Osteoarthritis and Cartilage 19 (2011) 809–815

Osteoarthritis and Cartilage

Weight gain and the risk of total hip replacement a population-based prospective cohort study of 265,725 individuals

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ARTICLE INFO

Article history:
Received 21 September 2010
Accepted 17 March 2011

Keywords:
Osteoarthritis
Body mass index
Epidemiology
Hip
Obesity
Weight gain

SUMMARY

Objective: To study the association between change in the body mass index (BMI) at different ages and the risk of a later total hip replacement (THR) due to primary osteoarthritis (OA).
Design: A total of 265,725 individuals who had two repeated measurements of weight and height were included from national health screenings. These individuals were followed prospectively. The data were matched with the Norwegian Arthroplasty Register and 4,442 of these individuals were identified as having received a THR for primary OA. Cox proportional hazard regression was used to calculate sex-specific relative risks for having a THR according to age at screening and BMI change.
Results: Men and women aged 20 years or younger at the first screening in the quartile with the greatest BMI change per year had more than twice the risk of later having a THR compared with those in the quartile with the smallest BMI change per year. For men older than 30 years at the first screening, there was no relationship between BMI gain, or weight gain, and later risk of THR. For older women, BMI gain was associated with risk of THR, but to a lesser degree than in younger women.
Conclusion: There was a clear relationship between change in BMI and the risk of later THR in young men and women, whereas the association was absent in older men and weaker in older women. It is important to focus on weight control to prevent future OA, and the preventive strategy should be focused on the young population.

Knowledge of the pathogenesis and risk factors for hip osteoarthritis (OA) is increasing. A strong hereditary component has been identified[1–4], and high body mass index (BMI), and high physical activity are established as strong risk factors[5–12], as is previous joint injury[13,14].

BMI is a modifiable risk factor; therefore, studies of the effect of weight change on development, progression and treatment of OA would provide valuable information that could be used to advise people about lifestyle changes to prevent future OA.

Weight reduction has proven effective in relieving pain in symptomatic knee OA[15], and it has been associated with lower risk of knee OA later in life[16]. Weight gain from normal to obese weight in adult life has also been shown to lead to a higher risk for needing a total knee replacement[17]. An increase in BMI in early adult life was associated more strongly with later knee OA than an increase in BMI in middle age[18].

Two studies have investigated the effect of weight change on the risk of having a total hip replacement (THR). One study examined the effect of spontaneous weight change between ages 34 and 47 years in 38,868 men and women and found no effect[19]. The Nurses' Health Study included 93,442 female nurses and found a moderate effect of weight gain from the age of 18 years until the date of THR, and no effect of weight loss[20]. A third study investigated the effect of weight change between ages 20 and 49 years on self-reported hip OA in 1,180 male physicians[18]. This study found no effect of weight change, but with only 26 men reporting hip OA, the power to detect an association was limited.

In the Nurses' Health Study, the recalled BMI at 18 years was highly associated with later THR, more than BMI close to the date of THR[20]. A large cohort study of almost 1.2 million individuals also found that the impact of a high BMI on the risk of having a later THR

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doi:10.1016/j.joca.2011.03.013

was much higher at a young age[21], which indicates that the risk for OA is established early in life.

Animal studies have revealed changes in the architecture and collagen content of the cartilage during growth and maturation[22]. The timescale of this maturation in humans is not elaborated. The authors of the animal study indicate that regular physical exercise with physiological loading at a young age may prevent future OA.

The current study investigates the effect of change in BMI on the risk of having a THR for primary OA. Previous studies have found no effect of weight gain in middle age[19], but a difference in the impact of a high BMI between different age groups[21]; therefore, this study assesses the effect of weight gain in subgroups of patients according to age. The study hypothesis is that weight gain in young adults is more damaging to the hip joint than weight gain later in life.

Patients and methods

The **National Health Screening Service** (now the Norwegian Institute of Public Health) has performed a series of population-based health screenings in Norway, including a nationwide compulsory tuberculosis screening during 1963–1975[23], and numerous cardiovascular screenings from 1974 to 1999[24]. In addition, population-based health screenings have been performed in the city of Oslo[25], Tromsø[26], and the county of Nord-Trøndelag[27].

Information obtained in the screenings varies according to the different purposes of the screenings. We gathered information from these surveys on weight and height measured twice in 304,011 individuals. The first weight and height measurements were from screenings performed between 1963 and 1975; the Tuberculosis Screening[23], and the Oslo Study[25]. The second weight and height measurements were obtained from screenings performed between 1974 and 1997; the First and Second Cardiovascular Survey of Oppland, Finnmark and Sogn og Fjordane, the Second and the Third Tromsø Study, the First Nord-Trøndelag Health Study (HUNT), and the 40-year Surveys. Body weight and height were measured in a standardized way at a consultation in all the included screenings. The second screening also included information on smoking habits, which were classified as never smoker, former smoker, or current smoker. Data from the health surveys were matched with the data on THRs performed from the Norwegian Arthroplasty Register using the national 11-digit personal identification code. The Norwegian Arthroplasty Register was started in 1987 by the Norwegian Orthopedic Association[28]. The operating orthopedic surgeon submits a standardized form to the register for each arthroplasty performed. The form contains information about the patient, the diagnosis that leads to the arthroplasty, the procedure and the type of implant used. The Norwegian Arthroplasty Register was fully operational from 1989. Data on death and emigration were collected from the Norwegian Registry of Vital Statistics.

The start of follow up in this study was January 1 1989, except for individuals who had their second weight measured in a health survey performed later than January 1 1989. For these, the start of follow up was the date of the second weight measurement. End of follow up was February 1 2006. There is no information on THRs performed before the start of follow up, except for 242 cases where there is information on surgery performed before the start of follow up that was given in connection with later surgery and is found in the Norwegian Arthroplasty Register. These cases were excluded.

Inclusion: all individuals invited to the Tuberculosis Screening or the Oslo Study who also participated in later screenings, and so had their weight and height recorded twice, were included in the study.

Exclusion: all individuals younger than 16 years at the first screening ($n = 29{,}764$), or older than 80 years at the start of follow up ($n = 2{,}816$) were excluded. Individuals were also excluded if they: had their second weight and height measurement after they had received a THR ($n = 133$); had already received a THR before start of follow up, according to the Norwegian Arthroplasty Register ($n = 242$), or had died or emigrated before start of follow up, according to the Norwegian Registry of Vital Statistics ($n = 4{,}864$). Also excluded were individuals who had information in the register about revision surgery, but no information on primary surgery, and individuals for whom there were irregularities in the data from the Norwegian Arthroplasty Register ($n = 467$).

A total of 304,011 individuals had repeated measurements of weight and height. Of these, 265,725 were eligible for the study after exclusion.

BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Change in body stature was expressed as change in BMI per year: the difference in BMI between the last and the first screening divided by the number of years between the screenings (ΔBMI/Year). The cohort was divided into quartiles according to the change in BMI per year and the quartiles with greater changes in BMI per year were compared with the quartile with the least change in BMI per year (the reference quartile). There are some limitations to the use of change in BMI per year as an exposure variable. There is no information on how each individual's stature evolved between the two screenings, e.g., if he or she gained weight rapidly during 1 year, or if the weight change was gradual throughout the whole interval between the two screenings. Because of this uncertainty, the analyses were also performed using absolute weight change in kilograms between the two screenings.

The cohort was divided into strata of 10 years according to the age at the first screening, and the results are presented accordingly. For example, for the strata who were 20 years and younger at the first screening, the effect of weight change between screenings was studied at mean ages of 18 and 41 years (Table I). The cohort was also stratified by sex.

Adjustments were made for the continuous variables age, BMI and height at the first screening, and for the smoking habits recorded at the second screening. Analyses were also performed with BMI and height measured at the first screening, categorized into sex-specific quartiles.

The analyses were performed as a survival study using the Cox proportional hazard regression method, calculating hazard ratios (hereafter called relative risks) for having a THR. The event was defined as the first recorded THR performed for the diagnosis of primary OA. Censoring occurred for THR performed for diagnosis other than primary OA, for death, for emigration, and at end of follow up.

Tests and visual inspection of plotted scaled Schoenfeld residuals[29] showed that the proportional hazard assumption of the Cox model was satisfied. The analyses were performed using the statistical program package SPSS version 16 (SPSS Inc., Chicago, IL, USA), and the statistical software R, version 2.9.0 (R: A language and environment for statistical computing. Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org).

The study was approved by the Data Inspectorate and the Regional Committee for Research Ethics in Norway.

The numbers of individuals included in the tables may vary slightly due to some missing values.

Results

A total of 124,894 men and 140,831 women were included in the study. The mean time between the two screenings was 18.1 years [standard deviation (SD) 4.8] and was somewhat longer in the youngest age group (Table I). Mean follow-up time was 15.3 years (SD 2.5). The mean increase in BMI between the two screenings was

Table I
Background characteristics of the cohort of 265,725 participants according to age at the first screening

	Age group at first screening (y)				
	≤20	21–30	31–40	41–50	51–60
Men					
No.	46,606	44,665	20,610	10,038	2,969
Age at first screening (1963–1975)*	17.8 (1.3)	24.4 (2.6)	35.6 (2.8)	44.4 (2.6)	54.6 (2.6)
Years between screenings*	21.8 (3.5)	16.5 (3.3)	13.4 (4.5)	16.4 (4.5)	16.0 (1.5)
Age at second screening (1974–1997)*	40.2 (3.4)	41.3 (2.7)	49.5 (5.6)	61.3 (5.7)	71.1 (2.8)
Age at start of follow up (01.01.1989, or for persons with second screening after 01.01.1989, date for second screening)*	40.9 (1.6)	43.9 (3.1)	56.7 (3.9)	65.2 (3.0)	75.0 (2.7)
Age at end of follow up (01.02.2006)*	54.6 (2.2)	60.2 (3.6)	73.1 (3.6)	80.9 (2.5)	90.5 (2.4)
Women					
No.	51,417	52,783	21,875	11,105	3,647
Age at first screening (1963–1975)*	17.9 (1.4)	24.1 (2.6)	35.6 (2.8)	44.5 (2.6)	54.6 (2.6)
Years between screenings*	21.9 (3.4)	16.7 (3.3)	13.9 (4.7)	16.9 (4.2)	16.0 (1.5)
Age at second screening (1974–1997)*	40.3 (3.3)	41.3 (2.6)	50.0 (5.8)	61.9 (5.4)	71.1 (2.8)
Age at start of follow up (01.01.1989, or for persons with second screening after 01.01.1989, date for second screening)*	41.0 (1.6)	43.8 (3.1)	56.9 (4.0)	65.4 (2.9)	75.1 (2.7)
Age at end of follow up (01.02.2006)*	54.7 (2.3)	60.1 (3.7)	73.5 (3.5)	81.2 (2.6)	90.8 (2.4)

* Mean (SD).

2.45 kg/m^2 (SD 2.64) for men, and 1.76 kg/m^2 (SD 3.0) for women, with a corresponding mean increase in weight of 8.4 kg (SD 8.4) in men, and 5.1 kg (SD 8.3) in women (Table II). During follow up, 1,521 men, and 2,921 women received their first THR because of primary OA. A total of 1,945 individuals were censored because they received the prosthesis for a condition other than primary OA. The main indications for surgery in these cases were dysplasia ($n = 705$) and sequelae after hip fracture ($n = 616$). A total of 30,980 individuals were censored because they died or emigrated during follow up.

The cohort was divided into groups according to age at the first screening. Men aged 20 years or younger in the quartile with the greatest BMI change per year had a more than double relative risk of having a THR compared with men in the same age group in the quartile with the smallest BMI change per year. The corresponding relative risk in men aged 21–30 years at the first screening was 37%. There was no statistically significant increased risk associated with change in BMI in men aged over 31 years at the first screening (Table III).

For women aged 20 years or younger at the first screening, the relative risk of having a THR in the quartile with the greatest BMI change per year was also more than double that in the quartile with the smallest BMI change per year. An increased relative risk for women in the quartile with the greatest BMI change per year compared with that with the smallest BMI change per year was found to a lesser degree in those aged 21–30 years, and 31–40 years at the first screening. In the oldest age group of women, 51–60 years at the first screening, the quartile with the greatest BMI change per year had a statistically significant increased risk compared with the quartile with the smallest BMI change per year (Table IV).

Additional analyses were conducted with the covariates BMI and height at the first screening, categorized into sex-specific quartiles, and gave similar results (data not shown). Analyses with BMI from the first screening categorized into quartiles specific for each 10-year age group also showed comparable results.

The possibility of an interaction between the first measured BMI and the change in BMI was investigated using an interaction term and no interaction was found.

Multivariate analysis was conducted with BMI change per year as a continuous variable (Table V). There was a six-fold increased relative risk per 1 kg/m^2 increase in BMI per year for men aged 20 years or younger at the first screening. For men in the older age groups there was no significant increase in risk. There was also a markedly increased relative risk associated with BMI change per year for women aged 20 years or younger at the first screening. The relative risk associated with BMI change per year was also elevated, but to a lesser degree, for women in the age groups 21–30 years, 31–40 years and 51–60 years.

The analyses were also performed using absolute weight change in kilograms (Table V). The results followed the same trends as those observed for BMI change per year. An effect of weight gain in men was only seen in those aged younger than 31 years at the first screening. In the youngest age group, a 10 kg weight gain was associated with a 33% increased risk of having a THR in men, and a 24% increased risk in women.

As the first screenings were performed over a period of 12 years (1963–1975), the analysis was repeated stratified to whether the first screening was early or late in the period, dividing the period in two by using the median. This did not have any effect on the results (data not shown).

High BMI at the second screening was not in itself a risk factor for needing a THR. The mean age at the second screening was 44.6 years. These findings concur with the findings in previous studies where high BMI in the young had a greater impact on the risk for needing a THR than high BMI in the older age[21].

Table II
Change in BMI, weight and height for the 265,725 participants according to the age at the first screening

Age at the first screening (y)	Change in BMI kg/m^2 (mean; SD)	Change in weight kg (mean; SD)	Change in height cm (mean; SD)
Men			
17–20	3.94 (2.64)	14.40 (9.15)	2.4 (3.4)
21–30	2.11 (2.23)	6.92 (7.17)	0.2 (1.3)
31–40	0.95 (1.89)	2.66 (5.83)	−0.3 (1.4)
41–50	0.77 (2.05)	1.71 (6.30)	−0.8 (1.4)
51–60	0.30 (2.06)	0.05 (6.19)	−1.0 (1.4)
Women			
17–20	2.49 (3.29)	7.59 (8.99)	1.1 (1.5)
21–30	1.78 (2.80)	5.16 (7.56)	0.4 (1.4)
31–40	0.93 (2.54)	2.20 (6.56)	−0.3 (1.5)
41–50	0.68 (2.69)	0.96 (6.96)	−1.0 (1.6)
51–60	−0.35 (2.84)	−2.20 (7.19)	−1.5 (1.8)

Discussion

This study in a large cohort of men and women showed that weight gain in young individuals increased the risk of later THR due

Table III
Absolute and relative risk of THR due to primary OA according to BMI change per year in 124,894 men

	Quartile of BMI change per year (kg/m^2/year)			
	First <0.04	Second 0.04–0.12	Third 0.12–0.21	Fourth >0.21
17–20 years at first screening				
No. of participants	4,578	9,879	14,989	17,148
Person–years	65,174	135,858	202,833	232,764
No. of THR	11	18	31	60
THR per 100,000 person–years (crude rate)	16.88	13.25	15.28	25.78
Crude relative risk	1	0.78	0.91	1.53
Multivariate-adjusted relative risk [95% confidence interval (CI)]*	1	1.00 (0.46–2.14)	1.23 (0.60–2.51)	2.15 (1.10–4.20)
21–30 years at first screening				
No. of participants	11,181	11,412	11,347	10,723
Person–years	184,574	186,172	184,335	174,341
No. of THR	90	78	91	94
THR per 100,000 person–years (crude rate)	48.76	41.90	49.37	53.92
Crude relative risk	1	0.86	1.01	1.11
Multivariate-adjusted relative risk (95% CI)*	1	1.05 (0.77–1.43)	1.30 (0.96–1.75)	1.37 (1.02–1.85)
31–40 years at first screening				
No. of participants	8,823	5,032	3,662	3,087
Person–years	146,688	82,942	60,603	51,506
No. of THR	256	161	128	96
THR per 100,000 person–years (crude rate)	174.52	194.11	211.21	186.39
Crude relative risk	1	1.11	1.21	1.07
Multivariate-adjusted relative risk (95% CI)*	1	1.13 (0.93–1.38)	1.23 (0.99–1.53)	1.06 (0.84–1.35)
41–50 years at first screening				
No. of participants	5,001	2,466	1,574	995
Person–years	79,891	39,114	25,143	16,198
No. of THR	167	88	61	25
THR per 100,000 person–years (crude rate)	209.03	224.98	242.61	154.34
Crude relative risk	1	1.08	1.16	0.74
Multivariate-adjusted relative risk (95% CI)*	1	1.08 (0.83–1.41)	1.14 (0.85–1.54)	0.74 (0.48–1.13)
51–60 years at first screening				
No. of participants	1,728	665	394	182
Person–years	28,889	11,080	6,577	3,038
No. of THR	35	15	10	5
THR per 100,000 person–years (crude rate)	121.15	135.38	152.05	164.58
Crude relative risk	1	1.12	1.25	1.36
Multivariate-adjusted relative risk (95% CI)*	1	1.19 (0.65–2.18)	1.38 (0.68–2.80)	1.49 (0.58–3.83)

* Adjusted for age, BMI, and height at first screening, and for smoking at second screening.

to primary OA. The association was weak or absent in men and women older than 30 years at the first screening.

One of the strengths of this study is the very large number of participants. In the older age groups, the number of events was particularly large, lending the analyses a high statistical power to detect a possible effect of weight gain. This supports our conclusion that weight gain is more damaging in the young.

The Norwegian Arthroplasty Register is functioning well, with a reporting rate of more than 97%[30]. The register was shown to have a very high validity when compared with local records from one hospital[31]; therefore, the number of undetected events in the current study population within the follow-up period is likely to be insignificant.

Body weight and height were measured in a standardized way at a consultation. This standardized measurement circumvented the problems associated with self-reporting weight and height. These problems vary systematically with BMI: individuals with a high BMI tend to under-report their weight and over-report their height[32].

A substantial proportion of individuals aged over 80 years may have medical conditions that render them unfit for surgery, and may not receive a THR even if they have severe symptomatic OA; therefore, all individuals aged over 80 years at the start of follow up were excluded from the analysis. As some of the individuals might have received a THR before the start of follow up (1989), the risk set at the time of an event could be overestimated. This would have the greatest effect on the oldest age groups, resulting in too low prosthesis rates. Accordingly, caution should be exercised when comparing rates across age categories; however, the effect within age categories would be small and the Cox regression analyses valid.

Death is a competing risk when studying the need for THR, and could lead to an overestimate of the risk for needing a THR, particularly in the oldest age group. There was no difference in the number of deaths in the different quartiles in the same age group. Again, caution should be exercised when comparing rates across age categories, but within age categories, the Cox regression analyses should be valid.

The mean time between the last weight and height measurements and THR was 14.9 years (SD 5.2). With such a long interval it is unlikely that weight gain in patients who later received a THR was caused by early OA symptoms inducing a sedentary lifestyle. To double check this, further analyses excluded all participants who had a THR performed before 1995, thus allowing for an even longer mean time between the weight measurements and surgery. These analyses gave similar results. Other studies have shown that obesity precedes the development of OA of the knee joint[16,33]. Among those who had their second weight measurement before the start of follow up, the time between the weight change and the start of follow up varied. Analyses were conducted including only the individuals who had their second weight measurement after January 1 1989, i.e., there was no time gap between the weight change and start of follow up (127,183 individuals). The results were no longer statistically significant; however, the trends in the results were the same (data not shown). The cohort study of 38,868 individuals that failed to find an effect of weight change between the age of 35 and 47 years included some of the same individuals in our cohort, using health surveys performed in Norway[19]. The majority of the individuals from that study are represented in the age group 31–40 years at their first screening in our study. Like the previous

Table IV
Absolute and relative risk of THR due to primary OA according to BMI change per year in 140,831 women

	Quartile of BMI change per year (kg/m^2/year)			
	First <−0.01	Second −0.01 to 0.08	Third 0.08–0.18	Fourth >0.18
17–20 years at first screening				
No. of participants	9,677	13,018	14,416	14,303
Person–years	138,795	177,885	193,476	191,981
No. of THR	27	52	49	69
THR per 100,000 person–years (crude rate)	19.45	29.23	25.33	35.94
Crude relative risk	1	1.50	1.30	1.85
Multivariate-adjusted relative risk (95% CI)*	1	1.88 (1.17–3.02)	1.75 (1.08–2.84)	2.38 (1.51–3.75)
21–30 years at first screening				
No. of participants	11,596	12,621	13,991	14,570
Person–years	190,854	205,548	226,175	234,724
No. of THR	136	144	141	200
THR per 100,000 person–years (crude rate)	71.26	70.06	62.34	85.21
Crude relative risk	1	0.98	0.87	1.20
Multivariate-adjusted relative risk (95% CI)*	1	1.29 (1.02–1.64)	1.21 (0.94–1.54)	1.47 (1.17–1.83)
31–40 years at first screening				
No. of participants	6,917	5,284	4,660	5,005
Person–years	113,703	85,911	75,578	81,818
No. of THR	350	287	254	295
THR per 100,000 person–years (crude rate)	307.82	334.07	336.08	360.56
Crude relative risk	1	1.09	1.09	1.17
Multivariate-adjusted relative risk (95% CI)*	1	1.23 (1.05–1.44)	1.23 (1.04–1.45)	1.26 (1.08–1.47)
41–50 years at first screening				
No. of participants	4,031	2,900	2,352	1,821
Person–years	63,140	44,510	36,244	28,543
No. of THR	230	232	164	122
THR per 100,000 person–years (crude rate)	364.27	521.23	452.49	427.43
Crude relative risk	1	1.43	1.24	1.17
Multivariate-adjusted relative risk (95% CI)*	1	1.46 (1.21–1.75)	1.24 (1.01–1.52)	1.14 (0.91–1.43)
51–60 years at first screening				
No. of participants	1,858	847	583	358
Person–years	30,267	13,625	9,485	5,715
No. of THR	81	44	18	26
THR per 100,000 person–years (crude rate)	267.62	322.94	189.77	454.94
Crude relative risk	1	1.21	0.71	1.70
Multivariate-adjusted relative risk (95% CI)*	1	1.20 (0.82–1.73)	0.71 (0.42–1.18)	1.64 (1.05–2.56)

* Adjusted for age, BMI, and height at first screening, and for smoking at second screening.

study, there was no effect of weight gain for men in this age group, although there was some effect for women. The present study has a greater population, and the follow up period is longer; therefore, this study captured THRs that were missed in the previous study. This may explain the difference in the results for women.

In the present study, THR was used as a marker of OA, and enabled identification of participants who developed severely symptomatic OA, who wanted a joint replacement, and who did not have contraindications to surgery. This may have introduced a bias as severe obesity is a relative contraindication to surgery. Such a bias would presumably work independently of age, and should not distort the association between age, weight gain, and later THR.

Table V
Multivariate adjusted relative risk of THR due to primary OA per unit of BMI change per year, and per 10 kg increase in weight

Age at the first screening (y)	Relative risk/kg/m^2/year (95% CI)*	Relative risk/10 kg weight gain (95% CI)*
Men		
17–20	5.98 (1.79–20.01)	1.33 (1.10–1.60)
21–30	1.82 (0.94–3.53)	1.16 (1.01–1.6.34)
31–40	1.23 (0.77–1.96)	1.10 (0.97–1.26)
41–50	1.40 (0.66–2.97)	1.03 (0.87–1.23)
51–60	5.05 (0.80–32.00)	1.33 (0.90–1.95)
Women		
17–20	3.66 (1.71–7.83)	1.24 (1.09–1.41)
21–30	1.86 (1.27–2.72)	1.17 (1.07–1.28)
31–40	1.41 (1.09–1.83)	1.14 (1.05–1.23)
41–50	1.31 (0.88–1.96)	1.08 (0.97–1.19)
51–60	2.41 (1.02–5.73)	1.22 (0.99–1.51)

* Adjusted for age, BMI, and height at first screening, and for smoking at second screening.

The difference in findings between men and women, with women also having a possibly higher risk of THR with weight gain at older age, may be due to a more complex association between OA and weight in women. Hormonal and reproductive factors have been shown to affect the risk of THR in women. Although there are conflicting results on the effect of estrogens on the cartilage[34], increasing parity and early menopause have been shown to increase the risk of THR[35].

Another possible explanation for the increased risk of THR among the young weight gainers is that their hip joints suffered a high load for more years than in those who gained weight later in life. More measurements of each participant in the current study would have been needed to accurately evaluate this hypothesis. A biological explanation of the findings is that the hip joint cartilage has a changing susceptibility to load throughout life. Wolff's law states that bone adapts to different types of loading with a change in its architecture[36], and similar adaptation to load has been demonstrated in cartilage[37]. Animal studies have shown that the cartilage during maturation responds to regular loading with a positive effect on the collagen architecture[38]. Loads beyond a certain threshold, however, will exceed the tissue's ability to adapt. Such excess load may induce permanent weakening of the cartilage. It is possible that in the hip joint this threshold is not constant throughout life. If the threshold is lower during the first decades of life, overweight at this age would increase the risk of hip OA more than overweight in old age. In the current study, there has been no adjustment for other known risk factors for THR like

physical activity, family history of OA, and previous joint injury. It could be that young participants appeared to be more affected by weight gain only because they were more physically active. A strong relationship between low physical activity and obesity is well documented[39]. As a high level of physical activity is unlikely among the overweight, it is not considered to be a major cause for hip OA in this group.

There is already good evidence that a high BMI increases the risk of later THR due to primary hip OA[20,21]. To our knowledge this is the first study that also demonstrates an adverse effect on the hip joint of a BMI increase, and that this effect is most significant when the weight gain occurs at a young age. This concurs with our previous study in which THR was shown to have no association with BMI changes that occurred during the fourth and fifth decades of life[19].

Obesity is spreading, and the young population is severely affected[40,41]. We have found that weight gain during early adulthood is particularly associated with severely symptomatic OA of the hip. This indicates that addressing early obesity and weight gain is particularly important in preventing the development or progression of OA.

Contributions

H. Apold; conception and design of the study, analysis and interpretation of the data, drafted the article.

H. Meyer; conception and design of the study, analysis and interpretation of the data, revised the article for important intellectual content.

B. Espehaug; statistical expertise, analysis and interpretation of the data, critically revised the article for important intellectual content.

L. Nordsletten; obtaining of funding; conception and design of the study, critically revised the article for important intellectual content.

L.I. Havelin; conception and design of the study, critically revised the article for important intellectual content.

G.B. Flugsrud; conception and design of the study, interpretation of the data, critically revised the article for important intellectual content.

All the authors have given their final approval of the version submitted.

H. Apold and G.B. Flugsrud take responsibility for the integrity of the work as a whole.

Funding sources

The work is in part supported by grants from Dr Trygve Gythfeldt og frues forskningsfond, from Helse Sør-Øst Artrose, and from The Norwegian Orthopedic Association. These sponsors have no involvement in any parts of the study itself.

Conflict of interest

The authors have no conflict of interest.

STROBE statement

We adhered to the strengthening of reporting of observational studies in epidemiology guidelines for cohort studies.

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