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ORIGINAL ARTICLE

Case–control study of knee osteoarthritis and lifestyle factors considering their interaction with physical workload

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Abstract
Aims The aim of this study is to examine the dose–response relationships between age, "lifestyle factors" (body mass index, tobacco smoking, sports), and symptomatic knee osteoarthritis in a population-based case–control study. Additionally, the study aims to investigate the mode of interaction between body mass index (BMI) and physical workload (occupational kneeling/squatting and lifting/carrying of loads) with respect to the risk of symptomatic knee osteoarthritis.
Methods In five orthopedic clinics and five practices, 295 male patients aged 25–70 with radiographically confirmed knee osteoarthritis associated with chronic complaints were recruited. The control group comprised 327 male control subjects. In a structured personal interview, body weight at different ages, body height, cumulative amount of smoking, and cumulative duration of different sports activities until the date of first diagnosis of knee osteoarthritis were elicited. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated using unconditional logistic regression analysis. An interaction analysis for the parameters BMI and kneeling/squatting respective lifting/carrying of loads was performed. Population attributable risks (PAR) for knee osteoarthritis were determined for BMI solely and for the combination of BMI with occupational kneeling/squatting and lifting/carrying of loads, respectively.
Results Age and overweight were strongly associated with the diagnosis of knee osteoarthritis. Compared with persons less than 35 years old, persons who were at least 65 years old had an odds ratio (OR) of 19.0 (95% CI 6.1–58.7) for knee osteoarthritis. Persons with a BMI $\geq$ 28.41 kg/m^2 had a strongly elevated risk of knee osteoarthritis (OR 10.8; 95% CI 4.8–24.3) compared to persons with a BMI $<$ 22.86 kg/m^2. Heavy tobacco smoking ($\geq$55.5 pack years) was associated with a decreased knee osteoarthritis risk in comparison with never-smoking (OR 0.2; 95% CI 0.1–0.5). Ball games (handball, volleyball, basketball) and cycling were associated with symptomatic knee osteoarthritis (OR 4.0; 95% CI 1.8–8.9 and OR 3.7; 95% CI 1.7–7.8 in the highest category of cumulative duration, respectively); to a weaker degree jogging, swimming, and soccer also were positively related to symptomatic knee osteoarthritis.

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Combining the two parameters, BMI and kneeling/squatting into one variable led to a multiplicative interaction mode for symptomatic knee osteoarthritis. For persons with elevated BMI in combination with moderate to high exposure to occupational kneeling/squatting, the population attributable risk (PAR) was 4%. The PAR for elevated BMI in combination with moderate to high exposure to occupational lifting/carrying of loads was 7%.

Conclusions In accordance with the literature, we find a strong association between BMI and knee osteoarthritis risk. Considering the relatively high prevalence of occupational manual materials handling, prevention of knee osteoarthritis should not only focus on body weight reduction, but should also take into account work organizational measures particularly aiming to reduce occupational lifting and carrying of loads.

Keywords Case–control study · Knee osteoarthritis · Body mass index, smoking, sports · Interaction · Physical workload

Introduction

Osteoarthritis, a major contributor to functional impairment, is becoming increasingly prevalent worldwide due to its association with an aging population and due to a growing prevalence of obesity (Berenbaum 2008). Knee osteoarthritis is a common cause of pain and disability (Lementowski and Zelicof 2008). The scientific literature on the association between physical workload (e.g., kneeling/squatting, lifting/carrying of loads) and knee osteoarthritis has been summarized by Jensen (2008). Currently, knee osteoarthritis is not mentioned in the European Commission's recommendation 2003/670/EC of 19 September 2003 concerning the European schedule of occupational diseases. However, some European countries (e.g., Denmark, Germany) have introduced knee osteoarthritis into their national lists of occupational diseases.

While age is strongly associated with the risk of knee osteoarthritis, overweight is arguably the most important modifiable risk factor (Coggon et al. 2001). Obesity is consistently found to be a risk factor for knee osteoarthritis (Anderson and Felson 1988; Teichtahl et al. 2008; Manninen et al. 1996). Body mass index (BMI) has been associated with the incidence and progression of knee osteoarthritis, independently of age and sex (Reijman et al. 2007). Even a moderate increase in BMI, within the normal range, was shown to be significantly related to knee osteoarthritis (Holmberg et al. 2005). The mechanisms by which obesity is linked to the pathogenesis of knee osteoarthritis are not completely understood. Biomechanical factors (e.g., reduced physical activity and immobility, abnormal knee adductor moment, high pressure on the articular cartilage) and metabolic mechanisms (e.g., hormonal dysregulation, adipokines) have been suggested as possible mediating factors for this joint disorder (Teichtahl et al. 2008).

Lifestyle factors, such as tobacco smoking, performing sports, and exercising, are inconsistently associated with a higher risk of knee osteoarthritis (Lane 1996). Available data with regard to an association between cigarette smoking and knee osteoarthritis remain controversial. Smoking has been associated with a lower risk of radiographic knee osteoarthritis (Felson et al. 1989). On the other hand, Hart and Spector (1993) do not find a clear association between smoking and the development of knee osteoarthritis. Besides tobacco smoking, physical activity is another controversially discussed risk factor related to the development of knee osteoarthritis (McAlindon et al. 1999). Whereas some studies reveal no association between physical activity and the risk of knee osteoarthritis, others again show a significant association (Urquhart et al. 2008; Spector et al. 1996; Kujala et al. 1995).

The aim of this study is to estimate the risk of knee osteoarthritis related to the lifestyle factors BMI, tobacco smoking, and the following sports activities: jogging/athletics; cycling; swimming; soccer; ball games (handball, volleyball, basketball); apparatus gymnastics, shot put, javelin, hammer throwing, wrestling; and body building, strength training.

Overweight and physical workload independently have been shown to be risk factors for knee osteoarthritis (Teichtahl et al. 2008; Cooper et al. 1994a). This study also sought to examine the combined impact of the two parameters BMI and physical workload (kneeling/squatting and lifting/carrying of loads) on the risk of knee osteoarthritis, as well as to examine their mode of interaction.

Subjects and methods

Study population

The study design has been described in detail in a previous publication (Seidler et al. 2008). Briefly, male patients with symptomatic knee osteoarthritis, aged 25–70, were recruited from orthopedic clinics and practices located in the area around the cities Frankfurt/Main and Offenbach in Germany. Women were not included in the study because of the low prevalence of knee straining work among female workers (compared to males); if women had been included, the required study sample size would have been considerably larger to analyze the relationship between physical workload and knee osteoarthritis and the interaction between lifestyle and occupational factors, with sufficient statistical power.

Of eligible patients, 61% agreed to participate. Knee X-rays of participants were collected and re-assessed by a reference radiologist (N.A.) according to the criteria defined by Kellgren (1963). Based on the radiologist's assessment, patients had to have at least grade 2 osteoarthritis to be included in the study. Population-based control subjects were selected from a 1% random sample of male Frankfurt residents, aged 25–70, drawn by the Frankfurt and Offenbach population registration office. Of the eligible population controls, 55% agreed to participate.

Exposure assessment

A detailed computer-assisted personal interview was developed and adopted by intensively trained interviewers to elicit information about work time physical workload including kneeling, squatting, lifting and carrying, working postures, whole body vibration; psychosocial workload, leisure activities, life events, and complaints. For each occupational phase, participants were asked to describe specific objects they had been lifting or carrying frequently, followed by questions considering the objects' weights (categories of weights: >5 to 10, >10 to 20, >20 to 30, >30 to 40, >40 to 50, >50 to 100, and >100 kg, respectively), frequency of lifting/carrying (about every minute, every two minutes, every 5 min, every quarter of an hour, less than every quarter of an hour, respectively; alternatively, exact frequency of lifting/carrying), and duration of lifting/carrying as directly related to these objects. To calculate cumulative exposures to lifting/carrying, all weights >5 kg lifted or carried at work were multiplied by the corresponding durations (assuming 2.5 s duration per single lifting act) and summed. Similarly to the procedure adapted for the calculation of cumulative lifting and carrying of loads, all occupational kneeling/squatting activities were multiplied by their corresponding durations and summed.

Generally, in cases only exposures up to the date of first diagnosis were considered for analysis. Subjects were asked about their age, education, smoking behavior, height, and weight at different ages. A detailed history of sports activities allowed the calculation of cumulative hours spent in the following sports: (1) jogging/athletics; (2) cycling; (3) swimming; (4) soccer; (5) ball games (handball, volleyball, basketball); (6) apparatus gymnastics, shot put, javelin, hammer throwing, wrestling; and (7) bodybuilding, strength training.

As an a priori defined procedure, all variables were categorized in tertiles based on the distribution of the exposed control subjects (see Seidler et al. 2008). If less than 20% of the control subjects were non-exposed, the reference category combined non-exposed subjects and subjects in the first exposure tertile. If the highest tertile of exposed control subjects comprised more than 10% of all (exposed plus non-exposed) control subjects, a high-dose category was generated according to the 95th percentile of control subjects. To give an example, BMI was categorized according to the distribution of the control subjects' BMI as follows: the first tertile of control subjects comprised persons with a BMI < 22.86 kg/m^2; the second tertile comprised persons with a BMI between 22.86 and <24.92 kg/m^2; the third tertile comprised persons with a BMI of 24.92 kg/m^2 or more; and the 95th percentile of control subjects comprised persons with a BMI of 28.41 kg/m^2 or more.

Statistical analysis

Odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression analysis. All statistical analyses were adjusted for age and place of residence, referred to as "region" in this text. Besides the odds ratios solely adjusted for age and region, odds ratios for the "final model" are given. In the final model, the following confounders were included: age, region, body mass index, kneeling/squatting, cumulative lifting/carrying, and jogging/athletics (at a time, excluding the considered variable).

Interaction analysis for BMI and physical workload

An interaction analysis was performed, combining the parameters BMI and kneeling/squatting on the one hand, and BMI and lifting/carrying of loads on the other hand, to one variable. Detailed information on the knee osteoarthritis risks for occupational kneeling/squatting respective lifting/carrying of weights alone (disregarding the interaction with BMI) can be found in Seidler et al. (2008). Briefly, the OR for knee cumulative exposure to kneeling and squatting was 2.4 (95% CI 1.1–5.0) in the highest exposure category (>10,800 h) adjusted for lifting/carrying of weights. Cumulative exposure to lifting/carrying resulted in an OR of 2.6 (95% CI 1.1–6.1) for knee osteoarthritis in the highest exposure category (>37,000 kg × h) adjusted for kneeling/squatting. The knee osteoarthritis risk was strongly increased for high exposures to kneeling/squatting combined with high exposures to lifting/carrying of weights (OR 7.9; 95% CI 2.0–31.5).

To estimate the combined effects of overweight and kneeling/squatting, persons with both a BMI ≥ 24.92 kg/m^2 and a moderate to high cumulative exposure to kneeling/squatting (defined as having been exposed ≥4,757 h) were compared to persons with a BMI < 24.92 kg/m^2 who were not exposed to kneeling/squatting. A similar procedure was adapted in order to analyze the interaction for the combination of overweight and lifting/carrying of loads: persons with both a BMI $\geq$ 24.92 kg/m^2 and a moderate to high cumulative exposure to lifting/carrying of loads (defined as having been exposed to lifting/carrying of loads $\geq$5,120 h) were compared to persons with a BMI of <24.92 kg/m^2 who had not been exposed to lifting/carrying.

To estimate the mode of interaction, the method described by Saracci and Boffetta (1994) was applied. Generally, this method is based on the comparison of the expected OR on the basis of single exposures (OR_1 and OR_2) with the observed OR for the combined exposure. The absolute interaction magnitude is classified with reference to the additive (A) and multiplicative (M) models, according to Table 1.

Population attributable risks (PAR) were calculated for the categories mentioned above taking into account at first BMI elevations alone, at second combined exposure to elevated BMI and to occupational kneeling/squatting, and at third combined exposure to elevated BMI and to occupational lifting/carrying of loads. PAR calculations were based on the adjusted OR, including the above mentioned confounders of the final model.

Results

Age, body mass index, and smoking

A steep dose–response relationship between age and the diagnosis of knee osteoarthritis was found: compared with persons less than 35 years old, persons $\geq$65 years old had a 19-fold elevated knee osteoarthritis risk (OR 19.0; 95% CI 6.1–58.7; Table 2). Considering age as a continuous variable, the risk increase for knee osteoarthritis was $\sim$8% per year. The mean BMI was also strongly associated with knee osteoarthritis: compared to persons with a BMI < 22.86 kg/m^2, persons with a BMI of 28.41 kg/m^2 or more had an OR of 10.8 (95% CI 4.8–24.3). Assuming a linear dose–response relation, there was a "doubling risk" for each 3.4 kg/m^2 increase in the BMI; this means, for example, those persons with a BMI of 28.4 kg/m^2 have a knee osteoarthritis risk of 2 compared with persons with a BMI of 25 kg/m^2. Heavy smokers (tobacco consumption according to a quantity of $\geq$55.5 pack years) showed an adjusted OR of 0.2 (95% CI 0.1–0.5) for the risk of knee osteoarthritis, in comparison to never-smokers.

Sports activities

Cycling was associated with knee osteoarthritis, with an OR of 3.7 (95% CI 1.7–7.8) for persons having cycled 7,000 or more hours. A positive dose–response relationship between the cumulative duration of playing soccer and the diagnosis of knee osteoarthritis with an OR of 2.2 (95% CI 1.0–5.0) in the second-highest category (4,000 to <7,800 h) was found; however, the knee osteoarthritis risk was not significantly elevated among subjects in the highest category ($\geq$7,800 h). The knee osteoarthritis risk was clearly elevated among subjects having played ball games as handball, volleyball, or basketball for 2,100 h or more (OR 4.0; 95% CI 1.8–8.9). The final model did not reveal statistically significant associations between knee osteoarthritis and high cumulative durations of the following sports activities: jogging/athletics; swimming; apparatus gymnastics, shot put, javelin, hammer throwing, wrestling; weight lifting (with low numbers); and body building/strength training.

Interaction analysis for BMI and physical workload

Overweight persons, showing the combination of BMI $\geq$ 24.92 kg/m^2 and moderate to high exposure to kneeling/squatting ($\geq$4,757 h), had an OR of 8.9 (95% CI 4.4–17.9), adjusted for age and region (Table 3). The value of this OR of 8.9 is within the range of values of the expected OR of 8.1 for defining an interaction as of being multiplicative. Therefore, a multiplicative interaction

Table 1 Interpretation of interaction mode, for example, between BMI and physical workload (adapted from Saracci and Boffetta 1994)

Observed OR among subjects with combined "exposure" (e.g., to both BMI and specific physical workload)	Interpretation of interaction mode
More than 25% below expected OR assuming A[a]	Less than additive
Within ±25% of expected OR assuming A	Near additive
Within ±10% of expected OR assuming A	Additive
More than 25% above expected OR assuming A and more than 25% below expected OR assuming M	Intermediate
Within ±25% of expected OR assuming M[a]	Near multiplicative
Within ±10% of expected OR assuming M	Multiplicative
More than 25% above expected OR assuming M	More than multiplicative

[a] "A" refers to the expected OR assuming *additive* interaction ($OR_1 + OR_2 - 1$), whereas "M" refers to the expected OR assuming *multiplicative* interaction ($OR_1 \times OR_2$)

Table 2 Individual/lifestyle factors and symptomatic knee osteoarthritis

Variable	Cases		Controls		Adj. OR[a]	95% CI	Adj. OR[b]	95% CI
	N	%	*N*	%				
Age								
<35 years	5	1.7	58	17.7	1.0	–	1.0	–
35 to <45 years	14	4.7	79	24.2	1.9	0.6–5.8	2.1	0.6–7.1
45 to <55 years	49	16.6	73	22.3	7.7	2.8–20.8	7.3	2.4–22.3
55 to <65 years	134	45.4	81	24.9	19.8	7.5–52.1	14.8	5.0–43.6
≥65 years	93	31.5	36	11.0	28.4	10.4–77.7	19.0	6.1–58.7
Body mass index								
<22.86 kg/m^2	32	10.9	108	33.0	1.0	–	1.0	–
22.86 to <24.92 kg/m^2	74	25.2	108	33.0	1.9	1.1–3.3	1.8	1.0–3.3
24.92 to <28.41 kg/m^2	112	38.1	92	28.1	2.9	1.7–5.1	2.7	1.5–4.9
≥28.41 kg/m^2	76	25.9	17	5.2	12.5	5.8–26.9	10.8	4.8–24.3
Smoking								
Never-smoker	104	35.3	122	37.5	1.0	–	1.0	–
>0 to <11.5 pack years	60	20.3	67	20.6	1.2	0.7–2.0	1.2	0.6–2.1
11.5 to <27.3 pack years	64	21.7	68	20.9	1.0	0.6–1.7	1.2	0.7–2.1
27.3 to <55.5 pack years	57	19.3	51	15.7	0.9	0.5–1.5	0.8	0.4–1.4
≥55.5 pack years	10	3.4	17	5.2	0.4	0.2–0.9	0.2	0.1–0.5
Jogging/athletics								
No jogging/athletics	210	71.2	203	62.1	1.0	–	1.0	–
>0 to <700 h	21	7.1	37	11.3	0.8	0.4–1.5	0.8	0.4–1.7
700 to <1,695 h	16	5.4	37	11.3	0.8	0.4–1.5	1.0	0.5–2.3
1,695 to <3,530 h	25	8.5	21	6.4	1.5	0.7–3.1	1.9	0.8–4.1
≥3,530 h	23	7.8	16	4.9	1.6	0.7–3.3	1.9	0.8–4.3
Cycling								
No cycling	153	51.9	204	62.4	1.0	–	1.0	–
>0 to <1,050 h	13	4.4	36	11.0	0.6	0.3–1.3	0.6	0.2–1.4
1,050 to <3,700 h	50	16.9	36	11.0	2.0	1.2–3.6	2.3	1.2–4.4
3,700 to <7,000 h	33	11.2	21	6.4	1.6	0.8–3.0	1.8	0.8–3.8
≥7,000 h	46	15.6	15	4.6	3.2	1.6–6.5	3.7	1.7–7.8
Swimming								
No swimming	233	79.3	261	79.8	1.0	–	1.0	–
>0 to <500 h	13	4.4	17	5.2	0.9	0.4–2.1	0.6	0.2–1.9
500 to <1,900 h	17	5.8	18	5.5	1.1	0.5–2.5	1.7	0.7–4.2
≥1,900 h	31	10.5	18	5.5	2.1	1.0–4.3	2.0	0.9–4.4
Soccer								
No soccer	178	60.3	208	63.6	1.0	–	1.0	–
>0 to <1,660 h	29	9.8	35	10.7	1.3	0.7–2.3	1.1	0.5–2.1
1,660 to <4,000 h	41	13.9	34	10.4	1.9	1.0–3.4	2.0	1.0–3.8
4,000 to <7,800 h	32	10.8	19	5.8	2.2	1.1–4.4	2.2	1.0–5.0
≥7,800 h	15	5.1	16	4.9	1.2	0.5–2.8	1.4	0.6–3.6
Ball games (handball, volleyball, basketball)								
No ball games	240	81.4	251	76.8	1.0	–	1.0	–
>0 to <1,050 h	14	4.7	19	5.8	1.3	0.5–3.2	1.2	0.4–3.2
1,050 to <2,100 h	9	3.1	18	5.5	0.6	0.2–1.4	0.7	0.2–2.1
≥2,100 h	32	10.8	19	5.8	2.9	1.4–6.0	4.0	1.8–8.9

Table 2 continued

Variable	Cases N	Cases %	Controls N	Controls %	Adj. OR[a]	95% CI	Adj. OR[b]	95% CI
Apparatus gymnastics, shot put, javelin, hammer throwing, wrestling								
No apparatus gymnastics, etc.	260	88.1	289	88.4	1.0	0.2–4.3	1.0	–
>0 to <400 h	5	1.7	6	1.8	1.0	0.2–4.3	0.5	0.1–3.1
400 to <2,200 h	21	7.1	6	1.8	4.0	1.3–12.0	3.2	1.0–9.8
≥2,200 h	9	3.1	7	2.1	1.7	0.5–5.4	0.9	0.2–3.6
Weight lifting								
No weight lifting	289	98.0	300	91.7	1.0	–	1.0	–
>0 to <1,000 h	2	0.7	2	0.6	–	–	–	–
1,000 to <1,500 h	2	0.7	2	0.6	–	–	–	–
≥1,500 h	2	0.7	3	0.9	1.4	0.2–9.8	0.6	0.1–4.3
Body building, strength training								
No body building, strength training	280	94.9	262	80.1	1.0	–	1.0	–
>0 to <600 h	2	0.7	16	4.9	0.2	0.05–1.2	0.4	0.1–2.6
600 to <1,700 h	8	2.7	15	4.6	0.8	0.3–2.3	1.2	0.4–3.8
≥1,700 h	5	1.7	16	4.9	0.7	0.2–2.1	0.9	0.3–3.0

[a] Adjusted for age and region (without considered variable)

[b] Adjusted for age, region, body mass index, jogging/athletics, kneeling/squatting, and lifting/carrying (without considered variable)

Table 3 Interaction of body mass index and physical workload (kneeling/squatting; lifting or carrying of loads) and the risk of knee osteoarthritis

Variable	Cases N	Cases %	Controls N	Controls %	Adj. OR[a]	95% CI	Adj. OR[b]	95% CI
Body mass index (BMI) combined with kneeling/squatting								
0. BMI < 24.92 kg/m^2 and no kneeling/squatting	60	20.3	145	44.3	1.0	–	1.0	–
1. Kneeling/squatting >0 to <4,757 h	47	15.9	79	24.2	1.7	1.0–2.9	1.2	0.7–2.2
2. BMI ≥ 24.92 kg/m^2 and no kneeling/squatting	85	28.8	62	19.0	2.7	1.6–4.6	2.5	1.5–4.3
3. BMI < 24.92 kg/m^2 and kneeling/squatting ≥4,757 h	32	10.8	23	7.0	3.0	1.5–6.0	1.8	0.8–3.9
4. BMI ≥ 24.92 kg/m^2 and kneeling/squatting ≥4,757 h	69	23.4	15	4.6	8.9	4.4–17.9	5.3	2.4–11.5
Expected OR assuming additive interaction ($OR_2 + OR_3 - 1$)*					*4.7*		*3.3*	
Expected OR assuming multiplicative interaction (OR_2 x OR_3)*					*8.1*		*4.5*	
Mode of interaction based on Saracci and Boffetta					Multiplicative		Near multiplicative	
Body mass index (BMI) combined with lifting/carrying of weights								
0. BMI <24.92 and no lifting/carrying	32	10.8	110	33.6	1.0	–	1.0	–
1. Lifting/carrying >0 to <5,120 h	89	30.2	115	35.2	2.6	1.5–4.6	2.4	1.3–4.3
2. BMI ≥ 24.92 kg/m^2 and no lifting/carrying	43	14.6	42	12.8	2.7	1.4–5.1	2.4	1.2–4.7
3. BMI < 24.92 kg/m^2 and lifting/carrying ≥5,120 h	37	12.5	30	9.2	3.9	1.9–7.9	2.4	1.1–5.4
4. BMI ≥ 24.92 kg/m^2 and lifting/carrying ≥5,120 h	89	30.2	27	8.3	6.8	3.6–12.9	5.0	2.4–10.5
Expected OR assuming additive interaction ($OR_2 + OR_3 - 1$)*					5.6		3.8	
Expected OR assuming multiplicative interaction (OR_2 x OR_3)*					10.5		5.8	
Mode of interaction based on Saracci and Boffetta					Near additive		Near multiplicative	

Probands with missing BMI and/or missing kneeling/squatting respective lifting/carrying are analyzed in a separate category (not shown)

[a] Adjusted for age and region

[b] Adjusted for age, region, body mass index, jogging/athletics, kneeling/squatting, and lifting/carrying (without considered variable)

* OR_2 and OR_3 refer to the odds ratios for the exposures as defined in the lines numbered 2 and 3 of the table, respectively

between BMI and kneeling/squatting with regard to the risk of symptomatic knee osteoarthritis was observed. Applying the final model, the corresponding interaction was nearly multiplicative (observed OR 5.3; 95% CI 2.4–11.5; expected OR on the basis of an assumed multiplicative interaction mode 4.5).

Overweight persons, showing BMI $\geq$ 24.92 kg/m^2 combined with moderate to high exposures to lifting/carrying of loads ($\geq$5,120 kg $\times$ h), had an OR of 6.8 (95% CI 3.6–12.9), adjusted for age and region. This OR was slightly higher than the expected OR of 5.6, assuming an additive interaction mode (Table 3). Therefore, a nearly additive interaction for the combination of BMI and lifting/carrying of loads with regard to the risk for symptomatic knee osteoarthritis was observed. Applying the final model, the observed OR of 5.0 (95% CI 2.4–10.5) was within the range of values of the expected OR of 5.8 for defining the mode of interaction as of being nearly multiplicative.

Population attributable risks (PAR) for BMI and physical workload

The adjusted population attributable risk (PAR) for a BMI of 22.86 or more compared with a BMI of less than 22.86 was 37% (no table). The adjusted PAR for kneeling/squatting for 4,757 h or more was 6% (no table). The adjusted PAR for occupational lifting and carrying of weights $\geq$5,120 kg $\times$ h was 9%.

When population attributable risks were calculated for the combination of BMI elevations and occupational exposures, for persons with a BMI $\geq$ 24.92 kg/m^2 exposed to kneeling/squatting for 4,757 h or more, the PAR was 4%. The population attributable risk for the combined exposure to BMI $\geq$ 24.92 kg/m^2 and occupational lifting/carrying of weights $\geq$5,120 kg $\times$ h was 7%. When persons with occupational lifting/carrying of weights $\geq$630 kg $\times$ h were regarded as exposed, the population attributable risk for the combined exposure to BMI $\geq$ 24.92 kg/m^2 and occupational lifting/carrying increased to 16%.

Discussion

In this study, age and overweight were strongly associated with the diagnosis of symptomatic knee osteoarthritis. Ball games (handball, volleyball, basketball) and cycling, to a weaker degree also jogging, swimming, and soccer were positively related to symptomatic knee osteoarthritis. Tobacco smoking showed a negative association with regard to the risk of symptomatic knee osteoarthritis for heavy smokers ($\geq$55.5 pack years).

The power of the study to detect effects of kinds of sports that are associated with high internal joint forces (weight lifting, body building) on the knee osteoarthritis risk is limited. Low physical activity, according to the lowest exposure groups (jogging/athletics up to 700 h; cycling up to 1,050 h; swimming up to 500 h; soccer up to 1,660 h; ball games, including handball, volleyball, and basketball, up to 1,050 h; apparatus gymnastics, shot put, javelin, hammer throwing, wrestling up to 400 h; body building and strength training up to 600 h; see Table 2) was not associated with symptomatic knee osteoarthritis. These results are in accordance with findings from other studies where light and moderate physical activities did not appear to increase the study population's knee osteoarthritis risk (McAlindon et al. 1999) and where recreational exercise was shown neither to protect against nor to increase the risk of knee osteoarthritis (Felson et al. 2007).

Potential bias

For a detailed discussion on potential bias, refer to Seidler et al. 2008. Briefly, substantial residual confounding by age and through choosing of participating medical facilities (orthopedic clinics and practices) is regarded as an improbable explanation of the results. The low participation rate (61% among patients, 55% among referents) might have introduced selection bias (potential overestimation of knee osteoarthritis risks). One major potential limitation of self-reported data concerns the possibility of differential and non-differential recall bias. In general, a differential overestimation of physical workload by patients would lead to an overestimation of risks. Otherwise, a non-differential overestimation of physical workload (in both cases and control subjects) would lead to an underestimation of risks. We therefore cannot reliably estimate the true effect of potential recall bias on the risk estimates. However, recall bias should not have played an important role in the participants' report of job titles. As the occupational group analysis reveals elevated risks in occupations with suspected high exposure to kneeling as well as to lifting/carrying of loads (e.g., metal workers, terrazzo layers, painters, see Seidler et al. 2008), recall bias is not a sufficient explanation for the positive association between physical workload and symptomatic knee osteoarthritis. Finally, adjustment for different interviewers did not substantially alter the results, so that interviewer bias can be regarded as negligible.

Plausibility of results

The finding of a clear dose–response relationship between BMI and knee osteoarthritis risk is in accordance with the literature (Felson 1996; Stürmer et al. 2000). The dose–response relationship between weight and knee osteoarthritis as well as the dose–response relationship between kneeling, respectively, lifting/carrying of loads and knee osteoarthritis can be explained by elevated joint forces with subsequent chronic cartilage damage: factors that lead to a high pressure on the articular cartilage of knee joints have been shown to be associated with a high knee osteoarthritis risk (Cooper et al. 1994b, Schouten et al. 1992, Manninen et al. 1996, Stürmer et al. 2000, Coggon et al. 2000). Lifting and carrying of heavy weights as well as overweight result in high forces acting on parts of the knee joints' cartilage. Therefore, it appears biologically plausible that pressure on knee joints might damage the articular cartilage and might consequently lead to knee osteoarthritis. However, an alternative hypothesis regards obesity as a systemic rather than a mechanical risk factor (as in some studies hand osteoarthritis is also associated with obesity).

In a large cohort study including 320,192 male Swedish construction workers, Järvholm et al. (2005) found a doubling of the risk ("doubling dose") of severe knee osteoarthritis with an increase in BMI of 5 kg/m^2. In the present study, the weight-related knee osteoarthritis risk is even higher with a "doubling dose" of 3.4 kg/m^2 increase in BMI.

Furthermore, the association between BMI and risk of symptomatic knee osteoarthritis is in accordance with data regarding a higher risk of knee replacement related to obesity (Liu et al. 2007). In a prospective cohort study including 490,532 women aged 50–69, who were recruited in the United Kingdom in 1996–2001 and followed over almost 3 years, Liu et al. (2007) examined among others the effect of BMI on the risk of knee replacement. Based on these data, the risk of knee replacement increased with increases in both BMI and weight. Comparing the heaviest group of women ($\geq$75 kg) with the lightest one (<60 kg) the relative risk for knee replacement was 9.71 (95% CI 7.39–12.77). When obese women ($\geq$30 kg/m^2) where compared to those in the lowest BMI group (<22.5 kg/m^2), the relative risk for knee replacement was 10.51 (95% CI 7.85–14.08). Adjusting for potential confounders (time since menopause, smoking, alcohol use, parity, or other illnesses reported at baseline) the calculated risks for BMI were not altered substantially: comparing the highest with the lowest BMI group, the relative risk for knee replacement was 9.49 instead of 10.51. On the basis of this data, Liu et al. (2007) estimated that 69% (95% CI 64–73%) of knee replacements are attributable to overweight and obesity (BMI $\geq$ 25 kg/m^2). Based on the present study data, 37% of symptomatic knee osteoarthritis is attributable to overweight/obesity (PAR = 37%, see above). The discrepancy between the attributable risk fraction of the data of Liu et al. (2007) and the present data could be resulting from the older age structure of the longitudinal cohort study design (50–64 vs. 25–70 years) of the former study. Another reason for this discrepancy could be found in the missing adjustment for occupational factors. Finally, Liu et al. (2007) did not focus on the risk factors of knee osteoarthritis, but on the risk factors of knee replacements: BMI might not only constitute an etiologic factor for the development of knee osteoarthritis, but also a prognostic factor for the requirement of knee replacement.

The present data reveal a negative relationship between the amount of smoking and diagnosis of knee osteoarthritis. Similarly, other studies have also found that smoking seems to decrease the risk of osteoarthritis (Järvholm et al. 2005; Liu et al. 2007; Sandmark et al. 1999). As a possible explanation, Järvholm et al. (2005) hypothesize that smoking might be associated with decreased performance of sports activities. However, in our study, the negative relationship between the amount of smoking and knee osteoarthritis remains stable after adjustment for sports activities.

The association between specific sports activities (playing soccer or ball sports) and knee osteoarthritis is partly in accordance with Kujala et al. (1994): these authors find an elevated osteoarthritis risk for Finish elite athletes from all types of competitive sports. The lack of a monotonous dose–response relationship between playing soccer and knee osteoarthritis might be explained by a "healthy athlete" effect: soccer players with knee complaints might quit playing soccer earlier than persons without knee complaints. The association between cumulative cycling time and knee osteoarthritis has to be verified in further studies.

Interaction between BMI and physical workload

Combining the two parameters BMI and kneeling/squatting into one variable led to a multiplicative interaction mode. This form of interaction could point to potentially different pathological pathways of overweight and kneeling/squatting in the etiology of knee osteoarthritis. The findings of a multiplicative interaction are in accordance with Coggon et al. (2000) who found that the interaction of occupational kneeling and squatting with obesity was approximately multiplicative. Persons exposed to occupational kneeling and squatting who had a BMI $\geq$ 30 kg/m^2 had an OR of 14.7 (95% CI 7.2–30.2) in comparison with unexposed subjects (BMI < 25 kg/m^2).

Based on the present data, it is not possible to conclude if the mode of interaction between BMI and lifting/carrying of loads can be defined as of being rather additive or rather multiplicative. A similar pathologic pathway for overweight and lifting/carrying of loads (for example, acting through elevated compressive forces within the knee joint) might explain the lower synergistic effect of these two factors compared to the combined effect of overweight and kneeling/squatting.

Population attributable risks (PAR) for knee osteoarthritis regarding the combination of the highest risk categories of BMI ($\geq$24.92 kg/m^2) with occupational kneeling/squatting ($\geq$4,757 h) and occupational lifting/carrying of loads ($\geq$5,120 h) were 4 and 7%, respectively. Preventive strategies aiming to reduce the prevalence of knee osteoarthritis should therefore take into consideration both occupational and non-occupational factors. Because of the high prevalence of overweight as well as of occupational lifting/carrying of loads, an appropriate public health strategy should include appropriate work organizational interventions targeted to reduce lifting/carrying of loads as well as interventions to reduce overweight.

Conclusion

This study supports a dose–response relationship between age, BMI and the risk of symptomatic knee osteoarthritis, respectively. Assuming a linear dose–response-relation, a "doubling risk" for each 3.4 kg/m^2 increase in the BMI is found. Heavy smoking is associated with a lower risk of knee osteoarthritis. Sports activities are associated to different degrees with the risk of knee osteoarthritis. Taking into consideration the interaction of exposures, BMI and kneeling/squatting show a multiplicative mode of interaction, whereas the interaction mode between BMI and lifting/carrying of loads cannot be clearly classified as of being rather additive or multiplicative. Considering the relatively high prevalence of occupational manual materials handling, in a public health perspective, prevention of knee osteoarthritis should not only focus on weight reduction alone, but should also take into account work organizational measures particularly aiming to reduce occupational lifting and carrying of loads.

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Conflict of interest statement The authors declare that they have no competing interests.

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