DOI: 10.63583/g6f8fb67

Endoscopic and pathological characteristics of large colorectal polyps in patients with hereditary cancer syndromes

CHU TIEN THINH[1], DINH VAN HANH[2]
1. Ha Hoa District Medical Center, Phu Tho Province, 2. Thanh Thuy District Medical Center, Phu Tho Province

Abstract

Objective: *To describe the endoscopic and histopathological characteristics of large colorectal polyps in patients with hereditary cancer risk factors.* ***Subjects and method:*** *A cross-sectional descriptive study with a control group was conducted using convenience sampling on 127 patients diagnosed with large colorectal polyps from January 2020 to January 2024.* ***Result:*** *The mean age of the hereditary group was lower than that of the non-hereditary group (52.3 ± 10.1 vs. 60.8 ± 12.5 years). The gene mutation rate in the hereditary group was 52.9%, significantly higher than in the non-hereditary group (3.2%). Polyps in the hereditary group were more frequently located in the right colon (55.6%) and had a flat morphology (31.1%). The mean polyp size was larger in the hereditary group (16.8 ± 4.2mm vs. 13.5 ± 3.6mm). The rate of adenoma, especially tubulovillous/villous type, was higher in the hereditary group (77.8% and 48.9%, respectively). High-grade dysplasia was more common in the hereditary group (40.0% vs. 15.0%). There was no significant difference in the rates of carcinoma in situ and submucosal invasive carcinoma between the two groups. Patients with FAP had a higher number of polyps, and higher rates of villous morphology and high-grade dysplasia compared to those with Lynch syndrome.* ***Conclusion:*** *The adenoma rate in hereditary colorectal polyps was 77.8%, with the tubulovillous/villous type accounting for 48.9%. High-grade dysplasia was significantly more frequent in the hereditary group than in the non-hereditary group (40.0% vs. 15.0%, p<0.05).*

Keywords: *Colorectal cancer, polyp, hereditary factors.*

I. Introduction

Colorectal cancer (CRC) is one of the most common malignancies worldwide. According to GLOBOCAN 2020, there were over 1.9 million new cases of CRC and more than 930,000 related deaths globally. The highest incidence rates are observed in regions such as Europe and Australia/New Zealand, while Eastern Europe reports the highest mortality rates [1]. CRC typically develops through three major stages: initiation, promotion, and progression. The initiation phase begins when genetic, metabolic, and carcinogenic factors damage the DNA of normal cells, leading to the emergence of abnormal cell clones [2]. Large colorectal polyps are defined endoscopically as lesions measuring ≥ 20 mm in diameter [3]. Numerous studies have demonstrated that most colorectal cancers arise from adenomatous polyps, following the accumulation of genetic mutations that result in

Received:: 03/6/2024, Accepted: 30/7/2024
Corresponding author: bsthinh@gmail.com - Ha Hoa District Medical Center, Phu Tho Province

DOI: 10.63583/g6f8fb67

dysplasia and eventual invasion of the submucosa. A high rate of adenocarcinoma has also been reported in large colorectal polyps. Historically, polyp size was considered the most important factor for predicting malignant potential. However, recent studies suggest that size alone is a poor predictor of submucosal invasion particularly in non-pedunculated polyps compared to other morphologic features [4]. In Vietnam, there is limited research on the characteristics of large colorectal polyps in patients with hereditary cancer risk factors. Therefore, we conducted the present study titled: "Characteristics of Large Colorectal Polyps in Patients with Hereditary Cancer Risk Factors", with the objective to: Describe the endoscopic and histopathological features of large colorectal polyps in patients at risk for hereditary cancer.

2. Subjects and Methods

2.1. Subjects

A total of 127 patients with colorectal polyps ≥ 20 mm in size were included in the study. Among them, 34 patients had hereditary risk factors, and 93 patients had no identifiable hereditary risk. All patients were diagnosed and treated between January 2020 and January 2024.

Inclusion Criteria

Patients diagnosed with colorectal polyps based on colonoscopy and confirmed by histopathology. Diagnosis was established according to the World Health Organization (WHO) 2019 classification.

Provided informed consent to participate in the study.

Exclusion Criteria

Patients with a concurrent malignancy other than colorectal polyps.

Inadequate tissue samples for histopathological evaluation.

Patients who refused to participate in the study.

2.2. Methods

Study Design

This was a cross-sectional descriptive study with an analytical case–control component.

Sample Size

The sample size was estimated using the following formula for comparing two proportions:

$$N = \frac{\left(Z_{1-\frac{\alpha}{2}}\right)^2 \times p\,(1-p)}{d^2}$$

N: Minimum required sample size for the study

Z: Z-score corresponding to a 95% confidence level (Z = 1.96)

p: Estimated prevalence of large colorectal polyps

Based on a previous study by Nguyen Truong Son et al. [5], the estimated prevalence p = 0.25, with a margin of error d = 0.08. Using the standard sample size formula for estimating a proportion, the minimum required sample size was calculated as n = 113. In practice, 127 patients were included in this study.

Sampling Method: All patients diagnosed with colorectal polyps ≥ 20 mm between January 2020 and January 2024, who met the inclusion and exclusion criteria, were consecutively enrolled in the study.

Data Collection and Analysis

Primary Study Parameters:

Endoscopic features: Location (right colon/left colon/rectum), Paris classification (Ip/Is/IIa/IIb), and polyp size.

Histopathology: Polyp type (adenoma, sessile serrated lesion [SSL], carcinoma), and dysplasia grade (low-grade/high-grade).

Hereditary risk factors: Family history of FAP or Lynch syndrome, or confirmed gene mutations.

DOI: 10.63583/g6f8fb67

Data Processing and Statistical Analysis:

Data were entered and managed using SPSS version 22.0.

Categorical variables were compared using Chi-square test, Fisher's exact test, or McNemar's test as appropriate.

A p-value < 0.05 was considered statistically significant.

III. Results

Table 1. Demographic Characteristics and Hereditary Risk Factors

Characteristic	Hereditary Risk Group (n = 34)	Non-Hereditary Group (n = 93)	p-value
Mean age (years)	52,3 ± 10,1	60,8 ± 12,5	<0,05
Sex (Male/Female)	20/14 (58,8%/41,2%)	58/35 (62,4%/37,6%)	0,72
History of FAP*	8 (23,5%)	0 (0%)	<0,001
History of Lynch syndrome	12 (35,3%)	0 (0%)	<0,001
Gene mutation (if tested)	18 (52,9%)	3 (3,2%)	<0,001

**FAP: Familial adenomatous polyposis.*

Interpretation: Patients in the hereditary risk group (n = 34) had a significantly younger mean age (52.3 ± 10.1 years vs. 60.8 ± 12.5 years, p<0.05) compared to those without hereditary factors. The prevalence of gene mutations was markedly higher in the hereditary group (52.9%) than in the non-hereditary group (3.2%). FAP and Lynch syndrome histories were exclusively found in the hereditary group, with proportions of 23.5% and 35.3%, respectively.

Table 2. Endoscopic Characteristics of Colorectal Polyps (n = 152)

Characteristic	Hereditary Group (n = 45 polyps)	Non-Hereditary Group (n = 107 polyps)	p
Location			
- Right colon + hepatic flexure	25 (55,6%)	37 (34,6%)	0,02
- Left colon + splenic flexure	12 (26,7%)	23 (21,5%)	0,49
- Transverse colon	5 (11,1)	23 (21,5)	0,12
- Sigmoid colon	2 (4,4)	15 (14,0)	0,08
- Rectum	1 (2,2%)	9 (8,4%)	1,00
Paris Classification			
- Flat type (IIa/IIb)	14 (31,1%)	11 (10,3%)	0,003
- Mean polyp size (mm)	16,8 ± 4,2	13,5 ± 3,6	<0,01

Comment: Polyps in the hereditary group were more frequently located in the right colon (55.6% vs. 34.6%) and exhibited a higher proportion of flat morphology (31.1% vs. 10.3%) compared to the

DOI: 10.63583/g6f8fb67

non-hereditary group. Additionally, the mean polyp size was significantly larger in the hereditary group (16.8 ± 4.2 mm) than in the non-hereditary group (13.5 ± 3.6 mm).

Table 3. Histopathological Classification of Polyps

Histopathological type	Hereditary Group (n = 45)	Non-Hereditary Group (n = 107)	p-value
Adenoma	35 (77,8%)	63 (58,9%)	0,03
Tubulovillous/Villous	22 (48,9%)	11 (10,3%)	<0,001
Sessile serrated lesion	6 (13,3%)	12 (11,2%)	0,72
Invasive carcinoma	4 (8,9%)	10 (9,3%)	0,93

Comment: The hereditary group had a significantly higher proportion of adenomas (77.8% vs. 58.9%), especially those of tubulovillous or villous type (48.9% vs. 10.3%, p<0.001). The prevalence of invasive carcinoma was similar between the two groups (8.9% vs. 9.3%, p=0.93).

Table 4. Dysplasia Severity and Malignant Features

Feature	Hereditary Group (n = 45)	Non-Hereditary Group (n = 107)	p-value
High-grade dysplasia	18 (40,0%)	16 (15,0%)	<0,001
Carcinoma in situ (Tis)	5 (11,1%)	8 (7,5%)	0,45
Submucosal invasion (T1)	3 (6,7%)	2 (1,9%)	0,12

Comment: High-grade dysplasia was significantly more frequent in the hereditary group (40.0% vs. 15.0%, p<0.001). There were no statistically significant differences between the two groups in the rates of carcinoma in situ (Tis) and submucosal invasion (T1).

Table 5. Comparison of Polyp Characteristics Between Hereditary Syndromes

Characteristic	FAP (n = 8)	Lynch Syndrome (n = 12)	p-value
Mean number of polyps per patient	5,6 ± 2,1	2,3 ± 1,4	<0,01
Villous-type polyps	6 (75,0%)	2 (16,7%)	0,01
High-grade dysplasia	7 (87,5%)	5 (41,7%)	0,03

Comment: Patients with familial adenomatous polyposis (FAP) had a significantly higher mean number of polyps per patient compared to those with Lynch syndrome (5.6 ± 2.1 vs. 2.3 ± 1.4, p<0.01). The proportion of villous-type polyps and high-grade dysplasia was also significantly higher in the FAP group (75.0% and 87.5%, respectively) compared to the Lynch group (16.7% and 41.7%).

IV. Discussion

Our study found that patients with hereditary risk factors (n = 34) had a significantly younger mean age than those without such factors (52.3 ±

DOI: 10.63583/g6f8fb67

10.1 vs. 60.8 ± 12.5 years), consistent with previous reports of earlier onset in Lynch syndrome and familial adenomatous polyposis (FAP) [6]. The gene mutation rate in the hereditary group was markedly higher than in the non-hereditary group (52.9% vs. 3.2%), emphasizing the prominent role of genetic predisposition in colorectal polyp formation. These findings highlight the importance of genetic screening in patients with a family history or hereditary syndromes, as early detection may improve the management of malignant transformation risk.

Endoscopically, a significantly higher proportion of polyps in the hereditary group were located in the right colon (55.6% vs. 34.6%), in line with findings by Firas Al-Kawas, who reported the ascending colon as the most common site (24%) [3]. Notably, flat-type polyps (Paris IIa/IIb) were more common in the hereditary group (31.1% vs. 10.3%).

Histopathological analysis revealed a significantly higher proportion of adenomas in the hereditary group (77.8% vs. 58.9%), particularly tubulovillous/villous adenomas (48.9% vs. 10.3%). These histological subtypes are known to have a higher malignant potential. However, the rate of invasive carcinoma did not differ significantly between the two groups (8.9% vs. 9.3%), contrary to some previous studies [7]. This discrepancy may be due to differences in inclusion criteria or insufficient follow-up duration.

When comparing FAP and Lynch syndrome specifically, patients with FAP had a significantly higher mean number of polyps per patient (5.6 ± 2.1 vs. 2.3 ± 1.4), reflecting the hallmark of FAP hundreds to thousands of polyps developing in adolescence, with nearly 100% risk of malignant transformation if left untreated [8]. The rate of high-grade dysplasia was also significantly higher in the FAP group (87.5% vs. 41.7%), possibly explained by the accumulation of APC gene mutations during polyp progression.

These results support the hypothesis that colorectal polyps in patients with hereditary risk factors differ not only in number but also in clinical and histopathological characteristics. The presence of flat, large-sized polyps with a tendency for high-grade dysplasia in younger patients with familial predisposition underscores the need for more intensive surveillance strategies in this population.

5. Conclusion

Patients with hereditary risk factors exhibited more distinct polyp characteristics, including predominant localization in the right colon, flat morphology, larger size, and higher rates of high-grade dysplasia and advanced histologic features. Gene mutations, as well as diagnoses of FAP and Lynch syndrome, were observed exclusively in this group. Among hereditary syndromes, patients with FAP had a higher polyp burden and greater histologic malignancy potential compared to those with Lynch syndrome. These features warrant close attention in the development of targeted screening and surveillance strategies for high-risk populations.

References

1. Morgan E., Arnold M., Gini A. et al (2023). Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut*, 72(2), 338–344.
2. Alzahrani S.M., Al Doghaither H.A., Al-Ghafari A.B. (2021). General insight into cancer: An overview of colorectal cancer (Review). *Mol Clin Oncol*, 15(6), 271.
3. Al-Kawas F., Gupta N., Benjamin S.B. et al (2008). Large Colorectal Polyps: Endoscopic Resection and Rate of Malignancy. Does Size Matter?. *Gastrointestinal Endoscopy*, 67(5), AB325.

DOI: 10.63583/g6f8fb67

4. Park W., Kim B., Park S.J. et al (2014). Conventional endoscopic features are not sufficient to differentiate small, early colorectal cancer. *World J Gastroenterol*, 20(21), 6586-6593.
5. Nguyễn Trường Sơn, Hoàng Mai Hương, Đỗ Khắc Trường (2021), Nghiên cứu tỷ lệ polyp đại trực tràng ung thư theo kích thước, *Tạp chí Y học Việt Nam*, 507(2). 126-129.
6. Lynch H.T., Snyder C.L., Shaw T.G. et al (2015). Milestones of Lynch syndrome: 1895-2015. *Nat Rev Cancer*, 15(3), 181-194.
7. Jass J.R., Cottier D.S., Pokos V. et al (1997). Mixed epithelial polyps in association with hereditary non-polyposis colorectal cancer providing an alternative pathway of cancer histogenesis. *Pathology*, 29(1), 28-33.
8. Roberts M., Marshall M.L., Webb E.M. et al (2018). Polyp burden in Lynch syndrome patients ascertained via multigene panel testing. *JCO*, 36(4_suppl), 596-596.