

EXTENDED REPORT

Weight changes and the risk of knee osteoarthritis requiring arthroplasty

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Objective: To examine the effect of weight changes between 20 and 50 years of age on the risk of severe knee osteoarthritis (OA) requiring arthroplasty.**Subjects and methods:** Cases were 55–75 year old men and women (n=220) having had knee arthroplasty for primary osteoarthritis at the Kuopio University Hospital in 1992–93. Controls (n=415) were randomly selected from the population of Kuopio Province. Weight at the age of 20, 30, 40, and 50 years was collected retrospectively with a postal questionnaire.**Results:** After adjustment for age, sex, history of physical workload, recreational physical activity, and previous knee injury, weight gain resulting to a shift from normal body mass index (BMI ≤ 25 kg/m²) to overweight (BMI >25 kg/m²) was associated with a higher relative risk of knee OA requiring arthroplasty than persistent overweight from 20–50 years of age, compared with those with normal relative weight during the corresponding age period. The odds ratios (OR) were 3.07 (95% confidence interval 1.87 to 5.05) for those with normal weight at the age of 20 years and overweight at two or three of the ages 30, 40 or 50 years, 3.15 (1.85 to 5.36) for those with overweight from the age of 30 years, and 2.37 (1.21 to 4.62) for those with overweight from the age of 20 years, respectively.**Conclusion:** In adult life, a shift from normal to overweight may carry a higher risk for knee OA requiring arthroplasty than does constant overweight.

Knee osteoarthritis (OA) is a common cause of disability in ageing populations.^{1,2} Prevention of knee OA is important, because so far there is no effective treatment for slowing down the disease process. Known risk factors for knee OA are heredity,^{3,4} age,⁵ sex,⁵ injuries,^{6,7} physical loading,^{5,8–12} and obesity.^{13–28} Of these risk factors, obesity, knee injury, and physical loading are in theory modifiable.^{29–30}

Obesity is an important risk factor, because it explains a substantial part of the occurrence of knee OA. In one study, a decrease in the risk of knee OA was observed after weight loss.³⁴ It also accelerates the disease progress^{30,31} and contributes to disability.^{2,32,33} However, there is no firm evidence on the effect of weight change on the risk of knee OA.

The purpose of this case–control study was to explore the effect of changes in relative weight from 20 to 50 years of age on the risk of severe knee OA requiring knee arthroplasty in later life.

SUBJECTS AND METHODS

Subjects

All 55–75 year old inhabitants living in Kuopio province in Finland comprised the study population. Cases were patients who had received their first knee arthroplasty because of primary osteoarthritis in Kuopio University Hospital during the years 1992 and 1993 (n = 358). They were identified through the Finnish Arthroplasty Register.³⁵ Controls (n = 799) were randomly selected from the study population and frequency matched according to age (SD 2.5 years) and sex.

Of the study group, 239 controls (29.9%) and 61 cases (15.9%) could not be interviewed owing to the following reasons: telephone number could not be found, not reached by telephone, poor health condition, and refusal. One subject had died.¹²

A total of 874 subjects were interviewed. The interviewers considered 17 of the interviews to be unreliable and those

were excluded. Other reasons (35 controls, 17 cases) for exclusion were secondary OA due to cerebral palsy, rheumatoid arthritis, lower extremity disease other than OA such as status following rachitis, osteomyelitis, or tuberculosis, and marked length difference of lower extremities. There was no difference in the proportion of exclusion due to secondary osteoarthritis between the cases and controls. Data on body weight were incomplete for 61 cases and 109 controls. In the final analyses, there were 220 (61.4%) cases and 415 (51.9%) controls.

Mean age of the cases was 66.7 (SD 5.6) years and that of the controls 68.6 (SD 5.5) years. Owing to a low proportion of men (38%), analyses were made for both sexes together.

Questionnaire

An introductory letter was sent to all cases and controls. A few days later they were contacted by telephone. Those agreeing to participate in the study were interviewed by the computer assisted telephone interviewing system.³⁶ The interviews were carried out in 1994, and the interviewers were blinded to the case/control status of the subjects. The questionnaire included work history, recreational physical exercise, knee injuries, chronic diseases, weight at different ages, adult height, and smoking habits.^{12,37}

Body weight was obtained by the question: what was your weight at the age of 20, 30, 40, and 50 years. BMI (kg/m²) at different ages was calculated, and dichotomised as normal (BMI ≤ 25.0 kg/m²) and overweight (BMI >25.0 kg/m²) (table 1). To estimate the effect of overweight at different ages and weight change on the risk of knee OA, a variable describing weight changes between the ages of 20 and 50 years was formulated. The reference class included those with normal weight at all ages. Second, third, and fourth classes included those with normal weight at the age of 20 years and overweight at one, two, or three of the ages 30,

Abbreviations: BMI, body mass index; OA, osteoarthritis

Table 1 Distribution of body mass index (BMI) and overweight at the age of 20, 30, 40, and 50 years in cases and controls

	Age (years)							
	20		30		40		50	
	Cases (n = 252)	Controls (n = 479)	Cases (n = 255)	Controls (n = 482)	Cases (n = 263)	Controls (n = 508)	Cases (n = 271)	Controls (n = 526)
BMI (kg/m ²), mean (SD)	22.2 (2.7)	22.1 (2.7)	23.8 (2.7)	23.2 (2.7)	25.5 (3.4)	24.3 (3.0)	26.7 (3.7)	25.3 (3.2)
Overweight (BMI >25 kg/m ²), %	11.2	12.1	31.1	21.7	55.6	35.1	68.8	48.1

40, or 50 years, respectively. In the fifth class the subjects had been overweight at the age of 20 years and thereafter normal weight at one of the later ages at least (small numbers made it impossible to have a more detailed classification). The sixth class comprised those who had been overweight at all ages. BMI was also divided into tertiles to consider its association with knee OA. Cumulative BMI years were calculated by multiplying the mean BMI for each 10 year period (20–30, 30–40 and 40–50 years) by 10 and summing up.

History of knee injury was considered positive, if the injury had led to a physician's consultation. Selfreported physical workload was classified as high, medium, or low based on sweating and rapid heartbeat frequently, occasionally, or seldom, respectively.^{12–37} History of knee OA confirmed by radiography was asked for the controls in the questionnaire.

Statistical analysis

The data were analysed by logistic regression modelling.³⁸ The adjusted relative risks were expressed as OR with 95% confidence intervals. Age, sex, knee injury, physical workload, and recreational activity were entered as potential confounders. Statistical significance was tested with likelihood ratio test. Two way *t* test was used to compare BMI values between the cases and controls at different age

RESULTS

At the age of 20 years there was no difference in the mean BMI between the cases and the controls (table 1), but at the age of 30, 40 and 50 years the cases had higher BMI than the controls, *p* values being 0.003, 0.000, and 0.000, respectively. Proportion of overweight individuals among the cases exceeded that among the controls at the age of 30 years and thereafter. Overweight at the age of 20 years showed no association with the risk of knee OA in later life, but overweight at older ages did. In older age, an association could be observed between BMI and sex with the risk of knee OA, but not at the age of 20 and 30 years. At the age of 40 and 50 years, the ORs for the women were 1.45 (0.99 to 2.13) and 1.40 (0.96 to 2.05), respectively. Weight change from normal to overweight seemed to carry an equal risk of knee OA requiring arthroplasty than constant overweight from the age of 20 to 40 years (table 2).

The risk of knee OA requiring arthroplasty was also estimated by tertiles at different ages. At the age of 20 years, after adjustment of the potential confounders, OR (95% CI) was 1.07 (0.72 to 1.59) in the middle tertile and 1.18 (0.80 to 1.76) in the highest tertile; 1.12 (0.75 to 1.68) and 1.87 (1.25 to 2.79) at 30 years; 1.19 (0.79 to 1.80) and 2.87 (1.94 to 4.26) at 40 years; and 1.38 (0.93 to 2.06) and 2.87 (1.93 to 4.26) at 50 years. After adjustment for age, sex, history of knee injury, physical workload, and recreational activity, relative weight increase from normal to overweight after the age of 20 years was associated with an increased risk of knee OA in later life even more strongly than constant overweight between the ages from 20 to 50 years (table 3): OR (95% CI) was 3.07 (1.87 to 5.50) for those with normal weight at the age of 20 years and thereafter overweight at two of the ages 30, 40, or 50 years, and 3.15 (95% CI 1.85 to 5.36) for those with normal weight at the age of 20 years and thereafter overweight at three of these ages, compared with those with normal weight all the time. Estimation of the effect of weight loss on the risk of knee OA requiring arthroplasty was inconclusive because of the small number of the subjects. The risk of knee OA increased with increasing cumulative BMI years (test for trend *p* = 0.000). In the second, third, and fourth quartiles of BMI years, OR (95% CI) was 0.90 (0.53 to 1.51), 1.66 (1.01 to 2.75), and 2.41 (1.47 to 3.96), respectively, compared with the subjects in the lowest quartile.

DISCUSSION

Shifts from normal to overweight between the ages from 20 and 50 years were more closely associated with the risk of knee OA requiring arthroplasty than constant overweight.

The cases were subjects with severe primary knee osteoarthritis requiring arthroplasty. The age was limited because knee OA requiring arthroplasty is rare under the age of 55 years and recalling lifetime exposure after the age of 75 years could increase uncertainty about the data. All joint prostheses in Finland are reported to the Finnish Registry of Arthroplasty,³⁵ through which the cases were identified. During the observation period, almost all arthroplasty operations in Kuopio province were carried out in the public health care sector and therefore all inhabitants should have had the same opportunity to receive prosthesis if necessary. Controls were drawn from the general population of Kuopio

Table 2 Unadjusted risk of knee OA requiring arthroplasty and weight changes during different age periods

Relative weight at the beginning and at the end of age range	From 20 to 30 years				From 30 to 40 years				From 40 to 50 years			
	Cases (n = 229)	Controls (n = 424)	OR	95% CI	Cases (n = 238)	Controls (n = 446)	OR	95% CI	Cases (n = 248)	Controls (n = 375)	OR	95% CI
Normal/normal	154	313	1.00		104	280	1.00		70	242	1.00	
Normal/overweight	49	61	1.63	1.07 to 2.49	60	70	2.30	1.52 to 3.48	40	66	2.09	1.30 to 3.36
Overweight/normal	3	17	0.35	0.10 to 1.24	1	8	0.33	0.04 to 2.72	6	7	2.96	0.96 to 9.10
Overweight/overweight	23	33	1.41	0.80 to 2.49	73	88	2.23	1.52 to 3.27	132	60	2.85	2.00 to 4.05

OR, odds ratio; CI, confidence interval. Normal, BMI ≤25 kg/m²; overweight, BMI >25 kg/m². Logistic regression modelling was used.

Table 3 Adjusted risk of knee OA requiring arthroplasty and weight changes between the ages from 20 to 50 years

Relative weight changes between ages 20 and 50 years	Cases (n = 220)	Controls (n = 415)	OR	95% CI
Normal all the time	58	191	1.00	
Normal at the age of 20 years, thereafter overweight at one of the ages 30, 40, or 50 years	38	66	1.86	1.11 to 3.12
Normal at the age of 20 years, thereafter overweight at two of the ages 30, 40, or 50 years	54	58	3.07	1.87 to 5.05
Normal at the age of 20 years, thereafter overweight	46	51	3.15	1.85 to 5.36
Overweight at the age of 20 years, thereafter normal at least one of the ages 30, 40, or 50 years	3	18	0.60	0.16 to 2.21
Overweight all the time	21	31	2.37	1.21 to 4.62

OR, odds ratio; CI, confidence interval. Logistic regression modelling, adjusted for age, sex, knee injury, physical workload, and recreational physical activity.

province, representing the catchment population of Kuopio University Hospital. History of knee OA confirmed by radiography was asked of the controls in the questionnaire and 19.6% reported having knee OA. Considering this in the analyses did not change the results (data not shown).

The participation rate was higher among the cases than among the controls. The most common reasons for non-participation among the controls were problems in obtaining their telephone numbers and incomplete weight data. The average failure rate was about 15% when Statistics Finland provided telephone numbers. The failure rate might have been higher for older persons because some of them already resided in an institution and thus may not own a telephone. The telephone numbers of the cases were obtained from the Arthroplasty Register, where the numbers were recently updated.

Weight was obtained retrospectively and that may have reduced the validity of this study; however, the validity of self-reported weight has been assessed in several studies and seems to be good.^{39–43} Stunkard and Albaum³⁹ found reported weight slightly lower than measured weight. In two studies the correlations between measured and reported weight was 0.99 and 0.98.⁴¹ In a study comparing the reports of weight at the age of 25 years, recalled 20 to 30 years later, the correlation was 0.80.⁴³ In a case–control study, differential recall error cannot be excluded.⁴⁴ The cases may have recalled their weight more reliably, but magnitude of bias in this kind of settings is not known. We did not have any information as to whether the recall error was different between cases and controls. Information bias may also occur when interviewers do not treat cases and controls equally, but in this study the interviewers were blinded to the subjects' status.

Obesity as a risk factor of knee OA has been well documented,^{13–28} but there are only a few studies assessing the effect of overweight and weight changes at different ages on the risk of knee OA, an important factor in planning preventive measures. Recalled obesity at the age of 20 years was found to be a significant risk factor for later knee OA in a study by Hart and colleagues.¹⁷ In a case–control study,¹⁶ subjects who later developed knee OA had higher BMI at the age of 20 and 40 years than controls. In a study by Felson,²⁷ obesity before the age of 35 years was associated with an increased risk of knee OA in later life. Correspondingly, in a study by Gelber *et al.*⁴⁵ the incidence of knee OA was strongly associated with BMI at the ages of 20–29, 30–39, and 40–49 years. Change in BMI between 20 and 49 years was not associated with the risk of knee OA.

In the current study, weight changes seemed to be more closely associated with risk of knee OA than did constant overweight. This may be due to the adaptation of knee joints to overweight. Another possible explanation is some metabolic factor. However, it cannot be excluded that early

symptoms of knee OA reduce physical activity and lead to consequent weight increase.

It has been proposed that in addition to the mechanical burden due to overweight metabolic or biomechanical changes may also have importance in the aetiology of OA.^{17, 46–52} In a study by Silveri,⁴⁸ serum insulin levels were higher in subjects with OA than in controls. In a study by Hart and colleagues,⁴⁹ the risk of knee OA was higher in subjects with elevated blood glucose levels and a history of hypertension. In a study by Haara *et al.*, high BMI was found to be associated with finger OA that may be explained by metabolic rather than mechanical factors.⁵² Moreover, that study showed an association between finger OA and cardiovascular mortality in men. In addition, two studies have suggested that lipid abnormalities are associated with degradation of articular cartilage^{53, 54} However, the results of the earlier studies are not consistent concerning metabolic changes and the risk of arthroplasty due to knee OA.^{50, 51} The association of biomechanical factors in the risk of knee OA has been studied; Sharma and colleagues⁴⁶ observed that BMI was related to OA severity in those with varus, but not with valgus knees.

In conclusion, weight gain after the age of 20 years is deleterious for the knee joints. A shift from normal to overweight may carry a higher risk of knee OA than constant overweight. For prevention of knee OA requiring arthroplasty, weight control during early adulthood should be encouraged.

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