



Personal, reproductive, and familial characteristics associated with bilateral oophorectomy in premenopausal women: A population-based case-control study

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ABSTRACT

Objectives: We investigated the association of personal, reproductive, and familial characteristics with bilateral oophorectomy performed for nonmalignant indications in a US population.

Study design: In an established cohort study, we used the records-linkage system of the Rochester Epidemiology Project (REP <http://www.rochesterproject.org>) to identify 1653 premenopausal women who underwent bilateral oophorectomy in Olmsted County, Minnesota between 1988 and 2007 for a nonmalignant indication. Each woman was matched by age (± 1 year) to a population-based referent woman who had not undergone bilateral oophorectomy as of the index date. We used case-control analyses to investigate several characteristics associated with bilateral oophorectomy. Odds ratios and their 95% confidence intervals were adjusted for race, education, and income.

Results: In the overall analyses, infertility was more common in women who underwent bilateral oophorectomy than in the controls, whereas use of oral contraceptives, a history of breast feeding, and fibrocystic breast disease were less common. The women who underwent bilateral oophorectomy weighed more than controls, had a higher body mass index and were younger at menarche. The associations were more pronounced for women who underwent the bilateral oophorectomy before age 46 years, and some associations were different for women with or without a benign ovarian indication. Reported family histories of uterine and other cancers were more common in women without a benign ovarian indication.

Conclusions: We identified a number of personal, reproductive, and familial characteristics that were associated with bilateral oophorectomy over a 20-year period. Our historical findings may help inform decision-making about oophorectomy in the future.

1. Introduction

Bilateral oophorectomy continues to be performed in isolation or more commonly with hysterectomy in women before the age of natural menopause [1,2]. In the majority of cases, these surgeries are

performed to treat nonmalignant gynecological symptoms or conditions. In addition, a large number of bilateral oophorectomies are performed at the time of a hysterectomy without a specific ovarian indication. For example, recent data from California suggest that approximately 38% of women undergo bilateral oophorectomy at the time

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of a hysterectomy in the absence of a documented ovarian condition [2]. This practice reflects the unresolved controversy about the advantages and disadvantages of removing healthy ovaries in premenopausal women for the prevention of ovarian and breast cancer [3–9]. In addition to a family history of ovarian cancer, intraoperative events, surgeons' preferences, women's preferences and past experiences, and social, reproductive, and familial factors may be involved in the decision to remove healthy ovaries [10,11]. We recently reported on the association between adverse childhood or adult experiences and the risk of bilateral oophorectomy [10,11]. However, other characteristics associated with bilateral oophorectomy have not been investigated extensively.

We conducted a case-control study to investigate the personal, reproductive, and familial characteristics associated with bilateral oophorectomy in the Mayo Clinic Cohort Study of Oophorectomy and Aging-2 (MOA-2). We report a series of case-control analyses contrasting premenopausal women who underwent bilateral oophorectomy to their respective age-matched controls in a geographically defined US population with a special focus on women who underwent oophorectomy at younger ages and on women who did not have a specified ovarian indication.

2. Methods

2.1. Study population

The overall study design and the clinical characteristics of the women included in the MOA-2 study were reported elsewhere [12–14]. In brief, MOA-2 included a cohort of premenopausal women who underwent bilateral oophorectomy for a nonmalignant indication, and a corresponding cohort of age-matched referent women. Both cohorts were representative of the geographically defined population of Olmsted County, Minnesota (USA) for the 20-year period 1988–2007. All data collection was through the records-linkage system of the Rochester Epidemiology Project (REP) that has been described elsewhere [15–18]. The women originally sampled to serve as exposed and referent women for the cohort analyses were re-labeled as cases and controls to be used in the case-control analyses reported here.

2.2. Data collection

A physician (LGR) and a trained nurse abstractor reviewed the medical records of all women who received a surgical code for unilateral or bilateral oophorectomy. For those women confirmed to have undergone surgery, detailed information about surgical characteristics was abstracted (e.g., indication for the surgery, pathology of the removed ovaries, and pathology of the removed uterus, if applicable). In addition, for both women with oophorectomy and their age-matched controls, the complete medical records were reviewed to collect an extensive series of demographic, social, and reproductive history data, and information about adult life characteristics and family history of cancer. Only characteristics documented before the index date were considered in the case-control analyses. Data were abstracted and recorded using an electronic data entry application. The application provided real time data checks (e.g., range of valid values), and comprehensive data checks were performed regularly during abstraction. To increase the consistency of the data collected, the two data abstractors followed a manual of instructions providing definitions and examples for the characteristics of interest. The manual was updated iteratively during the data collection phase. Information about income was derived from the 2000 United States Census (Summary File 3) [19]. Each woman was assigned the median household income for the census block group in which she lived at the index date.

2.3. Statistical analysis

Cases and controls were compared using conditional logistic regression models for matched pairs, and the associations were measured using odds ratios and 95% confidence intervals. Because socio-demographic characteristics were considered possible confounding variables [12], analyses for personal, reproductive, and familial characteristics were adjusted for race (white; non-white), education (≤ 12 ; 13–16; > 16 years), and household income (quartiles: $< \$42,000$; $\$42,000$ – $\$56,999$; $\$57,000$ – $\$71,999$; $\geq \$72,000$). We conducted a set of analyses including the complete sample, and three sets of analyses stratified by age at the index date (≤ 45 years and 46–49 years), by indication (benign ovarian condition and no ovarian indication), and by calendar year (1988–1997 and 1998–2007). We also conducted a set of sensitivity analyses for the overall sample after excluding 165 case-control pairs in which the control had undergone hysterectomy before the index date and 24 pairs in which the case had not undergone hysterectomy as of the index date. All analyses were conducted using SAS v.9.4 (SAS Institute), and tests of statistical significance were conducted at the two-tailed alpha level of 0.05.

2.4. Ethical approval

All study procedures and ethical aspects were approved by the institutional review boards of both Mayo Clinic and Olmsted Medical Center. Because the data collection was historical, women did not need to provide a study-specific informed consent but rather a general consent to use their medical records for research (Minnesota legal requirements) [16,17].

3. Results

Supplementary Table 1 shows the results of case-control analyses for race, education, and income overall and in strata by age at oophorectomy and by indication for the oophorectomy. Non-white race was significantly less common in cases than controls overall and in all stratified analyses. However, the numbers for non-white women were small. Cases had significantly fewer years of education than controls overall, in the age stratum ≤ 45 years, and in women with a benign indication (with a dose-effect trend). Finally, cases had significantly lower income in women with age ≤ 45 years and in women with a benign indication (with a dose-effect trend).

Fig. 1 provides details about the indications for the oophorectomy and the pathological findings in the ovaries removed. Of the 1653 pairs of ovaries removed for any indication, 847 (51.2%) were found to be healthy at pathological examination (bolded numbers). Interestingly, 333 women underwent removal of their ovaries and uterus in the absence of any recognized ovarian or uterine condition (shaded boxes in right lower corner). The only indication in these women was excessive bleeding or abdominal pain.

Table 1 shows the results of case-control analyses for personal characteristics in the overall sample after adjusting for race, education, and income. Infertility, higher weight (with a dose-effect trend), and higher body mass index (BMI; with a dose-effect trend) were more common in women who underwent bilateral oophorectomy. By contrast, older age at menarche (with a dose-effect trend), any use of oral contraceptives, longer use of oral contraceptives (with a dose-effect trend), history of breast feeding, and fibrocystic breast disease were less common in women who underwent bilateral oophorectomy (Table 1; all ages, all indications). The results were similar in a set of sensitivity analyses in which we removed controls who had undergone hysterectomy and cases who had not undergone hysterectomy as of the index date (data not shown).

Table 2 shows case-control analyses for bilateral oophorectomy stratified by age at the time of oophorectomy (or index date; all indications). The median age at oophorectomy was 41 years (IQR, 38–44)

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