

Oophorectomy in the prevention of ovarian cancer

ELLEN MERETE MADSEN, ØJVIND LIDEGAARD AND ANN TABOR

From the Departments of Obstetrics and Gynecology, Centralsygehuset i Næstved, Næstved, Hvidovre Hospital and Rigshospitalet, Copenhagen, Denmark

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The question of whether to remove macroscopically normal ovaries at the time of hysterectomy for non-malignant conditions in women aged 40-50 years or older is still controversial.

Estimation of the benefits and potential risks of prophylactic bilateral oophorectomy is difficult. The spokesmen for bilateral oophorectomy claim that this operation prevents subsequent development of ovarian cancer and prevents operation for non-malignant conditions caused by symptoms from the 'residual ovarian syndrome'. The opponents of bilateral oophorectomy claim that healthy organs should be left in situ and that bilateral oophorectomy may cause hormonal deficiency also in postmenopausal women.

Ultimately the decision must be taken by the patient, but this decision should be based on as reliable data as possible. Our aim is to try to quantify some of the aspects of bilateral oophorectomy.

The life-time risk of developing ovarian cancer in Denmark is about 2% (1). The mortality from ovarian cancer has remained unchanged in the western world for decades; nearly 500 women die annually from this cancer in Denmark. The corresponding figures from Canada, the United States and Norway are 1200, 12,000 and 300 (2). This high mortality is mainly due to the fact that more than 50% of the patients have a disseminated disease at the time of diagnosis. The late diagnosis is due to the few and vague symptoms and the lack of efficient screening methods for this disease. Furthermore treatment for ovarian cancer has not improved significantly. Attempts to decrease the incidence of and mortality from ovarian cancer have focused on causal research, early detection/im-

proved diagnostic methods, better treatment and prophylactic surgery by performing bilateral oophorectomy.

In some cases it may be relevant to perform elective bilateral oophorectomy, if the woman has been exposed to etiological factors of importance for the development of ovarian cancer. Women with a family history of ovarian cancer are at increased risk of developing ovarian cancer. In the familiar ovarian cancer syndrome, available data suggest an autosomal dominant inheritance. Women in these families may have a 50% life-time risk of developing ovarian cancer (3), and bilateral oophorectomy may be considered as soon as these women have finished their reproductive career.

In families with a single case of ovarian cancer, first- and second degree relatives have been reported to have a relative risk of developing ovarian cancer between three and 18 (3-5). The incidence of ovarian cancer is also increased in relatives of patients with cancer of the breast, colon and endometrium. In a woman with a first-degree relative with endometrial cancer, the risk of developing ovarian cancer is about 3.5% (5).

It is known that prolonged anovulation caused by the use of contraceptive pills or by pregnancies has a protective effect on ovarian cancer and conversely that the risk is increased in nulliparous and infertile women, as well as in women with a late menopause (6-8).

All the above mentioned women, known to be at an increased risk of developing ovarian cancer, could be a primary target group for ovarian cancer screening, if a reliable and sensitive test is developed. They are also those in whom bilateral

oophorectomy at hysterectomy before the menopause should be considered.

Most of the available data concerning the effect of bilateral oophorectomy is from retrospective studies dealing with the frequency of prior hysterectomy and/or pelvic surgery among patients with ovarian cancer. In pooled data from 13 investigations, 542 (9%, range 4.5–19.0) of 6,017 ovarian cancer patients had previously had a gynecological laparotomy. Of these 542 women two-thirds were 40 years old or more at the time of the first operation and a quarter were 50 years or more. Thus, if bilateral oophorectomy had been performed at the time of the first operation in women aged 40 years or more, two-thirds of the ovarian cancers diagnosed at the second operation would have been prevented. These figures suggest the preventive potential of bilateral oophorectomy at different ages (9).

In eight prospective studies a total of 24,159 hysterectomized, but not oophorectomized women were followed up to 10 years. Fifty women corresponding to 0.2% (range 0–0.3%) developed ovarian cancer (9). This 0.2% risk of developing ovarian cancer after hysterectomy is much lower than the mentioned life-time risk of 2.0%, and cannot solely be explained by the effect of visual screening for ovarian pathology at the time of hysterectomy. A more probable explanation is the short follow-up period in the prospective studies and the fact that more than 75% of the hysterectomies were performed in women aged 50 years or less. As the maximum age incidence of ovarian cancer lies beyond 60 years, it is clear that the life-time risk of developing ovarian cancer is much higher than 0.2%. By applying the incidence of ovarian cancer in different age groups, the age of the women at the time of hysterectomy and the length of the follow-up periods in the prospective studies, it is possible to calculate what percentage of the life-time cancer risk each study has theoretically detected. The risk of developing ovarian cancer, if all women had been followed until death, can then be estimated. We find that these estimates are approximately 10 times higher than the published 0.2% risk. Although some uncertainty applies to these calculations, it appears that the life-time post-hysterectomy risk of ovarian cancer approximates the corrected figures, i.e. 2%. This implies that to prevent one case of ovarian cancer we have to perform bilateral oophorectomy in about 50 women (9).

Another minor benefit of bilateral oophorectomy is the prevention of the residual ovarian syndrome, whose symptoms consist of abdominal pain with or without relation to the menstrual cycle, dyspareunia and distension caused by ovarian cysts (10). This syndrome may be caused by peri-ovarian adhesions or ovarian dysfunction due to compro-

mised blood flow. The incidence of second operations for non-malignant conditions in the ovaries among hysterectomized women varies between 0.33% and 4.30% (9). As the follow-up periods in these studies were also short, these figures may underestimate the life-time re-operation risk.

In summary, we estimate that removal of the ovaries in all women over 40 years, if hysterectomized for non-malignant conditions, would prevent the development of 5–6% of all ovarian cancers. Furthermore, reoperation for benign conditions would be prevented in 4–5% of the hysterectomized women. If the hysterectomy rate increases the preventive effect will be greater.

The clinical decision of whether to perform bilateral oophorectomy or not is of course more complex, especially in women with preserved ovarian function. The clinical decision has to include physical and psychological aspects for the patient, as well as compliance problems in relation to hormone replacement therapy.

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Address for correspondence:

Ellen Merete Madsen
Margrethevej 20
DK-2840 Holte
Denmark