

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

Improving the Quality of Endoscopic Surveillance of Patients with Lynch Syndrome



Silvia Sanduleanu, MD, PhD
 Consultant Gastroenterologist
 Department of Internal Medicine
 Division of Gastroenterology and Hepatology
 GROW, School for Oncology and Developmental Biology
 Maastricht University Medical Centre
 Maastricht, The Netherlands

G&H What is Lynch syndrome?

SS Lynch syndrome, an autosomal-dominant condition caused by germline mutations in one of the DNA mismatch repair genes, accounts for approximately 5% of all colorectal cancers (CRCs). Depending on the type of mutation, CRC will develop in 40–80% of patients with Lynch syndrome during their lifetime. In patients with Lynch syndrome, CRC is diagnosed at a relatively young age compared with sporadic CRC. Of particular importance, nearly 70% of the CRCs diagnosed in patients with Lynch syndrome are located in the proximal part of the colon, where colonoscopy has shown limited effectiveness for preventing CRC. For these reasons, high-quality endoscopic surveillance is vital in patients with Lynch syndrome.

G&H What endoscopic techniques are currently used for surveillance of patients with Lynch syndrome?

SS In routine practice, white-light colonoscopy is usually used for the surveillance of patients with Lynch syndrome. In a few gastroenterology practices, as well as in research settings, panchromoendoscopy can be used via either dye-based techniques, such as indigo carmine, or digital chromoendoscopy techniques, such as narrow-band imaging, high-definition I-scan, autofluorescence, or Fujinon intelligent chromoendoscopy. Chromoendoscopy has the potential for improving the detection of subtle-appearing mucosal lesions, such as

small and flat lesions, as the technique helps to delineate the borders of these lesions, thus facilitating their resection (Figure). Finally, newly developed endoscopic techniques such as confocal laser endomicroscopy offer the opportunity of *in vivo* histologic diagnosis of colorectal neoplasms in patients with Lynch syndrome. It is important to keep in mind, however, that irrespective of the technology used, the ability of the endoscopist to perform high-quality colonoscopy has the most significant impact on surveillance outcomes.

G&H What is the optimal surveillance interval in patients with Lynch syndrome?

SS Patients with Lynch syndrome are advised to participate in colonoscopic surveillance programs with intervals of 1–2 years, starting at the age of 20–25 years. In the past, surveillance colonoscopy performed every 2–3 years appeared to be associated with a 10% risk of CRC. Shortening the surveillance interval from 2–3 years to 1–2 years has been demonstrated to reduce the CRC risk to 6%, during a 10-year follow-up period. Of note, the risk of CRC may differ among patients with Lynch syndrome, with the highest risk occurring in patients carrying the *MLH-1* or *MSH-2* mutation.

Several studies have examined whether shortening the surveillance interval improves surveillance outcomes, but only a few have addressed the role of colonoscopy quality. High-quality colonoscopic examination is vital for further reducing the risk of CRC, in terms of accurate detection and complete resection of precursor lesions.

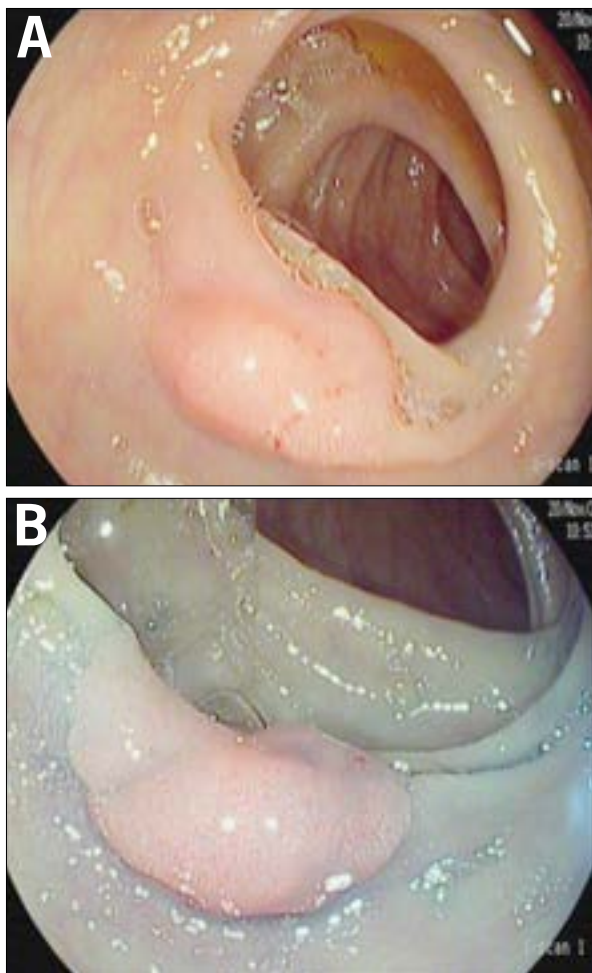


Figure. A nonpolypoid colorectal neoplasm in a patient with Lynch syndrome seen via (A) white-light colonoscopy and (B) chromoendoscopy using indigo carmine 0.4%, which allows better demarcation prior to endoscopic resection.

G&H Do all patients with Lynch syndrome require surveillance?

SS All carriers of a mutation in the mismatch repair genes (eg, *MLH-1*, *MSH-2*, *MSH-6*, and *PMS-2*) require colonoscopic surveillance, per international guidelines. These patients are usually highly motivated and comply with their surveillance programs.

G&H What challenges are associated with endoscopic surveillance of patients with Lynch syndrome?

SS Due to the fast polyp dwell-time (ie, rapid progression to cancer) in patients with Lynch syndrome, vigilance is needed to accurately detect and completely resect all colorectal lesions.

G&H Could you discuss the study that you and your colleagues conducted on this issue?

SS In February 2008, an initiative was undertaken to improve the quality of colonoscopy in South Limburg, The Netherlands. Using lectures, accredited video educational programs, and individual feedback, we trained endoscopists at our university hospital to recognize nonpolypoid (flat and depressed) colorectal neoplasms. We subsequently embarked on a prospective study of 59 patients with Lynch syndrome and 590 age- and sex-matched patients at average risk for CRC (controls) who underwent elective colonoscopy at our university hospital. Nonpolypoid colorectal neoplasms were defined as lesions with a height of less than one half of their diameter. When it was unclear if a lesion was nonpolypoid, selective chromoendoscopy was used with indigo carmine 0.4%.

We found that patients with Lynch syndrome had colorectal adenomas significantly more often than did controls (47.5% vs 30.7%; $P=.001$). Furthermore, in patients with Lynch syndrome, adenomas were nearly 4-fold more likely to be nonpolypoid than in controls. This was particularly seen with proximally located adenomas. Of note, adenomas containing advanced histology were also more often nonpolypoid in patients with Lynch syndrome than in controls (4/5 vs 5/17; $P=.19$). Serrated polyps were significantly more frequent (16.6% vs 11.4%; $P<.001$) and more often nonpolypoid in patients with Lynch syndrome than in controls.

We therefore concluded that, in patients with Lynch syndrome, colorectal neoplasms are more likely to have a nonpolypoid shape than in patients at average risk for CRC, particularly in the proximal colon. This may partly explain the limited effectiveness of colonoscopic surveillance in the proximal colon in patients with Lynch syndrome. Our data indicate that proficiency in the recognition and endoscopic resection of nonpolypoid colorectal lesions is of utmost importance for improving surveillance outcomes in patients with Lynch syndrome.

G&H How do your findings compare with those of previous studies?

SS Our data extend and substantiate findings from a previous Dutch nationwide study, which showed that there is still room for improvement in the colonoscopic prevention of CRC in patients with Lynch syndrome. A recent study by Haanstra and colleagues found that interval cancers in patients with Lynch syndrome are most often attributable to the incompleteness of a previous colonoscopy or incomplete polyp resection.

A new finding from our study is that nonpolypoid lesions—either adenomas or serrated polyps—are more

frequent in patients with Lynch syndrome than in patients at average risk for CRC. This is important, as endoscopic recognition of nonpolypoid neoplasms and their resection require training, particularly familiarity with the use of chromoendoscopy and skills for performing endoscopic resection techniques. Endoscopic mucosal resection and endoscopic submucosal dissection have been introduced only recently in routine practice in the West, and sustained practice is needed to attain and maintain these skills.

G&H What significance do serrated polyps have in Lynch syndrome?

SS Our study is one of the first to report on the prevalence and endoscopic appearance of serrated polyps in patients with Lynch syndrome. We categorized serrated polyps based on the World Health Organization classification and found that serrated polyps are significantly more common in patients with Lynch syndrome than in controls. More studies are needed, however, to elucidate the role of the serrated neoplastic pathway in CRC carcinogenesis in patients with Lynch syndrome.

G&H Should surveillance of Lynch syndrome be limited to specialist centers?

SS In our experience, patients with Lynch syndrome had a 3.6 greater odds of having nonpolypoid lesions compared with average-risk patients. This finding underscores the need for training and expertise in the recognition and endoscopic resection of such lesions to maximize protection against CRC via colonoscopy.

G&H What are the next steps in research in this area?

SS It is important to know whether high-quality colonoscopy may further reduce the risk of CRC during surveillance in patients with Lynch syndrome. Moreover, studies are needed to identify subgroups of patients with Lynch syndrome who are at greater risk for CRC (eg, *MLH-1* and *MSH-2* mutation carriers), as this information may form the basis for personalized genotype-specific surveillance in the future.

Dr. Sanduleanu does not have any conflicts of interest to disclose.

Suggested Reading

- Rondagh EJ, Gulikers S, Gómez-García EB, et al. Nonpolypoid colorectal neoplasms: a challenge in endoscopic surveillance of patients with Lynch syndrome. *Endoscopy*. 2013;45(4):257-264.
- Sanduleanu S, Driessen A, Gómez-García EB, et al. In vivo diagnosis and classification of colorectal neoplasia by chromoendoscopy-guided confocal laser endomicroscopy. *Clin Gastroenterol Hepatol*. 2010;8(4):371-378.
- Vasen HF, Abdirahman M, Brohet R, et al. One to 2-year surveillance intervals reduce risk of colorectal cancer in families with Lynch syndrome. *Gastroenterology*. 2010;138(7):2300-2306.
- Vasen HF, Blanco I, Aktan-Collan K, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. *Gut*. 2013;62(6):812-823.
- Haanstra JF, Vasen HF, Sanduleanu S, et al. Quality colonoscopy and risk of interval cancer in Lynch syndrome [published online July 16, 2013]. *Int J Colorectal Dis*. doi: 10.1007/s00384-013-1745-2.
- Sanduleanu S, Rondagh EJ, Masclee AA. Development of expertise in the detection and classification of non-polypoid colorectal neoplasia: experience-based data at an academic GI unit. *Gastrointest Endosc Clin N Am*. 2010;20(3):449-460.