Effects of Running on the Development of Knee Osteoarthritis

An Updated Systematic Review at Short-Term Follow-up

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Background: Some studies have suggested that running increases the risk of knee osteoarthritis (OA), while others believe it serves a protective function.

Purpose: To perform an updated systematic review of the literature to determine the effects of running on the development of knee OA.

Study Design: Systematic review; Level of evidence, 4.

Methods: A systematic review was performed by searching the PubMed, Cochrane Library, and Embase databases to identify studies evaluating the effect of cumulative running on the development of knee OA or chondral damage based on imaging and/or patient-reported outcomes (PROs). The search terms used were "knee AND osteoarthritis AND (run OR running OR runner)." Patients were evaluated based on plain radiographs, magnetic resonance imaging (MRI), and PROs (presence of knee pain, Health Assessment Questionnaire-Disability Index, and the Knee injury and Osteoarthritis Outcome Score).

Results: Seventeen studies (6 level 2 studies, 9 level 3 studies, and 2 level 4 studies), with 7194 runners and 6947 nonrunners, met the inclusion criteria. The mean follow-up time was 55.8 months in the runner group and 99.7 months in the nonrunner group. The mean age was 56.2 years in the runner group and 61.6 years in the nonrunner group. The overall percentage of men was 58.5%. There was a significantly higher prevalence of knee pain in the nonrunner group ($P < .0001$). Although 1 study found a significantly higher prevalence of osteophytes in the tibiofemoral (TF) and patellofemoral (PF) joints within the runner group, multiple studies found no significant differences in the prevalence of radiographic knee OA (based on TF/PF joint-space narrowing or Kellgren-Lawrence grade) or cartilage thickness on MRI between runners and nonrunners ($P > .05$). One study found a significantly higher risk of knee OA progressing to total knee replacement among nonrunners (4.6% vs 2.6%; $P = .014$).

Conclusion: In the short term, running is not associated with worsening PROs or radiological signs of knee OA and may be protective against generalized knee pain.

Keywords: knee joint; osteoarthritis; running

Osteoarthritis (OA) is the most common joint disorder in the United States and a leading cause of disability in the elderly population.[8,28] This chronic condition commonly affects load-bearing joints such as the knee and is characterized by pain, impaired physical function, and other adverse effects that may have a profound effect on the quality of life.[8,29] Knee OA is seen radiographically in 33% of the population >60 years, although there is considerable discordance between joint symptoms and radiographic findings.[2] The prevalence of symptomatic knee OA (SOA) in adults >60 years is approximately 10% in men and 13% in women.[8,31]

Knee OA is not a localized, degenerative disease of cartilage alone but is regarded as a chronic disease of the entire joint, including articular cartilage, meniscus, ligament, and periarticular muscle.[8] Age, obesity, occupation, and trauma to the joint because of repetitive movements such as kneeling or squatting have been identified as several risk factors for knee OA. Other factors, including cytokines, leptin, and mechanical forces, are pathogenic components of knee OA.[8] However, the association between physical activity such as running and the development of knee OA is less transparent, as some believe running increases the risk of knee OA, while others believe it is protective.[16,29]

The Orthopaedic Journal of Sports Medicine, 11(3), 23259671231152900
DOI: 10.1177/23259671231152900

Several studies have investigated the role of physical activity, particularly running, in the development of knee OA and have been inconclusive or contradictory.[9,29] The purpose of the present study was to perform an updated systematic review of the literature to determine the effects of running on the development of knee OA. We hypothesized that there would be no significant differences in the development of knee OA between high-volume runners and nonrunners.

METHODS

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines using a PRISMA checklist. Two independent reviewers (J.D., J.W.B.) searched the PubMed, Embase, and Cochrane Library databases up to October 3, 2021. The following electronic search strategy was used: knee AND osteoarthritis AND (run OR running OR runner). A total of 1485 studies were reviewed by title and/or abstract to determine study eligibility based on inclusion criteria, and 13 additional studies were identified through a gray literature search. In cases of disagreement, a third reviewer (M.J.K.) made the final decision. The inclusion criteria were as follows: studies evaluating the effect of cumulative running on the development of knee OA or chondral damage based on imaging or patient-reported outcomes (PROs). The exclusion criteria were as follows: studies unrelated to the knee, nonhuman studies, and non-English studies. The full text of 1 study was not available in online databases and therefore was excluded. Data extraction from each study was performed independently and then reviewed by a second author (M.J.K.).

Reporting Outcomes

Outcomes assessed included PROs and radiological outcomes. Six studies[12,14,15,17,18,24] assessed the presence of knee pain, 2 studies[6,9] used the Knee injury and Osteoarthritis Outcome Score (KOOS),[25] and 1 study[3] used the Health Assessment Questionnaire Disability Index (HAQ–DI).

Six studies[3,5,14,17,18,27] assessed the presence of radiographic knee OA (ROA) using the Kellgren-Lawrence[11] (KL) scale, 1 study[21] used magnetic resonance imaging (MRI) T2 mapping, 1 study[9] used the MRI Osteoarthritis Knee Score[10] (MOAKS), 3 studies[3,14,17] assessed the presence of ROA according to the Ahlbäck criteria,[1] and 3 studies[5,18,27] assessed joint-space narrowing using the Osteoarthritis Research Society International Atlas.[1] Two studies[14,27] assessed the presence of osteophytes at the tibiofemoral (TF) and patellofemoral (PF) joints using the Osteoarthritis Research Society International Atlas.[1]

Study Methodology Assessment

The Modified Coleman Methodology Score (MCMS)[4] was used to evaluate the methodology quality of studies. The MCMS has a scaled potential score ranging from 0 to 100. Scores ranging from 85 to 100 are excellent, 70 to 84 are good, 55 to 69 are fair, and <55 are poor. The primary outcomes assessed by the MCMS are study size and type, follow-up time, attrition rates, number of interventions per group, and proper description of study methodology.

Statistical Analysis

A weighted average was calculated for numerical demographics (age, sex, body mass index [BMI], and follow-up). The chi-square test was used to compare the presence of knee pain and total knee replacement (TKR) between the runner and nonrunner groups.

RESULTS

A total of 17 studies met the inclusion and exclusion criteria (Figure 1), with 14,141 patients (7194 runners and 6947 nonrunners) (Table 1). The mean age among runners was 56.2 years (range, 26-81 years) and 61.6 years among nonrunners (range, 25-73 years). The mean BMI was 26.7 kg/m^2 in the runner group and 28 kg/m^2 in the nonrunner group. The mean follow-up time was 55.8 months in the runner group and 99.7 months in the nonrunner group. The overall percentage of men was 58.5%.

[a]Patient age and follow-up are reported as mean ± SD (range, when reported), with the "Total" row reported as a

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Final revision submitted September 10, 2022; accepted November 8, 2022.

One or more of the authors has declared the following potential conflict of interest or source of funding: A.J.S. has received consulting fees from DePuy/Medical Device Business Services; and hospitality payments from Globus Medical. E.C.M. has received education payments from Gemini Mountain Medical; consulting fees from Medical Device Business Services, Flexion Therapeutics, and Zimmer Biomet; and nonconsulting fees from Arthrex. P.C.M. has received education payments from MedInc and Smith & Nephew; consulting fees from Smith & Nephew; and speaking fees and honoraria from Vericel. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

weighted mean. "n" refers to the number of runners/nonrunners who were included in each study. BMI, body mass index; LOE, level of evidence; Non, nonrunners; NR, not reported; Run, runners.

Modified Coleman Methodology Score

Table 2 shows the MCMS scores from the 17 included studies. Two studies[15,28] received an excellent score, 4 studies[6,12,18,26] received good scores, 6 studies[3,5,13,14,17,27] received fair scores, and 5 studies[9,19-22] received poor scores.

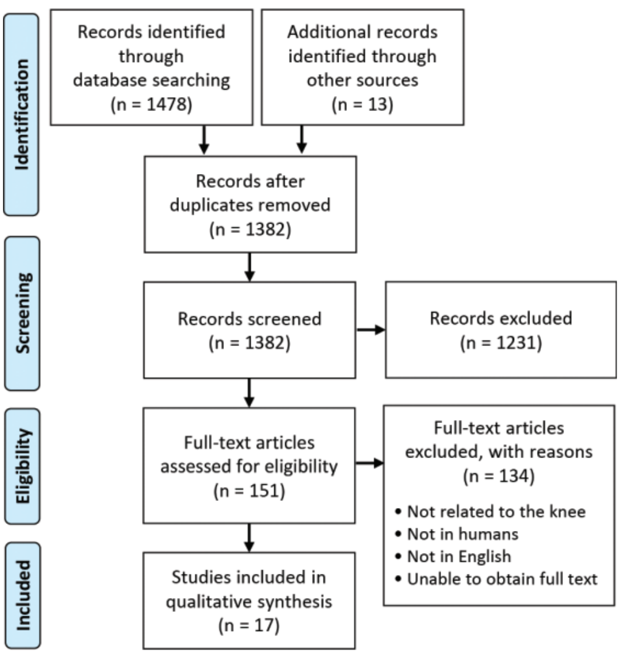

Figure 1. A PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Patient Characteristics/Study Methodology

Eight studies[5,12,14,17,18,26-28] evaluated the association of running on OA symptom and structure progression in patients with baseline knee OA. Two studies[3,22] evaluated the differences in progression to knee OA in runners compared with healthy nonrunners with radiographic observation. Horga et al[9] evaluated the short-term impact of long-distance running using MRI and the KOOS subscores, while Miller et al[20] compared peak and per-unit distance knee joint loads between human walking and running. Mosher et al[21] evaluated the effects of age and physical activity level on cartilage thickness and MRI T2 response immediately after running. Kujala et al[15] investigated whether men participating in competitive endurance sports in middle and old age are at increased risk of lower-limb OA and disability. Greaves et al[6] analyzed the effects of a rehabilitative exercise program on pain, function, kinesiophobia, running biomechanics, quadriceps strength, and quadriceps muscle inhibition in individuals with PF pain. Manninen et al[19] examined the association between physical exercise and the risk of severe knee OA requiring arthroplasty. Kujala et al[13] compared the incidence of hospital admission for OA of the hip, knee, or ankle between former elite athletes and control participants.

Seven studies[3,12,14,18,21,22,27] reported physical activity in the runner group. In 1 study,[18] 74.6% (103/138) of runners ran for 6 or more years and 92.7% (128/138) ran for 5 to 12 months per year, 88.4% (122/138) of runners ran more than 4 times per month, and 13% (18/138) participated in competitive running. In a study by Chakravarty et al,[3] runners

TABLE 1
Studies Included[a]

Study, Lead Author (year)	LOE	n (Run; Non)	Patient Age (Run; Non), y (range)	Follow-up (Run; Non), mo	BMI (Run; Non), kg/m^2	Sex, % male
Chakravarty[3] (2008)	3	45; 53	59.8 ± 1; 60.2 ± 1 (50-72)	216; 216	22.3 ± 0.3; 24 ± 0.5	67.3
Felson (2007)	2	1279; 0	53.2 (26.0-81)	8.8 ± 1.04	27.4	44
Greaves[6] (2021)	4	16; 0	30.8 ± 6.3	1.5	22.9 ± 1.6	56.3
Horga[9] (2019)	2	71; 11	44.0 ± 8.5; 44 ± 7 (25-73)	7.5; 7.5	25.2 ± 3.6; 24.2 ± 2.2	50.2
Kujala[13] (1994)	2	2049; 1403	NR	NR	NR	100
Kujala[14] (1995)	2	117; 0	59.1 (45-68)	NR	22.8, NR	100
Kujala[15] (1999)	2	269; 179	58.5; 60.3 (47-71)	132; 132	23.2; 25.5	100
Konradsen[12] (1990)	3	27; 27	58; 57; (50-68)	NR	22.9; 23.9	100
Lo[17] (2017)	3	778; 1859	62 ± 8.4; 65.3 ± 9	96; 96	27.9 ± 4.7; 28.8 ± 5	44.2
Lo[18] (2018)	3	138; 1065	62.9 ± 7.3, 63.2 ± 8	96; 96	28.4 ± 4; 29.6 ± 4.7	45.3
Manninen[19] (2001)	3	281, 524	NR	NR	NR	NR
Miller[20] (2014)	4	14; 0	25 ± 11	NR	24.2	50
Mosher[21] (2010)	2	22; 15	40; 37	NR	23.7, 25.4	47.8
Mühlbauer[22] (2000)	3	9; 9	27.4 ± 3.3; 22.2 ± 1.9	NR	22.4 ± 1.1; 23.1 ± 3.1	100
Sandmark and Vingård[26] (1999)	3	1173; 0	NR	NR	NR	50.2
Spector[27] (1996)	3	81; 977	52.3 ± 6.1; 54.2 ± 6 (40-67)	NR	22.1 ± 2.8; 25.6 ± 4.3	0.0
Thelin[28] (2006)	3	825; 825	NR (51-70)	NR	NR	43.2
Total	—	7194; 6947	56.2; 61.6	55.8; 99.7	26.7; 28	58.5

TABLE 2
Modified Coleman Methodology Score[a]

Study (year)	MCMS
Thelin et al[28] (2006)	89
Kujala et al[15] (1999)	88
Konradsen et al[12] (1990)	79
Sandmark and Vingård[26] (1999)	77
Greaves et al[6] (2021)	73
Lo et al[18] (2018)	70
Felson et al[5] (2007)	64
Spector et al[27] (1996)	64
Lo et al[17] (2017)	57
Chakravarty et al[3] (2008)	55
Kujala et al[13] (1994)	55
Kujala et al[14] (1995)	55
Manninen et al[19] (2001)	54
Mühlbauer et al[22] (2000)	54
Miller et al[20] (2014)	49
Horga et al[9] (2019)	48
Mosher et al[21] (2010)	44
Total	63.2 ± 13.9

[a]MCMS, Modified Coleman Methodology Score.

ran for a mean of 213.9 ± 18.7 minutes per week. In a study by Mosher et al,[21] runners ran for a mean of 23.1 miles per week. In a study by Konradsen et al,[12] it was found that 90% of runners (27/30) ran for a range of 12 to 24 miles per week for 40 years. Three runners had stopped running because of OA of both lower and upper extremity joints. In a study by Mühlbauer et al,[22] the runners trained for 10 hours per week for at least 3 years. In a study by Spector,[27] the runner group averaged 14.6 miles per week. The runners in the study of Kujala et al[14] ran for a mean of 9408 ± 4213 hours over a mean of 31.7 ± 16.6 years. In 10 studies,[5,6,9,13,15,17,19,20,26,28] the authors did not report on the running distance within the running groups. In all 17 studies,[3,5,6,9,12-15,17-22,26-28] the runners were running before the initiation of the study.

Four studies[3,21,22,27] reported physical activity in the nonrunner group. In the study[21] by Mosher et al, 2 patients in the nonrunner group reported occasionally running 5 miles per week over the past 2 years, and the rest of the patients reported no history of running exercise. In a study[27] by Spector et al, 81.3% (811/977) of nonrunners participated in little to no physical activity during the study. In a study by Mühlbauer et al,[22] participants in the nonrunner group reported <1 hour of physical activity per week throughout life. In a study by Chakravarty et al,[3] nonrunners ran for a mean of 0.9 ± 0.7 minutes per week. In 9 studies,[9,12,13,15,17-19,26,28] the authors did not report the level of physical activity in the nonrunner group.

Patient-Reported Outcomes

Six studies[12,14,15,17,18,27] assessed the presence of knee pain at the final follow-up (Table 3). Konradsen et al[12] did not report their findings for knee pain. Overall, the presence of knee pain ranged from 10.2% to 35.4% in the runner group and 13.4% to 58.8% in the nonrunner group. Lo et al[17] found a significantly higher prevalence of knee pain in the nonrunner group.

TABLE 3
Knee Pain[a]

Study	Runners	Nonrunners	*P*
Lo et al[18] (2018)	33/123 (26.8)	293/1009 (29)	.61
Lo et al[17] (2017)	274/775 (35.4)	1093/1859 (58.8)	**<.0001**
Kujala et al[14] (1995)	23/117 (19.7)	—	NA
Kujala et al[15] (1999)	27/264 (10.2)	24/179 (13.4)	.30
Spector et al[27] (1996)	27/81 (33.3)	248/994 (24.9)	.096
Total	384/1360 (28.2)	1658/4041 (41)	**<.0001**

[a]Data are reported as knee pain/total No. of patients within each group at the latest follow-up (%). Bold *P* values indicate statistically significant differences between runners and nonrunners ($P < .05$). NA, not applicable.

Chakravarty et al[3] reported results for the HAQ–DI and found no significant difference between runners and the control group ($P > .05$). Horga et al[9] reported results for the KOOS and found no significant changes between premarathon and postmarathon KOOS scores in the runner group in the subscales of symptoms ($P = .981$), pain ($P = .121$), activities of daily living ($P = .303$), sports and recreational activities ($P = 0.133$), and quality of life ($P = .096$). These authors also found no changes between baseline and final follow-up KOOS subscale scores in the nonrunner group—symptoms ($P = .375$), pain ($P = .250$), activities of daily living ($P > .999$), sports and recreational activities ($P > .999$), and quality of life ($P = .250$). Greaves et al[6] reported results for the KOOS subscales for pain and function and found that both subscores significantly improved after a 6-week exercise program was implemented ($P = .0001$, for both).

Radiological Outcomes

Three studies[5,18,27] assessed knee joint-space narrowing on a plain radiograph (Table 4). Spector et al[27] found a significantly higher prevalence of PF joint-space narrowing in the runner group at the final follow-up ($P < .05$). Two studies[14,27] assessed the presence of osteophytes at the TF and PF joints, of which Spector et al[27] found a significantly higher prevalence of osteophytes about both joints in the runner group at the final follow-up ($P < .05$). Three studies[3,14,17] assessed ROA. The 2 studies[3,17] that compared ROA between runners and nonrunners found no differences between groups. Chakravarty et al[3] assessed the progression of ROA by using a modification of the KL method. The study by Lo et al[17] defined ROA as a KL grade ≥2 in at least 1 knee and also assessed SOA, which was defined as having at least 1 knee with both ROA and frequent knee pain present. No difference was found in the prevalence of SOA between groups.

Chakravarty et al[3] assessed the total knee score and joint-space width. No significant differences were found between runners and the community control group regarding the total knee score or joint-space width ($P > .05$, for both).

TABLE 4
Radiological Outcomes[a]

Study	Outcome Measure	Results		P
		Runners	Nonrunners	
Felson et al[5] (2007)	TF JSN	222/2259 (9.8)	—	NA
Lo et al[18] (2018)	Medial JSN	40/205 (19.5)	378/1063 (23.6)	>.05
Spector et al[27] (1996)	TF JSN	28/81 (34.6)	359/911 (36.7)	>.05
Spector et al[27] (1996)	PF JSN	11/81 (13.6)	27/215 (12.6)	**<.05**
Spector et al[27] (1996)	Osteophytes (TF joint)	18/81 (22.2)	145/977 (14.8)	**<.05**
Spector et al[27] (1996)	Osteophytes (PF joint)	34/81 (42)	60/215 (28)	**<.05**
Lo et al[17] (2017)	ROA	416/778 (53.5)	1093/1859 (58.8)	>.05
Lo et al[17] (2017)	SOA	177/778 (22.8)	547/1859 (29.4)	>.05
Chakravarty et al[3] (2008)	ROA	9/45 (20)	17/53 (32.1)	>.05
Kujala et al[14] (1995)	ROA	31/117 (26.5)	—	NA
Kujala et al[14] (1995)	Osteophytes (TF joint)	11/117 (9.4)	—	NA
Kujala et al[14] (1995)	Osteophytes (PF joint)	22/117 (18.8)	—	NA

[a]Results are reported as patients affected/total No. of patients within each group at the latest follow-up (%). Bold P values indicate statistically significant differences between runners and nonrunners ($P < .05$). JSN, joint-space narrowing; NA, not applicable; PF, patellofemoral; ROA, radiographic knee osteoarthritis; SOA, symptomatic knee osteoarthritis; TF, tibiofemoral.

Mosher et al[21] assessed cartilage MRI T2 values and cartilage thickness from the central femoral and tibial cartilage and found no significant differences between the runners and nonrunners at the final follow-up ($P > .05$). A study by Mühlbauer et al[22] assessed cartilage thickness in the patella, trochlea, lateral femoral condyle, medial femoral condyle, and the medial and lateral tibial plateau and found no significant differences between the runner and control groups ($P > .05$). Konradsen et al[12] assessed cartilage thickness, grade of degeneration, and osteophytosis of the knee and found no significant differences between runners and nonrunners ($P > .05$).

Horga et al[9] assessed findings of the knee joint using the MOAKS score and found a significant improvement in the following structures within the runner group at the final follow-up: cartilage of the lateral patella ($P = .0005$); semimembranosus tendon ($P = .016$); iliotibial band ($P < .0001$); and the prepatellar bursa ($P = .016$). Furthermore, the authors assessed the presence of meniscal tears and found no significant differences in the prevalence of meniscal lesions between runners and nonrunners ($P > .05$).

Progression to Surgery

Three studies[17-19] reported on patients undergoing TKR due to OA. In the Lo et al (2018) study,[18] TKR was performed in 3.9% (8/205) of runners and 4.3% (69/1603) of nonrunners ($P = .79$). Lo et al[17] (2017) reported performing TKR in 2.6% (20/778) of runners and 4.6% (86/1859) of nonrunners ($P = .014$). Manninen et al[19] assessed physical exercise as it related to the risk of knee arthroplasty. In both men and women, the risk was significantly less in those with a high number of cumulative hours of exercise. This was defined by at least 8654 total exercise hours in men and at least 6862 total exercise hours in women by the age of 49 years, compared with those who had no regular physical exercise ($P < .05$).

DISCUSSION

Based on the findings of this systematic review, we found a significantly higher prevalence of knee pain in the nonrunner group. Although a single study[27] found a significantly higher prevalence of osteophytes in the TF and PF joints among runners, multiple studies[3,17,18,27] found no significant differences in the prevalence of ROA (based on TF/PF joint-space narrowing or KL grade) between runners and nonrunners. Additional studies[12,21,22] found no significant differences in cartilage thickness on MRI between runners and nonrunners. Finally, 2 studies[17,18] assessed the risk of progression of knee OA to TKR, with 1 study[17] finding a significantly lower risk of TKR among runners compared with nonrunners.

A 2017 meta-analysis by Timmins et al,[29] with a total of 6197 patients, found no significant differences in PROs between runners and nonrunners. While the authors reported mixed outcomes with regard to the presence of knee OA, there did appear to be a protective effect of running against surgery due to OA. The present systematic review builds upon this previous review with 7944 additional patients included for a more robust set of clinical findings.

Animal studies have shown that immobilization of the knee joint[30] as well as prolonged activity[24] can lead to osteoarthritic degeneration and that beneficial effects are determined by a dose-dependent relationship.[12,23] Furthermore, runners typically have a lower BMI, which could protect against knee OA.[17] How the distinct knee structures respond to dynamic, cyclical loading patterns during running—especially over prolonged periods—remains unclear.[29] Various intrinsic and extrinsic factors affect a joint's ability to withstand destructive forces. Intrinsic factors include the thickness and composition of the articular cartilage as well as the strength of the adjacent bone, muscle, and periarticular ligaments. Extrinsic factors consist of nutrition; training technique; and the magnitude, direction, and duration of the applied force.[7] Running may have a protective effect if the resulting mechanical loading stimuli help elicit beneficial adaptation to the joints and surrounding structures. On the contrary, if a joint's tolerance to loading is surpassed as a consequence of running, it could be a risk factor for knee OA. This relationship is further complicated because running is both directly and indirectly associated with other risk factors such as joint injury and BMI.[29] More recently, barefoot running has been proposed as a potential strategy to decrease the risk of acquiring running injuries because of its effects on the biomechanics of running and joint loading.[7]

Limitations

The limitations of this study should be noted. First, the included studies demonstrated heterogeneity in the amount of running, age of the patients included, outcomes reported, and study designs. It also should be noted that some studies included a small number of patients and that 5 studies[5,6,14,20,26] lacked a control group. There is also the potential for confounders and selection bias (eg, runners may have a better baseline joint health compared with nonrunners). Furthermore, there was a difference in the follow-up duration and age of the runners versus nonrunners included in the studies. Finally, most studies were retrospective in study design and could not assess changes in radiological or PROs based on running.

CONCLUSION

In the short term, running is not associated with worsening PROs or radiological signs of knee OA and may be protective against generalized knee pain.

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