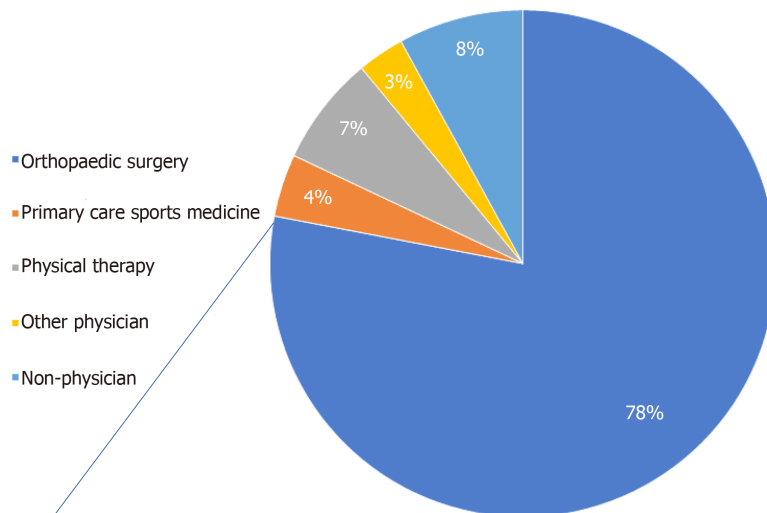
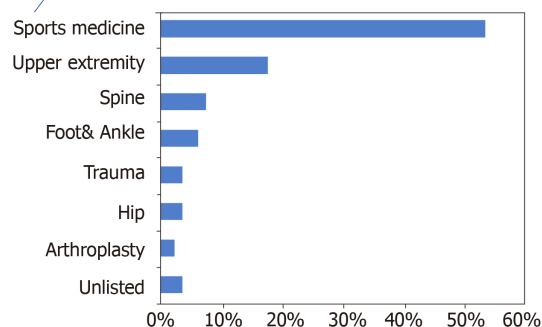
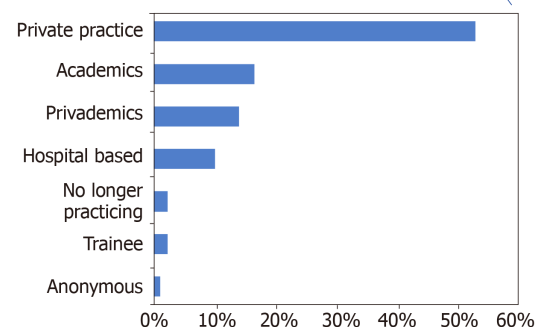
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Figure 1 Occupations of the top 100 social media influencers in orthopaedic surgery. A: Occupation of the top 100 influencers; B: Subspecialties of the 78 orthopaedic surgeon influencers; C: Practice setting of the 78 orthopaedic surgeon influencers. Primary care sports medicine refers to internal medicine, family practice, or pediatric doctors who undergo additional fellowship training in sports medicine. Physical therapy refers to those practicing physical therapy/physiotherapy.

own. This would be in line with the predominance of top orthopaedic surgeon influencers in this study working in private practice and prior work demonstrating lower social media utilization among academic orthopaedic surgeons^[4,25,30]. Given who is controlling the social media conversation on sports medicine may be unintuitive, here we identify many of the sports medicine physicians that have the highest influence in orthopaedic surgery.

Social media is uniquely equipped to have a positive impact for the sports medicine surgeon. First, given the overlapping demographics, skilled social media use may be used to help attract patients and grow one's practice. Moreover, patients may expect an online presence from their sports medicine surgeon, given it is such a primary means of communication for many sports medicine patients^[5]. Next, it provides a platform familiar to and highly utilized by many sports medicine patients to share relevant education materials. In an anecdotal analysis of many of the top influencers accounts, there were myriad educational posts and links to blogs on topics such as rehabilitation, injury prevention, injury descriptions, sports technology, etc. In addition, Twitter provides a network for sports medicine surgeons to learn from each other. Many of the top influencers shared videos of their operative techniques and conversed with each other on topics such as management of challenging cases, interpretation of imaging, and discussing the latest orthopaedic literature. By following the top influencers in this study, sports surgeons can join this rich community and continue to grow their own influence.

Despite the applicability of social media to the practice of sports medicine and the widespread social media influence of sports medicine physicians found in this study, there still exists a limited body of scientific work related to sports medicine on social media^[5]. This is in contrast to fields such as hand and upper extremity, which have

Table 2 Locations of the top 100 most influential individuals

United States		International	
California	13	United Kingdom	7
Florida	8	Australia	3
New York	7	Spain	2
Colorado	6	Chile	1
Minnesota	6	Denmark	1
Washington	5	Ireland	1
Illinois	4	United Arab Emirates	1
Texas	4	Venezuela	1
Massachusetts	3		
Missouri	3		
Ohio	3		
Tennessee	3		
Pennsylvania	2		
South Carolina	2		
Arizona	1		
Kentucky	1		
Louisiana	1		
Maryland	1		
North Carolina	1		
New Jersey	1		
New Mexico	1		
Nevada	1		
Utah	1		
Virginia	1		
Wisconsin	1		
Unknown	3		

received considerable attention^[7,24,25,31]. While this study identifies many of the top social media influencers in sports medicine and the work of Ramkumar *et al*^[5] examined social media use among patients and hospitals, future work examining the utilization and impact of social media on sports medicine practices may be helpful given the large social media influence sports medicine orthopaedic surgeons have on the topic of orthopaedics in general. On the other hand, our results demonstrate the paucity of top influencers from the other subspecialties within orthopaedics. Non-sports medicine physicians in the orthopaedics community should continue to work to get involved to help shape the face of orthopaedics to the public via social media and may benefit from engaging with and referencing the top influencers on this list.

Interestingly, over half of the top orthopaedic surgeon social media influencers—including 100% of the top ten—had personal websites (*i.e.*, websites about themselves that did not feature another physician). Moreover, 74% of these websites were solely portfolio/resume websites, separate from their practice website. It is unclear whether these results are due to the propensity for those with a larger online influence to have multiple online profiles, the propensity of top influencers to be sought after for employment by clinical institutions or consulting work resulting in the need for a portfolio website, or if the existence of such a website is actually useful in building influence. Notably, however, Garofolo *et al*^[24] reported that hand surgeons with a more robust online presence observed higher patient satisfaction scores on an online rating website (Healthgrades.com), and that the use of a professional personal website was the single most important social media platform to improve scores on this platform. They found the use of a group website was associated with more reviews, but did not improve Healthgrade scores, which was also recently corroborated by Donnally *et al*^[30] in a review of spine surgeons. Orthopaedic surgeons hoping to build their online influence may benefit from creating a personal website, which can promote their work as well as provide a platform to host content which can be linked to from social media platforms. As this is not the main focus of this study, future studies should examine effects of personal website use for branding, online presence, and patient acquisition.

Table 3 Board certification of orthopaedic surgeon influencers

Board Certification	<i>n</i>
American Board of Orthopaedic Surgery	63
United Kingdom General Medical Council ¹	5
American Osteopathic Academy of Orthopaedics	2
Australian Medical Board ²	2
Médicos Internos Residentes ³	2
Trainees	2
No publicly verifiable board	2

¹Certification in trauma and orthopaedic surgery;

²Certification in orthopaedic surgery;

³The Médicos Internos Residentes (Internal Medical Resident) is a certification program run by the Ministry of Health and Consumption of Spain—certification in Orthopaedic surgery and traumatology.

Influence, productivity, and impact within orthopaedic surgery are traditionally measured by publications, citations, and impact factors, collectively computed into an orthopaedic surgeon's *h*-index. Social media influence provides a new metric by which a surgeon's impact on the field can be measured, with some even arguing for the creation of academic tenure tracks based on social media influence^[32]. Our study reveals a strikingly high average *h*-index among the top social media influencers in orthopaedic surgery (mean: 13.67 ± 4.12 , median: 7), which can be compared to the median reported *h*-index for orthopaedic academic faculty (5) and the median *h*-index for orthopaedic chairpersons (13)^[19]. These findings provide further evidence legitimizing social media influencers as significant contributors to the field of orthopaedic surgery. Ultimately, social media simply provides a new way that orthopaedic surgeons can achieve the same goal of spreading new knowledge and information with both peers and the public.

While the high mean *h*-index observed among the top 100 social media influencers in orthopaedic surgery certainly reflects the overlap between the most influential researchers and social media users within our field, social media influencers may also benefit academically from using Twitter to support their work. For example, previous work in the *Journal of Medical Internet Research*^[33] found highly tweeted articles (top 25%) were nearly eleven times more likely to be cited than less tweeted articles. A randomized controlled trial in psychiatry found articles promoted on Twitter received nearly three times as many page visits as controls^[34]. Within orthopaedics, a recent study found Twitter mentions correlated with citation counts but accumulated more rapidly with time^[3]. Taken together, these results underscore the role of social media—much like academic research—in modern orthopaedic surgery to disseminate knowledge to fellow scientists, physicians, and patients alike. In fact, many journals have been recently promoting Altmetric scores of their articles as a measure of a manuscript's public impact, including social media and lay press.

Despite the fact the majority of top social media influencers were orthopaedic surgeons, 22% of the top influencers were not, including 3 of the top 10 influencers. Furthermore, several of these influencers were commercially-affiliated. Given the potential for these individuals to influence our patients' perceptions and expectations, it is important to be aware of what patients may encounter online. It is also vital for us as orthopaedic surgeons to be cognizant of the impact that who, and how, we engage with others through social media—especially commercial entities—can have. To be a top influencer within orthopaedics, these non-medical accounts are almost requisitely engaged by those within our profession on a regular basis. Nonetheless, identifying the existence of these influencers is important so that orthopaedic surgeons can continue to build influence and control the conversation about the specialty.

Limitations

A particular strength of this study was the examination of social media influence, rather than stand-alone metrics such as top tweets or followers. Nevertheless, an inherent weakness to any study of influence or impact (*e.g.*, *h*-index) is the use of a proprietary algorithm, in this case the Right Relevance API. It is possible other algorithms would assign different weights to certain variables of impact and thus arrive at slightly different results. However, we chose the Right Relevance API specifically because it uses sophisticated algorithms that account for engagement and connections to other influencers within the field, in addition to more simple metrics such as number of followers or retweets, helping to arrive at a truer value of

influence. Given our knowledge of many of the names on the list from using social media for orthopaedics, reading the orthopaedic literature, and attending conferences, coupled with the high *h*-index scores of the top influencers in this study, we are confident this list does represent the majority of the top social media influencers in orthopaedic surgery. Next, these results only represent a single time point. In contrast to many online studies where results may vary on a daily basis, however, influence is an integral of social media impact over time, requiring an extended time to build, and thus is subject to significantly less variability over time. Additionally, these results are limited to a single social media platform. However, Twitter has been shown to be particularly conducive to medical discussion^[3,13,15-18,35], as well as host to up to 82% of orthopaedic social media mentions^[3]. Moreover, given that orthopaedic surgeons frequently utilize multiple social media platforms and that many social media platforms allow for cross-platform posting, the results are likely correlated between social media platforms. As the use of social media in orthopaedics continues to grow, future work may be warranted to examine social media influence on additional platforms. Finally, we only performed one search ("orthopaedics"); however, Right Relevance includes several related topics (*e.g.*, "orthopaedic surgery," "orthopedics," "orthopedic surgery," *etc.*) when determining influence for a given niche. Nonetheless, it is possible a different search term may have yielded different results.

In conclusions, the top orthopaedic social media influencers on Twitter were predominantly board-certified, sports-medicine subspecialists working in private practice in the United States. Social media influence was highly concordant with academic productivity as measured by the academic *h*-index. Though the majority of influencers are orthopaedic surgeons, 22% of top influencers on Twitter are not, which is important to identify given the potential for these individuals to influence patients' perceptions and expectations. This study also provides the top influencer network for other orthopaedic surgeons to engage with on social media to improve their own social media influence.

ARTICLE HIGHLIGHTS

Research background

Social media is playing an increasingly large role in medicine, and several studies have described how orthopaedic patients use social media. In addition to patient use, Twitter was named an "essential tool" for the academic surgeon given its ability to serve as a tool to share findings, collaborate, network, and educate. Despite the large emerging role of social media in medicine, however, no study has assessed the top social media influencers in orthopaedic surgery.

Research motivation

Given that social media is playing an increasingly large role as a face by which patients are exposed to orthopaedics, identifying who is sharing information to patients is highly important. These individuals play a critical role in setting patient expectations, encouraging appropriate utilization, and providing accurate orthopaedic education.

Research objectives

The purpose of this study was to identify the top 100 social media influencers within orthopaedics, characterize who they are, and relate their social media influence to academic influence. This analysis will allow us to identify who is controlling the conversation about orthopaedics to the public.

Research methods

In this observational study, we queried the Right Relevance API for the topic of "orthopaedics." This API uses sophisticated partitioning techniques to calculate influence based on a variety of factors, including connections (follower/following) to other influencers and engagement (views, likes, retweets). We then used these individuals' public Twitter bios and other public sources to characterize them with respect to specialty, subspecialty, practice setting, location, board certification, and academic *h*-index.

Research results

We identified the 100 top influencers in orthopaedic surgery; these individuals represented 9 different countries. The mean academic *h*-index of the top influencers ($n = 79$) was 13.67 ± 4.12 (mean \pm 95%CI) and median 7 (range 1-89), which can be references against the median reported *h*-index of academic orthopaedic faculty of 5 and orthopaedic chairpersons of 13. Of the 100 top influencers, 78% were orthopaedic surgeons. Sports medicine (54%), hand and upper extremity (18%), and spine (8%) were the most common orthopaedic subspecialties. Most influencers worked in private practice (53%), followed by academics (17%), privademics (14%), and hospital-based (9%). All board-eligible orthopaedic surgeons were board-certified.

Research conclusions

The top orthopaedic social media influencers on Twitter were predominantly board-certified,

sports-medicine orthopaedic surgeons, representing countries from around the world. However, 22% of top influencers were not orthopaedic surgeons, which is important to identify given the potential for these individuals to influence patients' perceptions and expectations. Social media influence within orthopaedics was not disconnected from academic index: the median *h*-index among top influencers (7) was higher than the median reported *h*-index of orthopaedic academic faculty (5). Here we also provide the top influencer network for other sports surgeons to engage with on social media to improve their own social media influence.

Research perspectives

While we find that the majority of orthopaedic influencers are board-certified orthopaedic surgeons, more than 1/5 of the top influencers are not. Moving forward, orthopaedic surgeons should continue to increase their social media presence to ensure they are controlling the conversation about orthopaedics to the public. From an academic perspective, future work is indicated to identify the specific impact social media has on patient decision making and outcomes.

REFERENCES

- 1 Modahl M, Tompsett L, Moorhead T. *Doctors, Patients & Social Media*. September 2011; [cited 12 May 2018]. Available from: <http://www.quantiamd.com/q-qcp/DoctorsPatientSocialMedia.pdf>
- 2 Fox S. The Social Life of Health Information, 2011 [cited 21 July 2018]. Available from: <http://www.pewinternet.org/2011/05/12/the-social-life-of-health-information-2011/>
- 3 Evaniew N, Adili AF, Ghert M, Khan M, Madden K, Smith C, Bhandari M. The Scholarly Influence of Orthopaedic Research According to Conventional and Alternative Metrics: A Systematic Review. *JBJS Rev* 2017; **5**: e5 [PMID: 28557819 DOI: 10.2106/JBJS.RVW.16.00059]
- 4 Lander ST, Sanders JO, Cook PC, O'Malley NT. Social Media in Pediatric Orthopaedics. *J Pediatr Orthop* 2017; **37**: e436-e439 [PMID: 28719545 DOI: 10.1097/BPO.0000000000001032]
- 5 Ramkumar PN, La T, Fisch E, Fabricant PD, White AE, Jones KJ, Taylor SA. Integrating Social Media and Anterior Cruciate Ligament Surgery: An Analysis of Patient, Surgeon, and Hospital Use. *Arthroscopy* 2017; **33**: 579-585 [PMID: 27771170 DOI: 10.1016/j.arthro.2016.08.021]
- 6 Ramkumar PN, Navarro SM, Haeberle HS, Chughtai M, Flynn ME, Mont MA. Social Media and Total Joint Arthroplasty: An Analysis of Patient Utilization on Instagram. *J Arthroplasty* 2017; **32**: 2694-2700 [PMID: 28456560 DOI: 10.1016/j.arth.2017.03.067]
- 7 Ramkumar PN, Navarro SM, Cornaghi MM, Haeberle HS, Hameed H, Schickendantz MS, Ricchetti ET, Iannotti JP. Social Media in Shoulder & Elbow Surgery: An Analysis of Twitter and Instagram. *Int J Sports Med* 2018; **39**: 564-570 [PMID: 29758568 DOI: 10.1055/s-0043-124369]
- 8 Hirsch JE. An index to quantify an individual's scientific research output. *Proc Natl Acad Sci USA* 2005; **102**: 16569-16572 [PMID: 16275915 DOI: 10.1073/pnas.0507655102]
- 9 New research: The value of influencers on Twitter, 2016 [cited 12 May 2018]. Available from: https://blog.twitter.com/marketing/en_us/a/2016/new-research-the-value-of-influencers-on-twitter.html
- 10 Van Citters AD, Fahlman C, Goldmann DA, Lieberman JR, Koenig KM, DiGioia AM, O'Donnell B, Martin J, Federico FA, Bankowitz RA, Nelson EC, Bozic KJ. Developing a pathway for high-value, patient-centered total joint arthroplasty. *Clin Orthop Relat Res* 2014; **472**: 1619-1635 [PMID: 24297106 DOI: 10.1007/s11999-013-3398-4]
- 11 Tanzer D, Smith K, Tanzer M. Changing Patient Expectations Decreases Length of Stay in an Enhanced Recovery Program for THA. *Clin Orthop Relat Res* 2018; **476**: 372-378 [PMID: 29529671 DOI: 10.1007/s11999-0000000000000043]
- 12 Halawi MJ, Vovos TJ, Green CL, Wellman SS, Attarian DE, Bolognesi MP. Patient expectation is the most important predictor of discharge destination after primary total joint arthroplasty. *J Arthroplasty* 2015; **30**: 539-542 [PMID: 25468779 DOI: 10.1016/j.arth.2014.10.031]
- 13 Logghe HJ, Selby LV, Boeck MA, Stamp NL, Chuen J, Jones C. The academic tweet: Twitter as a tool to advance academic surgery. *J Surg Res* 2018; **226**: viii-vxii [PMID: 29622401 DOI: 10.1016/j.jss.2018.03.049]
- 14 Social Media. September. Twitter: An Essential Tool for Surgeons? JBJS OrthoBuzz Blog, 2018 [cited 12 May 2018]. Available from: <https://orthobuzz.jbjs.org/2018/04/12/twitter-an-essential-tool-for-surgeons/>
- 15 Logghe H, Jones C, McCoubrey A, Fitzgerald E. #ILookLikeASurgeon: Embracing diversity to improve patient outcomes. *BMJ* 2017; **359**: j4653 [PMID: 29018031 DOI: 10.1136/bmj.j4653]
- 16 Brady RRW, Chapman SJ, Atallah S, Chand M, Mayol J, Lacy AM, Wexner SD. #colorectalsurgery. *Br J Surg* 2017; **104**: 1470-1476 [PMID: 28881004 DOI: 10.1002/bjs.10615]
- 17 Sullivan SJ, Schneiders AG, Cheang CW, Kitto E, Lee H, Redhead J, Ward S, Ahmed OH, McCrory PR. 'What's happening?' A content analysis of concussion-related traffic on Twitter. *Br J Sports Med* 2012; **46**: 258-263 [PMID: 21406451 DOI: 10.1136/bjsm.2010.080341]
- 18 Chandawarkar AA, Gould DJ, Grant Stevens W. The Top 100 Social Media Influencers in Plastic Surgery on Twitter: Who Should You Be Following? *Aesthet Surg J* 2018; **38**: 913-917 [PMID: 29518179 DOI: 10.1093/asj/sjy024]
- 19 Ence AK, Cope SR, Holliday EB, Somerson JS. Publication Productivity and Experience: Factors Associated with Academic Rank Among Orthopaedic Surgery Faculty in the United States. *J Bone Joint Surg Am* 2016; **98**: e41 [PMID: 27194503 DOI: 10.2106/JBJS.15.00757]
- 20 Sculco PK, McLawhorn AS, Fehring KA, De Martino I. The future of social media in orthopedic surgery. *Curr Rev Musculoskelet Med* 2017; **10**: 278-279 [PMID: 28456946 DOI: 10.1007/s12178-017-9412-9]
- 21 Curry E, Li X, Nguyen J, Matzkin E. Prevalence of internet and social media usage in orthopedic surgery. *Orthop Rev (Pavia)* 2014; **6**: 5483 [PMID: 25317312 DOI: 10.4081/or.2014.5483]
- 22 Duymus TM, Karadeniz H, Çağan MA, Kömür B, Demirtaş A, Zehir S, Azboy İ. Internet and social media usage of orthopaedic patients: A questionnaire-based survey. *World J Orthop* 2017; **8**: 178-186 [PMID: 28251069 DOI: 10.5312/wjo.v8.i2.178]
- 23 Duymus TM, Karadeniz H, Şükür E, Atıç R, Zehir S, Azboy İ. Social media and Internet usage of orthopaedic surgeons. *J Clin Orthop Trauma* 2017; **8**: 25-30 [PMID: 28360492 DOI: 10.1016/j.jcot.2017.03.001]

- 10.1016/j.jcot.2016.10.007]
- 24 **Garofolo G**, Akinleye SD, Golan EJ, Choueka J. Utilization and Impact of Social Media in Hand Surgeon Practices. *Hand (NY)* 2018; 1558944718787285 [PMID: 30003808 DOI: 10.1177/1558944718787285]
- 25 **Rozental TD**, George TM, Chacko AT. Social networking among upper extremity patients. *J Hand Surg Am* 2010; 35: 819-823.e1 [PMID: 20227837 DOI: 10.1016/j.jhsa.2009.12.043]
- 26 **Ramski DE**, Kanj WW, Franklin CC, Baldwin KD, Ganley TJ. Anterior cruciate ligament tears in children and adolescents: A meta-analysis of nonoperative versus operative treatment. *Am J Sports Med* 2014; 42: 2769-2776 [PMID: 24305648 DOI: 10.1177/0363546513510889]
- 27 **Gornés D**, Rodríguez-Roiz JM, Fernández-Valencia J. Social media in orthopaedics: a case study analysis of twitter posts at the American Academy of Orthopaedic Surgeons (AAOS) Congress 2012 and the European Federation of National Associations of Orthopedics and Traumatology (EFORT) Congress 2012. *Int J Adv Joint Reconstr* 2014; 1: 17-19
- 28 **Chung A**, Woo H. Twitter in urology and other surgical specialties at global conferences. *ANZ J Surg* 2016; 86: 224-227 [PMID: 26631323 DOI: 10.1111/ans.13393]
- 29 **Lubowitz JH**, Provencher MT, Poehling GG. Follow us on twitter. *Arthroscopy* 2012; 28: 1747-1748 [PMID: 23200516 DOI: 10.1016/j.arthro.2012.10.004]
- 30 **Donnally CJ**, Li DJ, Maguire JA, Roth ES, Barker GP, McCormick JR, Rush AJ, Lebowitz NH. How social media, training, and demographics influence online reviews across three leading review websites for spine surgeons. *Spine J* 2018; 18: 2081-2090 [PMID: 29709552 DOI: 10.1016/j.spinee.2018.04.023]
- 31 **Lifchez SD**, McKee DM, Raven RB, Shafritz AB, Tueting JL. Guidelines for ethical and professional use of social media in a hand surgery practice. *J Hand Surg Am* 2012; 37: 2636-2641 [PMID: 23174079 DOI: 10.1016/j.jhsa.2012.10.002]
- 32 **Reissis D**, Shatis A, Nikkhah D. Advertising on Social Media: The Plastic Surgeon's Prerogative. *Aesthet Surg J* 2017; 37: NP1-NP2 [PMID: 27771608 DOI: 10.1093/asj/sjw174]
- 33 **Eysenbach G**. Can tweets predict citations? Metrics of social impact based on Twitter and correlation with traditional metrics of scientific impact. *J Med Internet Res* 2011; 13: e123 [PMID: 22173204 DOI: 10.2196/jmir.2012]
- 34 **Adams CE**, Jayaram M, Bodart AY, Sampson S, Zhao S, Montgomery AA. Tweeting links to Cochrane Schizophrenia Group reviews: A randomised controlled trial. *BMJ Open* 2016; 6: e010509 [PMID: 26956164 DOI: 10.1136/bmjopen-2015-010509]
- 35 **Hughes H**, Hughes A, Murphy C. The Use of Twitter by the Trauma and Orthopaedic Surgery Journals: Twitter Activity, Impact Factor, and Alternative Metrics. *Cureus* 2017; 9: e1931 [PMID: 29464138 DOI: 10.7759/cureus.1931]



Calcaneal osteochondroma masquerading as plantar fasciitis: An approach to plantar heel pain - A case report and literature review

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Abstract

BACKGROUND

Heel pain is a common orthopaedic complaint, and if left untreated can be a source of chronic morbidity. Accurate diagnosis can be challenging, owing to the complex anatomy and multiple pain generators present in the foot. We aim to share our clinical experience managing an unusual case of chronic heel pain secondary to osteochondroma.

CASE SUMMARY

A 41-year-old obese male who works as a porter presented with a long-standing history of left plantar heel pain. He was assessed to have point tenderness over the plantar insertion of the calcaneus as well as a positive Silfverskiöld test. He was treated for plantar fasciitis and tight gastrocnemius but failed conservative therapies as well as surgical intervention. Magnetic resonance imaging revealed the presence of a pedunculated bony protrusion over the plantar aspect of the calcaneus. The decision was made for excision of the osteochondroma, and the patient has been pain-free since.

CONCLUSION

Osteochondromas are rarely symptomatic in skeletally mature patients. While most are benign with a very low risk of malignant transformation, surgical excision can yield excellent results and significant pain relief in symptomatic patients.

Key words: Chronic heel pain; Recalcitrant heel pain; Osteochondroma; Diagnostic challenge; Case report

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Core tip: Heel pain is a common orthopaedic complaint. If not treated correctly, it can lead to chronic morbidity and disability. Plantar fasciitis is diagnosed clinically. Advanced imaging is rarely required and used to exclude underlying sinister pathology. Osteochondromas of the calcaneum are rare. In symptomatic patients, excision can improve outcomes.

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INTRODUCTION

Heel pain is a common orthopaedic complaint, constituting about 15% of foot pain^[1]. 1 in 8 people aged 50 years and older complain of heel pain, with more than half reporting that the severity is disabling^[2].

The various aetiologies of heel pain can be broadly classified into mechanical, neurological, traumatic and degenerative causes with the most common cause being mechanical^[3,4]. Accurate diagnosis can be challenging, owing to the complex anatomy and their interdependent mechanical relationships as well as vulnerable pain generators present in the foot^[5]. Heel pain is best defined by the Heel Pain Committee of the American College of Foot and Ankle Surgeons as pain either over the posterior or plantar aspect of the foot^[4]. For the purpose of this article, focus will be on plantar heel pain.

As with all foot and ankle pathologies, a good grasp of anatomy, clinical acuity, detailed history taking as well as physical examination are key to achieving an accurate diagnosis. Astute application of investigative modalities aid in confirming the diagnosis. Conversely, inappropriate treatment can lead to worsening or chronic pain that can result in morbidity^[2]. In this case report, we aim to share our clinical experience in managing one such patient whose plantar heel pain was refractory to all treatment modalities offered. We present an unusual case of chronic heel pain secondary to osteochondroma.

CASE DESCRIPTION

Chief complaints

A 41-year-old Malay gentleman who works as a hospital porter presented with a long-standing history of left plantar heel pain.

History of present illness

His gastrocnemius was also noted to be tight with positive Silfverskiöld test. He was treated for plantar fasciitis and tight gastrocnemius and underwent extensive physiotherapy sessions targeted at gastrocnemius stretching. He was started on anti-inflammatory and analgesic medications. However, his symptoms persisted, and he underwent left gastrocnemius release and endoscopic plantar fascia release. This provided temporal relief of his symptoms, and he was able to return to work.

Two and half years later, he presented with similar symptoms of left heel pain. His gastrocnemius was once again assessed to be tight demonstrating limited dorsiflexion in the absence of ankle osteoarthritis. A repeated minimally invasive gastrocnemius release was performed. He underwent a prolonged recovery with enforced rest and time off work, which improved his symptoms. However, his symptoms quickly reoccurred upon return to work.

History of past illness

He is obese (BMI: 31 kg/m²), has hyperlipidaemia but reports no history of diabetes or gout.

Physical examination

Patient ambulated with an antalgic gait. On physical assessment, his gastrocnemius remained tight with a positive Silfverskiöld test. Tenderness around the plantar aspect

of the calcaneum was non-specific and found along the distribution of the plantar fascia insertion.

Imaging examinations

Foot and calcaneal radiographs showed normal bony relationships of the foot with no features of arthritis (Figure 1). No fractures or obvious lesions were noted. Magnetic resonance imaging (MRI) of the left foot was performed. It reported the absence of plantar fascia thickening as well as no signal alteration in the adjacent soft tissue or bone marrow. MRI did reveal a pedunculated bony protrusion arising from the posterolateral plantar aspect of the calcaneus measuring 1.1 cm × 0.9 cm, which was consistent with an osteochondroma (Figure 2). Computed tomography scan was organised to better evaluate this lesion (Figure 3).

FINAL DIAGNOSIS

Osteochondroma of the calcaneum with a concomitant gastrocnemius contracture.

TREATMENT

Decision for surgical excision of left calcaneal lesion was made in view of chronic discomfort and limited relief from two other previous procedures. A mini-incision was made centred over the posterolateral border of calcaneum. A soft tissue flap was raised allowing access to the lesion. The bony lesion was excised *en bloc* and sent for histological analysis. Layered closure was attempted and wound dressed with Jones dressing. Patient was kept on non-weight bearing over the left lower limb before progressing to full weight bearing once the wound healed. Histology reported the lesions as a nodular lesion with mature lamellar bone consistent with a matured osteochondroma.

OUTCOME AND FOLLOW UP

The patient was followed up closely and remains pain-free 12 mo after surgery. He is back to work and very satisfied with the surgery.

DISCUSSION

Plantar fasciitis

This patient presented with typical signs and symptoms of plantar fasciitis, a common cause of heel pain especially amongst middle-aged patients^[6]. Plantar fasciitis is a condition attributed to biomechanical stress of the plantar fascia and its calcaneal insertion. Risk factors of developing plantar fasciitis involve those subjecting the plantar fascia to excessive biomechanical stress. Being obese is a well-documented risk factor^[7-9]. Abnormal strain on the windlass mechanism of the foot results in excessive plantar fascia tendon loading and subsequent injury^[10]. In non-athletic individuals, patients with BMI ≥ 27 kg/m² are 3.7 times more likely to suffer from plantar heel pain^[7]. In addition, this patient had a tight gastrocnemius^[8] as well as a job requiring excessive push-off force to manually transport heavy carts, patients and machines around the hospital. Tight gastrocnemius limits ankle dorsiflexion, thereby producing increased strain on the plantar fascia during the gait cycle^[11-13]. Pes cavus is another anatomical risk factor. Patients who have pes cavus have a reduced distance between the calcaneus and the metatarsal heads and rigid relationships between both bony and soft tissue structures^[14].

The initial management for plantar fasciitis is conservative. In keeping with the literature, this patient was started on a course of plantar fascia as well as gastrocnemius stretching with a physiotherapist^[11,15]. DiGiovanni *et al*^[16,17] demonstrated significant pain relief after 8 wk of plantar fascia specific stretches as compared to gastrocnemius stretches alone. Coupled with the use of non-inflammatory and analgesia medications, off-loading orthotics, heel cups and adequate rest, these treatments form the backbone of plantar fasciitis management^[4,5,18].

However, our patient remained symptomatic after a year of conservative management and decided to undergo endoscopic plantar fasciotomy and



Figure 1 Foot and calcaneal radiographs. Demonstrates normal bony relationships of the foot. No fractures or obvious lesions noted. Overlapping bony structures obscures view of the posteromedial pedunculated lesion noted on magnetic resonance imaging.

gastrocnemius release. This surgery offered significant relief in the acute setting. Plantar fasciotomy is the technique of choice in recalcitrant plantar fasciitis^[19,22]. In a survey of 64 patients who underwent plantar fasciotomy, Wheeler *et al*^[22] reported 84% of patients were satisfied or very satisfied, with almost three quarters of patients experiencing greater than 80% pain relief. However, owing to varying techniques described within the literature (namely open, mini-open and endoscopic ablation), there remains a paucity of good quality evidence supporting its role^[21]. Most agree with the use of the medial open approach releasing the medial third of the plantar fascia^[23,24], although there is a growing number of studies showing comparable results using endoscopic plantar fasciotomy^[5,25].

Proximal medial gastrocnemius release in the treatment of refractory plantar fasciitis has also shown excellent results without the complications associated with plantar fasciotomy^[20,24,26]. This technique was conceived after DiGiovanni *et al*^[27] reported plantar foot pain associated with gastrocnemius contracture and Barouk *et al*^[24] demonstrated the safe surgical technique most authors now perform.

However, results can be unpredictable, especially in patients with chronic heel pain^[28]. Our patient returned complaining of similar symptoms after two and half years. The use of advanced imaging modalities, such as ultrasound and MRI is not necessary in diagnosing plantar fasciitis. Toomey *et al*^[29] demonstrated poor correlation between plantar fascia thickness and plantar heel pain. Therefore, most authors believe that plantar fasciitis is a clinical diagnosis^[5,24,29,30]. In the case above however, recalcitrant heel pain despite surgical intervention is a red flag warranting further investigation^[4,5]. In addition, should the tenderness not be localised to the plantar fascia insertion or if the clinical picture appears inconsistent, then advanced imaging would be prudent.

Diagnosing recalcitrant plantar heel pain

In a diagnostically challenging case, astute clinical reasoning is key. Most heel pain arises from soft tissue structures such as tendons, fascia and nerves around the calcaneus and less commonly from bone and apophyses^[3]. Plantar foot pain pathologies are often mechanical in nature^[31].

The authors propose key considerations when approaching heel pain (Table 1). Location, age, precipitating events and nature of symptoms are all important clues to deriving an accurate diagnosis. Pinpointing the location of greatest discomfort is the most useful way of arriving at a diagnosis; it narrows potential differentials and

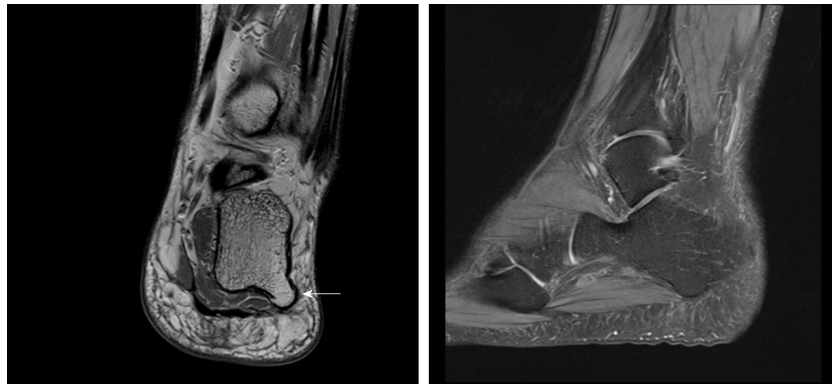


Figure 2 Magnetic resonance imaging of foot. A plantar osteochondroma arising from the posterolateral aspect of the calcaneus. No significant thickening in plantar fascia or signal alteration in the adjacent soft tissues or bone marrow to suggest recurrent plantar fasciitis

focuses history taking and clinical examination towards structures underlying the site^[30]. Patients are encouraged to point a finger at the location of greatest discomfort and through the application of clinical anatomy enquire about exacerbating factors as well as perform respective provocation manoeuvres (Table 1).

Age is another useful tool in diagnosing heel pain. Almost a quarter of the population aged 45 years and older suffer from foot pain^[32]. In the middle aged and elderly, osteoarthritis and tendinopathies as well as plantar fasciitis are more common^[24,33,34]. Scher *et al*^[35] reported increasing incidence of plantar fasciitis with increasing age of United States military service members suggesting that the loss of heel-pad elasticity and its ability to “shock-absorb” results in excessive strain to the plantar fascia. Whereas, in the younger, active populations, traumatic or repetitive stress injuries are more likely^[36-38].

In the absence of trauma or a fall, bony injury is less likely. Pain that worsens with activity and pushing off suggests a mechanical origin. However, in a patient with chronic heel pain not improved by surgery, sinister causes such as malignancy or infection need to be excluded. Other considerations include a neurological cause from radicular symptoms, referred pain or even systemic inflammatory pathologies (Table 1).

Bilateral dorsoplantar and lateral weight-bearing foot radiographs are fundamental investigations when assessing foot pain. It offers insight into the foot’s bony relationships and allows comparison with the contralateral limb (Figure 1A). Dedicated calcaneal radiographs provide an unobstructed axial view, commonly obscured by overlapping structures of the foot. The presence of osteochondroma on calcaneal radiographs was not obvious on either foot (Figure 1).

In patients with recalcitrant pain refractory to surgery, advanced imaging, such as MRI or computed tomography scans is indicated to evaluate other causes of pain. MRI would allow better assessment of soft tissue pathology as well as acute bony injury after trauma (Figure 2). On the other hand, computed tomography scans provide good bony definition (Figure 3).

Calcaneal osteochondroma

Osteochondromas are the most common benign tumour of the skeleton accounting for 36% to 41% of benign bone tumours^[39-41] and affecting about 2% to 3% of the general population^[41-43]. However, its presentation in a foot and ankle account for less than 10% of such cases^[42-46]. Osteochondromas are benign osseous lesions that originate from the metaphyseal regions of long bones and on histology classically present with normal bony trabeculae with a distinct hyaline cartilage cap^[41,42,44]. Most osteochondromas are usually asymptomatic and are incidentally picked up on radiographs^[42]. They are commonly found in adolescents and young adults presenting often as a painless mass, but it can be symptomatic as a sequelae of its size causing entrapment of neurovascular structures, restriction of movement and fractures^[42,44]. Malignant transformation is rare accounting for less than 1% of osteochondromas^[41,47,48]. Its presentation in a skeletally mature adult is rare. To date, only a handful of case reports are found in the literature^[42,45,46].

CONCLUSION



Figure 3 Computed tomography of foot showing a pedunculated bony protuberance at the lateral border without periosteal reaction nor bony destruction.

There are many causes of heel pain, with plantar fasciitis being the most common cause. However, in recalcitrant heel pain refractory to both conservative and surgical management, it would be astute to investigate the underlying cause further. Osteochondroma of the calcaneum is uncommon but a potential cause of debilitating plantar heel pain. Surgical excision can improve symptoms and reduce plantar heel pain.

Table 1 Key considerations when approaching heel pain

Location	Asking the patient to point with a finger over the point of greatest discomfort allows for narrowing of diagnosis. Subsequent provocation tests or history enquiring of exacerbating factors will provide greater clarity regarding the underlying pathology ^[30] .
Age	In the middle aged (> 45 years old) and elder patients (> 65 years old), degenerative causes such as tendinopathies should be considered ^[32-34,49] . Whereas in the young, traumatic or overuse injuries such as stress fractures and acute tendinitis are more common ^[31,36-38] .
Trauma and stress injuries	Fundamental to most orthopaedic history-taking, a recent traumatic injury should be ascertained. Radiographic evaluation to rule out fractures should there be a positive history of trauma ^[4] . In addition, nature of activity as well as occupation will provide insight as to whether patients are at risk of repetitive stress. Athletes as well as manual laborers are predisposed to repetitive strain injuries or tendinitis.
Pain characteristic	Characterising pain allows assessment of whether the pain is mechanical or non-mechanical. Start-up pain coupled with progressive worsening with activities may suggest a degenerative or inflammatory cause ^[30] , whilst pain at rest and in the night may suggest a more sinister pathology.
Red flags	Whilst rare, it is crucial to exclude sinister causes of plantar heel pain. Tumour: Constitutional symptoms like loss of appetite and loss of weight as well as pain disrupting sleep are red flags suggestive of more systemic pathology ^[50] . Prompt and advanced imaging modalities are warranted. Infection: Classic features of inflammation – <i>calor, dolor, rubor</i> and <i>tumour</i> coupled with systemic symptoms of fever and malaise are suggestive of an infective process. Both radiological and laboratory tests are crucial in establishing diagnosis as well as evaluating its severity.
Others	Neurologic: Patients with compressive neuropathy can present with foot discomfort. In the presence of paraesthesia or numbness, it would be prudent to screen the spine for potential nerve root compression. Rheumatologic: Patients with inflammatory arthritis can present with heel pain. In patients with polyarthropathy, laboratory investigations looking at inflammatory and autoimmune markers are advisable.

REFERENCES

- 1 Garrow AP, Silman AJ, Macfarlane GJ. The Cheshire Foot Pain and Disability Survey: a population survey assessing prevalence and associations. *Pain* 2004; **110**: 378-384 [PMID: 15275789 DOI: 10.1016/j.pain.2004.04.019]
- 2 Chatterton BD, Muller S, Roddy E. Epidemiology of posterior heel pain in the general population: cross-sectional findings from the clinical assessment study of the foot. *Arthritis Care Res (Hoboken)* 2015; **67**: 996-1003 [PMID: 25604329 DOI: 10.1002/acr.22546]
- 3 Tu P. Heel Pain: Diagnosis and Management. *Am Fam Physician* 2018; **97**: 86-93 [PMID: 29365222]
- 4 Thomas JL, Christensen JC, Kravitz SR, Mendicino RW, Schuberth JM, Vanore JV, Weil LS Sr, Zlotoff HJ, Bouché R, Baker J. American College of Foot and Ankle Surgeons heel pain committee. The diagnosis and treatment of heel pain: a clinical practice guideline-revision 2010. *J Foot Ankle Surg* 2010; **49**: S1-19 [PMID: 20439021 DOI: 10.1053/j.jfas.2010.01.001]
- 5 Lareau CR, Sawyer GA, Wang JH, DiGiovanni CW. Plantar and medial heel pain: diagnosis and management. *J Am Acad Orthop Surg* 2014; **22**: 372-380 [PMID: 24860133 DOI: 10.5435/JAAOS-22-06-372]
- 6 Buchbinder R. Clinical practice. Plantar fasciitis. *N Engl J Med* 2004; **350**: 2159-2166 [PMID: 15152061 DOI: 10.1056/NEJMc032745]
- 7 van Leeuwen KD, Rogers J, Winzenberg T, van Middelkoop M. Higher body mass index is associated with plantar fasciopathy/plantar fasciitis: systematic review and meta-analysis of various clinical and imaging risk factors. *Br J Sports Med* 2016; **50**: 972-981 [PMID: 26644427 DOI: 10.1136/bjsports-2015-094695]
- 8 Irving DB, Cook JL, Young MA, Menz HB. Obesity and pronated foot type may increase the risk of chronic plantar heel pain: a matched case-control study. *BMC Musculoskelet Disord* 2007; **8**: 41 [PMID: 17506905 DOI: 10.1186/1471-2474-8-41]
- 9 Hill JJ, Cutting PJ. Heel pain and body weight. *Foot Ankle* 1989; **9**: 254-256 [PMID: 2731839 DOI: 10.1177/107110078900900509]
- 10 Fuller EA. The windlass mechanism of the foot. A mechanical model to explain pathology. *J Am Podiatr Med Assoc* 2000; **90**: 35-46 [PMID: 10659531 DOI: 10.7547/87507315-90-1-35]
- 11 Bolívar YA, Munuera PV, Padillo JP. Relationship between tightness of the posterior muscles of the lower limb and plantar fasciitis. *Foot Ankle Int* 2013; **34**: 42-48 [PMID: 23386760 DOI: 10.1177/1071100712459173]
- 12 Carlson RE, Fleming LL, Hutton WC. The biomechanical relationship between the tendoachilles, plantar fascia and metatarsophalangeal joint dorsiflexion angle. *Foot Ankle Int* 2000; **21**: 18-25 [PMID: 10710257 DOI: 10.1177/107110070002100104]
- 13 Erdemir A, Hamel AJ, Fauth AR, Piazza SJ, Sharkey NA. Dynamic loading of the plantar aponeurosis in walking. *J Bone Joint Surg Am* 2004; **86**: 546-552 [PMID: 14996881]
- 14 Bolgla LA, Malone TR. Plantar fasciitis and the windlass mechanism: a biomechanical link to clinical practice. *J Athl Train* 2004; **39**: 77-82 [PMID: 16558682]

- 15 **Sweeting D**, Parish B, Hooper L, Chester R. The effectiveness of manual stretching in the treatment of plantar heel pain: a systematic review. *J Foot Ankle Res* 2011; **4**: 19 [PMID: [21703003](#) DOI: [10.1186/1757-1146-4-19](#)]
- 16 **Digiovanni BF**, Nawoczenski DA, Malay DP, Graci PA, Williams TT, Wilding GE, Baumhauer JF. Plantar fascia-specific stretching exercise improves outcomes in patients with chronic plantar fasciitis. A prospective clinical trial with two-year follow-up. *J Bone Joint Surg Am* 2006; **88**: 1775-1781 [PMID: [16882901](#) DOI: [10.2106/JBJS.E.01281](#)]
- 17 **DiGiovanni BF**, Nawoczenski DA, Lintal ME, Moore EA, Murray JC, Wilding GE, Baumhauer JF. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain. A prospective, randomized study. *J Bone Joint Surg Am* 2003; **85**: 1270-1277 [PMID: [12851352](#)]
- 18 **Lim AT**, How CH, Tan B. Management of plantar fasciitis in the outpatient setting. *Singapore Med J* 2016; **57**: 168-70; quiz 171 [PMID: [27075037](#) DOI: [10.11622/smedj.2016069](#)]
- 19 **Brown JN**, Roberts S, Taylor M, Paterson RS. Plantar fascia release through a transverse plantar incision. *Foot Ankle Int* 1999; **20**: 364-367 [PMID: [10395338](#) DOI: [10.1177/107110079902000604](#)]
- 20 **Abbassian A**, Kohls-Gatzoulis J, Solan MC. Proximal medial gastrocnemius release in the treatment of recalcitrant plantar fasciitis. *Foot Ankle Int* 2012; **33**: 14-19 [PMID: [22381231](#) DOI: [10.3113/FAI.2012.0014](#)]
- 21 **Rompe JD**. Plantar fasciopathy. *Sports Med Arthrosc Rev* 2009; **17**: 100-104 [PMID: [19440137](#) DOI: [10.1097/JSA.0b013e3181a3d60e](#)]
- 22 **Wheeler P**, Boyd K, Shipton M. Surgery for Patients With Recalcitrant Plantar Fasciitis: Good Results at Short-, Medium-, and Long-term Follow-up. *Orthop J Sports Med* 2014; **2**: 2325967114527901 [PMID: [26535314](#) DOI: [10.1177/2325967114527901](#)]
- 23 **Kitaoka HB**, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. *Foot Ankle Int* 1994; **15**: 349-353 [PMID: [7951968](#) DOI: [10.1177/107110079401500701](#)]
- 24 **Monteagudo M**, de Albornoz PM, Gutierrez B, Tabuenca J, Álvarez I. Plantar fasciopathy: A current concepts review. *EFORT Open Rev* 2018; **3**: 485-493 [PMID: [30237906](#) DOI: [10.1302/2058-5241.3.170080](#)]
- 25 **Bader L**, Park K, Gu Y, O'Malley MJ. Functional outcome of endoscopic plantar fasciotomy. *Foot Ankle Int* 2012; **33**: 37-43 [PMID: [22381234](#) DOI: [10.3113/FAI.2012.0037](#)]
- 26 **Monteagudo M**, Maceira E, Garcia-Virto V, Canosa R. Chronic plantar fasciitis: plantar fasciotomy versus gastrocnemius recession. *Int Orthop* 2013; **37**: 1845-1850 [PMID: [23959221](#) DOI: [10.1007/s00264-013-2022-2](#)]
- 27 **DiGiovanni CW**, Kuo R, Tejiwani N, Price R, Hansen ST, Cziernecki J, Sangeorzan BJ. Isolated gastrocnemius tightness. *J Bone Joint Surg Am* 2002; **84**: 962-970 [PMID: [12063330](#)]
- 28 **Martin RL**, Irrgang JJ, Conti SF. Outcome study of subjects with insertional plantar fasciitis. *Foot Ankle Int* 1998; **19**: 803-811 [PMID: [9872466](#) DOI: [10.1177/107110079801901203](#)]
- 29 **Toomey EP**. Plantar heel pain. *Foot Ankle Clin* 2009; **14**: 229-245 [PMID: [19501805](#) DOI: [10.1016/j.fcl.2009.02.001](#)]
- 30 **Alvarez-Nemegyei J**, Canoso JJ. Heel pain: diagnosis and treatment, step by step. *Cleve Clin J Med* 2006; **73**: 465-471 [PMID: [16708714](#)]
- 31 **Agyekum EK**, Ma K. Heel pain: A systematic review. *Chin J Traumatol* 2015; **18**: 164-169 [PMID: [26643244](#)]
- 32 **Thomas MJ**, Roddy E, Zhang W, Menz HB, Hannan MT, Peat GM. The population prevalence of foot and ankle pain in middle and old age: a systematic review. *Pain* 2011; **152**: 2870-2880 [PMID: [22019150](#) DOI: [10.1016/j.pain.2011.09.019](#)]
- 33 **Menz HB**, Dufour AB, Casey VA, Riskowski JL, McLean RR, Katz P, Hannan MT. Foot pain and mobility limitations in older adults: the Framingham Foot Study. *J Gerontol A Biol Sci Med Sci* 2013; **68**: 1281-1285 [PMID: [23704204](#) DOI: [10.1093/gerona/glt048](#)]
- 34 **Menz HB**, Tiedemann A, Kwan MM, Plumb K, Lord SR. Foot pain in community-dwelling older people: an evaluation of the Manchester Foot Pain and Disability Index. *Rheumatology (Oxford)* 2006; **45**: 863-867 [PMID: [16449369](#) DOI: [10.1093/rheumatology/kei002](#)]
- 35 **Scher DL**, Belmont PJ, Bear R, Mountcastle SB, Orr JD, Owens BD. The incidence of plantar fasciitis in the United States military. *J Bone Joint Surg Am* 2009; **91**: 2867-2872 [PMID: [19952249](#) DOI: [10.2106/JBJS.I.00257](#)]
- 36 **Sherman KP**. The foot in sport. *Br J Sports Med* 1999; **33**: 6-13 [PMID: [10027050](#)]
- 37 **Outerbridge AR**, Micheli LJ. Overuse injuries in the young athlete. *Clin Sports Med* 1995; **14**: 503-516 [PMID: [7553920](#)]
- 38 **Sammarco GJ**. Soft tissue conditions in athletes' feet. *Clin Sports Med* 1982; **1**: 149-155 [PMID: [6138162](#)]
- 39 **Wodajo FM**. Top five lesions that do not need referral to orthopedic oncology. *Orthop Clin North Am* 2015; **46**: 303-314 [PMID: [25771324](#) DOI: [10.1016/j.ocl.2014.11.012](#)]
- 40 **Dahlin DC**, Beabout JW. Dedifferentiation of low-grade chondrosarcomas. *Cancer* 1971; **28**: 461-466 [PMID: [5566365](#)]
- 41 **Sandell LJ**. Multiple hereditary exostosis, EXT genes, and skeletal development. *J Bone Joint Surg Am* 2009; **91** Suppl 4: 58-62 [PMID: [19571069](#) DOI: [10.2106/JBJS.I.00391](#)]
- 42 **Blitz NM**, Lopez KT. Giant solitary osteochondroma of the inferior medial calcaneal tubercle: a case report and review of the literature. *J Foot Ankle Surg* 2008; **47**: 206-212 [PMID: [18455666](#) DOI: [10.1053/j.jfas.2007.12.006](#)]
- 43 **Griffiths HJ**, Thompson RC, Galloway HR, Everson LI, Suh JS. Bursitis in association with solitary osteochondromas presenting as mass lesions. *Skeletal Radiol* 1991; **20**: 513-516 [PMID: [1754913](#)]
- 44 **Sella EJ**, Chrostowski JH. Calcaneal osteochondromas. *Orthopedics* 1995; **18**: 573-574; discussion 574-575 [PMID: [7675723](#)]
- 45 **Nogier A**, De Pinieux G, Hottya G, Anract P. Case reports: enlargement of a calcaneal osteochondroma after skeletal maturity. *Clin Orthop Relat Res* 2006; **447**: 260-266 [PMID: [16741480](#) DOI: [10.1097/01.blo.0000203474.96549.80](#)]
- 46 **Koplay M**, Toker S, Sahin L, Kilincoglu V. A calcaneal osteochondroma with recurrence in a skeletally mature patient: a case report. *Cases J* 2009; **2**: 7013 [PMID: [19829896](#) DOI: [10.4076/1757-1627-2-7013](#)]
- 47 **Murphy MD**, Choi JJ, Kransdorf MJ, Flemming DJ, Gannon FH. Imaging of osteochondroma: variants and complications with radiologic-pathologic correlation. *Radiographics* 2000; **20**: 1407-1434 [PMID: [10992031](#) DOI: [10.1148/radiographics.20.5.g00se171407](#)]

- 48 **de Souza AM**, Bispo Júnior RZ. Osteochondroma: ignore or investigate? *Rev Bras Ortop* 2014; **49**: 555-564 [PMID: [26229862](#) DOI: [10.1016/j.rboe.2013.10.002](#)]
- 49 **Dunn JE**, Link CL, Felson DT, Crincoli MG, Keysor JJ, McKinlay JB. Prevalence of foot and ankle conditions in a multiethnic community sample of older adults. *Am J Epidemiol* 2004; **159**: 491-498 [PMID: [14977645](#) DOI: [10.1093/aje/kwh071](#)]
- 50 **Flanagan AM**, Lindsay D. A diagnostic approach to bone tumours. *Pathology* 2017; **49**: 675-687 [PMID: [29110879](#) DOI: [10.1016/j.pathol.2017.08.003](#)]
- 51 **Scott A**, Khan KM, Cook JL, Duronio V. What is "inflammation"? Are we ready to move beyond Celsus? *Br J Sports Med* 2004; **38**: 248-249 [PMID: [15155418](#) DOI: [10.1136/bjism.2003.011221](#)]



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