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Universal Tumor Screening for Lynch Syndrome – Accreditation measure

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Background

Colorectal cancer (CRC) is the third most common cancer type and second most common cause of cancer death in the United States.[1] Approximately 10% of colorectal cancers are hereditary and 20% to 30% are familial.[2,3] The most common form of hereditary CRC is Lynch syndrome. Lynch syndrome is estimated to affect 1 out of every 279 individuals globally and 1 out of every 25-35 individuals with CRC.[4] Lynch syndrome is caused by pathogenic variants in the mismatch repair (MMR) genes *MLH1*, *MSH2*, *MSH6*, and *PMS2* or deletions of the 3' end of *EPCAM*.[5] Individuals with Lynch syndrome have a 20-60% lifetime risk of developing CRC without early identification and recommended surveillance, and are more likely to develop CRC at an age younger than 50.[6] Lynch syndrome is also associated with a high risk of endometrial cancer (15-40% lifetime risk) as well as moderately increased risks of gastric, ovarian, biliary, urinary tract, small bowel, brain and pancreatic cancers.[6]

Intensive surveillance is recommended, including colonoscopy every 1-2 years beginning at age 20-25 for individuals with *MLH1* and *MSH2* pathogenic variants and 30-35 for individuals with *MSH6* and *PMS2* pathogenic variants, as well as consideration of hysterectomy and bilateral salpingo-oophorectomy after child-bearing.[6-12] In addition, chemoprevention with aspirin can significantly reduce the long-term risk of colorectal cancer in Lynch Syndrome patients.[13,14] These interventions are effective at preventing cancer or potentially diagnosing the cancers early when they are most treatable. However, it is estimated that 90% of individuals with Lynch syndrome

are not aware of their diagnosis.[15] Furthermore, studies demonstrate disparities in access to genetic counseling and testing among ethnic/racial minorities.[16-17]

Universal Tumor Screening for Lynch Syndrome

Universal tumor screening of all newly diagnosed colorectal and endometrial cancer patients is one approach used to identify cases of Lynch syndrome.[15,18-20] Testing is performed using tumor tissue to identify features of deficient mismatch repair (MMR) including microsatellite instability (MSI) and/or absence of any of the four mismatch repair proteins.[7] This also provides prognostic and treatment information for the patients with several studies showing a better prognosis for cancers with microsatellite instability and convincing data that these tumors respond well to immune checkpoint inhibition therapy.[21-24] As a result, multiple professional organizations have recommended universal tumor screening for all colorectal and endometrial cancer patients as follows:

Tumor to Screen	Professional Organization	Year Recommendation Released
Colorectal Cancer	Evaluation of Genetic Applications in Practice & Prevention (CDC)[6]	2009
	Healthy People 2020[25]	2010
	National Comprehensive Cancer Network[6, 26]	2013
	European Society of Medical Oncology[8]	2013

	US Multi-Society Task Force on Colorectal Cancer[9]	2014
	American College of Gastroenterology[10]	2015
	American Society of Clinical Oncology[11]	2015
	National Institute for Health and Care Excellence (UK)[27]	2017
	American Society for Clinical Pathology College of American Pathologists Association of Molecular Pathology American Society of Clinical Oncology[28]	2017
Endometrial Cancer	American College of Obstetrics and Gynecology and the Society of Gynecologic Oncology[12]	2014

Adoption of Universal Tumor Screening

Universal tumor screening for Lynch syndrome remains underutilized. Barriers include lack of knowledge of guidelines, inadequate stakeholder involvement and champions, access to genetic testing and counseling services, and cost.[18] An assessment of National Cancer Institute (NCI)-designated Comprehensive Cancer Centers in 2012 found that only 71% were performing universal tumor testing for Lynch syndrome.[29] Furthermore, only 48% of American College of Surgeons–accredited Community Hospital Comprehensive Cancer Programs, 14% of Community Hospital Cancer Program sites, and approximately 4-5% of Veteran Affairs Medical Centers perform universal tumor testing on all CRCs.[29,30] Another study found that only 28.2% of colorectal cancer patients had universal tumor screening at the time of diagnosis according to the National Cancer Database.[31] The most recent study on this topic showed some

improvement with 86% of institutions surveyed performed universal tumor screening for Lynch syndrome with no difference between academic and nonacademic institutions.[32] Therefore, strategies are needed to improve implementation of universal tumor screening.

Quality Improvement Measures as a Strategy to Increase Uptake

Quality measures have been increasingly used in the United States over the last 20 years to assess the utilization of cancer care guidelines and stimulate improvement. Adoption of quality measures by accrediting entities have been shown to be effective in improving patient outcomes. For example, Shulman et al. demonstrated that the introduction of the Commission on Cancer 12 lymph node measure for colorectal cancer surgery resulted in an improvement of 39.3% increased compliance with the practice – from 52.8 to 92.1% compliance in a 13-year period. Hospitals with increased compliance concurrently experienced improved patient survival.[33] A Commission on Cancer (COC) Quality Measure would provide accountability and incentive for cancer centers and providers to implement universal tumor testing.

We propose that the COC adopt a new National Cancer Database (NCDB) accountability or quality improvement measure for use with standard 7.3 the Quality Improvement Initiative regarding universal tumor screening for Lynch syndrome. This standard would be added to the colorectal and endometrial cancer sections (https://www.facs.org/quality-programs/cancer/ncdb/qualitymeasurescocweb) as follows: Universal tumor screening for defective mismatch repair performed using either IHC for the four MMR proteins or MSI testing by PCR or NGS. The percent of tumors that receive this important screening would be reported.

This measure could dovetail nicely with the COC Genetic Counseling and Risk Assessment standard (4.4) since all colorectal and endometrial cancer patients with defective mismatch repair in their tumor (not caused by MLH1 promoter methylation) should be referred for cancer genetic counseling. Therefore, the new standard will identify a group of patients that could be selected to be tracked for the existing standard 4.4. While studies have shown that universal tumor screening of colorectal cancer and endometrial patients is performed at similar rates among Non-Hispanic White, Black, and Hispanic populations, minority populations are less likely to receive referral to genetic evaluation and complete germline genetic testing.[16-18] The pairing of these two measures could improve implementation of universal tumor testing among all populations and reduce racial and ethnic disparities in referral to genetic evaluation and post-test follow-up.

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