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REVIEW

A systematic review to evaluate exercise for anterior cruciate ligament injuries: does this approach reduce the incidence of knee osteoarthritis?

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Purpose: Among a variety of conservative and surgical options to treat anterior cruciate ligament (ACL) injuries, we do not understand which options could potentially prevent knee osteoarthritis (OA). The aim of this systematic review was to examine the evidence pertaining to exercise treatment of ACL injuries in the context of knee OA.

Methods: Medline, Embase, CINAHL, PubMed, and PEDro (Physiotherapy Evidence Database) databases were systematically searched using keywords encompassed within four primary key terms: knee, osteoarthritis, anterior cruciate ligament, and exercise. Clinical studies evaluating the effect of an exercise treatment for ACL injuries on the development of knee OA in adult humans were included. The PEDro scale was used to critically assess the studies included in the review.

Results: Eighteen studies were included in this review, with a median PEDro score of 6/11 (range, 2/11–9/11). Three studies provided statistical evidence that exercise following ACL injury lowered the risk for knee OA development. Nine studies demonstrated no benefit of exercise in preventing knee OA incidence relative to either operative treatment or the contralateral, unaffected knee. However, exercise resulted in higher knee instability. Nonetheless, there were no significant differences in subjective or objective knee outcomes for early versus late ACL reconstruction.

Limitations: This review was not registered through PROSPERO.

Conclusion: The relationship between a rehabilitative exercise for ACL injuries and long-term knee OA prevalence is inconclusive. However, research suggests initial conservative treatment with optional late ACL reconstruction because this treatment strategy may reduce the risk of knee OA. More research, ideally randomized controlled trials or comparable designs, is required prior to establishing clinical guidelines for ACL injury management.

Keywords: exercise therapy, knee, ligament, articular, osteoarthrosis, rehabilitation

Introduction

The most commonly injured ligament of the knee is the anterior cruciate ligament (ACL). Rupture, elongation, and/or fraying of the ACL often occur within activities that require pivoting movements such as soccer or basketball.[1] Therefore, ACL injuries occur most frequently among young, competitive athletes.[2] The primary function of the ACL is to stabilize the knee by resisting hyperextension, anterior tibial translation, and knee joint internal/external rotation.[3] The ACL also helps to resist varus and valgus forces when the knee is in a flexed position.[3] Injury of the ACL occurs when stresses applied directly or indirectly to the knee exceed the ACL tissue tolerance. Direct contact

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injuries generally occur through a forceful valgus stress and often result in concomitant injuries to the medial meniscus and the medial collateral ligament.[3] ACL injuries are most commonly caused through noncontact mechanisms. This indirect contact accounts for 70%–80% of all ACL injuries and is frequently attributed to poor body mechanics during jumping or pivoting.[3]

In the long term, elevated risks of knee osteoarthritis (OA) and poor knee function exist in those with ACL injuries, predominantly due to knee joint instability.[1,4,5] In fact, OA affects up to 50% of individuals that have had an ACL injury.[2] OA can lead to chronic pain, limited function, as well as an overall reduction in the quality of life.[6] To further contribute to knee OA risk, an ACL injury can occur concurrently with meniscal tears.[1] The meniscus acts as a secondary stabilizer of the knee, and knee instability is associated with a high risk of OA development.[5] A partial or total meniscectomy is often performed when the meniscus is injured, which is also recognized as a substantive risk factor in the development of knee OA.[1]

There are no specific guidelines whether ACL injuries should be treated conservatively with rehabilitation programs, or with surgical reconstruction.[2] Posttraumatic ACL injuries can be managed through different treatment options, including conservative (typically exercise combined with bracing and activity modification) and nonconservative (surgical repair of the ACL) approaches. The restoration of neuromuscular knee function after injury through exercise may play a key role in preventing the development of OA.[6] However, operative treatment for an ACL injury is common, primarily due to its associated improvements in knee stability and better restoration of activity level.[2] While there is an abundance of research reviewing the effect of operative treatment on the development of knee OA, there has been minimal research examining the long-term effects of exercise for ACL deficiency.[7] Since poor muscle function is implicated in the development of OA, exercise, and rehabilitation after an ACL tear may be advantageous for preventing the development of OA.[6] Through the use of rigorous neuromuscular training, muscular function after an ACL injury can be effectively regained, including improvements in strength, dynamic stability, postural awareness, and muscular coordination.[8] As well, a conservative approach to ACL injuries eliminates the risk of surgical complications.[8] These complications include the risk of infection, arthrofibrosis, graft failure, donor site morbidity, and pain.[8]

The purpose of this review was to critically examine whether exercise after an ACL injury reduces the risk of knee OA development compared to an operational approach. Treatment effectiveness was evaluated using several outcome measures, including signs of knee degeneration on images acquired with a variety of modalities, as well as both subjective and objective measures of knee stability and function.

Methods

Search and evaluation strategy

Medline (1946–Present), Embase (1974–Present), CINAHL (1981–Present), PubMed, and Physiotherapy Evidence Database (PEDro) databases were systematically searched using keywords encompassed within four primary key terms: knee (5 keywords), osteoarthritis (11 keywords), anterior cruciate ligament (4 keywords), and exercise (48 keywords) (Table 1). After each search was performed, the publication titles and abstracts were evaluated based on specific inclusion/exclusion criteria. Inclusion criteria included the following: 1) full text journal article, 2) longitudinal design, 3) prescribed exercise intervention for ACL rupture, and 4) measurement of incidence of knee OA using an imaging modality (ie, radiographs, magnetic resonance imaging [MRI]). Study design (ie, randomized controlled trial [RCT], prospective/retrospective case series or cohort) was not restricted, however review papers (ie, narrative, systematic, meta-analyses) were not included. Studies were excluded if they did not use human participants who were over 18 years of age. This search was last conducted in September 2015. All articles were imported into Mendeley Desktop© (version 1.14) through which duplicates were removed and articles were screened for inclusion.

Measurement of the incidence of knee OA

Several measurements of knee OA incidence were included in this review: 1) radiographs, 2) bone scans, 3) MRI, and 4) signs and symptoms associated with knee function. These outcome measures were required to provide evidence of joint degradation associated with knee OA. Signs of joint space narrowing and osteophyte formation were noted on radiographs. In one study, bone scans were used to complement radiographic findings, with the regional specific changes evaluated and scored.[9] MRI has been recently used to specifically evaluate regional changes in knee cartilage.[10,11] Finally, clinical measurements of signs associated with impaired knee function due to ACL deficiency and knee OA, such as knee laxity were included.

Apart from imaging evidence of joint degradation, subjective and objective assessments of knee stability and function were often reported. Subjective and objective measurements were recorded in this review. Knee instability, range of motion, and laxity measurements may be evaluated primarily using the Lachman test, pivot shift test, and side-to-side

Table 1 Search strategy; 68 key words within four key terms (knee, osteoarthritis, anterior cruciate ligament, exercise)

Knee (5)	**Osteoarthritis (11)**	**Anterior cruciate ligament (4)**
1. Knee	1. [a]Osteoarthrit*	1. Anterior cruciate ligament
2. Knee joint	2. Osteoarthritis, knee	2. Cruciate ligament, anterior
3. Menisci, tibial	3. Osteoarthrosis	3. Ligaments, articular
4. Patellofemoral joint	4. Arthritis, degenerative	4. Medial collateral ligament, knee
5. Superior tibiofibular joint	5. Cartilage	
	6. Cartilage, articular	
	7. Fibrocartilage	
	8. Menisci, tibial	
	9. Joint instability	
	10. Instability, joint	
	11. Laxity, joint	

Exercise (48)			
1. Exercises	13. Aerobic exercises	25. Static stretching	37. Weight-bearing strengthening program
2. Exercise, physical	14. Exercise movement techniques	26. Dynamic stretching	38. Resistance training
3. Exercises, physical	15. Movement techniques, exercise	27. Isometric stretching	39. Strength training
4. Physical exercise	16. Exercise movement technics	28. Active stretching	40. Rehabilitation
5. Physical exercises	17. Pilates-based exercises	29. Passive stretching	41. Exercise therapy
6. Exercise, isometric	18. Exercises, Pilates-based	30. Relaxed stretching	42. Physical therapy modalities
7. Exercises, isometric	19. Pilates based exercises	31. Static-active stretching	43. Physical therapy (specialty)
8. Isometric exercises	20. Muscle stretching exercise	32. Static-passive stretching	44. Physiotherapy
9. Isometric exercise	21. Muscle stretching exercises	33. Circuit-based exercise	45. Physical therapy
10. Exercise, aerobic	22. Exercise, muscle stretching	34. Weight-lifting exercise program	46. Manipulation, orthopedic
11. Exercises, aerobic	23. Exercises, muscle stretching	35. Weight-lifting strengthening program	47. Musculoskeletal manipulations
12. Aerobic exercise	24. Proprioceptive neuromuscular facilitation (PNF) stretching	36. Weight-bearing exercise program	48. Kinesiology, applied

Note: [a]The search term was specifically "osteoarthrit*" not osteoarthritis. This ensured that words such as osteoarthritic were also searched.

laxity (≥3 mm) using a KT-1000 arthrometer. Additional manual tests, such as the anterior drawer test, and flexion/extension range of motion may also be used to evaluate knee stability. Studies may quantify lower limb muscle strength differences between the injured and uninjured knees.[12–14] Also, standardized subjective reports of knee function may be assessed using scores obtained from questionnaires, including the Knee Injury and Osteoarthritis Outcome Score, International Knee Documentation Committee (IKDC), Lysholm, and Short Form-36. Self-reported knee instability, pain, and swelling were also recorded. Finally, the activity level was evaluated predominantly using Tegner scores, however, subjective reports of sport or occupational modifications due to injury or treatment were reported.

Each of the included studies was reviewed to determine whether specific trends could be identified with respect to the relationship between conservative management of ACL injuries through exercise and the incidence of knee OA. This included considering related factors such as knee instability, length of follow-up period, and late surgical intervention.

Critical appraisal

Included studies were critically reviewed using the PEDro critical appraisal scale. The PEDro scale was developed to assist researchers in identifying clinical trials with adequate internal validity and interpretable outcomes based on sufficient statistical information.[15] The PEDro scale appraises articles based on eleven criteria. These criteria involve the eligibility of study participants, allocation to groups, blinding procedures, and the use of outcome measures.[15] A high score on the PEDro scale indicates that the study has high internal validity.

Results

A total of 18 studies were included in this review. The search strategy elicited 2,260 articles. After duplicates were removed (562), 1,698 were screened by title and abstract. Thirty-seven full journal articles were reviewed for eligibility, with 18 articles meeting all of the inclusion criteria. Studies were primarily excluded due to not specifically assessing OA using an imaging approach and/or describing the approach used to address cartilage changes, as well as not specifically describing an exercise treatment plan to conservatively treat the ACL injury. In addition, any review papers, those studies evaluating nonhuman participants or children (<18 years) were excluded. A summary of the included studies, specifically the PEDro score, sample, and intervention as well as the results, are shown in Table 2. Three of the studies reported a different set of outcome measures from the same sample and thus their results are integrated within the table.[1,16,17]

Table 2 Summary of studies included in review

Author (year); PEDro scale score	Sample information; length of follow-up; retention	Intervention; retention	Results summary
Giove et al[13] 6/11	Sample: n=24 M (24) Age (FU): 30.2±5.2 y Length of FU: time from rehabilitation to FU: 12.8±4.73 mo Time from I to FU: 44.25±48.91 mo	Intervention: All treated with exercise program (minimum of 7 mo)	1. Radiographic (n=22; two patients refused radiographs) No statistically significant differences between injured and healthy contralateral knees 13/22 injured knees, 7/22 contralateral knees had degenerative changes 2. Instability, range of motion and laxity High percentage of participants had positive anterior drawer (neutral [96%], 15° (external rotation [79%]), and Lachman tests (96%) No significant differences in ranges of motion between injured and contralateral knees 3. Muscle strength No difference in strength between injured and contralateral knees, but quadriceps 12% stronger than hamstrings in injured limb and 15% stronger in contralateral limb (P=0.005) 4. Activity level Of n=24 returning to activity: 3= preinjury level (no symptoms), 11= full activity (occasional symptoms), 8= limited activity (moderate to severe symptoms), 2= minimal participation
Hawkins et al[22] 2/11	Sample: n=40 M (31): W (9) Age (I): 22±13 y Length of FU: 45 (rng, 24–79 mo)	Intervention: All treated with an exercise program Late reconstruction (30%) Retention: 28/40 (nonoperative) 23/28 radiographs 28/28 interviewed and examined	1. Radiographic 10/23 had some degenerative changes 1/23 had moderate OA 4/23 had mild or minimal OA 2. Self-reported symptoms/rating Participants reported instability/giving way (86%), adequate or fully functional (61%), participating in sports with little or no limitation (57%), no pain (46%) or mild pain with activity (36%), occasional or no swelling (89%) Overall ratings good (12.5%), fair (57.5%), poor (30%)
Kannus and Jarvinen[14] 5/11	Sample: n=98 M (71): W (27) Age (I): 32±13 y Injury from sport related trauma (48%) Length of FU: 8.0±2.3 y	Intervention: All treated with exercise program (only initial operative procedure was meniscectomy) Late ACL reconstruction (35%); during the FU period (20%) and at FU (15%) Retention: 90/98 Grade III injury (49/90) Grade II injury (41/90)	1. Radiographic Grade III: 70% had signs of OA (including osteophytes, subchondral sclerosis and joint space narrowing) Grade II: 15% had signs of OA (similar changes to grade III) 2. Instability, range of motion and laxity Grade III: 95% were severely (3+) or grossly (4+) unstable anteriorly (as per anterior drawer and Lachman tests) Grade II: instability less severe but comparable frequency to Grade III 3. Muscle strength Grade III: strength deficits – extension (20%±18%) and flexion (16%±15%) Grade II: strength deficits – extension (6%±10%) and flexion (4%±8%) 4. Activity level Grade III: 80% reduced activity level, 25% changed occupations due to knee symptoms; 40% sustained several re-injuries Grade II: 66% had same preinjury activity level, 7% changed occupations; 15% sustained several re-injuries

Pattee et al[21] 3/11	Sample: n=68 M (37): W (12) Age (l): 27 (rng, 16–46 y) Length of FU: 67 (rng, 48–122 mo)	Intervention: All treated with exercise program Late ACL reconstruction (n=9, 18%) (excluded from analysis) Retention: 49/68 9 excluded from analysis 40/68 questionnaires 31/40 physical exam 20/31 radiographs	1. Radiographic (n=20/31) 35% showed normal radiographs, 50% had mild flattening of the femoral condyle, 15% had mild subchondral sclerosis and osteophytes, none had joint space narrowing 2. Instability, range of motion and laxity (n=31/40) Physical exam: 87% had pivot shifts; all participants had positive Lachman tests Clinical test (KT-1000): average of 3.1 mm greater anterior displacement compared to contralateral knee 3. Self-reported symptoms/rating (n=40) Participants reported instability (65%), giving way (35%), pain (60%), and mild swelling (40%)
Daniel et al[9] 6/11	Sample: n=298 Age (l): (rng, 15–44 y; in 91% of participants) Sample at FU: n=292 M (204): W (88) Length of FU: 64 (rng, 46–113 mo)	Intervention: 1. Group 1: early stable, exercise (n=54) 2. Group 2: early unstable, exercise (n=147) 3. Group 3: early reconstruction (n=45) 4. Group 4: late reconstruction (n=46) Retention: 292/298 285/292 interviewed and examined 7/292 interviewed 231/292 radiographs 245/292 functional tests 263/292 motion measurements	208 knees underwent arthroscopy to verify tears; n=2 (1%) of unstable and n=9 (50%) of stable knees did not have tears Reconstructed patients had higher incidence of meniscal surgery 49% of patients with an ACL injury had a meniscal tear 1. Radiographic (n=231/292) and bone scan (n=165/292) Greater degenerative changes on both scans in operative groups All scores were generally low; radiograph (5.8, rng 0–32; maximum possible score: 83), bone scan (8.6, rng 0–24; maximum possible score: 24) 2. Instability, range of motion and laxity Difference between normal and injured knee in Group 1 significantly different from other groups ($P<0.001$) for KT-1000 tests, quadriceps active test and manual muscle test 89%–93% of Group 1, 16%–55% of Group 2, 33%–64% of Group 3 and 30%–61% of Group 4 had displacement measurements <3 mm, depending on the test 3. Standardized Subjective scores Group 1 performed better one-legged hop compared to all other groups ($P<0.05$) 4. Self-reported symptoms/rating No participant changed occupations, but sports participation reduced in all groups (44%–55%) Group 1 had lower symptoms and impairments compared to all other groups
Fink et al[12] 5/11	Sample: n=113 No difference in sports participation or activity-related symptoms between groups ($P>0.05$) Sample at FUII: Operative n=46 M (37): W (9) Age (l): 33.6±8.0 y Exercise n=25 M (18): W (7) Age (l): 32.3±9.9 y Length of FU: First FU (FUI): 74.2±8.1 mo Second FU (FUII): 132.2±8.1 mo	Intervention: Operative (n=72) Exercise (n=41) Late ACL reconstruction (n=2 between FUI and FUII) Retention: Operative FUI =72.2%; FUII =63.9% (n=46) Exercise FUI =78.1%; FUII =61% (n=25)	1. Radiographic Mild-to-moderate degenerative changes were not different between operative and exercise groups ($P>0.05$) but did increase over time (preinjury to FUI and FUII) in both groups ($P<0.05$) 2. Instability, range of motion and laxity KT-1000: greater side-to-side laxity ($P<0.05$) and higher increase over time ($P<0.05$) for exercise group compared to operative 3. Standardized Subjective scores FUI and II – operative higher Lysholm and Orthopaedische Arbeitsgruppe Knie scores than exercise ($P<0.05$) Note: FUI and FUII not different ($P>0.05$) IKDC scores at FUII: No patients scored "normal" 43.5% operative/4.3% exercise "nearly normal" 52.1% in operative group and 52.1% in exercise group were "abnormal" 4.3% operative/43.5% exercise "severely abnormal"

(*Continued*)

Table 2 (*Continued*)

Author (year); PEDro scale score	Sample information; length of follow-up; retention	Intervention; retention	Results summary
			4. Muscle strength Higher knee extensor torque ($P<0.05$) in contralateral limb of each group compared to injured limb Similar knee flexor torque ($P>0.05$) between limbs of each group 5. Self-reported symptoms/rating FUI and II – operative higher self-reported rating than exercise ($P<0.05$) 6. Activity level Operative maintained higher activity level than exercise, but both groups reduced over time ($P<0.05$) Higher percentage of operative group ($P<0.05$) could maintain occupation at preinjury level (95.6%) compared to exercise (73.9%)
Fithian et al[19] 5/11	Sample: n=287 Sample at FU: M (101): W (108) Age (FU): 39 (rng, 16–69 y) Length of FU: 6.6 (rng, 3–10 y)	Intervention: Participants assigned to 1/3 groups based on initial knee stability testing and preinjury sports participation level: 1. High risk (n=55) Early operative (n=31) Early exercise (n=24) (n=18 no late operative [ACL reconstruction]) 2. Moderate risk (n=72) Early operative (n=26) Early exercise (n=46) [n=30 no late operative] 3. Low risk (n=82) Early operative (n=6) Early exercise (n=76) [n=65 no late operative] Note: "exercise" will indicate no early or late ACL reconstruction Retention: 210/287 at FU 1 excluded due to surgery received elsewhere; 11 injured nonindex knee (excluded from analysis that required comparisons to nonindex knee)	Low risk group had fewer later surgeries (16%) than moderate and high risk groups, collectively (33%; $P=0.008$) 1. Radiographic Operative had higher prevalence of OA than exercise at lateral (39%/25%; $P=0.03$), patellofemoral (71%/57%; $P=0.03$) and anterior (18%/6%; $P=0.004$) joint spaces 2. Instability, range of motion and laxity Pivot shift and Lachman test: operative had lower scores than exercise ($P<0.001$) KT-1000: high risk ($P=0.002$), moderate risk ($P=0.002$), and low risk ($P=0.04$) had less manual maximum displacement than exercise in same risk groups 3. Standardized Subjective scores Short Form-36 (SF-36): operative higher on all subscales compared to exercise IKDC: operative had higher percentage of participants scored as normal or nearly normal (83%) compared to exercise (33%; $P<0.001$) Lysholm score: operative higher score than exercise ($P<0.05$) 4. Activity level Tegner score: all groups had reduced scores ($P<0.001$), early operative had higher scores than exercise ($P<0.001$) and late operative ($P=0.007$) 5. Self-reported symptoms/rating Exercise group had higher instability rate (giving-way episodes) than operative ($P=0.009$) Operative better able to walk ($P=0.04$) and climb ($P=0.047$), but had more difficulty kneeling ($P=0.02$) than exercise
Meunier et al[20] 7/11	Sample: n=100 Operative n=44 M (33): W (11) Age (I)= 22 (rng, 14–30 y)	Intervention: Operative (n=42) Exercise (n=52) Late ACL reconstruction (n=16, 31%)	Meniscus injury prevalence lower in the operative group (12%) compared to exercise group (35%) ($P=0.015$) 1. Radiographic No significant difference in OA prevalence between operative and exercise groups 50% showed OA changes after 15 y, but <10% showed severe OA changes

	Exercise n=56 M (35): W (21) Age (I) = 21 (rng, 14–30 y) Length of FU:15±1 y	Retention: Operative (42/44) Exercise (52/56)	2. Instability, range of motion and laxity Operative group had reduced range of motion (P=0.0013) but better knee stability (Lachman tests (P=0.02); KT-1000 (P=0.0018)) compared to exercise group 3. Standardized Subjective scores Operative group had better Lysholm scores, but similar KOOS scores, compared to exercise group
Kostogiannis et al[16] 6/11	Sample: n=100 M (58): W (42) Age (FU): 42.1 (rng 30–57 y) Length of FU: 15 (rng, 13–20 y)	Intervention: Randomly assigned to supervised neuromuscular training or self-monitored traditional training After 6 weeks 49% of self-monitored training group were transferred to supervised 23% had undergone reconstruction at FU (time from injury to reconstruction =4 [rng, 0.5–11.5 y]) Retention: 67/100 M (40): W (27)	No differences between patients who underwent self-monitored or supervised rehabilitation 1. Standardized Subjective scores KOOS score: Lower scores for those injured in contact sports compared to noncontact ($P<0.05$) Lower scores compared to matched controls on all subscales except pain (P=0.06) IKDC score: 15 y FU score 83.3 (rng, 39.1–100) Significantly lower scores for those injured in contact sports, compared to noncontact (P=0.007) Lysholm score: Postinjury scores similar at 1 y (96 [rng, 61–100]) and 3 y (95 [rng, 60–100]) 15 y FU score decreased to 86 (rng, 32–100; $P<0.001$) 2. Activity level Tegner score: Score at injury (7, rng 3–9); 1 y postinjury (6, rng 2–9, $P<0.001$); 3 y postinjury (6, rng 3–9); 15 y FU (4, rng 1–7, $P<0.001$) At 3 y postinjury, 60% of exercise group had same or higher activity level as preinjury
Neuman et al[1] 7/11	Sample: n=100 Age (I): 26±8 y M (58): W (42) Length of FU: 15.7±1.4 y	Intervention: All subjects treated initially with activity modification and physical therapy without ACL reconstruction Late ACL reconstruction (n=22, 23%) Retention rate: 94/100 93/100 KOOS 84/100 Lysholm 84/100 Tegner 79/100 radiographs	1. Radiographic 15% of participants developed tibiofemoral (TF) OA (all had meniscal surgery) None of the participants that had no (or minor) meniscal tear developed TF OA ($P<0.0001$) 6/17 in operative group and 7/62 exercise group had TF OA (P=0.03) No TF OA in n=4 of operative group that did not have major meniscal injury 2. Standardized Subjective scores Lysholm Score: Higher score in exercise group compared to operative group (P=0.049) IKDC: 92/100 participated in sports at time of injury, 44/79 continued to participate at 15 y FU ($P<0.0001$) KOOS: Higher pain scores in participants who had meniscal surgery (P=0.042) and ACL reconstruction (P=0.035); lower scores in those with radiographic TF OA 3. Activity level Tegner score: Rating reduced from 7 (at injury) to 4 (15 y FU) Operative group had higher score than exercise (P=0.085)
Neuman et al[17] 5/11	Sample: n=100 Age (I): 26±8 y Length of FU: 15.7±1.4 y	Intervention: All subjects treated initially with activity modification and physical therapy without ACL reconstruction Late ACL reconstruction (n=22, 23%)	Radiographic results described in Neuman et al.[1] At FU, 48% had meniscal surgery (18/22 operative group, 26/72 exercise group) 1. Instability, range of motion and laxity Pivot shift and Lachman test: Both exercise and operative showed improved stability from baseline to 15 y FU ($P<0.0001$) Operative more stable (P=0.007) and lower pivot shift grade ($P<0.001$) than exercise

(*Continued*)

Table 2 (*Continued*)

Author (year); PEDro scale score	Sample information; length of follow-up; retention	Intervention; retention	Results summary
		Retention rate: 94/100 74/94 Laxity test, Radiographs 4/94 Laxity test only 5/94 radiograph only 11/94 interview	KT-1000: Sagittal laxity correlated with Lachman (*P*=0.0001) and pivot shift (*P*=0.001) tests Difference between injured and contralateral knees was 1.8±4.2 mm for operative group and 2.4±2.7 mm for exercise group (*P*=0.46)
Kessler et al[5] 6/11	Sample: n=109 M (68): W (41) Age (I): 30.7 (rng, 12.5–54.0 y) Length of FU: 11.1 (rng, 7.5–16.3 y)	Intervention: Operative (n=60) Exercise (n=49)	1. Radiographic No OA present in 52% of participants at FU (45% in operative and 61% in exercise group) Significantly greater risk of OA (≥ Grade II) in operative group (45%) compared to exercise group (24%) (*P*=0.03) 2. Instability, range of motion and laxity KT-1000: Statistically significant difference between injured and contralateral knees for operative (3.9, rng 0–12 mm) and exercise (5.7, rng 0–16 mm) groups ($P<0.05$) 3. Standardized Subjective scores IKDC: operative group had better scores at FU compared to exercise group (*P*=0.008) 4. Activity level Tegner score: no difference present between groups ($P>0.05$)
Meuffels et al[2] 7/11	Sample: n=50 Operative M (19): (6) Age (FU) = 37.6±6.2 y Exercise M (19): (6) Age (FU) = 37.8±6.8 y Length of FU: 10 y	Intervention: Operative (n=25) Exercise (n=25) Participants were matched for sex (*P*=1.0), age (*P*=0.808), BMI (*P*=0.443), and activity level (*P*=0.831)	68% of operative and 80% of exercise group had meniscal surgery by 10 y FU (*P*=0.333) 1. Radiographic 48% of operative group and 28% of exercise group had radiographic OA at FU (*P*=0.145) 2. Instability, range of motion and laxity KT-1000: 17% of exercise group and 6% of operative group had maximum side-to-side differences >3 mm (*P*=0.002) Pivot shift: 21% of exercise group and 5% of operative group had scores ≥1 ($P<0.001$) 3. Standardized Subjective scores IKDC: no significant differences between groups for IKDC (*P*=0.442), Lysholm (*P*=0.683) or one-legged hop test (*P*=0.522) 4. Activity level Tegner score: scores not significantly different between operative and exercise groups after ACL injury (*P*=0.420) or at FU (*P*=0.188)
Mihelic et al[18] 6/11	Sample: n=54 M (44): W (10) Operative n=36 Age (I) = 25.3 y Exercise n=18 Age (I) = 25.5 y Length of FU: 17–20 y	Intervention: Operative (n=36) Exercise (n=18)	1. Radiographic Operative group: 50% had mild and 16.5% had severe OA Exercise group: no participants had knees classified as normal and 56% had severe OA ($P<0.05$) 2. Instability, range of motion and laxity Anterior drawer test: 83% of operative group and 16% of exercise treated group had normal/near normal knees Patients with stable knees had better function and more sport activity 3. Standardized Subjective scores Lysholm score: operative group had higher score (84.3) than exercise group (53.3) ($P<0.05$) IKDC: operative group had higher score (83.15) than exercise group (64.6) ($P<0.05$)

			4. Activity level Tegner score: significantly lower activity level in exercise group compared to operative group after injury ($P<0.05$), but no difference prior to injury ($P<0.05$)
Streich et al[7] 6/11	Sample: n=126 Sample at FU: n=80 Operative M (28): W (12) Age (FU): 26±6.2 y Exercise M (28): W (12) Age (FU): 24±6.8 y Length of FU: Operative 15.4±0.76 y Exercise 15.2±0.69 y	Intervention: Operative (n=40) Exercise (n=40) Participants were matched for age, sex, BMI and concomitant injuries (no statistically significant differences) Retention rate: 80/126 n=14 lost to follow-up n=8 lost to graft rupture n=6 lost to late reconstruction n=18 lost to age, sex, BMI and concomitant injuries	Significantly higher rate of meniscal surgery in exercise group than operative group (P=0.028) 1. Radiographic Significant difference in radiographic OA between initial assessment and FU for both groups (Wilcoxon test $P<0.001$); 62.5% of operative and 55% of exercise 2. Instability, range of motion and laxity KT-1000: no statistically significant differences in anterior laxity at either 20° Flexion (P=0.389) or 60° Flexion (P=0.732) Pivot shift: Better rotational stability in operative group compared to exercise group, but not statistically significant (Fisher exact test P=0.662) Significant relationship between a positive pivot shift at FU and OA prevalence ($P<0.001$) Range of motion: reduced flexion range of motion at FU for n=17 in the operative group ($P<0.05$) 3. Standardized Subjective scores IKDC: no statistically significant differences between groups (P=0.066) 4. Activity level Tegner score: significant decrease between preinjury and postinjury in both groups (P=0.036) but no difference between groups
Potter et al[11] 7/11	Sample: n=40 (42 knees) Operative n=28 M (14): W (14) Age (I): 35.1±8.2 y Exercise n=14 M (4): W (10) Age (I): 41.5±9.7 y Length of FU: yearly FU (to maximum of 11 y)	Intervention: Operative (n=28) Exercise (n=14)	1. Standardized Subjective scores Short Form-36 (SF-36) scores: no significant differences between groups for physical (P=0.139) or mental (P=0.476) IKDC scores: delayed return to function, but by 2 y exercise was comparable to operative 2. Activity levels Activity of Daily Living scores: No significant differences between groups Activity Rating Scale scores: 1 y: operative (8.5±5.7), exercise (1.3±1.5), ns (P=0.056) 2 y: operative (8.5±6.1), exercise (8.2±5.6) 3 y: operative (5.6±3.9), exercise (10.0±4.9), ns (P=0.088) 3. MRI Across both groups, by 7–11 y postinjury, risk of cartilage loss compared to baseline was 50× greater for lateral femoral condyle, 30× for the patella and 19× for the medial femoral condyle Significantly higher odds ratio effect for cartilage loss over medial tibial plateau in exercise group compared to operative group
Frobell et al[4] 9/11	Sample: n=121 M (88): W (32) Sample at FU: n=120	Intervention: Operative (n=61) Exercise (n=59) Late ACL reconstruction (n=30, 51%)	1. Radiographic No statistically significant differences between operative, late reconstruction and exercise groups for tibiofemoral OA (P=0.25) or patellofemoral OA development (P=0.21) 23/58 (40%) of operative group, 7/29 (24%) of late reconstruction group and 5/26 (19%) of exercise group developed OA (tibiofemoral/patellofemoral)

(*Continued*)

Table 2 (*Continued*)

Author (year); PEDro scale score	Sample information; length of follow-up; retention	Intervention; retention	Results summary
	Operative n=61 M (49): W (12) Age (I): 26.4±5.1 y Exercise n=59 M (39): W (20) Age (I): 25.8±4.7 y Length of FU: Operative 60 (95% CI, 59–61) mo Exercise 59 (95% CI, 57–60) mo	Retention: 120/121	2. Instability, range of motion and laxity Operative group had significantly better knee instability compared to exercise: Lachman test ($P<0.001$); Pivot shift ($P<0.001$) 3. Standardized Subjective scores KOOS: no significant differences between groups (P=0.45) Short Form-36 (SF-36) scores: no significant differences between groups: physical component (P=0.78), mental component (P=0.34) 4. Activity level Tegner score: no significant differences between groups (P=0.73)
Neuman et al[10] 7/11	Sample: Cohort from Neuman et al.[1,17] n=32 M (17): W (15) Age (FU): 45 (rng, 35–61 y) Length of FU: 20.6 (rng, 18–23 y)	All treated with exercise program No radiographic OA (grade ≤1) at 16 y FU Compared to healthy reference group (n=24) matched for level of physical activity and BMI (M [14]: W [10]), Age: 25 y	1. MRI (dGEMRIC) No significant differences in T1Gd (used to estimate cartilage quality) values between ACL injured and healthy control group (matched for physical activity and BMI) both medially (P=0.065) or laterally (P=0.31) No difference in T1Gd values between participants with and without radiographic OA (grade ≤1) (P=0.85) No significant difference in T1Gd values between participants with and without major medial (P=0.48) and lateral (P=0.41) meniscal injury in their respective sides 2. Standardized Subjective scores KOOS: ACL injured participants had comparable results to healthy controls; with significantly higher values for pain (P=0.034) and ADL (P=0.0084) subscales

Abbreviations: ACL, anterior cruciate ligament; BMI, body mass index; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; OA, osteoarthritis, n, number of participants; M, men; W, women; y, years; mo, months; rng, range; FU, follow-up; I, injury; ns, not significiant; dGEMRIC, delayed gadolinium-enhanced magnetic resonance imaging of cartilage; MRI, magnetic resonance imaging.

The median PEDro score of the included studies was 6/11 and ranged from 2/11 to 9/11. A variety of intervention approaches was used to determine the effect of an exercise program on knee OA development. Eight of the included studies employed solely a rehabilitative exercise intervention, while ten compared this conservative treatment with an operative ACL reconstruction treatment. Exercise programs varied across the included studies, however, several adopted similar neuromuscular training themes, including the quadriceps and hamstrings muscle training, in addition to stability, mobility, and range of motion exercises (Table 3). In two studies, while researchers indicated that a rehabilitation program was provided, specific details of the program were not indicated. As well, in addition to the exercise program, some treatment strategies included activity modification, such as avoiding competitive sport, or activities involving contact or pivoting movements.[5,16,18]

While all included studies contained participant groups initially treated with an exercise intervention, several required late surgical intervention within the follow-up period. Specifically, in twelve of the included studies, a median of 23% (range, 5%–51%) of participants in the exercise group required late ACL reconstruction (Table 2). Despite this, it appears there is a minimal disadvantage to having delayed reconstruction.[19] While a higher risk of meniscal surgery was evident in those who underwent ACL reconstruction later than 3 months post-ACL injury, the risk of radiographic degenerative changes was lower in this later reconstruction group. Across included studies, the mean and median follow-up period post-ACL injury, was 11 years with a range of 4–20 years.

Each study included a different combination of outcome measures (Table 2). Fourteen studies used radiographic imaging to evaluate OA prevalence, while two studies specifically assessed cartilage morphology or composition using MRI. Among the studies that captured radiographs, five different grading systems were adopted. The criteria for each of these scales used to address OA severity were comparable; predominantly evaluating joint space narrowing and osteophyte formation, while some also considered the presence of sclerosis, flattening of the femoral condyles, subchondral cysts, calcification of ligaments, or varus/valgus deformity.[4,9,14] Grading systems included the following: the Kellgren and Lawrence classification,[2,5] IKDC radiograph grading system,[7,18,19] the Fairbanks scale,[12,13,20,21] and recommendations posed by the Osteoarthritis Research Society International.[1] The remaining studies did not use a standardized radiographic grading scale and/or used the alternate subjective and objective measures of knee stability, laxity, and function to evaluate the treatment success.

Three of the included studies provided statistical evidence that an exercised-based rehabilitation program for ACL injury treatment lowered the risk for knee OA development.[1,5,19] Several studies demonstrated no statistically

Table 3 Exercise intervention description in the included studies

Author (year)	Exercise intervention
Giove et al[13]	Muscle rehabilitation program targeting the quadriceps and hamstrings, including: isometric, isotonic and isokinetic exercises (at least 7 months)
Hawkins et al[22]	Physiotherapist supervised exercise program targeting the quadriceps and hamstrings
Kannus and Jarvinen[14]	Initial immobilization; isometric quadriceps exercises; rehabilitation (at least 6 months)
Pattee et al[21]	Exercise/rehabilitation program targeting the quadriceps and hamstrings (supervised 3–6 weeks; encouraged to continue)
Daniel et al[9]	Initial immobilization; home exercise of cycling, swimming, isotonic exercises targeting the hamstrings
Fink et al[12]	Home exercise program of cycling, swimming and strengthening exercises targeting the hamstrings
Fithian et al[19]	Initial range of motion and nonimpact closed chain strengthening; jogging and sport-specific exercise (6–12 weeks after injury); return to competitive sports (3 months after injury, if not symptomatic)
Meunier et al[20]	Rehabilitation program targeting strength and coordination
Kessler et al[5]	Rehabilitation program including: bracing (6 weeks), quadriceps and hamstring muscle exercises, proprioception exercises, no loaded flexion greater than 60° (6 weeks), return to sports (3 months, if not symptomatic), return to contact/pivoting sports (9 months, if not symptomatic)
Kostogiannis et al[16] Neuman et al[1,10,17]	Either physiotherapist supervised neuromuscular training or self-monitored training; both programs targeted stability and mobility, strength, performance, muscle activation strategies, proprioception and postural control
Meuffels et al[2]	Swelling reduction and range of motion; quadriceps and hamstrings strengthening program (at least 3 months)
Mihelic et al[18]	Initial immobilization; rehabilitation program including: range of motion, quadriceps strengthening (2 months); activity modification
Streich et al[7]	Physiotherapist supervised neuromuscular based rehabilitation program targeting stability and mobility; closed chain kinetic exercises, activity level progression
Potter et al[11]	Standard rehabilitation program
Frobell et al[4]	Rehabilitation program consistent with literature consensus

significant difference between surgical reconstruction and the conservative exercise treatment for ACL injury, despite some showing trends of higher OA prevalence in either operative[2,4,7,9] or exercise[5,18,20] treatment groups. However, research demonstrated trends that both knee instability[2,17,19] and meniscal tear prevalence[5,19] are associated with an elevated risk for OA incidence following exercise as compared to operative treatment, though this trend was inconsistent across studies. Additionally, while researchers in one study showed a reduction in subjective outcome scores and activity levels at the end of the follow-up period (15 years), reasonable scores were still reported (Lysholm score =86, IKDC score =83.3 at 15-year follow-up), with authors suggesting that this decline may be partially attributed to age-related changes.[16] In fact, at the 3-year follow-up, 60% of participants who underwent rehabilitative exercise and activity modification, had comparable activity levels to their preinjury state. Thus, this strategy of combining exercise with activity modification appears effective.

Discussion

Exercise and knee OA prevalence

The current available evidence regarding the effectiveness of exercise in reducing the risk of OA development is not conclusive. While some researchers demonstrated a lower prevalence of knee OA following exercise,[1,5,19] most of the included studies showed no statistical advantage of exercise in reducing the risk of knee OA.

It is possible that the study sample sizes prohibited finding significant differences. Over half of the included studies had initial sample sizes ≥100 participants; however, many of these studies subdivided participants into two treatment groups (operative and conservative). The sample size within each group was often unequal because, instead of random allocation, the treatment allocation was generally selected based on a combination of participant preference, physician recommendation, and activity level, with a competitive, athletic population generally recommended for surgery.[5,7,19] As well, within the conservative group, up to 51% of participants had reconstructive surgery by the end of the follow-up period. Cross-over from exercise to operative treatment resulted from either clinical signs and symptoms, notably chronic instability and giving way,[7,12,14,20] and/or physical activity level, with a higher incidence of late surgery in a high risk group of young athletes;[19–21] this subsequently resulted in a lower exercise group sample size. Additionally, the sample size was reduced by retention rates at follow-up, as well as the inability to obtain all outcome measures from study participants that completed the follow-up evaluation.

The length of the follow-up period could have contributed to the difference in OA prevalence between treatment groups, as degenerative changes may not have yet become evident.[13,22] While progressive degradation has been noted in participants with established knee OA over as little as 2 years, these studies used measures from MRI which are more sensitive to change than many radiographic measures.[23,24] The necessary study follow-up period to detect cartilage degradation post-ACL injury is unclear. However, in the current review, the studies showing a lower prevalence of OA in the exercise treatment group, represented short (6 years), moderate (11 years), and long (15 years) follow-up durations.

Exercise and associated risk factors for knee OA

Apart from radiographic evidence, several other outcome measures can be used to predict the risk of knee OA development. In particular, knee instability and laxity are highly evident following an ACL injury, with research showing that 96% of participants had positive anterior drawer and Lachman stability tests.[13] Knee instability, identified using a pivot shift test, was significantly related to OA prevalence ($P<0.001$).[7] Further, despite similar radiographic outcomes, higher pivot shift, and Lachman test scores and maximal side-to-side displacements (KT-1000) indicative of knee instability, were identified in the exercise group.[2,17,19] These findings may suggest that while exercise may pose higher risk for OA development, the progression may not occur for several years.

Among those with an ACL injury, meniscal tears have been consistently recognized as a risk factor for OA development. It was suggested that the loss of meniscal integrity, which acts to stabilize the knee in the absence of an intact ACL, may contribute to knee instability and subsequent risk of OA.[5] However, while certain studies demonstrated a higher incidence of meniscal tears with exercise,[5,19] others showed a similar prevalence of meniscal tear between treatment groups, despite the increased knee instability and laxity in the exercise group.[4,12] Additionally, in one study, no differences in radiographic degeneration were shown in those participants requiring a meniscectomy.[13]

Similar to the divergence in objective outcome measures of stability and degeneration, subjective measures of knee pain and function following treatment were inconsistent across studies. Several researchers showed that, compared to operative treatment, exercise resulted in lower outcome scores at follow-up, as noted by IKDC scores,[5,12,18,19] self-reported ratings,[12,19] and Lysholm scores.[12,20] Additionally, participants treated with exercise demonstrated lower relative activity, sports and occupation-related capabilities compared to both operative treatment and their baseline (preinjury) measurement.[12,19] Alternatively, other researchers showed no difference in subjective knee function scores between treatment groups.[1,2,4,7,11]

Additional risk factors related to ACL injury and OA development exist, including sex, age, and body mass. Researchers have identified a higher incidence of ACL injuries sustained in women compared to men, with a ratio of 3:1.[25] As 70%–80% of ACL injuries result from noncontact, often occurring during sport, younger females are at a high risk for injury.[3] Alternatively, OA is a progressive degenerative disease that exists more prominently in women ≥55 years of age.[26] Obesity has been identified as a risk factor for OA development. High body mass leads to cartilage degeneration by increasing the mechanical load incurred at the knee joint.[27] Reducing body mass will concurrently reduce knee joint loading, with a ratio of 1:4.[28] As well, both greater age (P=0.03) and body mass index (P=0.03) related to OA development in those with ACL ruptures.[5] This suggests that ACL injuries sustained at a young age pose risk for OA development and that this risk may be exacerbated by higher body mass. Thus, while rehabilitative exercise strives to improve muscle strength and knee joint stability, a secondary target of the exercise should be reducing total body mass. For example, rehabilitation strategies that aim to initiate weight loss would in turn reduce knee joint loading and subsequently reduce the risk of OA.

Factors contributing to treatment outcome

With inconsistencies present across the literature regarding the effectiveness of exercise after ACL injuries, it is important to consider possible factors that may confound treatment outcomes. ACL tear severity and the duration between injury and operative treatment were two factors evaluated within the included research studies. Kannus and Jarvinen[14] compared OA prevalence, instability, muscle strength, and activity level for those with grade II and grade III ACL injuries. Overall, tear severity was inversely related to all outcomes measures. This could partially explain the lack of statistical findings between treatment groups, as the participant sample may have included several grades of injury. Similarly, only one study included individuals who had sustained an isolated ACL injury with no concomitant ligament, meniscal, or chondral injuries. While the results favored exercise due to the lower prevalence of radiographic OA, the results of this study may not be generalizable to most ACL injuries, as isolated ACL-ruptures rarely occur.[5] Research by Fithian et al[19] included three treatment levels across the three study groups (high risk, moderate risk, low risk). Participants were initially prescribed exercise or early operative treatment, however, several undergoing exercise treatments opted for late operative treatment (>3 months postinjury). While those who solely underwent exercise had poorer stability and subjective function scores than operative groups, no statistically significant differences were present between early and late operative treatments with the exception of showing greater prevalence of meniscal tears in the late operative group. However, the exercise treatment group had significantly lower radiographic degeneration than operative groups. These findings, particularly the little added benefit of early ACL reconstruction, suggest that the best outcome after ACL injury results from late operative repair, after a period of exercise, following injury.

Limitations

The difficulty in evaluating the effectiveness of exercise after ACL injuries stems from the limited ability to conduct RCTs. Predominant limitations include a lack of randomization and concealed allocation, which subsequently results in low PEDro scores (median, 6/11) across the included studies. The use of randomization could create an ethical issue because clinical recommendations and patient preference may not match random allocation.[1] Also, with regards to exercise or operative treatment of ACL injuries, it is not feasible to blind participants to treatment group. As well, it is not possible to blind the surgeons performing reconstruction, or the therapists leading the exercise. In practice, the treatment adopted stems primarily from patient preference and physician recommendation, which often considers the current activity level of the patient. For example, one study stratified participants by activity level, with all high risk individuals (defined as young and participating in competitive activity) recommended for operative treatment.[19] Despite the physician recommendation, 44% of high risk participants declined and were treated with exercise. The only RCT included in this review (Frobell et al[4]) studied 121 active adults with an ACL injury. Participants were randomized to receive either early reconstruction or rehabilitation with the option of delayed ACL reconstruction. At a 5-year follow-up, the two groups did not differ in terms of the presence of radiographic knee OA. This RCT had the highest PEDro score of 9/11.

Table 4 PRISMA 2009 checklist

Section/topic	Number	Checklist item	Reported on page number
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	1,2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	2
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (eg, web address), and, if available, provide registration information including registration number	N/A
Eligibility criteria	6	Specify study characteristics (eg, PICOS, length of follow-up) and report characteristics (eg, years considered, language, publication status) used as criteria for eligibility, giving rationale	2,3
Information sources	7	Describe all information sources (eg, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	Table 1
Study selection	9	State the process for selecting studies (ie, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	2
Data collection process	10	Describe method of data extraction from reports (eg, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	2
Data items	11	List and define all variables for which data were sought (eg, PICOS, funding sources) and any assumptions and simplifications made	2,3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	3
Summary measures	13	State the principal summary measures (eg, risk ratio, difference in means)	3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg, I2) for each meta-analysis	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (eg, publication bias, selective reporting within studies)	N/A
Additional analyses	16	Describe methods of additional analyses (eg, sensitivity or subgroup analyses, meta-regression), if done, indicating which were prespecified	N/A
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	3
Study characteristics	18	For each study, present characteristics for which data were extracted (eg, study size, PICOS, follow-up period) and provide the citations	Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (Item 12)	11, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot	Table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (Item 15)	13–15
Additional analysis	23	Give results of additional analyses, if done (eg, sensitivity or subgroup analyses, meta-regression [Item 16])	N/A
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg, health care providers, users, and policy makers)	12,13
Limitations	25	Discuss limitations at study and outcome level (eg, risk of bias), and at review level (eg, incomplete retrieval of identified research, reporting bias)	13–15
Conclusion	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	15
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (eg, supply of data); role of funders for the systematic review	N/A

Note: Reproduced from Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med.* 2009;151(4):264–249.[31]

Abbreviations: N/A, not applicable; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Despite the overall median PEDro score, several aspects of the included studies were conducted well, adding to the overall rigor of the evidence. Notably, many studies had longer follow-up times (up to 20 years). This time frame is highly advantageous for examining OA development, as OA is a disease that slowly progresses over variable time periods, but typically over several years. The studies also included reasonably large sample sizes (in some cases matching participants between treatment arms) and had rigorous inclusion/exclusion criteria. Additionally, independent assessors, who were unaware of the treatment received, often evaluated the radiographs; thereby limiting potential bias.

It is possible that variation in exercise programs also limited the ability to identify an effect of exercise after ACL injury on knee OA risk. Common goals included neuromuscular rehabilitation, reduction of swelling, increased joint mobility, and the modification of activities, which included a reduction in participation in sports and activities. However, because the description of the exact treatment plan was limited in most studies, comparing the effectiveness of different exercise programs was challenging. In fact, it is possible that research addressing the incidence of OA following conservative management of ACL injuries should be excluded from this review, due to not explicitly reporting their exercise management program. Future research should provide detailed reports of conservative treatment protocols and exercise programs, which would assist in offering more definitive conclusions regarding the effectiveness of exercise in reducing OA prevalence following an ACL injury.

Comparisons between exercise and operative management of ACL injuries was also limited by late operative procedures (notably ACL reconstruction). Many of the included studies initially prescribed exercise, but several participants underwent late reconstruction during the follow-up period. Finally, radiographic measurement of OA, which was included in 14 studies, is the current gold standard in diagnosing OA.[10] However, radiography is insensitive to early degenerative changes and may not be the best available tool for determining the risk of OA development. Research examining the sensitivity of different imaging modalities to evaluate OA changes in the knee, namely radiographs, computed tomography and MRI, demonstrated that MRI was better able to detect changes while also being able to evaluate soft tissue abnormalities (meniscus, ligaments).[29] Additionally, the diagnostic capability of ultrasound for OA has been recently studied.[30] While images from ultrasound denoting cartilage degeneration were a strong predictor of arthroscopic findings, negative findings from the ultrasound exam were identified in cases where arthroscopic OA was present. Thus, MRI, which is more sensitive to early cartilage changes, may be more effective in determining the risk of OA development.[10,11] Advances in imaging which enables assessment of cartilage composition with noninvasive techniques, such as transverse relaxation time (T2) mapping, may be useful in evaluating OA progression in future studies.

It should be noted that there is an important potential risk for assessor bias associated with this review due to not registering the protocol through PROSPERO. The lack of conclusive findings regarding the effectiveness of exercise treatment for ACL injuries reduces this risk. A PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) checklist, however, has been completed (Table 4) to demonstrate the scientific rigor in reporting this review.[31]

Conclusion

The collective results from this review demonstrated that the evidence regarding exercise after ACL injuries to reduce the risk of knee OA is inconclusive. However, compared to operative treatment, some evidence may suggest that exercise could increase the risk of knee instability and subsequent meniscal tears, which can further increase the risk of knee OA. However, this finding was not consistent. Additionally, research suggested that there was minimal benefit in undergoing early reconstructive treatment, with lower prevalence of OA shown in those who initially pursued exercise. Thus, initial exercise management, with the option of late ACL reconstruction, may be beneficial in reducing the risk of knee OA.

Future research specifically addressing the effect of knee stability and concomitant meniscus injuries on the development of OA and their relationship to exercise versus operative treatment of ACL injuries is required. Ideally, conducting randomized controlled or comparable trials would provide high quality evidence for ACL management and OA progression. Including activity modification treatment to prevent knee OA in ACL injured patients, rather than solely an exercise intervention may offer insight into conservative treatment strategies. Researchers suggest that modification of activity, including reduction of participation in physical activity and the avoidance of pivotal sports, may subsequently reduce the need for late ACL reconstruction.[16]

Understanding of the effects of exercise on the risk of developing knee OA is critical for the development of clinical treatment guidelines for ACL injuries. This may include differential treatment based on tear severity and activity level, in addition to combined treatments of exercise and activity modification.

Disclosure

The authors report no conflicts of interest in this work.

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