KNOWING ovarian cancer risks

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Women at high risk of ovarian cancer face tough decisions to maximise their chance of survival.

OVARIAN cancer is the most common cause of gynaecological cancer deaths. The absolute risk of ovarian cancer in the general population is 1.4%, with the median age at diagnosis being 57. Overall five-year survival is <45% due to advanced presentation in 75% of cases.

The strongest known risk factor is a positive family history (10–15% of cases). Women with a single family member affected by epithelial ovarian cancer (EOC) have a 4–5% risk, while those with two affected relatives have a 7% risk of developing the disease.

In contrast, women with hereditary ovarian cancer syndromes, defined as having at least two first-degree relatives with EOC, have a lifetime risk as high as 46% (Table 1).

The risk of ovarian cancer appears to be decreased in women with a history of pregnancy, oral contraceptive pill use, breastfeeding, tubal ligation and hysterectomy. Factors associated with a small increased risk of EOC include nulliparity, PCOS, endometriosis and obesity.

Screening with ultrasound and CA125 assays has not been associated with a statistically significant reduction in mortality from EOC.

It has an unacceptably high level of false positive results and attendant morbidity and mortality and therefore cannot be routinely recommended even in high-risk women.

Interval cancers can develop between screening visits and are often advanced at presentation. Serum CA125 is only elevated in 50–60% of stage I EOC. Screening should only be offered in women declining risk-reduction surgery (RRSx) in the absence of a better alternative.

For high-risk women declining RRSx, some expert groups have recommended screening with transvaginal ultrasound plus CA125 assays every six months, starting at the age of 35 years or 5–10 years earlier than the earliest age of first diagnosis of EOC in the family. While this may be a reasonable option, the evidence indicates limited effectiveness of screening in this population, and clinicians and patients should not be falsely reassured by negative screening results.

It has been suggested that women with a hereditary ovarian cancer syndrome who have not elected for RRSx and who are not trying to conceive should consider combined oral contraceptive use which has been found to reduce the ovarian cancer risk in BRCA carriers.

Lack of screening efficacy has prompted many clinicians to recommend risk-reducing bilateral salpingo-oophorectomy (RRBSO) at the completion of childbearing, as studies support its efficacy in significantly reducing the risk of gynaecological and breast cancer in women who carry BRCA1 or BRCA2 mutations and other high-risk genetic syndromes.

Woman with a positive family history of EOC but not suggestive of a hereditary cancer syndrome can consider RRSx based on individual considerations.

RRBSO in premenopausal women with BRCA mutations has the additional benefit of significantly reducing the risk of breast cancer by 30–75%.

Data regarding the finding of occult fallopian tube cancers in women who have undergone RRBSO suggest that at least some apparent ovarian cancers were initiated in the tubes.

The possibility that the fallopian tubes are the primary site of carcinogenesis in ovarian cancer has led to some experts advocating salpingectomy at the time of hysterectomy in the general population to reduce EOC risk.

Women who have not completed childbearing should be counselled regarding alternative reproductive options including embryo cryopreservation, preservation of ovarian tissue (under investigation) and surrogacy.

Hysterectomy may be performed concurrently when there are other gynaecological indications. For example, those with Lynch syndrome have a 40–60% risk of endometrial cancer, some BRCA carriers wanting to take tamoxifen for chemoprophylaxis of breast cancer (associated with an increased risk of endometrial pathology) and women wanting to take unopposed oestrogen therapy.

While combined HRT is associated with an increased risk of breast cancer in postmenopausal women, there is no association with unopposed oestrogen HRT in this group.

HRT is also recommended in the BRCA population after RRBSO up to the age of 50 as there is no decrease in the benefit in terms of breast cancer risk reduction.

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TABLE 1. EPITHELIAL OVARIAN CANCER RISK

BRAC1	35–46%
BRAC2	13–23%
Lynch syndrome	3–14%
Peutz-Jeghers syndrome	20%

TABLE 2. AGE OF ONSET OF EPITHELIAL OVARIAN CANCER IN THE BRAC POPULATION AND TREATMENT RECOMMENDATIONS

Mutation	2–3% incidence of EOC	Average age of diagnosis	Treatment recommendations
BRAC1	Age 40	Age 50	RRBSO >35 or after completing childbirth.
BRAC2	Age 50	Age 60	Could postpone RRBSO until 45 but would lose the additional benefit of reduced breast cancer risk.