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Hysterectomy with or without unilateral oophorectomy and risk of ovarian cancer

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Abstract

Objective. To analyze the role of hysterectomy, performed on benign indications, on the risk of developing ovarian cancer.

Methods. Multicenter case-control study conducted in four Italian areas. Cases were 1031 women with epithelial ovarian cancer. Controls were 2411 women admitted to the same network of hospitals for a wide spectrum of acute non-neoplastic conditions, unrelated to known risk factors for ovarian cancer.

Results. Compared to women with intact uterus and ovaries, the multivariate odds ratios (OR) was 0.6 (95% confidence interval 0.4–0.9) for women who reported hysterectomy. The OR was 0.5 ≥15 years after surgery. The OR was similar for women who had had pelvic surgery before age 45 and for those who had surgery later. No appreciable heterogeneity emerged across strata of parity and family history of ovarian/breast cancer.

Conclusion. Women who had undergone hysterectomy had a long-term reduced risk of epithelial ovarian cancer.

Keywords: Risk factor; Hysterectomy; Ovarian cancer

Introduction

Hysterectomy may influence ovarian cancer risk, but the issue is still open to debate. In a previous case-control study from Italy, hysterectomy about halved the risk of ovarian cancer [1]. In an Australian case-control study, hysterectomy was associated with a 36% reduction in risk of ovarian cancer, and the risk remained reduced up to 25 years after surgery [2]. Likewise, in an American cohort study [3], hysterectomy was inversely associated with ovarian cancer. In the pooled analysis of 12 case-control studies from the USA, hysterectomy without oophorectomy was associated with reduced ovarian cancer risk (OR 0.69 for six hospital-based studies, 0.88 for six population-based studies) [4]. Additional studies from the USA, Canada, and Sweden observed significant reductions in risk [5–7]. A recent population-based study confirmed a reduced risk of ovarian cancer associated with hysterectomy (OR 0.5) and unilateral oophorectomy (OR 0.2) [8].

However, other reports found that hysterectomy did not appreciably reduce the risk of ovarian cancer [9–13].

In this report, we consider the relation between hysterectomy with or without unilateral oophorectomy, performed

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on benign indication, and the risk of ovarian cancer, examining data from a large multicenter study conducted in Italy. This analysis does not include data reported in our previous paper [1].

Materials and methods

The data were derived from a case-control study of ovarian cancer, conducted between January 1992 and September 1999 in four Italian areas: the Greater Milan area, the provinces of Pordenone, Padua and Gorizia in northern Italy; the province of Latina in central Italy; and the urban area of Naples in southern Italy [14,15].

Cases were 1031 women (median age 56 years, range 18–79) with incident (diagnosed within the year before the interview; median time between diagnosis and interview was 1 month) histologically confirmed invasive epithelial ovarian cancer and with no previous diagnosis of cancer. Information on stage according to the International Federation of Gynecology and Obstetrics (FIGO) classification [16] was available for 587 (57%) ovarian cancer cases. The majority of cases (78%) had an advanced stage (III or IV) disease.

Controls were 2411 women (median age 57, range 17–79 years) residing in the same geographical areas and admitted to the same network of hospitals as cases for a wide spectrum of acute non-neoplastic conditions, unrelated to known risk factors for ovarian cancer. Women were excluded if admitted for hormonal and gynecological diseases and if they had undergone bilateral oophorectomy. Among the controls, 26% had traumatic conditions, 28% non-traumatic orthopedic disorders, such as low back pain and disc disorders, 15% acute surgical conditions, and 31% miscellaneous other illnesses, such as eye, ear, nose and throat, or dental disorders. Less than 4% of cases and controls approached refused interview, and the response rates did not vary across hospitals and geographic areas.

All interviews were conducted in hospital using a structured questionnaire, which included information on general characteristics and habits, socio-demographic factors, history of cancer in first-degree relatives, menstrual and reproductive factors, history of use of oral contraceptives and hormone replacement therapy, selected medical and surgical conditions, including hysterectomy with or without unilateral oophorectomy, as treatment for benign conditions. The interviewers routinely inspected clinical records to validate surgical information.

Data analysis

7Odds ratios (OR) of ovarian cancer and the corresponding 95% confidence intervals (CI) were derived from unconditional multiple logistic regression models, fitted by the method of maximum likelihood [17]. Two models were considered: the first one included terms for study center, and quinquennia of age; the second one included further terms for education, parity, oral contraceptive use, and family history of ovarian/breast cancer in first-degree relatives. The same models were also fitted to data stratified by age, parity, and family history of ovarian/breast cancer.

Results

Table 1 shows the distribution of cases and controls according to age and selected risk factors for ovarian cancer. By design, cases and controls had similar age distribution. Cases were more educated than controls, and reported earlier menarche and fewer children. An increased risk of ovarian cancer emerged in women with a family history of breast and/or ovarian cancer.

Table 1
Distribution of 1031 cases of epithelial ovarian cancer and 2411 controls according to age and selected characteristics; Italy 1992–1999[a]

	No. of cases (%)	No. of controls(%)	OR (95% CI)[b]	OR (95% CI)[c]
Age (years)				
<45	183 (17.8)	443 (18.4)		
45–54	287 (27.8)	615 (25.5)		
55–64	325 (31.5)	724 (30.0)		
≥65	236 (22.9)	629 (26.1)		
Education (years)				
≤7	570 (55.6)	1417 (59.4)	1[d]	1[d]
7–11	227 (22.2)	620 (26.0)	1.2 (1.0–1.5)	1.1 (0.9–1.4)
≥12	227 (22.2)	349 (14.6)	2.1 (1.7–2.7)	1.9 (1.5–2.4)
Parity				
Nulliparae	184 (17.8)	381 (15.8)	1[d]	1[d]
1–2	572 (55.5)	1268 (52.6)	1.0 (0.8–1.2)	1.1 (0.9–1.4)
Menopausal status				
Premenopausal	346 (33.6)	803 (33.4)	1[d]	1[d]
Postmenopausal	683 (66.4)	1603 (66.6)	1.0 (0.8–1.4)	1.0 (0.8–1.4)
Family history of ovarian/breast cancer				
No	902 (87.5)	2291 (95.0)	1[d]	1[d]
Yes	129 (12.5)	120 (5.0)	2.8 (2.1–3.7)	2.6 (2.0–3.5)
Age at menarche				
≤12	446 (43.4)	1003 (41.7)	1[d]	1[d]
13–14	444 (43.2)	1022 (42.5)	0.9 (0.8–1.1)	1.0 (0.8–1.1)
≥15	138 (13.4)	378 (15.7)	0.8 (0.6–1.0)	0.8 (0.6–1.0)

[a] In some cases the sum does not add up to the total because of some missing values.
[b] Odds ratios from multiple logistic regression including terms for age and center.
[c] Odds ratios from multiple logistic regression including additional terms for education, parity , oral contraceptive use, and family history of ovarian and breast cancer in first-degree relatives.
[d] Reference category.