

## Hereditary Breast-Ovarian Cancer Team of the University Medical Centre Groningen (UMCG) – a Report

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Female carriers of a germline BRCA1 or BRCA2 mutation have a cumulative lifetime ovarian cancer risk of 39-54% or 11-23%, respectively [1, 2]. Preventive health strategies for these women include gynaecological screening aiming at early cancer detection and prophylactic salpingo-oophorectomy aiming at cancer risk reduction. However, it is becoming increasingly clear that (bi) annual gynaecological screening by transvaginal ultrasonography and serum CA125 estimation in women at increased risk of ovarian cancer is ineffective in detecting presymptomatic ovarian cancer [4]. In a recent publication a positive predictive value of 17% and a sensitivity of less than 50% were found for screening for ovarian cancer in a high-risk population [3]. Preventive bilateral salpingo-oophorectomy (BSO) reduces ovarian cancer risk by 96% and breast cancer risk by 50% or less, depending on the age of preventive surgery. Preventive BSO at a premenopausal age is the most effective strategy to prolong life in the case of a BRCA1 mutation [5]. In our clinic, we therefore counsel women with a BRCA1/2 gene mutation to choose preventive surgery after childbearing age. From the age of 35-40 for BRCA1 mutation carriers and from the age of 40-45 for BRCA2 mutation carriers, these women are advised to undergo a laparoscopic BSO. Counselling is provided at our multidisciplinary outpatient clinic by an experienced gynaecologist who discusses the benefits and drawbacks of the decision for or against preventive surgery with the patient and the (contra) indications for hormonal replacement therapy (HRT). Additional psychological counselling is available from the team's psychologist. In our clinic, uptake of preventive BSO is more than 70%

in the total group of counselled mutation carriers and rises to more than 90% in women by the time they reach the age of 50 years.

The operation is performed in a day care setting and starts with peritoneal washing for a cytologic examination to detect subclinical (extra) ovarian or tubal cancer, followed by BSO. Atraumatic tissue handling is performed by grasping the ovarian pedicles instead of the ovarian epithelium. The fallopian tube is removed from the uterine corner by bipolar coagulation and only the intramural part of the tube is left in situ. After marking one adnex, the adnexa are taken out of the body by an endobag. The tissue is sent for histopathological examination.

Since the publications of case reports linking BRCA mutations to an increased risk of fallopian tube cancer as well, preventive oophorectomy is recommended to be replaced by BSO [6]. Although the rationale for removing the total fallopian tube by removing the uterus as well is clear, we could not find any evidence that a hysterectomy adds to reducing the risk of fallopian tube cancer more than a complete BSO alone. In a large clinicopathologic study of 105 cases of fallopian tube cancer, 92% were situated in the tubal portion, most often the distal part, while 8% were confined to the fimbriae [7].

Following preventive BSO, women who are younger than 45 years of age and have no history of breast cancer are counselled to use HRT, to treat vasomotor symptoms

and sexual side effects of oestrogen deprivation. In the case of prescription of HRT, we prescribe tibolone, because in contrast to oestrogen/progestogen treatment, it appears to exert little stimulation of breast tissue and does not increase the mammographic breast density [8].

Women who have been treated for breast cancer, or are older than 45-50 years of age, are advised not to use HRT. In the case of severe vasomotor symptoms, non-hormonal treatment is proposed by selective serotonin reuptake inhibitors (SSRI).

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