Lynch syndrome (also known as Hereditary Nonpolyposis Colon Cancer (HNPCC)) is caused by mutations in the MLH1, MSH2, MSH6, PMS2 or EPCAM genes. Lynch syndrome is responsible for approximately 2-4% of colorectal cancers (CRC) and 2% of endometrial cancers (EC). Individuals with Lynch syndrome are often diagnosed with cancer at younger ages and have an increased risk for additional cancers compared to the general population, highlighting the importance of early identification. Current professional medical society guidelines recommend Lynch syndrome evaluation for CRC and EC patients with early age of onset (< age 50) and family history as factors to be considered. To understand more about the phenotype of Lynch syndrome patients, we queried laboratory database, one of the largest databases of patients tested for Lynch syndrome.

Individuals with CRC had a 12.2% mutation rate. Among groups most likely to have a Lynch syndrome mutation with highest mutation rates were observed in patients diagnosed in their 20s, 30s, and 40s. However, patients diagnosed in their 50s and 60s had mutation rates of 16.5%, 11.5%, 10.9% and 8.3%, respectively.

The overall mutation rate for patients with colorectal cancer was 12.2%. The highest mutation rates were observed in patients diagnosed in their 20s, 30s, and 40s. However, patients diagnosed in their 50s and 60s also had an increased mutation rate.

The overall mutation rate for patients with endometrial cancer was 12.7%. The highest mutation rate was observed in patients diagnosed in their 40s, but the mutation rate for patients diagnosed in their 50s was comparable.

Finally, women with both CRC and EC diagnoses had a Lynch syndrome mutation rate of 29.4%. A peak mutation rate of 47.7% was observed in women diagnosed with their first cancer in their 40s. Women whose first cancer diagnosis occurred in their 20s, 30s, and 50s had Lynch syndrome mutation rates of 29.5%, 42.5%, and 25.4%, respectively.

The data presented here confirms that patients who have a personal history of early onset colorectal and/or endometrial cancer diagnosed less than age 50 have a considerable risk for having a Lynch syndrome genetic mutation.

The data also indicate that the mutation rate remains high for patients who are diagnosed with CRC and/or CRC and EC in their 50s and 60s and strongly supports evaluation of family history for genetic testing for Lynch syndrome.

The high mutation rate in women with both CRC and EC clearly demonstrates the elevated risk for second primary cancers in patients with Lynch syndrome. The identification of individuals who have a Lynch syndrome mutation after their first cancer diagnosis can lead to the prevention or early identification of a second cancer because of increased surveillance and/or prophylactic surgery.

**REFERENCES**


* All authors are employees of Myriad Genetic Laboratories, Inc. and receive salary and stock options as compensation.