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ORIGINAL RESEARCH—CLINICAL

Colonoscopy and Upper Endoscopy Surveillance in Lynch Syndrome: A Longitudinal Study From a Large Tertiary Healthcare System

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BACKGROUND AND AIMS: Lynch syndrome (LS) is caused by pathogenic mutations in mismatch repair (MMR) genes. There are limited data on differences in colorectal cancer (CRC) surveillance by MMR genes, and an international consensus on surveillance based on genes is not established. We aimed to evaluate colonoscopy and esophagogastroduodenoscopy (EGD) surveillance outcomes and compare CRC surveillance findings by the mutated gene. **METHODS:** One hundred one patients with LS were included and colonoscopy results were compared by MMR mutation. Primary outcomes included the development and recurrence of adenoma, CRC, high-grade dysplasia, advanced adenoma, and sessile serrated lesions. Logistic regressions evaluated the relationship between genes and the development or recurrence of primary outcomes. Survival analysis evaluated primary outcomes in patients with ≥ 2 colonoscopies. EGD results were summarized. **RESULTS:** Three hundred twenty seven colonoscopies were reviewed. Compared to *PMS2*, *MLH1* was associated with a higher risk of advanced adenoma/high-grade dysplasia/CRC development (odds ratio [OR] 9.85, 95% confidence interval [CI]: 1.97–77.24) and *MSH2* was associated with a higher risk of adenoma development (OR 4.17, 95% CI: 1.11–17.61). Among those with > 2 colonoscopies, *MLH1* (hazard ratio 18.98, 95% CI: 1.31–274.51) and *MSH6* (hazard ratio 15.03, 95% CI: 1.16–194.65) had a higher risk of sessile serrated lesions compared to *MSH2*. Among patients who had adenoma detected once, *MLH1* had a higher risk of adenoma recurrence compared to *MSH6* (OR 14.59, 95% CI: 1.53–244.30) and *PMS2* (OR 47.15, 95% CI: 4.26–984.28). *MSH2* had a higher risk of adenoma recurrence compared to *PMS2* (OR 11.89, 95% CI: 1.38–164.78). Of 170 EGDs, an actionable finding was identified in 16% of patients during their first 3 EGDs. **CONCLUSION:** Surveillance colonoscopy outcomes differed in patients with LS and suggest the need to guide surveillance based on MMR gene mutation.

Keywords: Lynch Syndrome; Colorectal Cancer; Colon Polyps; Upper Endoscopy; Surveillance

Introduction

Lynch syndrome (LS) is an autosomal dominant hereditary cancer predisposition syndrome caused by variants in DNA mismatch repair (MMR) genes including *MLH1*, *MSH2*, *MSH6*, and *PMS2*. Colorectal cancer (CRC) is the most common malignancy identified in patients with LS, and LS is diagnosed in 2%–3% of patients with CRC.[1,2] The risk of CRC development varies by the gene mutated, and *MLH1* and *MSH2* have been associated with an increased risk of CRC compared to *PMS2* and *MSH6*.[3–5] In the United States, CRC screening is recommended starting at age 20–25 years for *MLH1* and *MSH2* carriers with interval colonoscopy every 1–2 years.[6,7] For *PMS2* and *MSH6* carriers, screening is recommended starting at age 25–30 years with interval colonoscopy every 1–3 years.[6,7] However, an international consensus for optimal surveillance intervals based on MMR gene mutated has not been established and differences in recommendations remain.[8]

Prior studies of Lynch surveillance have identified a decreased time to development of advanced adenoma (AA) or CRC for *PMS2* and *MSH6* gene mutations. A retrospective study by Goverde et al. of colonoscopy surveillance based on pathogenic variant found patients with an *MSH6* variant had decreased time to development of AA or CRC.[9] Kastrinos et al. found that surveillance every 2–3 years would be cost-effective for individuals with a *PMS2* or *MSH2* variant compared to 1–2 years in patients with an *MLH1* or *MSH2* variant.[10] While these studies have identified variation in the risk of CRC and AA in patients with LS based on MMR genes, there are limited data concerning the prevalence of adenoma and sessile serrated lesion (SSL) development.

The risk of CRC in patients with LS is further influenced by individual factors including lifestyle, personal characteristics, and other genetic factors.[11] Individual factors

Abbreviations used in this paper: **AA, advanced adenoma; CRC, colorectal cancer; HGD, high-grade dysplasia; LS, Lynch syndrome; MMR, mismatch repair; SSL, sessile serrated lesions.**

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associated with an increased risk of CRC in patients with LS in prior studies include male sex, previous or ongoing smoking, and an increasing body mass index (BMI).[12] Furthermore, aspirin use has been associated with a decreased risk of CRC and adenoma recurrence.[13–15]

In addition to CRC risk, patients with LS are at an increased risk of developing extracolonic gastrointestinal malignancy. The cumulative lifetime risk of gastric cancer ranges from $<$ 1% to 9% and small bowel malignancy ranges from $<$ 1% to 11% in patients with LS. Recommendations for esophagogastroduodenoscopy (EGD) surveillance of extracolonic gastrointestinal malignancy are variable, with most guidelines recommending a baseline EGD and follow-up based on individual risk factors.[7,16] In recent years, some data have supported the potential benefit of surveillance EGD in identifying malignant and clinically significant nonmalignant lesions.[16,17] A recent US study of EGD surveillance in patients with LS by Farha et al. identified lesions associated with gastric malignancy in 6% of patients.[16] Kumar et al. described gastric intestinal metaplasia in 8% and *H. pylori* in 3% of their LS cohort in the United States.[18]

The primary aim of this study was to evaluate the outcomes of colonoscopy surveillance including CRC, AA, high-grade dysplasia (HGD), and SSL for patients with LS at our single institution based on which MMR gene is involved. The secondary aims were to (1) describe EGD surveillance outcomes in patients with LS and (2) evaluate for individual risk factors for CRC, AA, HGD, and SSL development in patients with LS.

Methods

We retrospectively reviewed colonoscopy and EGD results in patients with a diagnosis of LS at our single institution from January 2003 to July 2020. A total of 220 patients were identified by participation in the Hereditary Gastrointestinal Cancer Registry, and 101 were included in the study analysis after excluding those without $\geq$ 1 colonoscopy available. The Hereditary Gastrointestinal Cancer Registry is a registry of patients enrolled at the Huntsman Cancer Institute with a history of inherited cancer syndromes and/or a strong family history of cancer. Patients were grouped based on the gene mutated (*MLH1*, *MSH2*, *MSH6*, and *PMS2*). Endoscopy procedures were completed by 5 gastroenterologists at a single center with dedication to the field of high-risk CRC surveillance. All gastroenterologists had an Adenoma Detection Rate above the standard quality requirement (men $\geq$ 30% and women $\geq$ 20%). All patients included had Boston Bowel Prep Score of $>$ 7 and many patients from around the year 2017 onwards underwent chromoendoscopy during their surveillance colonoscopies. Baseline characteristics were compared between genes. Primary outcomes included the occurrence or recurrence of adenomas, SSL, or AA/HGD/CRC during the surveillance period.

Patient characteristics were summarized using median (interquartile range) for numeric variables and N (%) for categorical variables. We used the Kruskal-Wallis rank sum test for numeric variables and Fisher's exact test for categorical variables to compare the characteristics across the mutation types. We employed a logistic regression model to estimate the association between the mutation types and the development and recurrence of adenoma, SSL, and AA/HGD/CRC (Table 1 and Supplemental Table 3).

For patients who had two or more colonoscopies, we fitted Cox proportional hazards models on the time to development of adenoma, SSL, and AA/HGD/CRC (Table A2). We used the time of the first colonoscopy as the index date of the time-to-event outcome. For all the regression models, age, gender, BMI levels, smoking status, alcohol usage, aspirin usage, and any other cancer were included as confounders to control. All statistical analysis was performed using R Statistical Software (version 4.2.0).

Results

A total of 327 colonoscopies were reviewed for the 101 patients with LS included in the study. Patients with *MSH2* (31%) gene mutations had the most colonoscopy reports (31%) followed by *MLH1* (28%), *PMS2* (23%), and *MSH6* (18%). Baseline characteristics did not differ by gene, but patients with *MLH1* gene mutations had the highest average

Table 1. Association Between Adenoma, AA/HGD/CRC or SSL Development, and Gene Mutated

	OR when compared with *MSH6*	OR when compared with *PMS2*	OR when compared with *MSH2*
Adenoma			
PMS2	0.65 (0.14–2.88), $P = .575$		
MSH2	2.73 (0.69–11.43), $P = .156$	**4.17 (1.11–17.61), $P = .041$**	
MLH1	1.49 (0.36–6.26), $P = .577$	2.29 (0.60–9.30), $P = .234$	0.55 (0.14–1.99), $P = .369$
AA/HGD/CRC			
PMS2	0.28 (0.03–1.68), $P = .184$		
MSH2	1.31 (0.33–5.60), $P = .702$	4.70 (0.93–36.53), $P = .085$	
MLH1	2.75 (0.68–12.37), $P = .166$	**9.85 (1.97-77.24), $P = .011$**	2.09 (0.60–7.81), $P = .252$
SSL			
PMS2	0.25 (0.04–1.46), $P = .132$		
MSH2	0.50 (0.10–2.57), $P = .400$	2.03 (0.38–13.08), $P = .422$	
MLH1	0.41 (0.07–2.24), $P = .303$	1.66 (0.29–10.78), $P = .572$	0.82 (0.15–4.20), $P = .808$

AA, advanced adenoma; BMI, body mass index; CRC, colorectal cancer; HGD, high-grade dysplasia; SSL, sessile serrated lesion.
Logistic regression models were used; values are OR (95% CI); significant ORs, are bolded.
AA, advanced adenoma; CRC, colorectal cancer; HGD, high-grade dysplasia; OR, odds ratio; SSL, sessile serrated lesion.

Table 2. Baseline Characteristics and Screening Variables by Gene Mutated

Variables	Total N = 101	*MSH6* N = 18	*MSH2* N = 32	*PMS2* N = 23	*MLH1* *N = 28*	*P*
Baseline						
Age[a]	45 (24)	50 (20)	46 (25)	44 (20.5)	40.5 (22.5)	.509
BMI[a]	27.3 (8.5)	29 (5.9)	26.2 (5.8)	25.9 (12.3)	26.8 (10.6)	.584
Female[b]	61 (60.4)	11 (61.1)	24 (75)	13 (56.5)	13 (46.4)	.164
White[b]	95 (97)	18 (100)	28 (93)	22 (96)	27 (100)	.911
Hx of cancer[b]	53 (52.5)	12 (66.7)	19 (59.4)	8 (34.8)	14 (50)	.164
Reason tested[b]						.386
Personal history	36 (36.4)	10 (55.6)	10 (31.2)	7 (30.4)	9 (34.6)	
Family history	51 (51.5)	6 (33.3)	16 (50)	15 (65.2)	14 (53.8)	
Both	12 (12.1)	2 (11.1)	6 (18.8)	1 (4.3)	3 (11.5)	
Colonoscopy						
Total number	327	45	111	50	121	
Per patient[a]	2 (4)	1.5 (2.8)	3 (2.2)	2 (2)	4 (4)	.004
Surveillance (Y)[a]	4.5 (4)	4.5 (3.3)	5 (4.2)	3.7 (2.3)	4.9 (4)	.357
Surveillance outcomes						
Adenoma[b]	54 (53.5)	9 (50)	18 (56.2)	10 (43.5)	17 (60.7)	.65
SSL[b]	17 (16.8)	5 (27.8)	5 (15.6)	3 (13)	4 (14.3)	.621
AA/HGD/CRC[b]	29 (28.7)	5 (27.8)	10 (31.2)	2 (8.7)	12 (42.9)	.051

AA, advanced adenoma; BMI, body mass index; CRC, colorectal cancer; HGD, high-grade dysplasia; SSL, sessile serrated lesion.
Logistic regression models were used; values are OR (95% CI); significant ORs, are bolded.
AA, advanced adenoma; CRC, colorectal cancer; HGD, high-grade dysplasia; OR, odds ratio; SSL, sessile serrated lesion.
[a]Continuous variables; Values are median (IQR); Kruskal-Wallis test were used.
[b]Categorical variables; Values are n (%); Fisher's exact test were used.

number of colonoscopies completed (Table 2). Overall, there was no statistically significant risk in the overall occurrence of any adenoma, SSL, or AA/HGD/CRC between gene groups, although *MLH1* (43%) and *MSH2* (31%) patients had the highest proportions of AA/HGD/CRC occurrence.

The presence of an adenoma, SSL, or AA/HGD/CRC on each colonoscopy for each patient included in the study is represented by the gene mutated in Figure. Findings on the first colonoscopy included AA/HGD/CRC in 22 patients including 10 CRC, 10 AA, and 2 HGD. The median age (and range) of patients with CRC on the index colonoscopy was 38.5 (27.6, 66), and the gene mutated included 4 *MLH1*, 3 *MSH2*, and 3 *MSH6*. Overall, 10 patients had CRC identified on their index colonoscopy (4 *MLH1*, 3 *MSH2*, and 3 *MSH6*), and 6 patients developed CRC during the surveillance period including 4 *MSH2* and 2 *MLH1* gene carriers (Table A1).

Compared to *PMS2*, *MLH1* was associated with a higher risk of AA/HGD/CRC development (odds ratio [OR] 9.85, 95% confidence interval [CI] 1.97–77.24) and *MSH2* was associated with a higher risk of adenoma development (OR 4.17, 95% CI 1.11–17.61) (Table 1). Among those with ≥ 2 colonoscopies (n = 71), there was no significant difference in adenoma or AA/HGD/CRC development, but *MLH1* (hazard ratio 18.98, 95% CI 1.31–274.51) and *MSH6* (hazard ratio 15.03, 95% CI 1.16–194.65) had a higher risk of SSL compared to *MSH2* (Table A2). Among patients who had adenoma detected once (n = 54), *MLH1* had a higher risk of adenoma recurrence compared to *MSH6* (OR 14.59, 95% CI 1.53–244.30) and *PMS2* (OR 47.15, 95% CI 4.26–984.28). *MSH2* had a higher risk of adenoma recurrence compared to *PMS2* (OR 11.89, 95% CI 1.38–164.78) (Table A3).

Individual risk factors including a recorded personal history of smoking tobacco, alcohol use, or aspirin use at the time of LS diagnosis or the first encounter in our medical record system were evaluated for an association with the odds of adenoma, AA/HGD/CRC, and SSL development during the study period. Of 101 patients, 13 (12.9%) reported a positive personal history of smoking, 38 (37.6%) reported positive alcohol use, and 12 (11.9%) reported aspirin use. There was no statistically significant association between smoking, alcohol use, and aspirin use with the odds of developing an adenoma, AA/HGD/CRC, or an SSL during the study (Table 3).

A total of 76 patients had at least one EGD during the follow-up period, and a total of 170 EGD procedures were evaluated. Findings of interest from EGDs completed included Barrett's esophagus, *H. pylori* infection, eosinophilic esophagitis, esophageal or gastric ulcerations, fundic gland polyps with dysplasia, pyloric gland adenomas, tubular adenomas, tubulovillous adenomas, villous adenomas, hyperplastic polyps > 5 mm in size, and any malignancy. Details for the findings of the first 3 EGDs are included in Table 4. The median follow-up for all patients with > 1 EGD available was 4.0 years (3.1, 5.2). The median follow-up for patients with 2–3 EGDs available for review was 3.4 years (2.0, 4.5).

Of patients who had > 3 EGDs, 12 had 4 EGDs and 5 had ≥ 5 EGDs. There was one case of an ampullary adenoma identified on the fourth EGD for a patient with a history of

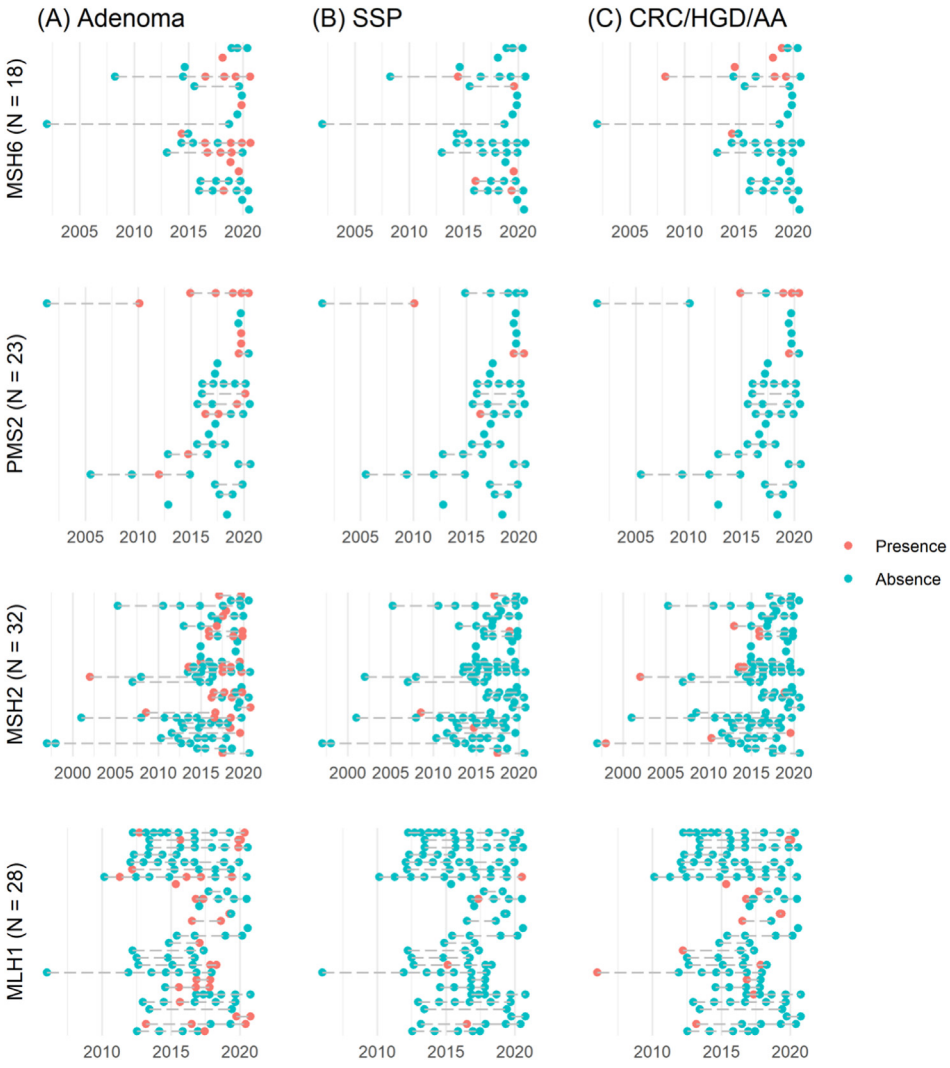

Figure. Visual representation of colonoscopy surveillance outcomes by gene mutated. Each patient is represented as a horizontal line and grouped based on the gene mutated and the colonoscopy findings of adenoma, SSP, or CRC/HGD/AA. Blue dots represent the absence of a lesion, and orange dots represent the presence of a lesion. Colonoscopies for each patient are indicated as a dot for the date when the procedure was performed.

ampullary adenocarcinoma and an *MSH2* variant. The patient was receiving yearly surveillance with an EGD, and the recurrence occurred 6 years after the index malignancy. There were no additional cases of identified malignancy.

Discussion

Surveillance colonoscopy outcomes in the present study, including SSL development, differed in patients with LS based on the gene mutated. *PMS2* was associated with decreased odds of AA/HGD/CRC and adenoma development compared to *MLH1* and *MSH2*, respectively. In patients with a prior adenoma, *PMS2* and *MSH6* were associated with decreased odds of adenoma recurrence compared to *MLH1*. No patients with *PMS2* were diagnosed with CRC during our study. These findings support the consideration of individualized surveillance intervals for patients with *PMS2* or *MSH6* gene mutations because they are associated with a lower risk of adenoma recurrence.

Overall, 10 patients had CRC identified on their index colonoscopy and only 6 patients developed CRC identified on a subsequent surveillance colonoscopy supporting the effectiveness of colonoscopy surveillance for patients with LS. Notably, no patients with *MSH6* or *PMS2* gene mutations

Table 3. Association Between Adenoma, AA/HGD/CRC or SSL, and Individual Risk Factors

	Adenoma	AA/HGD/CRC	SSL
Smoking	4.44 (0.93–26.81), $P = .076$	1.18 (0.28–4.76) $P = .819$	1.90 (0.30–10.47), $P = .466$
Alcohol use	0.95 (0.35–2.54), $P = .914$	1.84 (0.67–5.16), $P = .239$	1.46 (0.42–5.05), $P = .548$
Aspirin use	1.34 (0.28–6.68), $P = .708$	0.26 (0.04–1.19), $P = .102$	0.63 (0.08–3.49), $P = .626$

Logistic regression models were used; values are OR (95% CI).
AA, advanced adenoma; CRC, colorectal cancer; HGD, high-grade dysplasia; SSL, sessile serrated lesion.

Table 4. Findings From First Three EGDs

Variables	First EGD N = 76	Second EGD N = 40	Third EGD N = 25
Reason for endoscopy			
LS surveillance	62	28	17
Symptoms	13	7	4
Follow-up	0	5	4
Other	1	0	0
Findings			
Normal	64	33	22
EoE	2	3	2
H pylori	1	0	0
Barrett's	1	1	1
Ulceration	3	3	0
HP > 5 mm	2	0	0
Other	3	0	0
Actionable finding total	12 (16)	7 (17.5)	3 (12)

Values are n (%).
EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; HP, hyperplastic polyp; LS, Lynch syndrome.

developed CRC during the study surveillance period. Prior studies have found mixed results regarding variability in surveillance colonoscopy outcomes based on the gene in patients with LS, and only a limited number of studies have reported on longitudinal adenoma and SSL incidence in patients with LS.[9,19] In agreement with our results, prior studies have identified that *MLH1* and *MSH2* carriers have an increased risk of CRC development compared to MLH6 and PMS2 carriers.[9,12,20] A recent study by Del Carmen et al. of 163 patients at M.D. Anderson found an earlier incidence of adenomas in *MSH2* carriers compared to *MLH1* but found no significant difference in the overall odds of adenoma, AA, or CRC development between genes mutated.[20]

In addition to evaluating surveillance colonoscopy outcomes, we completed a descriptive review of EGD outcomes in 76 patients with LS. A recent study by Farha et al. found clinically actionable findings in 18% of patients with LS undergoing asymptomatic EGD surveillance over a median length of 3.5 years.[16] In our study, 15.8% of patients had clinically actionable findings identified on the first 3 EGDs reviewed including 3 (3.9%) with malignancy and 6 (7.9%) lesions with premalignant potential identified. These rates are similar to findings of malignancy in 1.5%–5.8% of patients with LS undergoing EGD surveillance in prior studies.[16–18,21] Interestingly, only one patient had *H. pylori* found on their baseline endoscopy.

Regarding individual risk factors, we did not identify a statistically significant difference in the odds of developing an adenoma, AA/HGD/CRC, or SSL based on smoking, alcohol, or aspirin use history. Previous studies have identified associations between male sex, current or prior smoking history, and increased BMI with an increased risk of CRC development in patients with LS.[12,22] The lack of an association between CRC and smoking, alcohol, or in our study could partially be explained by the relatively low number of patients with a personal history of smoking and aspirin use. Furthermore, the quantity of alcohol use was not specified for patients and risk could vary based on the amount and frequency of alcohol consumption.

The strengths of the study include collecting longitudinal data at a single institution with only a handful of providers performing endoscopic surveillance on patients allowing for more similarity between exams. Another strength is the quality of data being obtained from a well-established patient registry with a clearly defined cohort. Also, patients primarily followed their care at the same institution and were unlikely to have interval or missed data. The limitations of this study include the small sample sizes in each gene group leading to wide confidence intervals and potential instability of the estimates. We were not able to do multiple comparisons due to sample size and the risk of elevated type II errors potentially masking meaningful associations. The retrospective nature of the study is also a limit with variable time to follow-up leading to differences in the overall time of follow-up data.

Conclusion

Differences in the incidence of precancerous and advanced colonic lesions between genes mutated suggest that colonoscopy surveillance may be individualized and modified based on the gene involved. The effect of lifestyle risk factors in the development of colorectal neoplasia in Lynch patients needs further study in a larger cohort.

Supplementary Materials

Material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gastha.2024.07.004.

References

1. Yurgelun MB, Kulke MH, Fuchs CS, et al. Cancer susceptibility gene mutations in individuals with colorectal cancer. J Clin Oncol 2017;35(10):1086–1095.
2. 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 2020;22(1):15–25.
3. Møller P, Seppälä TT, Bernstein I, et al. Cancer risk and survival in path_MMR carriers by gene and gender up to 75 years of age: a report from the Prospective Lynch Syndrome Database. Gut 2018;67(7):1306–1316.
4. Møller P, Seppälä T, Dowty JG, et al. Colorectal cancer incidences in Lynch syndrome: a comparison of results from the prospective lynch syndrome database and the international mismatch repair consortium. Hered Cancer Clin Pract 2022;20(1):36.
5. Lamba M, Wakeman C, Ebel R, et al. Associations between mutations in MSH6 and PMS2 and risk of surveillance-detected colorectal cancer. Clin Gastroenterol Hepatol 2020;18(12):2768–2774.

6. Monahan KJ, Bradshaw N, Dolwani S, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCGG). Gut 2020;69(3):411–444.
7. Weiss JM, Gupta S, Burke CA, et al. NCCN Guidelines® Insights: Genetic/Familial High-Risk Assessment: Colorectal, Version 1.2021. J Natl Compr Cancer Netw 2021; 19:1122–1132.
8. 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(11):1082–1093.
9. Goverde A, Eikenboom EL, Viskil EL, et al. Yield of lynch syndrome surveillance for patients with pathogenic variants in DNA mismatch repair genes. Clin Gastroenterol Hepatol 2020;18(5):1112–1120.e1.
10. Kastrinos F, Ingram MA, Silver ER, et al. Gene-specific variation in colorectal cancer surveillance strategies for lynch syndrome. Gastroenterology 2021;161(2):453–462.e15.
11. International Mismatch Repair Consortium. Variation in the risk of colorectal cancer in families with Lynch syndrome: a retrospective cohort study. Lancet Oncol 2021; 22(7):1014–1022.
12. Jamizadeh N, Walton Bernstedt S, Haxhijaj A, et al. Endoscopic surveillance of Lynch syndrome at a highly specialized center in Sweden: an observational study of interval colorectal cancer and individual risk factors. Front Oncol 2023;13:1127707.
13. Burn J, Sheth H, Elliott F, et al. Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial. Lancet 2020;395(10240):1855–1863.
14. Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. N Engl J Med 2003; 348(10):883–890.
15. Logan RF, Grainge MJ, Shepherd VC, et al. Aspirin and folic acid for the prevention of recurrent colorectal adenomas. Gastroenterology 2008;134(1):29–38.
16. Farha N, Hrabe J, Sleiman J, et al. Clinically actionable findings on surveillance EGD in asymptomatic patients with Lynch syndrome. Gastrointest Endosc 2022; 95(1):105–114.
17. Chautard R, Malka D, Samaha E, et al. Upper gastrointestinal lesions during endoscopy surveillance in patients with lynch syndrome: a multicentre cohort study. Cancers (Basel) 2021;13(7):1657.
18. Kumar S, Dudzik CM, Reed M, et al. Upper endoscopic surveillance in lynch syndrome detects gastric and duodenal adenocarcinomas. Cancer Prev Res (Phila) 2020;13(12):1047–1054.
19. Sleiman J, Farha N, Beard J, et al. Incidence and prevalence of advanced colorectal neoplasia in Lynch syndrome. Gastrointest Endosc 2023;98(3):412–419.e8.
20. Del Carmen G, Reyes-Uribe L, Goyco D, et al. Colorectal surveillance outcomes from an institutional longitudinal cohort of lynch syndrome carriers. Front Oncol 2023;13: 1146825.
21. Ladigan-Badura S, Vangala DB, Engel C, et al. Value of upper gastrointestinal endoscopy for gastric cancer surveillance in patients with Lynch syndrome. Int J Cancer 2021;148(1):106–114.
22. Pande M, Lynch PM, Hopper JL, et al. Smoking and colorectal cancer in lynch syndrome: results from the colon cancer family registry and the University of Texas M.D. Anderson cancer center. Clin Cancer Res 2010; 16(4):1331–1339.

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Authors' Contributions:
Priyanka Kanth: Conceived and designed the study, data acquisition, analyzed the data, and manuscript preparation. Elena Gibson: Data acquisition, analyzed the data, and manuscript preparation. Judith Staub: Data acquisition and manuscript preparation. Megan Keener: Data acquisition and manuscript preparation. Deb Neklason: Data acquisition, analyzed the data, and manuscript preparation. Haojia Li: Analyzed the data and manuscript preparation.

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Ethical Statement:
The study was approved by the Institutional Review Board at the University of Utah and Huntsman Cancer Center, Salt Lake City, Utah.

Data Transparency Statement:
Data and analytic methods are available to other researchers upon request.

Reporting Guidelines:
None.