**MSI-HIGH HISTOLOGY IS A PREDICTIVE RISK FACTOR FOR LYNCH SYNDROME**

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**INTRODUCTION**

Patients whose colorectal tumor exhibits MSI-High histology (including mucinous, signet ring, tumor infiltrating lymphocytes, Crohn’s-like lymphocytic reaction, or medullary growth pattern) have previously been reported to have a higher risk of carrying a Lynch syndrome mutation. Based upon the Revised Bethesda guidelines, patients diagnosed with colorectal cancer (CRC) less than age 50 are appropriate for further evaluation, but the age limit for evaluation is increased to patients diagnosed under age 60 if the colorectal tumor has MSI-High histology. To understand more about the prevalence of Lynch syndrome mutations in patients who have CRC with abnormal histology (MSI-High histology), we queried a genetic testing laboratory database for patients with that diagnosis who underwent germline genetic testing for Lynch syndrome.

**METHODS**

Data were queried for patients with a personal history of CRC who underwent comprehensive germline genetic testing for Lynch syndrome (full sequencing and large rearrangement analysis of MLH1, MSH2/EPCAM, and MSH6 with or without PMS2) between July 2012 and August 2013. Patients who had testing for a specific Lynch syndrome mutation or single gene testing, presumably based upon immunohistochemistry results, were excluded from the analysis. Information regarding patients’ personal and family history of cancer and the histology of the patient’s colorectal tumor were ascertained from the Test Requisition Form (TRF). Patients’ histories were evaluated to determine what percentage would not have met testing criteria if information regarding histology were not included.

**CONCLUSIONS**

- The 13.9% mutation positive rate for patients whose colorectal tumor had MSI-High histology demonstrates that histology is a valuable element of Lynch syndrome risk assessment independent from tumor testing.
- The 77.2% of Lynch syndrome positive patients who would not have met Amsterdam II criteria supports the importance of including tumor histology in addition to personal and family history when assessing a patient’s risk of Lynch syndrome.
- Mucinous and signet ring were the most common histologies and had similar Lynch syndrome mutation rates.
- These results support MSI-High histology as a predictive risk factor for Lynch syndrome and the assessment of histology as a critical component for evaluating a colorectal cancer patient’s risk for having Lynch syndrome.