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Leisure and occupational physical activity at different ages and risk of endometriosis

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ABSTRACT

Objective: Cohort and case-control studies have suggested that adult physical activity (PA) may lower endometriosis risk and improve symptoms, but evidence is still controversial. To add information on leisure and occupational PA impact, if any, on endometriosis risk, we have analyzed data from a small case-control study conducted in Milan (Italy).

Study design: Ninety cases and 90 controls (median age 35 years, range 18–76) were compared. Endometriosis was laparoscopically diagnosed within the year before interview. Information on demographic variables, menstrual and reproductive history, occupational and recreational physical activity was collected.

Results: A consistent protective effect emerged between leisure PA and endometriosis risk. For <2–4 and ≥5 h/week (reference no PA), the estimated odds ratios (ORs) were, respectively: 0.36 (95% CI 0.18–0.74) and 0.83 (95% CI 0.27–2.53) as regards PA in early adolescence; 0.31 (95% CI 0.15–0.63) and 0.78 (95% CI 0.25–2.38) as regards PA in teenage years; 0.34 (95% CI 0.12–0.94) and 0.33 (95% CI 0.08–1.28) for PA in adulthood. However, no significant trend was seen according to hours spent in leisure PA. Occupational PA did not show statistical significant differences among different types or across age classes.

Conclusions: These results suggest that leisure PA in early adolescence, teenage years and adulthood may, to some extent, decrease the risk of endometriosis. In the interpretation of these results, however, the role of potential biases cannot be totally ruled out.

Introduction

Most cohort and case-control studies which analyzed the association between physical activity (PA) and endometriosis suggested that adult PA decreases endometriosis risk and tends to improve symptoms [1–3]. Several biological mechanisms have been proposed to explain the influence of exercise on endometriosis risk, possibly involving multiple but, in some cases, overlapping pathways [2,4,5]. Endometriosis is an estrogen dependent condition and one of the mechanisms may include the influence on body mass and body fat composition, changes in serum cholesterol and changes in levels and availability of sex hormones. It has to be considered, however, that a modest inverse correlation has been consistently demonstrated between endometriosis and BMI [6]. Proposed hypotheses for this inverse association include a synergy between weight and the underlying causes of infertility that in endometriosis may involve both ovarian and endometrial processes, possible different alimentary attitudes in endometriosis patients, involvement of alternative hormonal pathways other than estrogens or the possible role of in utero and childhood exposure in the causation of endometriosis [6]. Therefore, the well known inverse association between PA and BMI, in turn associated with higher endometriosis risk, conflicts with the studies reporting a protective effect of PA on endometriosis development [7,8].

Another possible explanation for the inverse association between PA and endometriosis may be linked to the ability of PA to reduce insulin resistance, thus avoiding stimulation possibly linked to hyperglycemia and hyperinsulinemia [4,6,9]. Hyperinsulinemia may increase levels of estrogens through decreasing concentrations of sex hormone binding globulin, and may increase

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levels of Insulin-like growth factor (IGF)-1 through decreasing levels of IGF binding protein (IGFBP)-1. Both estrogens and IGF-1 stimulates endometrial cell proliferation [10]. Exercise can also raise the production of some prostaglandins that, in turn, may influence the risk of endometriosis [11,12]. The activation of the immune system response has also been postulated [13] and a role of the immune system in the development of endometriosis has been consistently suggested [14]. Finally, it is not totally clear if the reported protective effect of high level PA on risk of endometriosis is "true" or at least partially explained by the fact that women affected by pain related to endometriosis may reduce their level of activity [15].

A problem related to the study of risk factors for endometriosis is that there is a substantial delay between the onset and the diagnosis of the diseases [16]. Thus, in order to investigate the role of PA in the pathogenesis of endometriosis, it is important to assess risk exposure at different ages, and in particular at young ages. Scanty data are available on the age at which PA may affect endometriosis risk. In fact most studies on occupational PA considered the usual lifetime occupation, while few studies have examined specific times prior to diagnosis. A large cohort study conducted in France has suggested a positive association between walking activity at 8–15 years of age, but not out-of-school physical activity at the same ages, and risk of endometriosis later in life [3].

To establish the ages at which leisure and occupational PA has an impact, if any, on endometriosis risk, we have analyzed data from a small case-control study conducted in Milan, Italy.

Materials and methods

Subjects

Subjects were enrolled in a case-control study of endometriosis conducted at the San Raffaele Hospital and Policlinico of Milan in the period 2012–2013. Cases of endometriosis included 90 women (median age 35, range 19–49) with incident, i.e. laparoscopically diagnosed within the year before interview, histologically confirmed endometriosis. Controls were 90 women (median age 35.5, range 18–76) admitted for a wide spectrum of acute conditions unrelated to known potential risk factors for endometriosis. Of these, 7.8% had traumatic or non-traumatic orthopedic conditions, 6.7% had acute surgical conditions (mostly abdominal, such as acute appendicitis or strangulated hernia), 47.8% gynecological benign conditions, 11.1% ear, nose and throat conditions and 26.6% miscellaneous other illnesses (such as eye and dental disorders). Less than 4% of cases and controls approached for interview refused to participate and the response rates did not vary across cases and controls.

All interviews were conducted in hospital using a structured questionnaire which assessed personal characteristics and habits, anthropometric variables, education and other socio-economic factors, general lifestyle habits, such as smoking, alcohol, coffee consumption, medical history and dietary habits. The section on PA included questions on self reported intensity of activity at work and in leisure time separately. Physical activity in leisure time was elicited for three specific periods of life: at the ages of 12 (early adolescence, mean menarche age in Italian women), 15 to 19 (teenage years, shortly after menarche) and 30 to 39 (adulthood; in Italy, most women are diagnosed with endometriosis in this age group). It was defined on the basis of the number of hours per week of a sport or activity such as walking, gardening, cycling, etc. The scores ranged between 1 and 5, corresponding to none, <2, 2–4, 5–7 and >7 h of PA per week. No information was available on intensity or amount of activity.

Occupational PA was elicited for teenage years and adulthood. Patients were asked about their jobs, which were classified into five categories (scores between 1 and 5) corresponding to 'very heavy', 'heavy', 'average', 'standing', 'mainly sitting'. Domestic work was also investigated in this questionnaire. The scores of the two highest levels of occupational PA, and the two intermediate and the highest levels of leisure-time PA were combined, in order to obtain adequate numbers in the categories.

Overall PA was evaluated combining occupational and leisure time PA. It was classified into three categories: 'none' (no leisure PA and 'mainly sitting' occupational PA), intermediate ('standing' or 'mainly sitting' occupational PA and <2–4 h/week leisure PA) and high (moderate/intense occupational PA and/or ≥5 h/week leisure PA).

The study was approved by the Hospital Institutional Review Boards.

Data analysis

Frequencies were compared using the chi-square test or Fisher's exact test or the Mantel–Haenszel chi-square, as appropriate. Odds ratios (ORs) for endometriosis, and the corresponding 95% confidence intervals (CI), for increasing levels of occupational and leisure-time physical activity at various ages were computed. In order to take into account potential confounding factors, ORs were also computed using unconditional multiple logistic regression, fitted by the method of maximum likelihood [17]. In the final PA model, the equations included age as a continuous variable, education, BMI and parity in classes.

A total of 20 comparisons were performed. Two PA levels were tested versus one reference group, on 10 variables: occupational PA in teenage years and adulthood; leisure PA in early adolescence, teenage years, and adulthood (whole sample and excluding women aged >41 years); overall PA in teenage years and adulthood (whole sample and excluding women aged >41 years); according to the Bonferroni's test [18] the level of significance was set at $P < 0.0025$.

Results

Table 1 shows the distribution of cases and controls according to BMI, education, smoking habits, parity, history of miscarriages and lifelong menstrual history. Overweight women (BMI > 25) had endometriosis less frequently than women with BMI ≤ 25 ($P = 0.07$). As expected, women with endometriosis were more educated ($P = 0.0005$) and less frequently parous than controls ($P < 0.0001$). On the same line, miscarriage was more frequent, though not significantly, in women with endometriosis ($P = 0.32$). In our sample, irregular menstrual cycle, days of bleeding and oral contraceptive use were not significantly related to endometriosis, and nor was smoking.

Table 2 shows the distribution of cases and controls with corresponding multivariate ORs in relation to the levels of leisure PA at different ages and occupational PA in teenage years and adulthood. In order to avoid biases due to diagnostic delay, we repeated the teenage years PA analysis excluding women aged less than 25 years (5 years delay), but the results did not substantially change. As 33 women were aged less than 30 years, they did not contribute to the PA evaluation in adulthood. The sample for the analysis of occupational and leisure PA in adult age was composed of 74 cases and 73 controls, and according to each subject's age, it included both current and past PA. Conversely, the early adolescence and teenage years PA analyses regarded past PA for all subjects.

A consistent protective effect emerged between leisure PA and endometriosis risk. For <2–4 and ≥5 h/week (reference no PA), the