

REVIEW

# Prevention of injury-related knee osteoarthritis: opportunities for the primary and secondary prevention of knee osteoarthritis

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## Abstract

Where risk factors have been identified in knee and hip osteoarthritis (OA), with few exceptions, no prevention strategies have proven beneficial. The major risk factors for knee OA are advanced age, injury and obesity. However, there is limited or no evidence that they are modifiable or to what degree modifying them is effective in preventing development of knee OA or in preventing symptoms and progressive disease in persons with early OA. The notable exception is the growing epidemic of (sports) injury related knee OA. This review details the biological and clinical data indicating the efficacy of interventions targeting neuromuscular and biomechanical factors that make this subset of OA an attractive public health target, and highlights research opportunities for the future.

## Introduction

Osteoarthritis (OA) is the most important rheumatic disease affecting mankind. Where risk factors have been identified, such as in knee and hip OA, with few exceptions, no prevention strategies are well substantiated enough or have proven benefit to justify widespread dissemination. The major risk factors for knee OA are advanced age, injury and obesity [1]. However, there is limited or no evidence that they are modifiable or to what degree modifying them is effective or what this would cost in primary prevention (avoiding development of knee OA) or secondary prevention (detecting knee OA early to treat or prevent symptoms and progressive disease).

The notable exception is the growing epidemic of (sports) injury related knee OA. The purpose of this

review is to detail the biological and clinical data that make this subset of OA an attractive public health target.

## Joint injury increases the risk of knee osteoarthritis

The incidence and prevalence of severe knee injuries requiring medical attention are not well documented. The differential diagnosis of knee injuries includes contusion, subchondral or chondral injury with and without meniscal tear and with and without ligamentous injury or complete tear. In the best studied sports injuries, even injury not precipitating a medical visit appears to be a risk factor for knee OA; the rate is high and increasing worldwide.

Meniscus injuries are common in athletes and the general population [2,3]. Lohmander and colleagues [2] estimate that the cumulative population risk of an anterior cruciate ligament (ACL) injury between 10 and 64 years of age is about 5% based on MRI findings of the acutely injured knee, and for meniscus injury leading to surgery is at least 15%. The incidence of ACL tears is unknown but the MRI-confirmed incidence has been reported at 81 per 100,000 in a hospital-based study [4], while a population-based study estimated rates 50 to 100% higher [5]. The true incidences of both meniscal and ligamentous injuries are likely to be higher since injuries are sometimes unreported, undiagnosed, or diagnosed without MRI.

Over the past two decades there has been an alarming increase in the rate of ACL injuries in young females in sports that involve cutting, jumping and pivoting. Adolescent and mature females in these sports have ACL injuries at a two- to eight-fold greater rate than males participating in the same sports [6-8]. This, along with a ten-fold increase in the number of women participating in sports since the inception of Title IX, has resulted in a dramatic increase in ACL injuries in females in the US [9].

The risk of knee OA from knee joint injury is high; approximately 50% of individuals with an ACL or meniscus tear develop knee OA [10-15]. A long-term prospective study indicated a relative risk for knee OA of approximately 5 for any previous injury of the knee [13].

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Thelin and colleagues [16] found that knee joint injuries (and not the type of sport or other factors) accounted for all knee OA in a population-based case-control study of Swedish adults aged 51 to 70 years.

#### **Knee osteoarthritis after anterior cruciate ligament injury**

Individuals with ACL ruptures comprise an estimated 25% of the overall knee OA population [17,18]. In male and female soccer players sustaining ACL tears, approximately 80% had radiographic OA 12 to 14 years later, irrespective of whether they had had surgical intervention; approximately 70% had functional limitations and reduced quality of life due to their knee [10,12]. While short- and mid-term results of ACL reconstruction are satisfactory, 10 to 20 years after injury approximately 50% of those with ACL or meniscus tear have OA with associated pain and functional impairment [2]. Since ACL injury often occurs in young adulthood, OA development for many, if not most, is a distinct probability by their late 30s or 40s. Identification and implementation of disease-delaying treatment would be a major advance.

#### **Knee osteoarthritis and meniscal injury**

Degenerative meniscal pathology, that is, horizontal cleavages, flap or complex, are common - present in approximately a third of the general population over 50 years of age [3] - and are associated with increasing age, existing OA, and progression of OA [19]. Traumatic tears usually occur in younger individuals, increase the risk of OA [19] and appear to be an early event in the disease process [20].

Meniscectomy is a significant risk factor for knee OA - the relative risk after total meniscectomy is six times greater than for un-operated controls [21]. In a prospective study of ACL-injured patients followed for 15 years, the primary risk factor for tibiofemoral OA was a prior meniscectomy [22].

The high incidence of OA after injury highlights a potential opportunity to improve population health and is a strong rationale to direct increased efforts toward primary prevention of knee injury and improved management of knee injury. A decade ago it was estimated that prevention of joint injuries would yield an approximately 14 to 25% reduction in OA prevalence [23]; with the alarming increase in female knee injuries in the past decade and an increased ability to detect injury using imaging, the risk of knee OA attributable to injury may be higher now.

#### **Primary prevention of injury-related knee osteoarthritis**

##### **Prevention of knee injuries**

It is possible to prevent a substantial number of knee injuries. Studies over the past decade have identified new

and modifiable risk factors for knee injury and mechanisms of injury and provide evidence from multiple interventional prospective longitudinal studies and randomized controlled trials of how these factors can be modified.

Risk factors for knee injury include intrinsic (anatomic, neuromuscular, hormonal) and extrinsic factors (environmental, including knee bracing, shoe-surface interface, weather). The efficacy of knee bracing to prevent knee injury has been studied - mostly in American football and soccer players - and has shown contradictory results, with some studies reporting relative risk reductions in injury incidence of 10 to 50% [24-26], while others have reported increased risks of similar magnitude [27-30]. Compliance is a major issue as athletes may fear impaired performance and discomfort [27,31]. Rigorous randomized controlled trials are needed.

The playing surface and variable friction at the shoe-ground interface might be a determinant of knee injuries. Higher friction can result from surface type, shoe type and, in outdoor fields, ground hardness, dryness, grass cover and weather conditions. Studies of grass versus artificial turf in soccer and American football show that risk of knee injury is either not related to playing surface [32-34] or is slightly more common on older artificial surfaces [35]. In European team handball, floor type (artificial versus wooden) was a significant risk factor for ACL injuries in women [36,37].

Several studies demonstrate that knee injuries are increased on shoe-surface interfaces with higher friction (older artificial turf, dry hard fields) [35,38,39]. A 10-year study of 5,910 NFL games found that cold weather is associated with lower knee and ankle injury risk in outdoor stadiums with both natural grass and artificial turf, probably because of reduced shoe-surface traction [38,39]. A controlled biomechanical laboratory study showed that a high shoe-surface friction alters biomechanical movement patterns that increase the risk of ACL injury [40].

There is strong evidence for the role of intrinsic risk factors in the etiology of knee injury. Studies of the neuromuscular and biomechanical substrate of knee injuries show that most knee injuries are not the result of contact or collision, and that distinctive biomechanical patterns, such as excessive coronal plane motion (valgus collapse), are seen when the knee is injured [41-43]. Other kinematic factors associated with ACL injury include less knee flexion [43,44], decreased core and trunk control [45] and increased hip flexion, landing flatfooted and with less plantar flexion [42]. These observations led to the hypothesis that the ACL 'epidemic,' especially in females, is primarily neuromuscular and biomechanical in nature and can be modified.

Prevention strategies based on neuromuscular training programs were subsequently designed to train athletes to

land and decelerate in a more controlled fashion with reduced valgus collapse, increased knee flexion and improved trunk control, balance and proprioception. While there is not a consensus on program parameters, training is typically in 6- to 8-week progressive sequences doing sport maneuvers in simulated game situations and/or in 10- to 15-minute pre-game and pre-practice warm-up routines. A meta-analysis examining the relative effectiveness of six interventions for reducing ACL injuries in females found that neuromuscular training may reduce ACL injuries if plyometrics, balance and strengthening are incorporated, and training sessions occur more than once per week and are a minimum of 6 weeks in length. The studies with the greatest impact on ACL risk incorporated high-intensity plyometric movements that progressed beyond footwork and agility [46].

From this has emerged a strong body of level 1 and 2 evidence that biomechanical risk factors for knee injury can be averted [47-49] and knee injuries substantially reduced [50-55]. Three recent large-scale randomized controlled trials [50-52] confirmed previous randomized controlled studies and support the utility of prevention programs in preventing knee and lower extremity injury [50-55]. The potential risk reductions for ACL injury are substantial, being 41 to 88% [50-52,54]. Of the few studies that have shown little or no effect on injuries, low athlete compliance likely played a role [56,57].

#### **Prevention of knee osteoarthritis after knee injury**

Once the knee is significantly injured, the incidence of eventual knee OA is dramatically increased. It poses a challenge for the clinician and for those involved in injury prevention [58] to devise a secondary prevention strategy. There is reason to be cautiously optimistic that this is possible.

#### ***Joint biomechanics and neuromuscular function in OA development after injury***

Biomechanical factors may be a potent driver of OA after injury [59], but because of the long latency period in knee OA, study is difficult.

Knee alignment is one such biomechanical factor. Varus alignment is associated with medial compartment OA and valgus alignment with lateral compartment OA, and there is strong circumstantial evidence that malalignment is important in disease progression [60]. Surgical re-alignment by osteotomy to unload the involved compartment appears to slow progression in the unloaded side and hastens progression on the loaded side in patients with uni-compartmental OA [61].

The injury itself alters biomechanics that may make the joint vulnerable to OA. Meniscus injury decreases the load bearing and shock absorbing function of the joint, increases tibial-femoral loading and decreases joint

stability [62-64]. Damage to ligaments and the joint capsule may shift contact pressure of the joint surfaces during gait, which can result in degenerative metabolic changes in localized regions of cartilage [65].

Neuromuscular function is the complex interaction between sensory and motor pathways [66]. Significant knee injuries that damage ligaments and joint capsule can result in reduced muscle strength and activation [67-69] and may damage normal mechanoreceptors [70]. These are critical to normal joint protection whereby loads are anticipated and muscles and tendons assume the correct tension to deflect and distribute loads across the whole joint surface or lessen the rate with which the load is applied to the joint [71].

Individuals with knee injuries have a host of demonstrable but treatable neuromuscular impairments after injury, such as decreased quadriceps strength [69], poor lower limb positioning and proprioceptive deficiencies [72-74] and impaired postural control [66,75], that may be caused or exacerbated by arthrogenic inhibition and muscle guarding [68,76,77]. Without addressing these impairments, it is probable that even low or moderate activity after injury may increase risk of knee OA. Reduced neuromuscular control impairs normal joint protection mechanisms, leaving the joint vulnerable to increased loads and shear forces. These and shifts in contact distribution may play a role in cartilage degradation [65,78,79].

#### ***Can OA be prevented or delayed after injury?***

##### *Surgical treatment*

Surgical reconstruction of the ACL restores short-term function and has good patient reported outcomes, but does not prevent knee OA [2,10,12,80]. While ACL reconstruction restores knee stability, it does not restore normal mechanics [81,82], resulting in a shift in functional load bearing with rotational malalignment that may direct weight-bearing loads on regions of cartilage that are not able to withstand them [82,83]. While the reasons are not entirely clear, a contributing factor in surgical reconstructions may be the placement of the ACL graft, in particular the sagittal/coronal orientation [84]. Several longitudinal studies [85-87] have shown higher rates of both tibiofemoral OA and patellofemoral OA with a patellar tendon autograft versus a semitendinosis or gracilis autograft. There is evidence that traditional surgical decision making based on passive anterior knee laxity and pre-injury activity level are not good predictors of dynamic knee stability and function after surgery. Screening for neuromuscular function using such tests as the timed hop test and self-reported symptoms, such as knee giving-way, may be better predictors of function and help guide individualized patient management after ACL injury [88,89].

Randomized controlled trials investigating arthroscopic treatment of meniscal and chondral damage show no benefit of surgery over conservative treatment [90,91] or placebo surgery [92]. Meniscectomy is associated with subsequent knee OA [19,93] and the higher risk is associated with the greater amounts of meniscal tissue removed [11]. Arthroscopy, while shown to be promising in uncontrolled studies, is not efficacious in OA [94].

#### *Exercise therapy*

While exercise and neuromuscular training are theoretically beneficial and common treatment for knee injury, their efficacy in treating knee injury and preventing OA and the superiority of one form of exercise intervention over another are not supported by high quality trials [95,96]. Several observational studies have investigated conservative exercise-based management of ACL injury, or compared it to reconstructive surgery for longer term outcomes [14,22,80]. There is some evidence that non-operative treatment may result in a lower rate of OA than surgical repair, particularly in patients willing to modify their activity. A prospective study [22] following up subjects 15 years after non-operative treatment of ACL injury found favorable functional outcomes and an exceptionally low incidence of radiographic knee OA. The primary treatment algorithm involved early activity modification and neuromuscular rehabilitation. The primary risk factor for OA was meniscectomy. Other observational studies have reported comparable outcomes with non-operative treatment versus reconstruction of ACL tears [97], some noting lower rates of OA in non-surgical groups [10,14,98]. In observational studies of surgery versus no surgery, unmeasured confounding, particularly confounding by indication, may bias the results. The first high quality randomized controlled trial comparing surgical and non-surgical treatments for ACL tear was recently published [99], and concluded that structured rehabilitation with early reconstruction was not superior to a strategy of structured rehabilitation plus optional delayed ACL reconstruction. In the latter treatment arm, 60% of ACL reconstructions were avoided without adversely effecting outcomes at 2 years.

The role of exercise alone in preventing OA after injury has received limited study. Decreased muscle performance is a risk factor for OA in the young and middle-aged adult [100]. Neuromuscular function of the quadriceps [101] and lower extremity performance [102] is impaired in subjects at risk for, but prior to onset of, radiographic OA, suggesting that muscle dysfunction precedes structural evidence of OA. There is evidence that moderate neuromuscular exercise improves joint symptoms and function and cartilage quality in those at high risk of developing OA [103]. From a population

perspective, there is evidence that moderate physical activity and specific exercise regimens play a significant role in prevention of knee OA. Animal and human studies demonstrate that being physically active or specific exercises enhance cartilage properties, suggesting a pathway to prevent or delay OA [103-105]. An epidemiologic study of 55 to 75 year olds showed that regular, moderate physical exercise over the lifetime decreased the risk of severe knee OA [106]. Whether exercise could prevent knee OA after knee injuries, however, has not been adequately studied.

#### **Prevention of knee OA may start with the young: the role of physical activity and screening**

There is circumstantial evidence that knee OA prevention might start in childhood. The benefits of physical activity in childhood on bone mass persist into adulthood [107], but the effect on joints and cartilage is less well known. An MRI study of children aged 9 to 18 years found younger children, males and those undertaking more vigorous sports have substantially higher articular cartilage accrual rates [108]. While there are limitations to the available studies, the current evidence supports a prescription of vigorous physical activity for optimum joint development in children [109]. Vigorous activity would also reduce childhood and possibly adult obesity - a leading risk factor for knee OA [1].

Citing the evidence that childhood and adolescent exercise and joint injury have long-term effects in adulthood, Nicholson and colleagues [110] have recently proposed a screening program of adolescents covering sports and activities, joint injury, body mass index and family history. There is evidence that screening may identify athletes at future risk of ACL rupture through assessment of neuromuscular activation in the lower limb [111] and core and trunk control [45], and standardized functional movement testing [112].

The identification of adolescents with early knee injury and those with potential neuromuscular and other risk factors might permit targeting of at-risk groups for exercise interventions, activity modification and education that may have an impact on prevention of knee OA, but this needs study.

#### **Future directions**

OA is the major public health problem in musculoskeletal medicine and the current evidence suggests that at least one subset, injury related knee OA, could be prevented and its incidence and prevalence markedly reduced. The strongest biological rationale is for implementing evidence-based interventions targeting neuromuscular and biomechanical factors. The attributable risk reduction from this alone can only be surmised at this time but is amenable to study.

The most pressing need is to disseminate what we know works - strong evidence from multiple studies confirms that large numbers of knee OA cases are preventable. Translating knowledge of proven, injury prevention programs is a necessary next step. The richest target may be school- and university-aged students, reached through physical education curriculums and improved sports associations. An example is FIFA, the international governing body of the world's largest sport (by participation). They have studied and developed an injury prevention program - the FIFA 11 - which is simple and accessible worldwide through its Internet site [113].

The injured knee joint presents a rich opportunity for investigation of neuromuscular and biomechanical factors - the mechanical and physiological changes post-injury place these joints essentially in a pre-OA state, but with no apparent clinical or radiological signs of OA. There is a need for a neuromuscular screening tool to identify which knee-injured individuals are at highest risk for future OA development, and to determine neuromuscular and biomechanical signatures that predispose to OA. Target components include measures of muscle strength and activation, functional movement patterns, proprioception and alignment. Advanced imaging, including MRI and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), which can detect early incident OA, are available to use as a gold standard to validate such screening instruments. Although the evidence is incomplete, health care professionals should target knee-injured individuals for primary prevention with respect to education, activity modification and the role of re-establishing neuromuscular function and exercise in surgical decision-making and rehabilitation.

There is a strong need to assemble early post-injury cohorts prior to OA development. Rigorous long-term randomized trials that evaluate surgical and conservative methods of treatment are required. In addition to established patient-reported outcomes, validated neuromuscular and biomechanical measures should be used since structural radiological change is a late sign.

Of particular interest, given the success of neuromuscular programs in altering risk factors and incidence of knee injury, is whether similar exercise strategies could be used to modify OA development and progression after injury. Similar trunk, hip and knee control strategies could be applied to knee-injured individuals.

Since most ACL and other types of knee injuries occur in the young population, the effectiveness of adolescent screening and the timing, nature, duration and compliance with intervention programs are other important areas of investigation.

Other chronic diseases with long latent periods (for example, osteoporosis, atherosclerotic vascular disease) have developed primary and secondary prevention

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strategies. OA has long been ignored. With new knowledge that goes beyond the description of risk factors, we have the opportunity to test a population strategy for one preventable subset. Knee injury prevention and injury management offer a significant opportunity to address knee OA at an earlier stage.

#### Abbreviations

ACL = anterior cruciate ligament; MRI = magnetic resonance imaging; OA = osteoarthritis.

#### Competing interests

The authors declare that they have no competing interests.

#### Acknowledgements

Supported by grants from the Molson Foundation, the Michael Smith Foundation for Health Research and a Canadian Institutes of Health Research Fellowship.

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Published: 31 August 2010

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doi:10.1186/ar3113

**Cite this article as:** Ratzlaff CR, Liang MH: **Prevention of injury-related knee osteoarthritis: opportunities for the primary and secondary prevention of knee osteoarthritis.** *Arthritis Research & Therapy* 2010, **12**:215.