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Lifetime body mass index, other anthropometric measures of obesity and risk of knee or hip osteoarthritis in the GOAL case-control study

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SUMMARY

Objective: To examine the risk of large joint osteoarthritis (OA) in those becoming overweight during early adult life, and to assess the risks associated with high body mass index (BMI) and other anthropometric measures of obesity.

Methods: BMI, waist and hip circumference were measured in the GOAL case-control study comprising hip OA cases ($n = 1007$), knee OA cases ($n = 1042$) and asymptomatic controls ($n = 1121$). Retrospective estimates of lifetime weight, body shape and other risk factors were collected using an interview-lead questionnaire. Odds ratios (ORs), adjusted OR (aOR), 95% confidence intervals (CIs) and P values were calculated using logistic regression analysis.

Results: BMI was associated with knee OA (aOR 2.68, 95% CI 2.33–3.09, P-trend < 0.001) and hip OA (aOR 1.65, 95% CI 1.46–1.87, P-trend < 0.001). Those who became overweight earlier in adulthood showed higher risks of lower limb OA (P-trend < 0.001 for knee OA and hip OA). Self-reported body shape was also associated with knee OA and hip OA, following a similar pattern to current and life-course BMI measures. Waist:hip ratio (WHR) at time of examination did not associate with OA independently of BMI, except in women-only analysis. Waist circumference was associated with lower limb OA risk.

Conclusions: Becoming overweight earlier in adult life increased the risks of knee OA and hip OA. Different distribution patterns of adiposity may be related to OA risk in women.

Introduction

Body mass index (BMI) is an established risk factor for knee osteoarthritis (OA). A recent systematic review found 36 studies on BMI and all showed a positive risk for knee OA[1]. Many studies have used the current BMI of their participants, but prospective studies have shown that BMI at baseline remains a strong risk factor[2–5], and is considered an important contributor to the causes of knee OA. Weight loss can help reduce the incidence of symptomatic knee OA[6] and its effect as a treatment of knee OA have been observed by randomised controlled trials[7]. Many studies have investigated the association between BMI and hip OA, but with conflicting results. A systematic review and meta-analysis published in 2002 concluded that moderate evidence existed to associate hip OA with obesity, with an odds ratio (OR) of approximately 2[8]. However, many studies also report no association between BMI and hip OA[2,9].

The mechanism of the association between BMI and knee and hip OA traditionally was thought to be purely biomechanical, with the excess weight inducing deleterious effects on the joints. This makes the differing associations between knee and hip OA with BMI surprising because the forces from body weight pass through the hips as well as the knees, although the different morphology of the joints might explain different abilities to withstand adverse mechanical loading. However, recent advances in adipose biology have suggested the possibility that other factors may affect the joints. Patterns of distribution of adipose tissue within the body and associations with metabolic syndrome are now known, and adipocytokines are secreted by and related to adipose tissue. The adipocytokine, leptin is related to metabolic syndrome but also has direct effects on chondrocytes[10]. Associations between hand OA and

Abbreviations: IVU, intravenous urography; BMI, body mass index; WHR, waist:hip ratio; WC, waist circumference; HC, hip circumference; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence intervals.

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obesity[11] and the increased prevalence of OA in women might favour a metabolic/hormonal contribution to OA causes, rather than a simple biomechanical mechanism. Evidence of such a factor is currently weak with associations between metabolic correlates, percentage fat and body fat distribution being non-significant after adjusting for BMI[12–16]. The Chingford study, a cohort comprised only of women, identified an association between metabolic factors (hypertension, hypercholesterolemia and blood glucose) and knee OA that was independent of obesity[17].

Studies on the distribution of adipose tissue use waist:hip ratio (WHR) which is considered a surrogate marker of the central obesity useful for determination of cardiovascular risks[18], but its value for OA research is unknown. Similarly, evidence on other obesity measures such as waist circumference (WC), hip circumference (HC), body shape and risk of knee and hip OA is sparse[4].

The aim of the current study was to assess the risk of obesity, using BMI and other related anthropometric measures, on severe knee and hip OA in the large case-control study "Genetics of Osteoarthritis and Lifestyle" (GOAL).

Methods

Study population

GOAL is a case-control study including hospital-referred hip OA cases, knee OA cases and controls, designed to investigate genetic and environmental risk factors[19–22]. All participants were unrelated Caucasians living within the Nottingham area. Cases were recruited from joint surgery lists from three Nottingham hospitals or from a large joint OA clinic and all had been referred with clinically severe OA for consideration of joint replacement surgery. Controls were recruited from intravenous urography (IVU) waiting lists at the same three hospitals and had experienced no knee or hip symptoms. For this study, the group sizes were knee OA, $n = 1042$; hip OA, $n = 1007$; controls, $n = 1121$. All participants were recruited with informed consent. Ethical approval was granted by the Nottingham City Hospital Local Research Ethics Committee (reference EC02/06).

Data collection

Data was collected in two stages; an interviewer-administered lifestyle questionnaire and a clinical examination. During the clinical examination weight (kg), height (cm), maximum WC (cm) at the natural waist or umbilicus and pelvic bone HC (cm) were measured by a trained research nurse. During the interviewer-administered questionnaire individuals estimated their weight and their body shape from a diagram (Fig. 1) at each decade of life[23]. Subjects were asked if they had been diagnosed with hypertension, stroke, heart disease; type I or type II diabetes; kidney problems, cancer, depression or thyroid diseases by their doctor. Participants were classified as having "metabolic disease" if they reported heart problems, type II diabetes, stroke or hypertension. Self-reported physical activities throughout life, smoking history and female reproductive history were also recorded.

Measurement of obesity-related variables

BMI was calculated in kg/m^2 and subjects were categorised into three groups according to WHO criteria, specifically normal ($<$25 kg/m^2), overweight ($\geq$25 and $<$30 kg/m^2) and obese ($\geq$30 kg/m^2). Prior to analysis, self-reported body shapes 6–7 and 8–9 were taken to represent approximately the WHO BMI classes of "overweight" and "obese" respectively. Individuals retrospective estimates of weight and current height were used to estimate mean BMI at three stages; 20–30's, 40–50's and at their current age. Subjects were then categorised into four groups of increasing exposure to BMI throughout life. The groups were: (1) BMI $<$25 throughout life, (2) BMI $\geq$25 only at recruitment, (3) BMI $\geq$25 from middle age (40–50's) onwards and (4) BMI $\geq$25 from 20's to 30's onwards. Similar groups were derived for self-reported overweight body shape (i.e., scale >5) throughout life (Fig. 1). Control data-derived tertiles were generated to categorise subjects for WC, HC and WHR (calculated as WC/HC).

Other variables

Major risk factors for OA were included for the adjustment purposes including age, gender, occupational risk, physical activity, smoking, female reproductive history and oestrogen exposure. Longest-held occupation was classified as manual or non-manual[24] (which was used as a surrogate for social class), and also used to estimate occupation risks. Heavy work standing ($\geq$1 h per day), lifting 25 kg ($\geq$10 times per week) or lifting 50 kg or 100 kg ($\geq$1 time per week) were score for hip OA (maximum score 3). Kneeling or squatting ($\geq$1 h per day) were added for knee OA (maximum score 5)[22]. Physical activity was measured in hours per week between the ages of 10 and 50, which was categorised into groups based upon tertiles of the control population. Smoking was categorised as never, current and ex-smoker. Exposure to oestrogen was determined as low, moderate or high derived from years of menstruation, number of pregnancies, years of HRT and contraceptive pill use; and was used in female-only analyses. Occupational exposures and female reproductive history were truncated to the age when first joint replacement took place. In average, cases were truncated 3 years earlier before the recruitment date. This was therefore used to truncate all controls.

Representativeness of GOAL

The GOAL study control group was compared to other large UK studies to assess how representative the sample group was. The other studies were Norfolk EPIC[25], the Hertfordshire cohort study (HFCS)[26], Prostate[27], British National Survey[28], British Regional Heart Survey[29] and Health Survey of England 1996[30].

Statistical analysis

ORs and 95% confidence intervals (CIs) were calculated to present the relative risk of exposure. Confounding factors were adjusted for using logistic regression to generate adjusted OR (aOR). Logistic regression was performed using the variables BMI/anthropometric measures, age, gender, physical activity, metabolic disease co-morbidity, oestrogen exposure (women only), social class, smoking and occupational risks. When men and women were analysed separately, only gender and oestrogen exposure were omitted from the models. Dose–response relationships were examined whenever the data were available for graded measures and P values for linear trend are calculated. The differences in co-morbidities were assessed using the χ^2 statistic. Correlations between obesity measures were assessed by Pearson's coefficient. Anthropometric measures and BMI were included together in logistic regression models to estimate whether both independently conferred risks for OA. All analyses were performed using SPSS version 14. Statistical significance was taken when $P < 0.05$.

Results

The demographics of the GOAL study are shown in Table I. The control group had lower BMI, WC, HC, and WHR and was younger than the knee OA and hip OA groups, but contained more current smokers. The control group also had fewer subjects with self-reported metabolic diseases but more subjects with depression, kidney diseases and cancer.