RAD51C and *RAD51D* Mutations

Brought to you by the *National Society of Genetic Counselors, Cancer Special Interest Group*

What you should know about *RAD51C* and *RAD51D* Mutations

RAD51C and *RAD51D* mutations are associated with an increased risk of ovarian cancer in women. It is possible that *RAD51C* and *RAD51D* mutations may also be associated with an increased risk of breast cancer in women, particularly triple-negative breast cancer, although additional research is needed to confirm this association. Men can also have *RAD51C* and *RAD51D* mutations. Men with a *RAD51D* mutation may have an increased risk for prostate cancer, although additional research is needed to confirm this association. There are currently no known cancer risks for men with a *RAD51C* mutation.

Cancer Risks Associated with *RAD51C* and *RAD51D* Mutations

Type of Cancer	General Population Risk	*RAD51C* Mutation Carrier Risk	*RAD51D* Mutation Carrier Risk
Ovarian	1.2%	5-9%	7-14%
Breast	12.5%	Possibly increased	Possibly increased
Prostate	11-12%	Unknown	Possibly increased

Genetics and Inheritance of *RAD51C* and *RAD51D* Mutations

Genes are our body's instructions. They provide our body with information about how to grow and develop. When there is a mutation in a gene, it can cause the gene to no longer function correctly. Each person has two copies of every gene. One copy is inherited from their mother and the other copy is inherited from their father.

Cancer risks associated with mutations in the *RAD51C* and *RAD51D* genes are inherited in an autosomal dominant manner. This means that children, siblings and parents of individuals with a *RAD51C* or *RAD51D* mutation have a 50% (1 in 2) chance of having the mutation as well. Both males and females can inherit a *RAD51C* or *RAD51D* mutation and can pass that mutation on to their children.

Individuals who have a single *RAD51C* mutation are also carriers of a rare condition called Fanconi anemia, which is inherited in an autosomal recessive manner. This means that if both parents each have a single *RAD51C* mutation, there is a 25% (1 in 4) chance of having a child who inherits both *RAD51C* mutations. Having two *RAD51C* mutations, one inherited from each parent, causes Fanconi anemia. Individuals with Fanconi anemia may have bone marrow failure, physical abnormalities, organ defects, and increased risks for certain types of cancer. There have been no reports to date of *RAD51D* mutations causing Fanconi anemia.

Managing Cancer Risks

- The National Comprehensive Cancer Network (NCCN) recommends consideration of risk-reducing bilateral salpingo-oophorectomy (the surgical removal of both ovaries and fallopian tubes to prevent ovarian cancer from occurring) for women with a *RAD51C* or *RAD51D* mutation.
- The optimal age at which this procedure should be performed has not yet been determined; some studies have suggested around 45-50 years of age, or earlier if there is a family history of early-onset ovarian cancer.
- There is currently not enough evidence to recommend changes to breast cancer screening based on having a *RAD51C* or *RAD51D* mutation; breast cancer screening should be guided by personal and family history.

When to Consider Evaluation for *RAD51C* and *RAD51D* Mutations

A cancer genetic evaluation for *RAD51C* and *RAD51D* mutations should be considered in the following cases:

- An individual whose family member was found to have a *RAD51C* or *RAD51D* mutation
- An individual with a personal or family history of ovarian cancer

Depending on an individual's personal and family history, a broader multigene panel test may be recommended to include testing of additional genes associated with hereditary cancer risk.

Genetic Counseling

In many families, the cancer history may be due to a combination of genetic and environmental factors. In addition, other genetic conditions (i.e. other gene mutations) may appear clinically similar to *RAD51C* and *RAD51D* mutations**.** For this reason, a detailed review of the family history by a genetics professional is important before pursuing genetic testing. A genetic counselor can help determine which, if any, genetic tests may be helpful for a family and review the benefits, risks and limitations of genetic testing. Genetic testing is usually performed through a blood or saliva sample.

Genetic test results can be complicated and are most useful when interpreted by a genetics professional in the context of an individual's personal and family history. To locate a genetic counselor near you, please visit www.nsgc.org and click on the 'Find a Genetic Counselor' link.

Genetic Discrimination

The Genetic Information Nondiscrimination Act (GINA) was signed into federal law in 2008. GINA prohibits health insurers and most employers from discriminating against individuals based on genetic information (including the results of genetic tests and family history information). According to GINA, health insurance companies cannot consider genetic information to be a preexisting condition, nor can they use it to make decisions regarding coverage or rates. GINA also makes it illegal for most employers to use genetic information in making decisions about hiring, firing, promotion, or terms of employment. It is important to note that GINA does not offer protections for life insurance, disability insurance, or long-term care insurance. More information about GINA can be found by contacting a local genetic counselor or by visiting www.ginahelp.org.

Resources

- Facing Our Risk of Cancer Empowered (FORCE): https://www.facingourrisk.org/

References

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