

# Effectiveness of a dedicated small bowel neoplasia screening program by capsule endoscopy in Lynch syndrome: 5 years results from a tertiary care center

Guillaume Perrod\*<sup>1</sup>, Elia Samaha\*, Enrique Perez-Cuadrado-Robles, Arthur Berger<sup>1</sup>, Hedi Benosman, Sherine Khater, Ariane Vienne, Charles-André Cuenod, Aziz Zaanan, Pierre Laurent-Puig, Gabriel Rahmi and Christophe Cellier

## Abstract

**Background and aims:** The role of small bowel neoplasia (SBN) screening in asymptomatic patients with Lynch syndrome (LS) is uncertain. The aim of our study was to assess the effectiveness of screening by capsule endoscopy (CE) in these patients.

**Methods:** This study was an observational, analytical, and retrospective single-center study within the PRED-IdF network. All consecutive asymptomatic patients older than 35 years-old with confirmed LS and no personal history of SBN who started the screening from 2010–2015 were included. The baseline screening and 24 months follow-up were performed by CE. The CE diagnostic yield (positive tumor or polyp) and accuracy, using the follow-up as gold standard, were evaluated.

**Results:** A total of 150 patients underwent the SBN screening program and 135 (52.7 ± 11.2 years-old, 37.8% male) met the inclusion criteria. The baseline CE diagnostic yield was 4.4% (3 polyps, 3 tumors) and the proximal small bowel was the most common location ( $n=4$ , 66.7%). In total, 87 patients underwent follow-up and the diagnostic yield was 4.6%. Four patients were considered positive at follow-up (2 adenomas, 2 adenocarcinomas). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CE were 60%, 100%, 100%, 96.9%, and 97%, respectively.

**Conclusions:** CE is an accurate procedure for baseline screening of SBN in LS patients and may be efficient for follow-up procedures. However, the optimal starting age of screening and intervals of follow-up must be clarified.

**Keywords:** capsule endoscopy, diagnostic yield, Lynch syndrome, small bowel neoplasia screening

Received: 4 December 2019; revised manuscript accepted: 11 May 2020.

## Introduction

Lynch syndrome (LS), also known as the hereditary non-polyposis colorectal cancer, is an autosomal dominant inherited disorder caused by a pathogenic variant in one of the mismatch repair genes (*path\_MMR*), mostly *path\_MLH1*, *path\_MSH2* and *path\_MSH6*. This disease is characterized by a very high risk of early-onset colorectal and endometrial cancer and an increased risk of other neoplasms, including cancers of the stomach,

ovary, urinary tract, and small bowel.<sup>1,2</sup> Recently, several studies have evaluated the life-time risk of small bowel neoplasia (SBN) in LS patients, which is estimated to be around 4–5%.<sup>3,4</sup> Although the SBN risk increases with age, LS patients may develop early adenocarcinoma usually located in the duodenum and jejunum.<sup>5,6</sup>

Currently, SBN screening by capsule endoscopy (CE) or radiological examinations in LS is not

*Ther Adv Gastroenterol*

2020, Vol. 13: 1–7

DOI: 10.1177/  
1756284820934314

© The Author(s), 2020.  
Article reuse guidelines:  
sagepub.com/journals-  
permissions

Correspondence to:

**Guillaume Perrod**  
Gastroenterology and  
Endoscopy Unit, Georges  
Pompidou European  
Hospital, 20 Rue Leblanc,  
Paris, 75015, France

Paris Descartes University,  
Paris, France

[perrodguillaume@gmail.com](mailto:perrodguillaume@gmail.com)

**Elia Samaha**  
**Enrique Perez-Cuadrado-Robles**

**Hedi Benosman**  
**Sherine Khater**  
**Ariane Vienne**  
Gastroenterology and  
Endoscopy Unit, Georges  
Pompidou European  
Hospital, Paris, France

**Arthur Berger**  
**Gabriel Rahmi**  
**Christophe Cellier**  
Gastroenterology and  
Endoscopy Unit, Georges  
Pompidou European  
Hospital, Paris, France

Paris Descartes University,  
Paris, France

**Charles-André Cuenod**  
Radiology Unit, Georges  
Pompidou European  
Hospital, Paris, France

Paris Descartes University,  
Paris, France

**Aziz Zaanan**  
Oncogenetic department,  
Georges Pompidou  
European Hospital, Paris,  
France

**Pierre Laurent-Puig**  
Oncogenetic department,  
Georges Pompidou  
European Hospital, Paris,  
France

Paris Descartes University,  
Paris, France

Authors designed with \*  
shared first co-authorship

recommended,<sup>7</sup> however, prospective studies in the literature analyzing the usefulness of CE in these patients are lacking. Indeed, CE<sup>8,9</sup> and magnetic resonance enteroclysis (MRE)<sup>10</sup> have shown to have a high diagnostic yield in the diagnosis of sporadic small bowel (SB) tumors. Similarly, the diagnostic yield of CE in LS has been assessed in two prospective studies with different outcomes. Saurin *et al.*<sup>11</sup> described an 8.6% SBN rate in 35 asymptomatic patients with LS who underwent CE, thus concluding that this technique could be better than Computed Tomography enteroclysis. Conversely, Haanstra *et al.*<sup>6</sup> reported a 1.5% SBN rate (200 asymptomatic patients), and all the lesions were located in the duodenum and within reach of conventional gastroduodenoscopy. In a follow-up study, the same group reported an SBN rate of 0% (155 patients) at 2 years, thus suggesting that small bowel screening by CE should not be warranted in asymptomatic LS patients.<sup>12</sup> In addition, the optimal interval time of surveillance after a baseline screening CE and the usefulness of this technique in the long term are uncertain. In this study, we aimed to evaluate, within our dedicated tertiary care center, the effectiveness of a dedicated SBN screening program by CE in asymptomatic patients with LS.

## Patients and methods

### Patients

This is an observational, analytical, and retrospective study performed in one center of the PRED-IdF network. All consecutive asymptomatic patients older than 35 years-old with genetically confirmed LS followed at our center were sent for SBN screening between January 2010 and December 2015. Baseline and demographic characteristics including family history of SBN and path\_MMR were collected. Patients with suspected SB or obscure gastrointestinal bleeding, suspected intestinal obstruction, previous diagnosis of SB tumor, or previous SB surgery were excluded.

### The SBN screening program

The PRED-IdF network is a French dedicated regional network for counselling and follow-up of patients with genetic predispositions to gastrointestinal cancers, coordinated by the Georges Pompidou European Hospital.

The baseline SBN screening was performed by CE (Pillcam SB2, Pillcam SB3, Medtronic Inc, Dublin, Ireland) in all cases. A 1.5L polyethylene glycol preparation was given the night before CE. The patients had fasted for 8 h and were allowed to drink water 2 h after the CE ingestion. Laxatives and prokinetic agents were not used. A positive diagnostic yield was retained in patients with SB polyps or tumors, while those presenting with other SB lesions (vascular lesions, ulcers, diverticula) or a normal examination were considered a negative result. CE-related adverse events were noted. All procedures were read by expert endoscopists (ES, GR) with a background of more than 2000 CE procedures.

### Follow-up

According to the PRED-IdF guidelines, patients were offered either CE or MRE follow-up procedures within 12–24 months in case of normal baseline findings and every 2 years thereafter. The choice between both modalities was made in accordance with patient preference. To ensure the homogeneity in the follow-up of our population, we only considered the first CE follow-up procedure.

In case of suspected SBN, double balloon enteroscopy (DBE) (Fujifilm Inc., Saitama, Japan) was performed under general anesthesia to obtain histological confirmation. Subsequently, endoscopic or surgical removal of the neoplastic lesions was decided based on patient and lesion characteristics.

### Ethics

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee. Written informed consent was obtained from all patients entering the PRED-IdF network, for both prospective and retrospective data analysis. The research proposal was reviewed and approved 7 September 2019 by the local ethics committee, the CERAPHP.5 (registration number of the committee: 00011928).

### Statistical analysis

Categorical variables were compared using the  $\chi^2$  test or Fisher's test. Normally distributed continuous variables were presented as the mean standard

**Table 1.** Characteristics of patients presenting with Lynch syndrome and a positive capsule endoscopy for baseline screening of small bowel neoplasms.

No.	Age, sex	Path_MMR	Lesion	Size (mm)	Location	Histology	Treatment
1	46, M	<i>MSH2</i>	Polyps ( $n=2$ )	6 and 5	Duodenum	Adenoma, LGD	Endoscopy
2	74, F	<i>MSH2</i>	Tumor	15	Ileum	Adenocarcinoma	Surgery
3	80, F	<i>MSH6</i>	Polyp	8	Jejunum	Adenoma, HGD	Endoscopy
4	71, F	<i>MSH2</i>	Tumor	20	Ileum	Adenocarcinoma	Surgery
5	41, M	<i>MLH1</i>	Polyp	6	Jejunum	Adenoma, LGD	Endoscopy
6	62, M	<i>MLH1</i>	Tumor	50	Jejunum	Adenocarcinoma	Surgery

F, female; HGD, high-grade dysplasia; LGD, low-grade dysplasia; M, male.

deviation and analyzed by Student's *t*-test. Non-normally distributed variables were expressed with the median and the range, and were analyzed by the Mann–Whitney *U* test. Preliminary sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for CE baseline diagnosis. Per-patient and per-procedure approaches were also considered. The gold standard for SBN screening was a composite criterion. A positive screening was retained when a histopathological confirmation of adenoma or adenocarcinoma, or the presence of an SBN (polyp or tumor) were achieved in follow-up examinations during a maximum period of 24 months following baseline CE. A negative result was retained in patients with a minimum of 12 months uneventful follow-up after baseline CE procedure. Per-procedure CE analysis was also carried out. *p*-values < 0.05 were considered statistically significant. SPSS version 24 was used (IBM, SPSS Inc., IL, USA).

## Results

### Patients

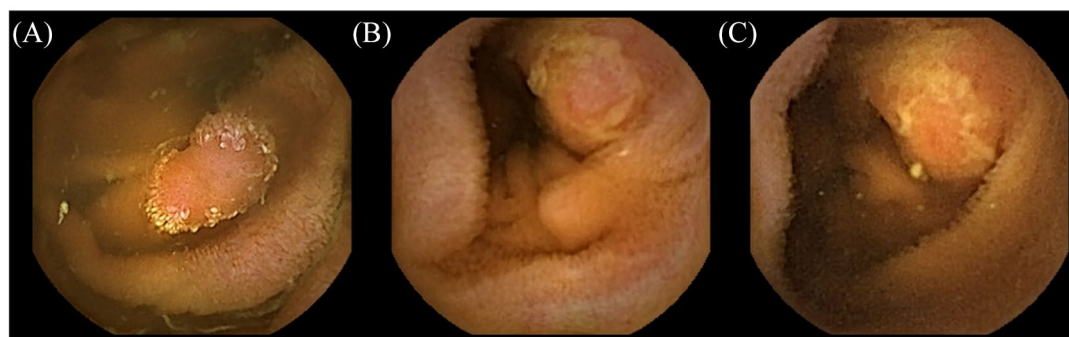
A total of 150 patients underwent the SBN screening program. Out of those, 15 were excluded as follows: obscure gastrointestinal bleeding ( $n=8$ ), SB obstruction ( $n=3$ ), and previous SB surgery ( $n=4$ ). Finally, 135 ( $52.7 \pm 11.2$  years-old, 37.8% male) patients were included in the data analysis. The LS pathogenic variants were *path\_MSH2* ( $n=59$ , 43.7%), *path\_MLH1* ( $n=52$ , 38.5%), *path\_MSH6* ( $n=20$ , 14.8%), *path\_PMS2* ( $n=3$ , 2.2%), and *path\_EPCAM* ( $n=1$ , 0.7%). There was a personal history of colorectal cancer in

30.4% of cases and a family history of SB cancer (SBC) in 25 patients (18.5%).

### CE diagnostic yield

CE reached the caecum in 132 cases (97.8%) and the SB preparation was considered adequate in all but one procedure (99.3%). The diagnostic yield was 4.4% because of the presence of tumors ( $n=3$ ) or polyps ( $n=3$ ) located in the jejunum ( $n=3$ , 50%), ileum ( $n=2$ , 33.3%), and duodenum ( $n=1$ , 16.7%). Characteristics of patients with a positive CE for screening are shown in Table 1. There was a difference in the median age of patients presenting with an SB tumor (71.4 years, range: 61.5–74.4), compared with those with no tumor detected by CE (52.2 years, range: 30.9–82.2), and this difference was statistically significant ( $p=0.021$ ). No patient with a positive-CE had a family history of SBN and there was no statistically significant association between the path\_MMR and the diagnostic yield ( $p=0.99$ ). All patients with an SB tumor (Figure 1) underwent surgery, and endoscopic resection by DBE was performed in those presenting with polyps. The capsule also detected angiodysplasias ( $n=15$ , 11.1%), erosions ( $n=3$ , 2.2%), caecal polyp, ( $n=1$ , 0.7%) and colorectal cancer ( $n=1$ , 0.7%), but all these results were considered as a negative-CE. There were no procedure-related adverse events.

Considering a per-procedure approach, a total number of 87 follow-up CEs were performed (64.4%). They were considered positive in four cases. After exclusion of the 48 patients in whom the follow-up CE was not performed, the overall diagnostic yield was 4.5%.



**Figure 1.** Capsule endoscopy findings in two asymptomatic path\_MMR carriers. (A) identification of a low-grade dysplasia adenoma of the jejunum, and (B, C) of a T2N0M0 ulcerated tumor of the ileum.

**Table 2.** Characteristics of patients with Lynch syndrome presenting with a negative baseline and a positive follow-up capsule endoscopy.

No.	Age, sex	Path_MMR	Lesion	Size (mm)	Location	Histology	Treatment
1	53, M	<i>MLH1</i>	Tumor	30	Duodenum	Adenocarcinoma	Surgery
2	57, F	<i>MLH1</i>	Polyp	10	Jejunum	Adenoma, LGD	Endoscopy
3	41, M	<i>MSH2</i>	Polyp	15	Duodenum	Adenoma, LGD	Endoscopy
4	63, F	<i>MLH1</i>	Tumor	25	ileum	Adenocarcinoma	Surgery

F, female; LGD, low-grade dysplasia; M, male.

#### Follow-up and CE accuracy

A total of 87 patients underwent follow-up CE. The mean interval between baseline and follow-up procedures was 24 (11–34) months. Four patients were considered positive at follow-up due to the presence of a tumor ( $n=2$ ) or polyp ( $n=2$ ), as described in Table 2. All of them presented with a negative baseline CE and a positive follow-up CE. Notably, these SBN were located in the duodenum ( $n=2$ ), ileum ( $n=1$ ), and jejunum ( $n=1$ ). Surgical or endoscopic therapy was carried out in all cases and a histopathological confirmation of adenoma or adenocarcinoma was made.

#### Predictive values of baseline CE

After follow-up analysis, the baselines sensitivity, specificity, PPV, NPV, and accuracy of CE for SBN screening (Table 3) were 60%, 100%, 100%, 96.9%, and 97%, respectively. Notably, there were four false negative-CE as previously described. The sensitivity, specificity, PPV, NPV, and accuracy for SBC (excluding adenomas) were 60%, 100%, 100%, 98.5%, and 98.5%, respectively.

#### Discussion

In the present study, we report the effectiveness of a dedicated screening program by CE in patients with LS. This technique achieved a baseline diagnostic yield of 4.4% in 135 asymptomatic patients with different pathogenic variants. In addition, using a composite gold standard that includes histology and follow-up by CE, we described a 96.9% accuracy for detecting tumors or polyps. Of note, the baseline and follow-up diagnostic yields were comparable, which implies that a short follow-up should be encouraged in these patients.

Presently, SBN screening in LS is offered to patients presenting with symptoms suggesting an SB disease, similarly to the general population. A Korean multicenter study<sup>13</sup> described that CE can effectively identify sporadic SB tumors undetectable by conventional radiological examinations, achieving a diagnostic effectiveness of 52.6%. This technique has also modified the therapeutic course in 12.3% of cases. Similarly, DBE has been reported as an accurate technique with a good concordance with CE<sup>14</sup> and has an effect on the clinical course of these patients.<sup>15</sup>



**Table 3.** Diagnostic accuracy values of baseline CE for screening of small bowel neoplasms in patients with Lynch syndrome.

Screening*		Positive	Negative
CE	Positive	6	0
	Negative	4	125

\*A positive screening was retained when a histopathological confirmation of adenoma or adenocarcinoma, or the presence of an SB neoplasm, in follow-up examinations was achieved.  
CE, capsule endoscopy.

There are few reports on patients with inherited polyposis syndromes. Caspari *et al.*<sup>16</sup> concluded that there is no significant difference between MRE and CE for the detection of large (i.e. more than 15 mm), clinically significant polyps in these selected cases. Recently, both the European Society for Paediatric Gastroenterology Hepatology and Nutrition and the European Society of Gastrointestinal Endoscopy (ESGE) recommend the gastrointestinal surveillance by upper-gastrointestinal (GI) endoscopy, colonoscopy, and CE in Peutz–Jeghers syndrome.<sup>17,18</sup>

In our study, we analyzed the diagnostic yield of CE in asymptomatic patients with LS under a dedicated screening program. The CE achieved baseline diagnostic yields of 4.4% for SBN and 2.2% for SBC, which were similar to those previously reported (1.5–8.6%).<sup>6,11</sup> We reported four false negatives. Among them, two presented with a duodenal SBN and two with a jejunal tumor during the follow-up. Of the two patients with SB adenocarcinoma, we report a 63 years-old female with poor SB cleanness at baseline and a positive CE at 1 year, and a 48 years-old female with a positive CE at 24 months from baseline CE. Both patients had a normal upper-GI endoscopy before baseline screening. Technical issues such as a faster transit and limited bowel distension may explain the proximal cases of false negative. In the same setting, Haanstra *et al.*<sup>6</sup> reported a false negative in a patient diagnosed with duodenal cancer 7 months after a negative CE. However, definition of a false negative in LS is complex and has to be balanced with the syndrome's specificities. First, Edelstein *et al.*<sup>19</sup> have reported in colorectal lesions a faster adenoma to carcinoma sequence compared with sporadic adenomas.<sup>19</sup> Second,

Kloor *et al.*<sup>20</sup> reported development of colorectal cancer from normal mucosa without a polyp precursor, probably arising from MMR deficient crypt foci. To our knowledge, these valuable data are not available for SB but may contribute to the development of a “false negative.”

In our series, baseline localizations of the SBN were as follows: duodenum 16.7% (1), jejunum 50% (3), and ileum 33.3% (2). Notably, the lesions were diagnosed equally between men and women (0.5 sex ratio). We reported only one patient with a duodenal neoplasia, and most of the adenocarcinomas (66.6%) were located in the ileum. Our reports emphasizes the results of previous and recent studies. Indeed, most of SBN are usually diagnosed in males with a majority of proximal lesions located in the duodenum and jejunum.<sup>21–23</sup> In the recent Dutch consortium study (200 LS patients), the baseline SBC diagnostic yield was 1%.<sup>6</sup> Characteristics of adenocarcinomas were consistent with the literature, both developing in males and located in the duodenum. More recently, Hammoudi *et al.*<sup>24</sup> reported the prevalence of duodenal lesions by upper-GI endoscopy performed every 3–4 years. Among the 154 patients included (*path\_MLH1* and *path\_MSH2*), a total of 12 duodenal neoplasia were diagnosed, including 3 invasive adenocarcinomas and 1 lesion arising from the ampulla. Of note, all patients included in our study also had an upper of upper-GI endoscopy every 4 years in accordance with the PRED-IdF guidelines, and no additional duodenal lesion was detected. Of the two patients with duodenal lesion, both had a normal upper-GI endoscopy before baseline CE. According to these findings, and because of the low reported prevalence of SBN among asymptomatic patients with LS, the ESGE published guidelines in 2019 that do not recommend routine SB screening in asymptomatic patients with LS. However, these guidelines may be challenged with regards to our results.

One of the strengths of our analysis is the comparison of CE with a gold standard. Indeed, not all abnormalities detected by CE are clinically relevant, and this technique can also have false positives. Haanstra *et al.*,<sup>12</sup> in a multicenter prospective study of 155 asymptomatic patients, analyzed the role of a second CE procedure 2 years after the first screening procedure. CE detected possibly significant lesions in 17 cases (11% diagnostic yield), but, interestingly, further investigations revealed no significant adenoma or cancer. In our

study, all positive-CE at baseline or follow-up had a histopathological confirmation and the diagnostic yield at follow-up was 4.6%.

The present study has several limitations aside from its retrospective design. All patients followed up at our center were sent for SB screening by CE and upper-GI endoscopy according to our guidelines. First, this strategy may lead to an over screening of proximal SB lesions. Second, a cost-effective analysis of our strategy is lacking and would be of interest. Finally, even if the overall CE accuracy was high (96.9%), the sensitivity was low (60%), which is an important feature for a screening test.

### Conclusion

CE is a safe and accurate procedure in the screening of SBN in asymptomatic patients with LS, allowing detection of both proximal and distal lesions. Our data suggest the use of CE as an initial workup, however the optimal starting age of screening and intervals of follow-up must be clarified in further studies.

### Acknowledgements

We would like to thank all patients followed up in our network who kindly authorized us to use their medical data and perform this study. We also would like to thank all physicians and nurses from our department who helped us to perform this study.

### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

### Conflict of interest statement

The authors declare that there is no conflict of interest.

### ORCID iDs

Guillaume Perrod  <https://orcid.org/0000-0003-4984-0310>

Arthur Berger  <https://orcid.org/0000-0003-0387-4734>

### References

- Giardiello FM, Allen JI, Axilbund JE, *et al.* Guidelines on genetic evaluation and management of Lynch syndrome: a consensus statement by the US Multi-society Task Force on colorectal cancer. *Am J Gastroenterol* 2014; 109: 1159–1179.
- Bonadona V, Bonaiti B, Olschwang S, *et al.* Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. *JAMA J Am Med Assoc* 2011; 305: 2304–2310.
- Koornstra JJ, Kleibeuker JH and Vasen HFA. Small-bowel cancer in Lynch syndrome: is it time for surveillance? *Lancet Oncol* 2008; 9: 901–905.
- Koornstra JJ. Small bowel endoscopy in familial adenomatous polyposis and Lynch syndrome. *Best Pract Res Clin Gastroenterol* 2012; 26: 359–368.
- Dominguez-Valentin M, Sampson JR, Seppälä TT, *et al.* Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database. *Genet Med Off J Am Coll Med Genet* 2020; 22: 15–25.
- Haanstra JF, Al-Toma A, Dekker E, *et al.* Prevalence of small-bowel neoplasia in Lynch syndrome assessed by video capsule endoscopy. *Gut* 2015; 64: 1578–1583.
- van Leerdam ME, Roos VH, van Hooft JE, *et al.* Endoscopic management of Lynch syndrome and of familial risk of colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2019; 51: 1082–1093.
- Pérez-Cuadrado-Robles E, Esteban-Delgado P, Martínez-Andrés B, *et al.* [Diagnosis agreement between capsule endoscopy and double-balloon enteroscopy in obscure gastrointestinal bleeding at a referral center]. *Rev Espanola Enfermedades Dig Organo Of Soc Espanola Patol Dig* 2015; 107: 495–500.
- Rondonotti E, Pennazio M, Toth E, *et al.* Small-bowel neoplasms in patients undergoing video capsule endoscopy: a multicenter European study. *Endoscopy* 2008; 40: 488–495.
- Van Weyenberg SJB, Meijerink MR, Jacobs MAJM, *et al.* MR enteroclysis in the diagnosis of small-bowel neoplasms. *Radiology* 2010; 254: 765–773.
- Saurin J-C, Pilleul F, Soussan EB, *et al.* Small-bowel capsule endoscopy diagnoses early and advanced neoplasms in asymptomatic patients with Lynch syndrome. *Endoscopy* 2010; 42: 1057–1062.
- Haanstra JF, Al-Toma A, Dekker E, *et al.* Incidence of small bowel neoplasia in Lynch

- syndrome assessed by video capsule endoscopy. *Endosc Int Open* 2017; 5: E622–E626.
13. Cheung DY, Lee I-S, Chang DK, *et al.* Capsule endoscopy in small bowel tumors: a multicenter Korean study. *J Gastroenterol Hepatol* 2010; 25: 1079–1086.
  14. Rahmi G, Samaha E, Lorenceau-Savale C, *et al.* Small bowel polypectomy by double balloon enteroscopy: correlation with prior capsule endoscopy. *World J Gastrointest Endosc* 2013; 5: 219–225.
  15. Robles EP-C, Delgado PE, Conesa PB, *et al.* Role of double-balloon enteroscopy in malignant small bowel tumors. *World J Gastrointest Endosc* 2015; 7: 652–658.
  16. Caspari R, von Falkenhausen M, Krautmacher C, *et al.* Comparison of capsule endoscopy and magnetic resonance imaging for the detection of polyps of the small intestine in patients with familial adenomatous polyposis or with Peutz-Jeghers' syndrome. *Endoscopy* 2004; 36: 1054–1059.
  17. Latchford A, Cohen S, Auth M, *et al.* Management of Peutz-Jeghers Syndrome in children and adolescents: a position paper from the ESPGHAN Polyposis Working Group. *J Pediatr Gastroenterol Nutr* 2019; 68: 442–452.
  18. van Leerdam ME, Roos VH, van Hooft JE, *et al.* Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2019; 51: 877–895.
  19. Edelstein DL, Axilbund J, Baxter M, *et al.* Rapid development of colorectal neoplasia in patients with Lynch syndrome. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc* 2011; 9: 340–343.
  20. Kloor M, Huth C, Voigt AY, *et al.* Prevalence of mismatch repair-deficient crypt foci in Lynch syndrome: a pathological study. *Lancet Oncol* 2012; 13: 598–606.
  21. Rodriguez-Bigas MA, Vasen HF, Lynch HT, *et al.* Characteristics of small bowel carcinoma in hereditary nonpolyposis colorectal carcinoma. International Collaborative Group on HNPCC. *Cancer* 1998; 83: 240–244.
  22. Schulmann K, Brasch FE, Kunstmann E, *et al.* HNPCC-associated small bowel cancer: clinical and molecular characteristics. *Gastroenterology* 2005; 128: 590–599.
  23. ten Kate GL, Kleibeuker JH, Nagengast FM, *et al.* Is surveillance of the small bowel indicated for Lynch syndrome families? *Gut* 2007; 56: 1198–1201.
  24. Hammoudi N, Dhooge M, Coriat R, *et al.* Duodenal tumor risk in Lynch syndrome. *Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver* 2019; 51: 299–303.

Visit SAGE journals online  
[journals.sagepub.com/  
 home/tag](http://journals.sagepub.com/home/tag)

 SAGE journals