UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

Lynch syndrome: *MSH2* Mutations

What You Should Know About Lynch syndrome (*MSH2* Mutations)

Lynch syndrome is the most common type of hereditary colon cancer and accounts for 2-4% of all colon cancers. Families with Lynch syndrome often have multiple family members with colon, uterine or other cancers, typically diagnosed before age 50. Lynch syndrome is caused by mutations in one of five different genes, and the specific cancer risks and management recommendations depend on the gene.

Cancer Risks Associated with Lynch syndrome (*MSH2* Mutations)

Males and females with an *MSH2* gene mutation have a 43-52% risk to develop colorectal cancer in their lifetime. Females have a 21-57% risk for uterine cancer, and a 10-38% risk for ovarian cancer. Males have a 30-32% risk for prostate cancer. Males and females with an *MSH2* mutation also have an increased risk for other types of cancer such as stomach cancer (0.2-16%), bladder cancer (4-17%), urothelial cancer (2-18%), and small bowel cancer (1-10%). These cancers tend to occur at a younger age.

Risks to Family Members

Mutations in the *MSH2* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *MSH2* mutation have a 1 in 2 (50%) chance of having the mutation as well. Individuals with a *MSH2* mutation may develop one cancer, more than one cancer, or none at all. Both males and females can inherit a familial *MSH2* mutation and can pass that it on to their children.

When an individual inherits two *MSH2* mutations (one from each parent), this causes a syndrome called Constitutional Mismatch Repair Deficiency (CMMRD). CMMRD is associated with an increased risk for childhood colon cancer, lymphoma, brain tumors, and cafe au lait spots.

Managing Cancer Risks

The following surveillance is recommended by the National Comprehensive Cancer Network (v3.2019):

Colon Cancer

- Colonoscopy every 1-2 years starting at age 20-25 or 2-5 years prior to earliest colon cancer diagnosis in the family, whichever comes first.
- If colon cancer is detected, partial or complete removal or colon should be considered

Uterine/Ovarian Cancer

- Screening via uterine biopsy every 1-2 years and transvaginal ultrasound may be considered
- CA-125 screening and transvaginal ultrasound can be considered (these tests have limited ability for early detection of ovarian cancer)
- Removal of ovaries and uterus after child-bearing is complete can be considered

Other Cancers

- Annual physical examination/ neurological exam starting at age 25-30
- Annual urinalysis beginning at age 30-35
- Upper endoscopy every 3-5 years, beginning at age 40

- Annual abdominal MRI and/or upper endoscopy beginning at age 50 or 10 years before the earliest diagnosed pancreatic cancer in the family for individuals a first or second degree relative with pancreatic cancer.
- Prostate screening may be considered based on personal risk factors and family history
- Additional screenings may be considered based on personal risk factors and family history

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