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Genetic Predisposition: BRCA Gene Mutations and Ovarian Cancer

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Abstract

Genetics plays a pivotal role in our susceptibility to various diseases and one of the most well-known connections between genetic mutations and cancer risk is the link between BRCA gene mutations and ovarian cancer. The discovery of these mutations has transformed our understanding of hereditary ovarian cancer and opened the door to proactive risk management and early detection strategies. BRCA1 and BRCA2 are tumor suppressor genes that are instrumental in DNA repair. Mutations in these genes increase the risk of developing breast and ovarian cancers. The BRCA1 gene is located on chromosome 17, while BRCA2 is situated on chromosome 13. These genes encode proteins that help repair damaged DNA, preventing the accumulation of genetic errors that can lead to cancer.

Keywords: Genetic predisposition • Mutations • Ovarian cancer

Introduction

Women who inherit certain BRCA1 or BRCA2 gene mutations have a significantly elevated risk of developing ovarian cancer. BRCA1 mutations are associated with a 35-70% lifetime risk of developing ovarian cancer, while BRCA2 mutations confer a 10-30% lifetime risk. In comparison, the general population's lifetime risk of ovarian cancer is around 1.3%. The precise mechanism through which BRCA gene mutations increase ovarian cancer risk is not fully understood, but it is believed to be related to the genes' roles in DNA repair. Mutations in these genes impair the body's ability to repair DNA damage, leading to a higher likelihood of genetic mutations that can trigger cancer. It is essential to distinguish between hereditary and sporadic ovarian cancer. Hereditary ovarian cancer is associated with BRCA gene mutations and is more likely to occur at a younger age. In contrast, sporadic ovarian cancer has no known genetic link and typically affects older women. To determine whether an individual carries BRCA gene mutations, genetic testing is necessary [1]. These tests analyze a person's DNA to identify mutations in the BRCA1 and BRCA2 genes. This information can help individuals understand their cancer risk and make informed decisions about prevention and screening.

Regular screening using methods like transvaginal ultrasound and CA-125 blood tests can help detect ovarian cancer at an earlier, more treatable stage. Some individuals may choose to undergo risk-reducing surgeries, such as bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes), to significantly reduce their risk of ovarian cancer. Certain medications, like oral contraceptives, may help lower ovarian cancer risk in individuals with BRCA mutations. A healthy lifestyle, including a balanced diet, regular exercise and avoiding tobacco, can contribute to overall well-being and potentially reduce the risk of cancer [2,3]. Ovarian cancer is a complex disease with various genetic mutations and alterations that contribute to its development and progression. These genetic mutations can be broadly categorized into two groups: somatic mutations and germline mutations. Somatic mutations are genetic changes that occur in the DNA of non-reproductive (somatic) cells during a person's lifetime. These mutations are typically not inherited and are acquired over time.

Description

TP53 mutations are the most prevalent genetic alterations in high-grade serous ovarian cancer, the most aggressive subtype of ovarian cancer. These mutations are associated with DNA repair deficiencies and uncontrolled cell growth. While these genes are often associated with hereditary breast and ovarian cancer, somatic mutations in BRCA1 and BRCA2 can also occur in ovarian cancer patients without a family history of these mutations. Such mutations can affect DNA repair pathways, increasing the risk of cancer development. Mutations in the PTEN gene are associated with an increased risk of several cancer types, including ovarian cancer. PTEN is a tumor suppressor gene and mutations can lead to uncontrolled cell growth. KRAS mutations are common in low-grade serous ovarian cancer. The KRAS gene is involved in cell signaling pathways and can contribute to cancer development when mutated. ARID1A is another frequently mutated gene in ovarian clear cell and endometrioid carcinomas. Mutations in ARID1A are associated with alterations in chromatin remodeling and gene expression regulation.

Germline mutations are inherited genetic alterations that are passed down from one generation to the next. Mutations in the BRCA1 and BRCA2 genes are well-known for increasing the risk of hereditary ovarian cancer. Individuals with these mutations have a higher likelihood of developing ovarian and breast cancer. Lynch syndrome is an inherited condition caused by mutations in genes involved in DNA mismatch repair (MLH1, MSH2, MSH6 and PMS2). Women with Lynch syndrome have an increased risk of ovarian cancer, in addition to colorectal and endometrial cancers. Mutations in these genes have been associated with an elevated risk of ovarian cancer, especially in individuals with a family history of the disease. PALB2 is another gene associated with hereditary breast and ovarian cancer syndrome. Mutations in PALB2 can increase the risk of both breast and ovarian cancer.

Understanding the specific genetic mutations in an individual's ovarian cancer can be essential for treatment decisions, as targeted therapies and precision medicine approaches are increasingly used to tailor treatments to the unique genetic characteristics of a patient's tumor [4,5]. It's important to note that the genetic landscape of ovarian cancer is continually evolving as research advances and new mutations and targeted therapies are identified. Regular genetic testing, especially for individuals with a family history of

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ovarian cancer or known genetic mutations, can help assess individual risk and guide treatment decisions.

Conclusion

BRCA gene mutations are a crucial factor in hereditary ovarian cancer, significantly increasing the risk of this disease. The discovery of these mutations has revolutionized the way we understand and manage ovarian cancer risk, enabling early detection and prevention strategies. For individuals with a family history of BRCA mutations, genetic testing and consultations with healthcare professionals are essential for informed decision-making. By proactively managing their risk, individuals with BRCA gene mutations can improve their chances of leading long and healthy lives, free from the shadow of ovarian cancer.

Acknowledgement

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Conflict of Interest

None.

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