REVIEW

Muscle dysfunction versus wear and tear as a cause of exercise related osteoarthritis: an epidemiological update

Ian Shrier

Br J Sports Med 2004;**38**:526–535. doi: 10.1136/bjsm.2003.011262

There are two main hypotheses for the cause of exercise related osteoarthritis: wear and tear of the articular cartilage and muscle dysfunction. This is a review of the clinical literature to see which hypothesis has the greatest support. Clinical studies support the muscle dysfunction hypothesis over the wear and tear hypothesis.

Osteoarthritis (OA) often limits activities of daily living—for example, climbing stairs, dressing[1]—and can prevent participation in the labour force for younger patients.[1] Patients seek advice from family doctors, internists, rheumatologists, and orthopaedic surgeons.

Recently sponsored symposia in both the United States[2] and Canada (co-sponsored by the Canadian Institutes of Health Research and the Canadian Arthritis Network, Toronto, Ont, April 2002) suggest that OA is a complex syndrome—that is, constellation of symptoms and signs with multiple causes—that involves the balance between cartilage synthesis and degradation, and affects all tissues surrounding the joint. That being said, the question remains as to which factors are directly related to the cause of OA and are modifiable so that doctors may counsel patients appropriately.

In the case of primary OA—that is, excluding genetic diseases, severe biomechanical abnormalities, post-septic arthritis, etc—many health-care professionals believe the major cause of OA is ''wear and tear''—that is, gradual thinning of the articular cartilage due to repeated weight bearing activity of the joints—and that therefore OA is caused and worsened by exercise. However, in 1999, Hurley[3] reviewed the basic science evidence and proposed that properly contracting muscles are the main force absorber for the joint, and that muscle dysfunction is the most important modifiable mediating factor for primary OA. Because regular exercise improves muscle function, this hypothesis predicts that exercise would not increase the incidence of or worsen OA. Hurley also suggested that whereas the wear and tear hypothesis predicts that cartilage thinning will be the first sign of OA, the muscle dysfunction hypothesis predicts that sclerosis would be the first sign. Finally, in the case of injury, the muscle dysfunction hypothesis predicts that injuries to muscles in a leg may increase the risk of OA in joints not immediately adjacent to the injured muscle because impact forces are not being properly absorbed. The wear and tear hypothesis suggests that injuries would only increase the risk of OA if articular cartilage injury occurs at the time of injury, or is more likely to occur after injury—for instance, anterior cruciate ligament (ACL) instability. The specific objective of this systematic review is to determine the clinical evidence in support of and against the hypotheses that exercise related OA is caused by (*a*) wear and tear or (*b*) muscle dysfunction.

The reader should not forget that OA is multifactorial and that there are other causes of OA. As such, there are two important limitations to the scope of this article. Firstly, it focuses on both hip and tibiofemoral OA and does not discuss patellofemoral OA, or OA in other areas of the body. Secondly, regardless of the initiating event of OA in a particular patient, the articular cartilage is eventually destroyed. The mechanism of articular cartilage destruction is also beyond the scope of this article.

MATERIALS AND METHODS

A systematic review of the literature was carried out. Medline and SportDiscus databases were searched using the strategy (osteoarthritis or osteoarthrosis) AND (activity or exercise or injury). Based on titles and abstracts, all potentially pertinent articles were retrieved and reviewed. The bibliographies of all articles retrieved were reviewed for additional references, and a search of Citation Search Index was conducted to find any article that may have cited one of the key articles previously retrieved. Data were abstracted by one person using a standardised form, and verified with a second reading by the same person at least four weeks later. This review is limited to exercise related primary OA, and studies investigating OA secondary to injury or previous surgery were not included in the results.

Results are presented as odds ratios (OR) or relative risks (RR) or hazard ratios (HR) with 95% confidence intervals (95%CI) in parentheses unless otherwise specified. Because many studies lacked the necessary power to determine if the differences were statistically significant, relying on p values or confidence intervals might result in a β error (incorrectly indicating that the differences between groups were not important). Therefore, the emphasis in this review is on the

Correspondence to: Dr Shrier, Lady David Institute for Medical Research, Centre for Clinical Epidemiology and Community Studies, SMBD-Jewish General Hospital, 3755 Cote Sainte-Catherine Road, Montreal H3T 1E2, Canada; ian.shrier@mcgill.ca

Accepted 29 March 2004

Abbreviations: OA, osteoarthritis; OR, odds ratios; RR, relative risk; HR, hazard ratio; 95%CI, 95% confidence intervals; ACL, anterior cruciate ligament; Exp, exercise group; Con, control group

direction and magnitude of the changes—that is, are the changes clinically relevant?— rather than whether a study had significant results.

Because the clinical studies reported different outcomes, used widely differing methodology, etc, a qualitative synthesis was more appropriate than an attempt to provide an overall summary statistic for the estimate of the effect.

RESULTS

Twenty three clinical articles (representing 18 studies) related to exercise and OA were retrieved. Table 1 presents studies on running, table 2 presents studies on football, and table 3 presents studies on other sports. Where studies reported on more than one type of exposure, the relevant details are repeated under each section and the duplication noted.

Table 1 Details of studies related to running exposure (95% CI in parentheses)

Article	Population	Design	Results	Comments
Exercise associated with OA				
Marti[16] (n = 59)	Males, age range not reported. Exp: 27 ex-elite long-distance runners and 9 bobsleigh from 1973. Con: 23 untrained men from "randomised training study" in 1973.	Historical cohort with 15 yrs follow-up. Information obtained by recall. Blinded assessment of X-rays. Follow-up in 1988.	Mean values Joint space: Runners 3.8 (3.4 to 4.2); Bobsleigh 4.7 (4.1 to 5.2); Control 4.0 (3.6 to 4.4) Composite knee score: Runners 1.4 (0.8 to 2.0); Bobsleigh 0.3 (–0.05 to 0.7); Control 0.3 (0.0 to 0.6) Grade 2 subchondral sclerosis and osteophytes only present in runners. Running pace was a better predictor of radiological hip OA. Hip pain was present in 30% of the runners, but 0% of bobsleigh or control groups.	Response rate 27/27 runner, 9/12 bobsleigh and 23/26 controls. OA scored separately as joint space, sclerosis and osteophytes, and also as a composite score ranging from 0–9. Although composite score worse for runners, the mean score was only 1.4 of a total score of 9. Still, 4/27 runners had joint space <3 mm whereas there were no bobsleigh or control subjects with this limited amount of joint space.
Cheng[17] (n = 16 961)	Males (n = 12 888 and females (n = 4073). Ages 20–87. Exp: Low = walk or jog <10 miles/wk (n = 3006) males, 1029 females), Mod = walk or jog 10–20 miles/wk (n = 1760 males, 495 females), High = walk or jog >20 miles/wk (n = 1003 males, 211 females). Other category (n = 2846 males, 1042 females) not included in this report. Control: sedentary (n = 4273 males, 1296 females).	Historical cohort with mean (SD) follow-up time ~10 (6) yrs. Information obtained by survey. Self-reported exposure and outcome so no blinding.	Hazard ratios for self-reported OA adjusted for BMI, alcohol, smoking, caffeine (reference category = sedentary). Males / Females **<50 yrs old** Low 1.0 (0.6 to 1.5) / 0.8 (0.8 to 1.6) Mod 1.2 (1.0 to 1.4) / 1.2 (1.2 to 1.5) High 2.4 (1.5 to 3.9) / 1.5 (1.5 to 5.1) **>50 yrs old** Low 1.3 (0.9 to 1.8) / 0.6 (0.3 to 1.2) Mod 1.0 (0.8 to 1.2) / 1.2 (0.9 to 1.5) High 1.2 (0.6 to 2.3) / 1.4 (0.4 to 4.6)	The inclusion of people as young as 20 for an outcome of OA may be inappropriate. The mean follow-up time suggests skewed distribution and we are not sure of minimum follow-up time. Some subjects in mod or high categories may have been walkers instead of runners. There was another category of "Other" referring to activity that is not walking or jogging. This was omitted in this review because details of the activity were not reported. Although results not significant for women, there does appear to be some association for young men involved in high levels of activity. However, this is not true for older men, suggesting that it is not simply the activity that is the problem.
Spector[18] (n = 1058)	Women, ages 40–65. Exp: ex-elite runners (middle and long distance) and tennis players (n = 81) Con: General population survey (n = 977).	Historical cohort (15–45 yr follow-up). OA status by x-ray and exposure status by recall. Blinding not reported.	OR for elite vs controls for different joints (adjusted for age, height and weight). Osteophytes / Narrowing Tibio-femoral 3.6 (1.9 to 6.7) / 1.2 (0.7 to 1.9) Patello-femoral 3.5 (1.8 to 6.8) / 3.0 (1.2 to 7.7) Hip 2.5 (1.0 to 6.3) / 1.6 (0.7 to 3.5) OR for control women with a history of different levels of physical activity (reference is low physical activity). Long term = ">4 units/wk", Moderate = "1–3 units/wk" Hip joint space narrowing / Tibio-femoral joint space narrowing Long-term 1.80 (0.73 to 3.48) / 0.85 (0.31 to 2.04) Moderate 1.05 (0.54 to 2.12) / 0.80 (0.52 to 1.08) The OR point estimates are estimated from a figure but the confidence intervals were exactly given.	Response rate 81/117 elite athletes and 977/1003 controls. Adequate information on physical activity in controls available in only 585/977 controls. OA assessed by joint space narrowing and osteophytes, but no total score. Among the control population with differnt levels of physical activity, the OR for joint space narrowing among the people with a past history of long-term physical activity was close to that of the elite athletes. The respective OR for osteophytes (among controls) was much higher than that of joint space narrowing. They were not reported here for space limitations. Note that the importance of osteophytes is not yet clear[56].
Vingård[18] (n = 569) The results of this study related to soccer are reported in table 2, and the results related to the total sport participation are reported in table 3.	Males, ages 50–70. Cases: Total hip replacement 2° idiopathic OA in 4 Swedish hospitals (n = 247 partial participation, 233 partial participation). Controls: Swedish men living in area of same 4 hospitals (n = 322 partial participation, 302 complete participation).	Case-contol. Information by recall. Blinding of evaluators for exposure not reported.	RR for total hip replacement among runners, adjusted for age, BMI, smoking and physical load at work. Medium / High Long-distance runners 1.7 (0.4 to 6.9) / 2.1 (0.6 to 6.8) Track & field and racquet sports had highest RR (~2.4 for medium exposure and ~3.5 for high exposure) among all sports.	Response rate 233/253 (92%) for full participation among cases, and 302/392 (72%) among controls. Slightly greater partial participation rates for both groups. Relative risks estimated from OR. Exposure information obtained by recall during interview. Authors note that recall in myocardial infarction patients and controls found no increased RR and they suggest that shows recall not a problem. However, if regular physical activity is protective against infarction, and recall not an issue, then physical activity should have been protective.

Table 1 Contd

Exercise not associated with OA

Lane[4; 19–21] (n = 55 for 9-yr follow-up)	Males and females, ages 50–72 at onset. Exp: Members of 50+ runners club, running 17.9 miles/wk at follow-up (25.3 miles/wk at onset, n = 28). Con: Sample from Lipid Research Clinics Study in same community, matched for age, sex, education and occupation (n = 27).	Prospective cohort with 9-yr follow-up. Blinded assessment of x-rays.	Change in x-ray score (higher score means progression of OA sign). Knee: Runners 0.80 (0.23) / 0.20 (0.10) / 0.96 (0.28); Non-runners 0.67 (0.32) / 0.32 (0.12) / 1.03 (0.42) Hip: Runners 0.50 (0.10) / 0.27 (0.10) / 1.14 (0.20); Non-runners 0.65 (0.30) / 0.52 (0.10) / 1.62 (0.50) Changes in hip not significantly different between groups for any score, but non-runners had more knee joint space narrowing and fewer knee osteophytes than runners (total score not significantly different).	Response rate: 43 subjects of original cohort (n = 98) followed for 9 years. No difference between group that returned and those that did not return. OA graded osteophytes, joint space and sclerosis separately, and then composite score. One paper was original cross-sectional analysis, followed by three papers published using the same subjects with 2, 5 and 9-yr follow-up report. Results used are from the 9-yr follow-up report. Results at 5 years were qualitatively similar for the knee (hip results not presented prior to 9 yr follow-up).
Kujala[13–15] (n = 2059) The results of this study related to soccer are reported in table 2, and the results related to overall sport are reported in table 3.	Males, ages 21–86. Exp: 1282 ex-elite male athletes from a wide variety of sports. Con: 777 men from medical exam for compulsory military service. Study 1[14] used hospital admission records as outcome. Study 2[15] used sub-sample of subjects (n = 28 runners, 31 soccer, 19 weight lifters and 29 shooters). Shooters (i.e. no impact or elevated joint pressure) were controls. Study 3[13] used self-reported pain and used follow-up of 30–75 yrs.	Three different studies, all historical cohort with 20–65 yr follow-up. Independent variables by recall. Blinded assessment of x-rays in Study 1 (National Registry) and Study 2. Outcome in study 3 was self-report.	Study 1: Survival analysis graph: Risk of hospital admission for OA (hip, knee or ankle) similar among controls and distance running/skiing until age 70, then controls less admissions. All other sports had higher admission rates throughout life. OR (adjusted for age, occupation and BMI): Sport: Distance running/cross-country skiing — OR 2.4 (1.3 to 4.7) Study 2: Used shooters as control group. Stepwise regression final model: BMI, previous injury, hours in team/endurance/power sport, hours in heavy or kneeling/squat work. Runners: OR 4.8 (0.48 to 47) age adjusted — OR (final model) "Not significant" Previous injury: OR 7.9 (univariate, from % data supplied) — OR (final model) 6.0 (1.3 to 27.8)	Study 1 response rate: 1282/1518 (84%) athletes and 777/1010 (77%) controls. The total number of approached subjects (n = 2528) represented 60.8% of original cohort (39.2% died before start of study). Study 2 response rate: 117/147 (80%). The 147 denominator represented all long-distance runners, soccer players, weight lifters and shooters. The results after controlling for previous injury are remarkable and strongly suggest the effect seen in Study 1 is due to injuries. OA defined as per hospital record diagnosis in Study 1, as per Kellgren and Lawrence (Grade 2 or more) for Study 2. Results for Study 3 are not shown because this study used pain as the outcome instead of OA, and used the same cohort.
Puranen[11] (n = 175)	Males, ages 31–81. Exp: ex-elite runners (winners of several Finnish Championships) who ran competitively for 8–21 years (n = 60). Con: male patients from University Hospital (n = 115).	Historical cohort with 8–50 years. Information obtained by recall. Blinding not reported.	Runners: Mild–Mod OA 2.7% — Severe OA 1.4% Control: Mild–Mod OA 7.0% — Severe OA 1.7% Although 9% of runners and 15% of controls had osteophytes, no subjects with only osteophytes complained of pain.	Response rate not reported. OA not defined but reported numbers mean that a diagnosis required more than just osteophytes. X-rays done between 1963 and 1974, but questionnaire on pain only in 1974. Follow-up time is therefore not clear.
Sohn[12] (n = 791)	Males and females (n not specified), ages 23–77. Exp: Ex-varsity runners (n = 504) Con: Ex-varsity swimmers (n = 287).	Historical cohort. Follow-up not clear. Information obtained by recall. Outcome = Pain, not OA. Blinding of evaluators not reported.	Main Outcome = Pain Runners: Severe hip or knee pain 2% — Any hip or knee pain 15% Swimmers: Severe hip or knee pain 2.4% — Any hip or knee pain 19% Proportion of group with surgery for pain: runners = 0.8%; swimmers = 2.1%. Average Mileage Among Runners Split by Age Age: Pain / No pain 0–40: 58.5 / 54 40–49: 33.4 / 27.9 50–59: 30 / 24.9 60–69: 17.9 / 16.3 70+: 18.8 / 18.8	Response rate = 504/658 (77%) for runners and 287/495 (58%) for swimmers. This study used pain rather than OA as the outcome. Exp subjects had competed between 1930–1960, and the age of subjects ranged 23–77. This means that survey had to be done in 1963, but the paper was published in 1985. Ex-runners with pain had slightly increased mileage compared with those who did not have pain, but the differences appear clinically irrelevant and were not statistically significant. Age not different between groups, but not formally analysed.

Running/soccer

Overall, the three cross sectional running studies concluded that exercise is not associated with OA,[4–6] and the three case-control running studies found mixed results but overall suggested that some higher intensity activities may be associated with the development of OA.[7–9]

With respect to historical cohort studies on running, there was no increased risk of OA in runners in four of seven historical cohort studies. This was true for (*a*) 27 elite Danish male orienteering runners compared with hospital controls,[10] (*b*) 60 Finnish male elite runners compared with hospital controls,[11] (*c*) 504 US college varsity cross country runners compared with varsity swimmers,[12] and (*d*) 1282 Finnish ex-elite male endurance athletes after controlling for previous injury (three papers published on the same cohort[13–15]).

In one study showing a possible increased risk of OA in runners,[16] running pace was a better predictor than running mileage even though the wear and tear hypothesis would predict that OA should increase with each vertical impact—that is, step—more so than horizontal speed. Horizontal speed would be important if the running technique was suboptimal, and the runner placed the foot in front of the body at heel strike, thereby creating a large breaking force. However, this breaking force slows the runner down and

Table 1 Contd

Lau[8] (n = 1868) Results for this study related to soccer and previous injury are reported in table 2.	452M, 1416F, ages not reported. Cases: Primary OA diagnosed in Hong Kong hospitals (n = 30 males and 108 females for hip, and 166 males and 492 females for knee). Controls: Consecutive patients without OA from 8 general practice clinics in same region, matched on age and sex (n = 90 males and 324 females for hip, and 166 males and 492 females for knee).	Case-control. Exposure defined as "performed sports activities regularly". Not clear when exposure occurred. No blinding but used standardised questionnaire for exposure data.	Univariate OR for OA of hip due to sport Males: Running 0.6 (0.3 to 1.4); Females: Running 1.4 (0.7 to 2.8) The above results are univariate as multivariate analysis only included variables found to be significant in univariate analysis. OR for gymnastics in multiple regressiion was 1.9 (1.3 to 11.1) and running not included as not significant.	Response rate not reported. Diagnosis by American College of Rheumatology criteria.
Panush[5] (n = 35)	Males, ages 50–74. Exp: runners with 20 miles/wk × last 5 yrs (n = 17). Con: sedentary, non-obese (n = 18)	Cross-sectional as Exp had to be currently running. Exposure information obtained by recall. Blinded assessment of x-rays.	OA Runners: Osteophytes 7.6 (5.7); Hip cartilage (mm) 4.6 (0.8); Degeneration in knee (%) 6% Control: Osteophytes 8.4 (4.6); Hip cartilage (mm) 4.3 (0.7); Degeneration in knee (%) 17% Knee OA in runners was all Grade 1, and control was split equally between Grades 1–3. There was no degeneration in the hips or ankles of either group. Pain Runners: Hip 23%; Knee 29%; Ankle 12%; Foot 5% Control: Hip 11%; Knee 22%; Ankle 5%; Foot 0%	Response rate not reported. OA grade on loss of joint space, sclerosis and osteophytes. The discrepancy between pain and OA underscores the importance for the need of radiological evidence of OA in these types of studies, i.e. runners often have knee and hip pain unrelated to OA. Study had 90% power to detect 30% difference in cartilage thickness. 53% of runners were marathon runners, which suggests a higher level of competitiveness than recreational runners. Because Exp had to be current runners, high danger of healthy worker bias.
Konradsen[10] (n = 54)	Males, ages 50–68. Exp: ex-elite Danish male orienteering runners from 1950–1955. Average years of running = 40 (range 32–50) (n = 27). Con: Sedentary males matched for age, height, weight (at follow-up) and physical workload (n = 27)	Cross-sectional. Runners had been running for 15–25 yrs. Information obtained by recall. Blinding not reported.	Degeneration (%) Runners: Hip 5%; Knee grade 3 4%; Ankle 0% Controls: Hip 4%; Knee grade 3 0%; Ankle 4% Cartilage thickness essentially the same. Osteophytes per subject essentially the same.	Response rate 30/33 for runners but not reported for Controls. 30 runners in study, but 3 are excluded from analysis because no longer runners. However, one of these had low back pain and one had stopped because of hip OA. OA defined by joint space narrowing and sclerosis, but osteophytes also enumerated. By matching on physical workload at follow-up, we cannot eliminate a "healthy worker" effect. This is because runners with pain would decrease their occupational loads, and therefore the "matched" controls would have lower occupational loads than normal population.

Studies are sorted by whether the results suggest an association between exercise and OA or not, and by study design within each category.

• OA: osteoarthritis

• Exp: Exercise group

• Con: Control group

• Historical cohort: For the purpose of this review, any observational study for which the exposure clearly predates the outcome was considered either a cohort study (groups assembled based on exposure history) or a case-control study (groups assembled based on presence or absence of OA). Although some historical cohort studies might be considered cross-sectional studies by other authors (e.g. when all information obtained by interview at one point in time), we felt that the important distinction between these two categories is the ability to determine if the exposure preceded the outcome (i.e. historical cohort study).

therefore would not be expected to correlate with running speed.

Another historical cohort study suggested an increased risk in runners younger than 50 who run >20 miles a week.[17] An effect of mileage was not seen in subjects older than 50, which again is contrary to what would be predicted by the wear and tear hypothesis. In the remaining study showing a possible increase in OA,[18] osteophytes were associated with elite exercise, but the OR for joint space narrowing was close to 1 for the knee (1.2, 95%CI 0.7 to 1.9) and for the hip (1.6, 95%CI 0.7 to 3.5). Within the control population, moderate exercise was not associated with joint space narrowing of the hip or knee, although there was a trend toward decreased joint space of the hip in the higher participation category (1.8, 95%CI 0.73 to 3.48).

In the only prospective study, Lane and colleagues[19–21] found no difference in the development or progression of OA between 41 runners and matched controls after two, five, or nine years. In another study that simply categorised exposure as ''sport participation'', there was again a lack of progression of OA.[22]

Besides pure running, team sports such as soccer have also been implicated as a cause of OA. Although Klunder *et al*[23] found a higher proportion of radiographic hip OA in soccer players, 13/30 patients with OA had previous injuries compared with only 3/19 controls. Lindberg *et al*[24] found hip OA was higher only in the elite soccer players (14.1% for elite, 4.2% for non-elite, and 4.2% for control).

In summary, these findings suggest that moderate intensity impact sports do not cause or worsen OA. OA in high intensity or elite sports could be due to a threshold effect—that is, wear and tear only occurs after a threshold—or some other factor, and a closer examination is warranted.

Table 2 Details of studies related to soccer exposure (95% CI in parentheses)

Article	Population	Design	Results	Comments
Klunder[23] (n = 114)	Males, ages 40–79. Exp: 57 ex-elite soccer players. Mean playing 6.7 hrs/wk during period of activity. Con: 57 admitted hospital patients matched for age and weight	Historical cohort with mean follow-up 22.8 yrs (range 11–41). Information obtained by recall. Blinding of evaluators not reported.	% with OA Hip: Exp 49%, Con 26% Fem-Tib: Exp 9%, Con 9% Fem-Pat: Exp 11%, Con 9% Injuries: 13/30 soccer players with OA had previous injury. 3/19 control subjects with OA had previous injury. Fracture: Exp (n = 13*) 3, Con (n = 3) 1 Meniscus: Exp 6, Con 2 Other: Exp 7, Con 0 *Numbers do not total for Exp group because some had more than one injury	Response 57/62 for Exp group. Response rate in control group not reported. OA defined as joint space narrowing, sclerosis or cysts. Osteophytes alone would not be considered OA. 8/30 soccer players with OA doing physical labour, 9/19 control subjects with OA doing physical labour. Higher rates of OA in Exp group may be due to increased injury prevalence. Other injuries were not clearly defined. The authors simply report "distortion, ligament injuries, ruptured tendons, etc".
Kujala[13–15] (n = 2059) The results of this study related to running are reported in table 1, and the results related to overall sport are reported in table 3.	Males, ages 21–86. Exp: 1282 ex-elite male athletes from a wide variety of sports. Con: 777 men from medical exam for compulsory military service. Study 1[14] used hospital admission records as outcome. Study 2[15] used sub-sample of subjects (n = 28 runners, 31 soccer, 29 weight lifters and 29 shooters). Shooters (i.e. no impact or raised joint pressure) were controls. Study 3[13] used self-reported pain and used follow-up of 30–75 yrs.	Three different studies, all historical cohort with 20–65 yr follow-up. Independent variables by recall. Blinded assessment of x-rays (knee OA) in Study 1 (National Registry) and Study 2. Outcome in Study 3 was self-report.	Study 1: Survival analysis graph: Risk of hospital admission for OA (hip, knee or ankle) greater throughout life compared with control group. OR (adjusted for age, occupation and BMI): Sport: Soccer/ice hockey/basketball/athletics OR: 2.37 (1.32 to 4.24) Study 2: Used shooters as control group. Stepwise regression final model: BMI, previous injury, hours in team/endurance/power sport, hours in heavy or kneeling/squat work. Soccer: OR 12.3 (1.35 to 111) (age-adjusted); OR (final model) 1.2 (1.0 to 2.3) Previous injury: OR 7.9 (univariate, from percent data supplied); OR (final model) 6.0 (1.3 to 27.8)	Study 1 response rate: 1282/1518 (84%) athletes and 777/1010 (77%) controls. The total number of approached subjects (n = 2528) represented 60.8% of original cohort (39.2% died prior to start of study). Study 2 response rate: 117/147 (80%). The 147 denominator represented all long-distance runners, soccer players, weight lifters and shooters. The results after controlling for previous injury are remarkable and strongly suggest the effect seen in Study 1 is due to injuries. OA defined as per hospital record diagnosed in Study 1, as per Kellgren and Lawrence (Grade 2 or more) for Study 2. Results for Study 3 are not shown because this study used pain as the outcome instead of OA, and used the same cohort.
Lau[8] (n = 1868) Results for this study related to running are reported in table 1.	452M, 1416F, ages not reported. Cases: Primary OA diagnosed in Hong Kong hospitals (n = 30 males and 108 females for hip, and 166 males and 492 females for knee). Controls: Consecutive patients without OA from 8 general practice clinics in same region, matched on age and sex (n = 90 males and 324 females for hip, and 166 males and 492 females for knee).	Case control. Exposure defined as "performed sports activities regularly". Not clear when exposure occurred. No blinding but used standardised questionnaire for exposure data.	Univariate OR for OA of Hip due to soccer. Males: Soccer (n = 1F, 30M) 1.3 (0.6 to 2.8) Females: N/A There was no association after adjustment for body weight, previous joint injury, smoking and occupation (results not reported) OR for OA of hip due to previous joint injury adjusted for body weight, sports, smoking and occupation. Hip: Males 25.1 (3.5 to 181); Females 43.3 (11.7 to 161) Knee: Males 12.1 (3.4 to 42.5); Females 7.6 (3.8 to 15.2) For women, the risk of knee OA was increased for exposure to gymnastics (OR = 74) and Kung Fu (OR = 22.5). There was no increased risk of hip OA with these exposures.	Response rate not reported. OA diagnosis by American College of Rheumatology criteria.
Vingård[7] (n = 569) The results of this study related to long-distance running are reported in table 1, and the results related to total sport participation are reported in table 3.	Males, ages 50–70. Cases: Total hip replacement 2° idiopathic OA in 4 Swedish hospitals (n = 247 partial participation, 233 partial participation). Controls: Swedish men living in area of same 4 hospitals (n = 322 partial participation, 302 complete participation).	Case-contol. Information by recall. Blinding of evaluators for exposure not reported.	RR for total hip replacement, adjusted for age, BMI, smoking and physical load at work compared with low exposure group. Exposure period: Soccer Medium exposure: 1.3 (0.4 to 3.9) High exposure: 2.3 (0.7 to 7.7) Low exposure = inactive + lowest 5% exposure; the remaining subjects equally split between medium exposure and high exposure	Response rate 233/253 (92%) for full participation among cases, and 302/392 (72%) among controls. Slightly greater partial participation rates for both groups. Relative risks estimated from OR. Exposure information obtained by recall during interview. Authors note that recall in myocardial infarction patients and controls found no increased RR and they suggest that shows recall not a problem. However, if regular physical activity is protective against infarction, and recall not an issue, then physical activity should have been protective.

Elite sports

Kulula's group[13–15] found that the risk of hip or knee disability was only increased in elite team sports (previous injury not controlled for[13]). When the same cohort of athletes was compared with 1403 controls without controlling for previous injury,[14] OA was increased in all types of athletes (OR range 1.73–2.17), but the greatest increase occurred in wrestling (OR 2.73, 95%CI 1.63 to 4.64), weight lifting (OR 2.74, 95%CI 1.27 to 5.9), soccer (OR 2.1, 95%CI 1.2 to 3.8), and ice hockey (OR 4.2, 95%CI 2.2 to8.0). Three of four of these exposures do not involve impact, suggesting that wear and tear is not a likely cause. In a subsequent study of a subgroup of the same population but now controlling for previous injury,[15] the risk was now considerably less (OR 1.2, 95%CI 1.0 to 2.3) and much less than the risk associated with previous injury (OR 6.0, 95%CI 1.3 to 27.8). The presence of previous injury may also partially explain the higher rate of OA in the previously mentioned Lindberg study.[24] Using the same population, the

Table 2 Contd

Lindberg[24] (n = 858)	Males, ages 40–88. Exp: ex-soccer players, with 71/286 being elite. Con: 572 males from same city population records, matched for age (soccer history unknown).	Cross-sectional study but exposure likely preceded outcome by 15–63 yrs. Information obtained from hip x-rays over 38 yrs. Blinding of evaluators not reported.	% Hip OA Older group (64–88) / Younger group (40–64) Elite: 14.7% / 13.5% Non-elite: 3.1% / 2.7% Control: 6.1% / 1.8%	Response rate not given. OA definition restricted so that joint space narrowing had to be present. History of soccer playing in control group is unknown, but control subjects did not play competitively for the teams included in the experimental group. Although timing between outcome and exposure not precisely reported, average age at diagnosis in Exp group was 47 yrs, and all Exp group subjects played competitive soccer until at least 25 years old.
Solonen[6] (n = 76)	Males, ages 18–37 for Exp and 18–88 for control. Exp: 36 active soccer players with 5–23 yrs experience (many national athletes). Con: 40 subjects with acute lower extremity injury and no known history of soccer.	Cross-sectional as all Exp group still active soccer players. Information obtained by recall. Blinding of evaluators not reported.	Hip: No OA in either group. Knee: 28% of soccer players mild-moderate OA of Pat-fem joint. Hip / Fem-Tib / Fem-Pat / Talo-crural Exp: 0% / 0% / 28% / 92% Con: 0% / 0% / 21% / 20% 73% of soccer players had moderate-severe knee injuries, and 80% had severe ankle injuries.	Response rate 36/60. As they were currently active and the reason for refusal was not provided, the subjects who refused may have been trying to hide their injuries. No precise definition for OA. No OA of hip or tibio-femoral component of the knee in either group. This is highly unusual.

All studies suggested soccer players were at risk of OA, but where studied, only in elite sports or those without injury. Studies are sorted by design.

- OA: osteoarthritis
- Exp: Exercise group
- Con: Control group
- Historical cohort: For the purpose of this review, any observational study for which the exposure clearly predates the outcome was considered either a cohort study (groups assembled based on exposure history) or a case-control study (groups assembled based on presence or absence of OA). Although some historical cohort studies might be considered cross-sectional studies by other authors (e.g. when all information obtained by interview at one point in time), we felt that the important distinction between these two categories is the ability to determine if the exposure preceded the outcome (i.e. historical cohort study).

subsequent publication[25] noted that 33% of elite soccer players with previous meniscectomy or ACL tear developed knee OA compared with 11% in those without these injuries. The same may also be true for hip OA, but this type of analysis has yet to be published.

DISCUSSION

The results of this literature review strongly suggest that regular mild-moderate impact exercise does not increase the risk of OA, and that there is some evidence that it does not increase symptoms in patients with mild-moderate OA. This evidence supports the muscle dysfunction hypothesis as a cause of OA over the wear and tear hypothesis.

Running/soccer

The wear and tear hypothesis predicts that any type of impact such as running would increase OA, or worsen it once developed. However, the clinical evidence suggests that recreational running and soccer do not increase the risk of OA. In the basic science literature, canine cartilage adapts favourably to moderate running,[26] and running did not worsen immobilisation induced OA in rabbit knees,[27] which is consistent with the prospective study reported by Lane *et al*.[21] In addition, the finding that degeneration occurs with forced exhaustive running in dogs[28 29] is also consistent with the muscle dysfunction hypothesis because exhaustion will prevent the muscles from absorbing force. Although some might believe that marathon running could be analogous to forced exhaustive exercise in dogs, most marathon training is done at much lower mileage. Although subjects may be tired, they are not exhausted. The actual marathon is run only a few times a year, whereas the dogs were run to exhaustion regularly.

Most of the subjects in the clinical studies in this review had intact menisci, and presumably no major malalignment. In subjects with previous meniscectomy, Roos *et al*[30] reported no effect of exercise on the incidence of OA. This contradicts the basic science finding that running increased the risk of OA in meniscectomised sheep.[31] Although there were no studies on the effect of exercise in subjects with malalignment, Sharma *et al*[32] reported that disease progression occurs more rapidly in this population. How does the muscle dysfunction hypothesis relate to these populations? The wear and tear hypothesis predicts that cartilage damage precedes bone sclerosis. However, the reverse occurred in adult rabbit knees subjected to one hour impulse loading a day.[33] The sclerosis was associated with numerous healing trabecular fractures, suggesting that the principle force absorber in anaesthetised animals is not cartilage but bone. This is supported by in vitro findings suggesting that articular cartilage does not absorb force,[34] but does redistribute force.[35–37] If enough microtrabecular damage occurs over a short period of time, sclerosis would occur as an adaptation—that is, damage would be less likely in sclerotic bone.[38] Within this paradigm, malalignment and meniscectomy could increase the risk of OA[30 32] because they prevent the normal redistribution of force—that is, even in normal knees, the muscles do not absorb 100% of the force—which makes micro-damage more likely to occur. Finally, the sclerotic changes in underlying bone stiffness may increase the stress on articular cartilage,[39] which would lead to increased degenerative changes in both meniscal and articular cartilage.

Elite sports

Although the findings suggest that recreational sports are innocuous with respect to developing OA, they do suggest that participation in elite sports increases the risk of OA. This

Table 3 Details of studies related to "other" exposure (95% CI in parentheses)

Article	Population	Design	Results	Comments
Exercise associated with OA				
Kujala[13–15] (n = 2059) The results of this study related to running are reported in table 1, and the results related to soccer are reported in table 2.	Males, ages 21–86. Exp: 1282 ex-elite male athletes from a wide variety of sports. Con: 777 men from medical exam for compulsory military service. Study 1[14] used hospital admission records as outcome. Study 2[15] used sub-sample of subjects (n = 28 runners, 31 soccer, 29 weight lifters and 29 shooters). Shooters (i.e. no impact or elevated joint pressure) were controls. Study 3[13] used self-reported pain and used follow-up of 30–75 yrs.	Three different studies, all historical cohort with 20–65 yr follow-up. Independent variables by recall. Blinded assessment of x-rays in Study 1 (National Registry) and Study 2. Outcome in Study 3 was self-report.	Study 1: Survival analysis graph: Risk of hospital admission for OA (hip, knee or ankle) similar among controls and distance running/skiing until age 70, then controls less admissions. All other sports had higher admission rates throughout life. OR (adjusted for age, occupation and BMI): Sport / OR Soccer/ice hockey/basketball/athletics / 2.37 (1.32 to 4.24) Box/wrestling/weight lifting/throwing / 2.68 (1.51 to 4.15) Study 2: Used shooters as control group. Stepwise regression final model: BMI, previous injury, hours in team/endurance/power sport, hours in heavy or kneeling/squat work OR (95% CI) Weight lifting / 12.9 (1.47 to 113) Increase in OA with training hours for weight lifting only. If previous injury included in model, OR only significant for team sports = 1.2 (1.0 to 2.3) and previous injury = 6.0 (1.3 to 27.8).	Study 1 response rate: 1282/1518 (84%) athletes and 777/1010 (77%) controls. The total number of approached subjects (n = 2528) represented 60.8% of original cohort. Study 2 response rate: 117/147 (80%). The 147 denominator represented all long-distance runners, soccer players, weight lifters and shooters. The results after controlling for previous injury are remarkable and strongly suggest the effect seen in Study 1 is due to injuries. OA defined in Study 1 as per hospital record, in Study 2 as Kellgren and Grade 2 or more. Results for Study 3 are not shown because pain was outcome instead of OA, and used the same cohort.
Vingård[9] (n = 503)	Women, ages 50–70. Cases: National Registry total hip replacement for primary OA (n = 230). Controls: local population registries (n = 273) matched for age and hospital referral area.	Case-contol study. Information on OA status from National Registry and exposure information obtained from interview. Blinding not reported.	RR (calculated from OR) adjusted for age and BMI (low sports and low workload group is the reference group). Exposure summed total hours of activity until age 50. Low = <100 hrs total, Med = 100–800 hrs total, High = >800 hrs total. Sports Exp / Physical load from work: Low / Medium / High Low / 1.0 / 1.1 (0.5 to 2.0) / 1.7 (0.8 to 3.5) Med / 1.1 (0.3 to 3.4) / 1.8 (0.8 to 4.1) / 2.7 (1.1 to 7.0) High / 2.0 (0.7 to 5.2) / 2.7 (1.2 to 5.9) / 4.3 (1.7 to 11.0) Overall RR (adjusted for age, BMI, occupational load, smoking and hormone replacement therapy) was 2.3 (1.5 to 3.7) for high vs low categories, and 1.5 (0.9 to 2.5) for medium vs low categories.	Response rate 242/255 (95%) for cases and 298/334 (89%) for controls. Outcome was total hip replacement for OA, so no precise definition of OA given. Not enough numbers to determine risks for individual sports. Very few women were elite atletes, but 3% of cases were elite and only 1% of controls were elite, suggesting a higher risk of OA requiring total hip replacement in elite athletes.
Vingård[7] (n = 569) The results of this study related to long-distance running are reported in table 1 and the results related to soccer are reported in table 2.	Males, ages 50–70. Cases: Total hip replacement 2° idiopathic OA in 4 Swedish hospitals (n = 247 partial participation, 233 partial participation. Controls: Swedish men living in area of same 4 hospitals (n = 322 partial participation, 302 complete participation).	Case-contol. Information by recall. Blinding of evaluators not reported.	RR for total hip replacement among those performing sport or not, adjusted for age, BMI, smoking and physical load at work. Exposure (Reference group: low) Exposure period / Medium / High Occurred <29 yrs ago / 2.0 (1.2 to 3.2) / 3.5 (2.2 to 5.6) Occurred 30–49 yrs ago / 1.3 (0.7 to 2.6) / 2.8 (1.8 to 4.5) Track & field and racquet sports (not long-distance running) had highest RR (~2.4 for medium exposure and ~3.5 for high exposure). RR increased if work had higher physical loads. Within each work category, relative risk increased with increasing participation.	Response rate 233/253 (92%) for full participation among cases, and 302/392 (72%) among controls. Slightly greater partial participation rates for both groups. Outcome was total hip replacement for OA, so no precise definition of OA given. Relative risks estimated from OR. Exposure information obtained by recall during interview. Authors note that recall in myocardial infarction patients and controls found no increased RR and they suggest that shows recall not a problem. However, if regular physical activity is protective against infarction, and recall not an issue, then physical activity should have been protective.

occurred in impact sports, such as soccer, and also in non-impact sports, such as weightlifting and hockey. Unlike the wear and tear hypothesis, the muscle dysfunction hypothesis predicts these results through the increased risk of injury that occurs with elite sports and the subsequent muscle dysfunction that occurs with injury. In support of these findings, others have found that young adults with previous knee injury are more likely to develop OA,[22 40] and that previous hip injury increases the risk of hip OA.[40]

There are three possible mechanisms by which previous injury could increase the risk of OA. Firstly, the damage may occur at the time of the injury and OA develops over the subsequent years. Secondly, the associated ligamentous instability with major injury leads to recurrent articular cartilage damage. Finally, the associated muscle dysfunction with injury leads to recurrent articular cartilage damage because the impact forces are no longer being absorbed appropriately.

If damage occurred at the time of injury, and the wear and tear hypothesis is correct, then articular cartilage damage should overlie areas of bone damage. However, there was no correlation between the location of a femoral bone bruise and articular or meniscal cartilage damage observed at surgery for ACL reconstruction.[41] The possibility of ''sub-clinical articular damage'' remains theoretical at the present time. Finally, Felson *et al*[42] recently found a strong correlation between location of bone marrow oedema on magnetic resonance images and progression of OA. If bone marrow oedema is indeed a strong predictor of progression, it suggests that bone injury is an early sign of damage. Future research should

Table 3 Contd

Roos[25] (n = 858)	Males, ages 40–88. Exp1: 71 ex-elite male soccer players. Exp2: 215 non-elite male soccer players. Con: Two age-matched male controls per Exp from population database.	Historical cohort with 15–63 yr follow-up. Historical information obtained by interview and current status by interview and exam. Blinded assessment of x-rays.	Prevalence of OA in groups. Category / % OA total group / % of Uninjured / % Major surgery Elite / 15.5% / 11% / 9% Non-elite / 4.2% / 3% / 2% Control / 1.6% / 0% / 0% 14% of soccer players (not separated by elite status) had menisectomies compared to 2% in control group. ACL injuries occurred in 4.2% of elites, 1.8% of non-elites and 0% of controls.	Response rate not reported. There was no standard follow-up and not all subjects had x-rays. Rather, x-ray records were pulled from radiology sources (only 253/858 had x-rays). OA defined by joint space narrowing >50% of other knee compartment or contralateral knee, or joint space less than 3 mm. The lower prevalence of OA in non-elite compared with elite suggests higher rates of OA in soccer mostly only in elite players. The difference in injury rates may be the mechanism (only ACL and menisectomy recorded).
Roos[30] (n = 175)	130 males and 45 females ages 35–78. Exp. Total menisectomy in 1973 (n = 107) without OA at the time of surgery. Con. From the National Population Registry (n = 68)	Historical cohort with 21-yr follow-up. Historical information obtained by recall and current status by interview and exam. Blinded assessment of x-rays.	Results for activity not shown. Article does say "neither occupation nor sports activity were significant risk factors for OA in this study."	Response rate 107/123 in Exp group. For control group, 214 originally designated but 16 excluded. Of remaining 198, 83 refused initially (leaving 115). Of those remaining, 40 excluded as double-controls, six refused to continue and 1 was excluded. OA required joint space narrowing. Power analysis suggested only needed 60 controls.
Cooper[22] (n = 354)	Males (n = 99) and females (255) with mean age 75.8 yrs (IQR = 69.5–80.9). Exp: weekly participation in sports for at least 10 yrs after leaving school. Con: Subjects who did not fit Exp definition.	Historical cohort with 5 yr follow-up. Exposure information obtained by interview and outcome by x-ray. Blinded assessment of x-rays. Grade I OA was presence of osteophytes. Grade II OA was presence of joint space narrowing.	OR for OA (adjusted for age, sex, BMI, knee pain at baseline and Heberden's nodes). / Grade I OA / Grade II OA Incidence Sports participation / 3.2 (1.1 to 9.1) / 1.0 (0.5 to 2.1) Previous injury / 4.8 (1.0 to 24.1) / 2.5 (0.8 to 8.1) Progression Sports participation / 0.7 (0.4 to 1.6) / 0.9 (0.3 to 2.5) Previous injury / 1.2 (0.5 to 3.0) / 1.1 (0.3 to 4.4)	Response rate = 354/583 (61%) of original cohort were available at follow-up. The increased risk of osteophytes with sport participation is consistent with other studies, as is the absence of the development or progression of joint space narrowing. The increased risk for incident Grade I or II OA with previous injury is consistent with previous studies. The lack of an increased risk for progression of OA with previous injury is new information and appropriate on face value. The injury may cause the OA, but once the damage is there, the mechanisms for progression would be based on the damage and not the original cause.

Studies are sorted by whether the results suggest an association between exercise and OA, and by study design within each category.

• OA: osteoarthritis

• Exp: Exercise group

• ACL: anterior cruciate ligament

• Con: Control group

• Historical cohort: For the purpose of this review, any observational study for which the exposure clearly predates the outcome was considered either a cohort study (groups assembled based on exposure history) or a case-control study (groups assembled based on presence or absence of OA). Although some historical cohort studies might be considered cross-sectional studies by other authors (e.g. when all information obtained by interview at one point in time), we felt that the important distinction between these two categories is the ability to determine if the exposure preceded the outcome (i.e. historical cohort study).

examine the subgroup of patients who had osteophytes without joint space narrowing at baseline to see if bone marrow oedema preceded the articular cartilage damage.

If ligamentous instability of the joint after an ACL tear causes OA, then ACL reconstruction should minimise the risk of OA. However, clinical studies (albeit with their limitations) suggest that it may not.[43 44] Other authors have suggested that it is the underlying bone injury that occurs at the time of ACL rupture that is the cause of OA. Yet, OA is produced in dogs and cats by isolated transection of the ACL without associated bone damage at the time of injury.[36 45 46] In the muscle dysfunction hypothesis, the loss of proprioception information from the ACL would result in increased force transmission to the bone, and increased OA. Further, evidence from biomechanical studies reveal an increase in loading of the non-transected knee, which does not develop OA,[47] which again suggests that normal muscles can absorb the regular amounts of stress and strain across a joint and that ''wear and tear'' is not the cause of OA in uninjured limbs.

The muscle dysfunction hypothesis is based on the finding that muscle fatigue increases the impact forces crossing a joint,[48 49] which suggests that properly contracting muscles are the main absorber of force. Whether the muscle cannot contract properly because of age or fatigue or disuse atrophy, or because of injury induced weakness (strains) or loss of proprioception (ACL tears), the effect is the same; more force is transmitted to the bone, which leads to increased microtrabecular damage, which leads to sclerosis, which could lead to changes in the stresses and strains across the articular cartilage, and then joint space narrowing. The added stress would then lead to the characteristic changes observed in periarticular tissue. Note that this hypothesis would predict an increased risk of OA with less severe injuries than are usually accounted for in studies—for example, quadriceps contusion could lead to increased risk of OA even though there was no ligamentous damage—and also the greater risk of hip OA compared with knee OA in soccer players[23]—that is, groin strains occur often in soccer but rarely with running. In addition, it would predict a higher rate of hip OA in

subjects with knee injuries, and vice versa because the muscles of the thigh would be expected to absorb force across both joints. However, this analysis has not yet been published.

Other activity and obesity

The objective of this article was to assess the risk of OA with exercise. Although a detailed discussion of the risk of OA with exposure to various occupations is beyond its scope, the muscle dysfunction hypothesis can explain findings in this area as well. Briefly, if a person is forced to work when fatigued or injured—for example, a farmer—the muscles no longer absorb the forces crossing a joint and there would be an expected increase in microtrabecular damage, then sclerosis, and then OA. For example, in the study by Lau *et al*,[8] for those subjects with occupational exposures that required climbing 15 flights of stairs or more, the OR for developing OA was 5.1 (95%CI 2.5 to 10.2) for women and 2.5 (95%CI 1.0 to 6.4) for men in the entire study, but 34.0 (95%CI 4.7 to 248.4) overall for those with previous injury. Similarly, the OR for developing OA in those subjects with occupational exposures that required lifting $\geqslant$10 kg more than 10 times a week was 2.0 (95%CI 1.2 to 3.1) for the entire group and 25.9 (95%CI 8.1 to 82.4) for those with previous injury.

Finally, obesity is a well recognised risk factor for OA.[2 50] The muscle dysfunction hypothesis explains this relation as well. The added weight means that muscles must absorb even more force and therefore must be stronger and have greater endurance or there will be a ''relative dysfunction''. However, obesity is associated with physical inactivity and therefore relative muscle dysfunction. With respect to mortality, most of the evidence suggests that obesity is not related to mortality if there is adjustment for physical fitness.[51] Future studies should explore whether the relation between obesity and OA is similar to that between obesity and mortality.

CONCLUSIONS

The muscle dysfunction hypothesis that was originally proposed based on basic science evidence is supported by the clinical literature as well. This includes:

- Strengthening and endurance exercise relieves symptoms in patients with mild and moderate OA,[52–54] and poor knee proprioception is associated with increased disability in patients with OA.[55]
- Regular running increases joint space width whereas forced exhaustive running—that is, fatigue—decreases joint space width.[28 29]
- Major injuries are associated with a high rate of OA.
- Because muscles provide the ''dynamic'' joint stability during movement, some signs of OA—that is, osteophytes and capsular thickening—may be an attempt by the body to increase joint stability in the presence of muscle dysfunction induced dynamic instability.
- A wide variety of elite sports, but not recreational exercise, are associated with OA. This effect is greatly reduced when major injuries are controlled for. Because elite athletes often play while injured—that is, on weak muscles—the muscle dysfunction hypothesis predicts that there would still be an increase in risk if minor injuries are not controlled for—for example, groin strain in soccer and hip OA.

The most important implication of the muscle dysfunction hypothesis is that proper rehabilitation after an injury may be important in the prevention of OA. A study designed to definitively test the role of muscle dysfunction would require detailed prospectively collected data, controlling for proper rehabilitation after major and minor injuries using appropriate strength testing and close supervision. That being said, the hypothesis that best explains the evidential relation between exercise and OA currently available today is the muscle dysfunction hypothesis.

ACKNOWLEDGEMENTS

Funding by the Chercheur-Boursier Clinicien program of the Fonds de Recherche en Santé du Québec is gratefully acknowledged.

REFERENCES

1 **Badley EM**. The effect of osteoarthritis on disability and health care use in Canada. *J Rheumatol Suppl* 1995;**43**:19–22.
2 **Felson DT**, Lawrence RC, Dieppe PA, *et al*. Osteoarthritis: new insights. Part 1. The disease and its risk factors. *Ann Intern Med* 2000;**133**:635–46.
3 **Hurley MV**. The role of muscle weakness in the pathogenesis of osteoarthritis. *Rheum Dis Clin North Am* 1999;**25**:283–98.
4 **Lane NE**, Bloch DA, Jones HH, *et al*. Long-distance running, bone density, and osteoarthritis. *JAMA* 1986;**255**:1147–51.
5 **Panush RS**, Schmidt C, Caldwell JR, *et al*. Is running associated with degenerative joint disease? *JAMA* 1986;**255**:1152–4.
6 **Solonen KA**. The joints of the lower extremities of football players. *Ann Chir Gynecol Fen* 1966;**55**:176–80.
7 **Vingard E**, Alfredsson L, Goldie I, *et al*. Sports and osteoarthrosis of the hip. *Am J Sports Med* 1993;**21**:195–200.
8 **Lau EC**, Cooper C, Lam D, *et al*. Factors associated with osteoarthritis of the hip and knee in Hong Kong Chinese: obesity, joint injury, and occupational activities. *Am J Epidemiol* 2000;**152**:855–62.
9 **Vingard E**, Alfredsson L, Malchau H. Osteoarthrosis of the hip in women and its relationship to physical load from sports activities. *Am J Sports Med* 1998;**26**:78–82.
10 **Konradsen L**, Hansen EB, Sondergaard L. Long distance running and osteoarthrosis. *Am J Sports Med* 1990;**18**:379–81.
11 **Puranen J**, Ala-Ketola L, Peltokallio P, *et al*. Running and primary osteoarthritis of the hip. *BMJ* 1975;**2**:424–5.
12 **Sohn RS**, Micheli LJ. The effect of running on the pathogenesis of osteoarthritis of the hips and knees. *Clin Orthop* 1985;**198**:106–9.
13 **Kettunen JA**, Kujala UM, Kaprio J, *et al*. Lower-limb function among former elite male athletes. *Am J Sports Med* 2001;**29**:2–8.
14 **Kujala UM**, Kaprio J, Sarna S. Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes. *BMJ* 1994;**308**:231–4.
15 **Kujala UM**, Kettunen J, Paananen H, *et al*. Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. *Arthritis Rheum* 1995;**38**:539–46.
16 **Marti B**, Knobloch M, Tschopp A, *et al*. Is excessive running predictive of degenerative hip disease? Controlled study of former elite athletes. *BMJ* 1989;**299**:91–3.
17 **Cheng Y**, Macera CA, Davis DR, *et al*. Physical activity and self-reported, physician-diagnosed osteoarthritis: is physical activity a risk factor? *J Clin Epidemiol* 2000;**53**:315–22.
18 **Spector TD**, Harris PA, Hart DJ, *et al*. Risk of osteoarthritis associated with long-term weight-bearing sports: a radiologic survey of the hips and knees in female ex-athletes and population controls. *Arthritis Rheum* 1996;**39**:988–95.
19 **Lane NE**, Bloch DA, Hubert HB, *et al*. Running, osteoarthritis, and bone density: initial 2-year longitudinal study. *Am J Med* 1990;**88**:452–9.
20 **Lane NE**, Michel B, Bjorkengren A, *et al*. The risk of osteoarthritis with running and aging: a 5-year longitudinal study. *J Rheumatol* 1993;**20**:461–8.
21 **Lane NE**, Oehlert JW, Bloch DA, *et al*. The relationship of running to osteoarthritis of the knee and hip and bone mineral density of the lumbar spine: a 9 year longitudinal study. *J Rheumatol* 1998;**25**:334–41.
22 **Cooper C**, Snow S, McAlindon TE, *et al*. Risk factors for the incidence and progression of radiographic knee osteoarthritis. *Arthritis Rheum* 2000;**43**:995–1000.
23 **Klunder B**, Rud B, Hansen J. Osteoarthritis of the hip and knee joint in retired football players. *Acta Orthop Scand* 1980;**51**:925–7.
24 **Lindberg H**, Roos H, Gärdsell P. Prevalence of coxarthrosis in former soccer players. *Acta Orthop Scand* 1993;**64**:165–7.
25 **Roos H**, Lindberg H, Gardsell P, *et al*. The prevalence of gonarthrosis and its relation to meniscectomy in former soccer players. *Am J Sports Med* 1994;**22**:219–22.
26 **Buckwalter JA**. Osteoarthritis and articular cartilage use, disuse, and abuse: experimental studies. *J Rheumatol Suppl* 1995;**43**:13–5.
27 **Videman T**. The effect of running on the osteoarthritic joint: an experimental matched-pair study with rabbits. *Rheumatol Rehabil* 1982;**21**:1–8.
28 **Kiviranta I**, Tammi M, Jurvelin J, *et al*. Articular cartilage thickness and glycosaminoglycan distribution in the canine knee joint after strenuous running exercise. *Clin Orthop* 1992:302–8.
29 **Palmoski MJ**, Brandt KD. Running inhibits the reversal of atrophic changes in canine knee cartilage after removal of a leg cast. *Arthritis Rheum* 1981;**24**:1329–37.
30 **Roos H**, Lauren M, Adalberth T, *et al*. Knee osteoarthritis after meniscectomy: prevalence of radiographic changes after twenty-one years, compared with matched controls. *Arthritis Rheum* 1998;**41**:687–93.
31 **Armstrong SJ**, Read RA, Ghosh P, *et al*. Moderate exercise exacerbates the osteoarthritic lesions produced in cartilage by meniscectomy: a morphological study. *Osteoarth Cartil* 1993;**1**:89–96.

32 **Sharma L**, Song J, Felson DT, *et al*. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA* 2001;**286**:188–95.
33 **Radin EL**, Parker HG, Pugh JW, *et al*. Response of joints to impact loading - III. *J Biomech* 1973;**6**:51–7.
34 **Radin EL**, Paul IL. Does cartilage compliance reduce skeletal impact loads? *Arthritis Rheum* 1970;**13**:139–44.
35 **Eckstein F**, Lemberger B, Stammberger T, *et al*. Patellar cartilage deformation in vivo after static versus dynamic loading. *J Biomech* 2000;**33**:819–25.
36 **Wu JZ**, Herzog W, Epstein M. Joint contact mechanics in the early stages of osteoarthritis. *Med Eng Phys* 2000;**22**:1–12.
37 **Clark AL**, Herzog W, Leonard TR. Contact area and pressure distribution in the feline patellofemoral joint under physiologically meaningful loading conditions. *J Biomech* 2002;**35**:53–60.
38 **Burr DB**, Turner CH, Naick P, *et al*. Does microdamage accumulation affect the mechanical properties of bone? *J Biomech* 1998;**31**:337–45.
39 **Brown TD**, Radin EL, Martin RB, *et al*. Finite element studies of some juxtarticular stress changes due to localized subchondral stiffening. *J Biomech* 1984;**17**:11–24.
40 **Gelber AC**, Hochberg MC, Mead LA, *et al*. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Ann Intern Med* 2000;**133**:321–8.
41 **Graf BK**, Cook DA, De Smet AA, *et al*. ''Bone bruises'' on magnetic resonance imaging evaluation of anterior cruciate ligament injuries. *Am J Sports Med* 1993;**21**:220–3.
42 **Felson DT**, McLaughlin S, Goggins J, *et al*. Bone marrow edema and its relation to progression of knee osteoarthritis. *Ann Intern Med* 2003;**139**:330–6.
43 **Daniel DM**, Stone ML, Dobson BE, *et al*. Fate of the ACL-injured patient. A prospective outcome study. *Am J Sports Med* 1994;**22**:632–44.
44 **Lohmander LS**, Roos H. Knee ligament injury, surgery and osteoarthrosis. Truth or consequences? *Acta Orthop Scand* 1994;**65**:605–9.
45 **Brandt KD**, Braunstein EM, Visco DM, *et al*. Anterior (cranial) cruciate ligament transection in the dog: a bona fide model of osteoarthritis, not merely of cartilage injury and repair. *J Rheumatol* 1991;**18**:436–46.
46 **McDevitt C**, Gilbertson E, Muir H. An experimental model of osteoarthritis; early morphological and biochemical changes. *J Bone Joint Surg [Br]* 1977;**59**:24–35.
47 **Hasler EM**, Herzog W, Leonard TR, *et al*. In vivo knee joint loading and kinematics before and after ACL transection in an animal model. *J Biomech* 1998;**31**:253–62.
48 **Christina KA**, White SC, Gilchrist LA. Effect of localized muscle fatigue on vertical ground reaction forces and ankle joint motion during running. *Hum Mov Sci* 2001;**20**:257–76.
49 **Mizrahi J**, Verbitsky O, Isakov E. Fatigue-related loading imbalance on the shank in running: a possible factor in stress fractures. *Ann Biomed Eng* 2000;**28**:463–9.
50 **Anderson JJ**, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol* 1988;**128**:179–89.
51 **Blair SN**. Effects of physical activity on cardiovascular disease mortality independent of risk factors. In Leon AS, ed. *Physical activity and cardiovascular health. A national consensus*. Champaign, IL: Human Kinetics, 1997:127–36.
52 **Penninx BW**, Messier SP, Rejeski WJ, *et al*. Physical exercise and the prevention of disability in activities of daily living in older persons with osteoarthritis. *Arch Intern Med* 2001;**161**:2309–16.
53 **Petrella RJ**, Bartha C. Home based exercise therapy for older patients with knee osteoarthritis: a randomized clinical trial. *J Rheumatol* 2000;**27**:2215–21.
54 **Ettinger WH Jr**, Burns R, Messier SP, *et al*. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;**277**:25–31.
55 **Birmingham TB**, Kramer JF, Kirkley A, *et al*. Association among neuromuscular and anatomic measures for patients with knee osteoarthritis. *Arch Phys Med Rehabil* 2001;**82**:1115–18.
56 **Altman RD**, Fries JF, Bloch DA, *et al*. Radiographic assessment of progression in osteoarthritis. *Arthritis Rheum* 1987;**30**:1214–25.