Genetic testing of tumor is recommended for colorectal cancer patients

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Of the 143,000 patients diagnosed with colorectal cancer annually in the U.S., up to 25 percent have a familial risk of colorectal cancer. A new guideline from the U.S. Multi-Society Task Force on Colorectal Cancer recommends genetic testing of tumors for all newly diagnosed colorectal cancer patients. The task force makes specific surveillance and management recommendations for those affected by a genetic condition called Lynch syndrome, the most common cause of inherited colorectal cancer, accounting for approximately 3 percent, or more than 4,000, of the newly diagnosed cases in the U.S. each year.

Universal Tumor Testing

Universal genetic testing of the tumors for evidence of mismatch repair (MMR) deficiency of newly diagnosed colorectal cancer patients is recommended for several reasons:

1. Use of clinical criteria and prediction models to identify patients with Lynch syndrome have less than optimal sensitivity and specificity.

2. It has been shown to be cost effective for the diagnosis of Lynch syndrome.

3. It has greater sensitivity for identification of Lynch syndrome compared with other strategies, including Bethesda guidelines, or a selective tumor testing strategy.

Genetic Counseling and Confirmatory Germline Genetic Testing

Individuals whose tumor shows evidence of MMR deficiency, have a known MMR gene mutation in the family, who meet clinical criteria for Lynch syndrome, or who have a personal risk of greater than or equal to 5 percent chance of Lynch syndrome based on prediction models should undergo a genetic evaluation for Lynch syndrome. Germline genetic testing has the following advantages:

1. It can confirm a diagnosis of Lynch syndrome in the patient.

2. It can determine the status of at-risk family members in families in which disease mutation has been found.

3. It can direct the management of affected and unaffected individuals.

Management of Lynch Syndrome

Patients with Lynch syndrome are at an increased risk of developing colorectal cancer, as well as cancers outside of the colon. The U.S. Multi-Society Task Force on Colorectal Cancer recommends that annual history, physical examination, and patient and family education regarding the risk of cancer should start between the ages of 20 and 25 years. In addition, the following recommendations are made for patients with or at risk of Lynch syndrome:

- Colorectal cancer
    - Colonoscopy screening every one to two years beginning at ages 20 to 25, or two to five years younger than the youngest age of CRC diagnosis in the family, if the

diagnosis was before the age of 25.

- Endometrial cancer
    - Conduct pelvic exam screening and endometrial sampling annually starting between the ages of 30 and 35.

- Ovarian cancer
    - Start annual transvaginal ultrasound screening at ages 30 to 35.
    - Hysterectomy and bilaterial salpingo-oophorectomy is recommended for women with Lynch syndrome at age 40 or after childbearing is complete.

- Gastric cancer
    - Screen via endoscopy with gastric biopsy beginning at ages 30 to 35. Continue every two to three years based on patient risk factors.

- Urinary cancer
    - Conduct annual urinalysis starting at ages 30 to 35.

Routine screening of the small intestine, pancreas, prostate and breasts are not recommended.

Treatment

There are two treatments recommended for patients affected with Lynch syndrome:

1. Removal of the large intestine: Colectomy with ileorectal anastomosis, which removes the large intestine and attaches the small intestine to the rectum, is the primary treatment for patients affected by Lynch syndrome who have colon cancer or precancerous colon polyps that cannot be removed by colonoscopy. Less extensive surgery can be considered for patients older than 60 to 65 years of age.

2. Aspirin therapy: There is growing evidence that the use of aspirin is beneficial in preventing cancer in Lynch syndrome patients. While the evidence is not conclusive, treatment of an individual patient with aspirin is a consideration after discussing patient-specific risks, benefits and uncertainties of treatment.

In the U.S., colorectal cancer is a major health problem—it is the second leading cause of cancer death, causing nearly 51,000 deaths each year. Environmental causes and inheritance play varying roles in different patients with colorectal cancer. About 20 to 30 percent of colorectal cancer patients appear to have a familial risk and a minority has a genetic mutation that contributed to the development of the disease.

The U.S. Multi-Society Task Force on Colorectal Cancer is composed of gastroenterology specialists with a special interest in colorectal cancer, representing the American Gastroenterological Association, the American College of Gastroenterology and the American Society for Gastrointestinal Endoscopy. Experts on Lynch syndrome from academia and private practice were invited authors of this guideline. Representatives of the Collaborative Group of the Americans on Inherited Colorectal Cancers and the American Society of Colon and

Rectal Surgeons also reviewed the manuscript.

The consensus statement, "Guidelines on Genetic Evaluation and Management of Lynch Syndrome: A Consensus Statement by the US Multi-Society Task Force on Colorectal Cancer," is published in *Gastroenterology*, the official journal of the AGA Institute; *American Journal of Gastroenterology*, the official journal of ACG; *Diseases of the Colon & Rectum*, the official journal of ASCRS; and *GIE: Gastrointestinal Endoscopy*, the official journal of ASGE.

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