PRIMEVIEW

OVARIAN CANCER

nature REVIEWS DISEASE PRIMERS

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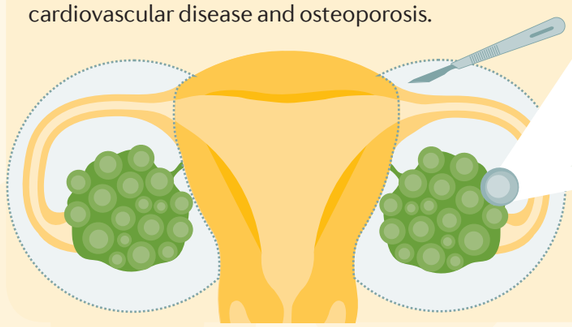
Ovarian cancer can be subdivided into different histological subtypes, such as high-grade serous, low-grade serous, clear-cell, mucinous and endometrioid carcinomas. Each subtype has different risk factors, molecular characteristics and clinical features.

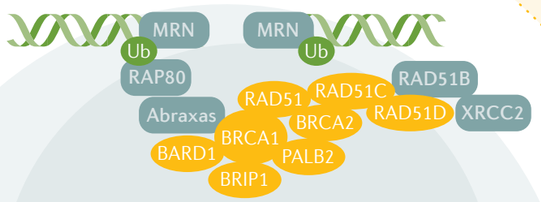
PREVENTION

Women at increased genetic risk of developing ovarian cancer can undergo risk-reducing surgery, such as bilateral salpingo-oophorectomy (removal of the fallopian tubes and ovaries). The timing of surgery is important, as this can be associated with adverse effects; in women <45 years of age, the hormonal effects of oophorectomy (that is, surgical menopause) can increase the risk of cardiovascular disease and osteoporosis.



MECHANISMS

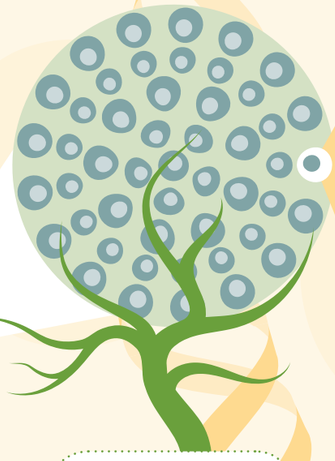
Alterations in genes encoding proteins involved in homologous recombination, for example, *RAD51*, *BRCA1*, *BRCA2* and *BARD1*, have been identified in up 50% of ovarian carcinomas



Of these, germline *BRCA1* and *BRCA2* mutations are the most significant known genetic risk factors for ovarian cancer and are found in up to 17% of patients

Other alterations associated with ovarian cancer include those in *TP53* and in genes involved in DNA mismatch repair, such as *MLH1* and *PMS2*

HOMOLOGOUS RECOMBINATION AND DNA REPAIR



Angiogenesis is important for the growth of ovarian cancer and metastasis

EPIDEMIOLOGY

225,000 new cases of ovarian cancer are diagnosed globally each year, with >140,000 cancer-specific deaths. Incidence and survival rates have been shown to vary by country. Risk factors for ovarian cancer include genetic, reproductive and lifestyle factors. In postmenopausal women, the use of hormone replacement therapy is associated with an increased risk. Other factors that affect risk include parity and the use of oral contraceptives, NSAIDs and cigarette smoking.

Genetic risk factors for ovarian cancer include mutations in *BRCA* and in genes involved in the Fanconi anaemia pathway

DIAGNOSIS

The median age of diagnosis of ovarian cancer is 63 years. Most ovarian cancers are asymptomatic in the early stages; symptoms such as ascites, gastrointestinal dysfunction, abdominal bloating and pain might initially be missed or attributed to another disease. Because of the lack of screening tests and the propensity for intra-abdominal tumour spread, ovarian cancer is most often diagnosed at a late stage.

Staging of ovarian cancer is based on surgical assessment of the cancer at initial diagnosis and requires assessment of the lymph nodes, abdominal fluid and histological examination of tissue

MANAGEMENT

The main treatment for women with ovarian cancer is surgical cytoreduction, which is followed by adjuvant chemotherapy for high-risk cancers. In some patients, such as those with extensive inoperable cancer burden, neoadjuvant chemotherapy can be administered before surgery with additional chemotherapy given post-surgery.

Most women with advanced-stage ovarian cancer will experience recurrence of disease

QUALITY OF LIFE

Ovarian cancer is associated with reductions in quality of life, which can affect physical, functional, social and sexual well-being.

Measures of quality of life, such as patient-reported outcomes, are being incorporated into clinical trials for ovarian cancer

OUTLOOK

Now is an exciting time for ovarian cancer research, with genomic analyses yielding more information about the histological subtypes of cancer and the pathophysiology of disease. Rational design of new treatments for ovarian cancer is also poised to move forward.

Designed by Laura Marshall

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