International Journal of Innovation Scientific Research and Review
Vol. 08, Issue, 05, pp.9927-9930, May 2026
Available online at http://www.journalijisr.com
SJIF Impact Factor 2025: 7.913

Research Article

ISSN: 2582-6131

CLINICAL, ENDOSCOPIC, HISTOPATHOLOGICAL, AND KRAS MUTATION CHARACTERISTICS IN NON-POLYPOID COLORECTAL CANCER PATIENTS AT CAN THO UNIVERSITY OF MEDICINE AND PHARMACY HOSPITAL

[1]Huynh Cong Tai, [1,] *Pham Thi Ngoc Nga, [1]Nguyen Phuc Duy, [2]Le Van Nho

[1]Can Tho University of Medicine and Pharmacy, No. 179, Nguyen Van Cu Street, Tan An Ward, Can Tho City, Vietnam.
[2]Da Nang University Of Medical Technology And Pharmacy, No. 99 Hung Vuong Street, Hai Chau District, Da Nang, Vietnam.

Received 18th March 2026; Accepted 19th April 2026; Published online 30th May 2026

ABSTRACT

Non-polypoid colorectal cancer is a distinct subtype of colorectal malignancy that is often associated with delayed detection and unfavorable clinical characteristics. A cross-sectional descriptive study was conducted on 56 patients diagnosed with non-polypoid colorectal cancer at Can Tho University of Medicine and Pharmacy Hospital from 2024 to 2026. Clinical manifestations, endoscopic findings, histopathological characteristics, and *KRAS* mutation status were analyzed, and *KRAS* exon 2 sequencing was performed to identify mutation subtypes. The mean patient age was 60.0 ± 11.37 years, with females accounting for 58.9% of cases. Hematochezia (58.9%) and abdominal pain (42.9%) were the most common symptoms. Most tumors were located in the rectum and presented as fungating lesions, while grade 2 adenocarcinoma was the predominant histopathological type (91.1%). *KRAS* mutations were detected in 5.4% of patients, with all mutations occurring at codon 12 of exon 2. Among these, G12A was the most common mutation subtype (66.7%), followed by G12D (33.3%). In conclusion, non-polypoid colorectal cancer was characterized by predominant rectal involvement, fungating morphology, and a low frequency of *KRAS* exon 2 mutations.

Keywords: colorectal cancer, KRAS mutation, exon 2, non-polypoid colorectal cancer, colonoscopy.

INTRODUCTION

Colorectal cancer is one of the most common malignancies worldwide and remains a major cause of cancer-related mortality. According to recent global cancer statistics, colorectal cancer ranks among the leading cancers in both incidence and mortality rates worldwide (Bray *et al.,* 2024). In Vietnam, the burden of colorectal cancer has continued to increase over recent years, posing significant challenges for early diagnosis and treatment.

Non-polypoid colorectal cancer is considered a distinct subtype characterized by flat or slightly elevated lesions that are often difficult to detect during endoscopic examination. These lesions are frequently associated with delayed diagnosis and potentially aggressive biological behavior compared with conventional polypoid lesions (Dekker *et al.,* 2019). Endoscopic morphology and histopathological characteristics play important roles in evaluating tumor progression and guiding therapeutic strategies.

*KRAS*is one of the most frequently mutated oncogenes in colorectal cancer and is involved in the EGFR signaling pathway, which regulates cell proliferation and differentiation (Fearon & Vogelstein, 1990; Pham *et al.,* 2023). Mutations in exon 2, particularly codons 12 and 13, have been associated with resistance to anti-EGFR therapy and may correlate with clinicopathological characteristics of colorectal cancer patients (Prior *et al.,* 2020). However, data regarding *KRAS* mutation profiles in non-polypoid colorectal cancer patients in Vietnam remain limited. Therefore, this study was conducted to describe the clinical and endoscopic characteristics of patients with non-polypoid colorectal cancer and to determine the frequency and mutation profile of *KRAS* exon 2 mutations at Can Tho University of Medicine and Pharmacy Hospital.

***Corresponding Author: Pham Thi Ngoc Nga,**
1Can Tho University of Medicine and Pharmacy, No. 179, Nguyen Van Cu Street, Tan An Ward, Can Tho City, Vietnam.

MATERIALS AND METHODS

Materials: The study included 56 patients diagnosed with non-polypoid colorectal cancer at Can Tho University of Medicine and Pharmacy Hospital from September 2024 to March 2026. Tumor tissue samples were collected during colonoscopy and used for histopathological examination and molecular analysis.

Inclusion criteria: Patients were eligible for inclusion if they met all of the following criteria: (1) diagnosed with non-polypoid colorectal cancer based on colonoscopic findings and histopathological confirmation of colorectal adenocarcinoma; (2) lesions classified as non-polypoid according to the Japanese Classification of Colorectal Carcinoma (JCCC) criteria (Japanese Society for Cancer of the Colon and Rectum, 2019); (3) underwent colonoscopy and tumor tissue sampling at Can Tho University of Medicine and Pharmacy Hospital from September 2024 to March 2026; and (4) agreed to participate in the study by providing written informed consent.

The diagnosis of colorectal adenocarcinoma was confirmed histopathologically according to the WHO Classification of Tumours of the Digestive System, 5th edition (Nagtegaal *et al.,* 2020).

Exclusion criteria: Patients were excluded if they met any of the following criteria: (1) recurrent colorectal cancer or history of previous colorectal cancer treatment; (2) inadequate tumor tissue samples for molecular analysis; (3) poor-quality DNA samples unsuitable for PCR amplification or sequencing; (4) patients with hereditary colorectal cancer syndromes or inflammatory bowel disease; or (5) incomplete clinical or endoscopic data.

Study design and sampling method: A cross-sectional descriptive study was conducted on patients with histopathologically confirmed non-polypoid colorectal cancer. Convenience sampling was applied

during the study period, and a total of 56 patients who met the inclusion criteria and agreed to participate in the study were enrolled consecutively.

Data collection and clinical measurements: Clinical information including age, sex, residence, family history, and gastrointestinal symptoms was collected using standardized questionnaires and medical records. Endoscopic findings including tumor location, tumor size, lesion morphology, and Japanese Classification of Colorectal Carcinoma were recorded during colonoscopy. Histopathological grading was classified according to the WHO Classification of Tumours of the Digestive System (5th edition).

Genetic analysis: Tumor tissue samples were collected and genomic DNA was extracted from formalin-fixed paraffin-embedded (FFPE) tissues using the TopPURE® FFPE DNA Extraction Kit (ABT-VN) according to the manufacturer's instructions. DNA concentration and purity were evaluated using a NanoDrop 2000 spectrophotometer (Thermo Scientific). *KRAS* exon 2, including codons 12 and 13, was amplified by polymerase chain reaction (PCR) using specific forward and reverse primers designed based on the reference *KRAS* sequence (F5'- TGTGTGACATGTTCTAATATAGTCAC -3'; R5'-AGAATGGTCCTGCACCAGTAA -3'). PCR amplification was performed in a total reaction volume of 25 µL under the following thermal cycling conditions: initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 58°C for 30 seconds, extension at 72°C for 30 seconds, and a final extension at 72°C for 5 minutes. PCR products were verified by 2% agarose gel electrophoresis, purified using ExoSAP-IT® PCR Product Cleanup reagent, and subsequently subjected to Sanger sequencing on the ABI 3500 Genetic Analyzer (Applied Biosystems) to identify *KRAS* mutation subtypes. Sequencing data were analyzed using reference *KRAS* gene sequences to determine mutation positions and mutation patterns (Pham *et al.,* 2023).

Statistical analysis: Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation or median values where appropriate. Fisher's exact test or Chi-square test was used to compare categorical variables. A p-value <0.05 was considered statistically significant.

Ethical considerations: The study protocol was approved by the Ethics Committee for Biomedical Research of Can Tho University of Medicine and Pharmacy under Approval No. 24.234.HV/PCT-HDDD dated June 28, 2024. All participants were informed about the objectives and procedures of the study, and written informed consent was obtained prior to enrollment. Patient confidentiality and privacy were strictly maintained throughout the study.

RESULTS

A total of 56 patients with non-polypoid colorectal cancer were included in this study. The mean age of the patients was 60.0 ± 11.37 years, ranging from 36 to 83 years. Most patients were aged ≥50 years (76.8%), and female patients accounted for 58.9% of the study population.

The distribution of clinical symptoms according to tumor location is presented in Table 1. Hematochezia and abdominal pain were the most common clinical manifestations. Significant differences among tumor locations were observed for abdominal pain, hematochezia, and weight loss.

Table 1. Clinical symptoms according to tumor location in patients with non-polypoid colorectal cancer

Clinical symptoms	Total n (%)	Right colon n (%)	Left colon n (%)	Rectum n (%)	Multiple sites n (%)	p value
Abdominal pain	24 (42.9)	5 (83.3)	10 (58.8)	6 (21.4)	3 (60.0)	0.005
Constipation	7 (12.5)	2 (33.3)	1 (5.9)	3 (10.7)	1 (20.0)	0.255
Diarrhea	9 (16.1)	1 (16.7)	4 (23.5)	3 (10.7)	1 (20.0)	0.616
Hematochezia	33 (58.9)	1 (16.7)	7 (41.2)	23 (82.1)	2 (40.0)	0.002
Mucous stool	15 (26.8)	1 (16.7)	6 (35.3)	7 (25.0)	1 (20.0)	0.839
Weight loss	11 (19.6)	0 (0.0)	2 (11.8)	5 (17.9)	4 (80.0)	0.011

Endoscopic characteristics of non-polypoid colorectal cancer according to tumor location are summarized in Table 2. Most tumors occupied ≥3/4 of the intestinal circumference and predominantly presented as fungating lesions. According to the JCCC, type 1 lesions accounted for the majority of cases.

Table 2. Endoscopic characteristics of non-polypoid colorectal cancer according to tumor location

Characteristics	Total n (%)	Right colon n (%)	Left colon n (%)	Rectum n (%)	Multiple sites n (%)	p value
Tumor size						0.010
<1/4 circumference	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	
1/4–<1/2 circumference	6 (10.7)	1 (16.7)	0 (0.0)	5 (17.9)	0 (0.0)	
1/2–<3/4 circumference	14 (25.0)	1 (16.7)	1 (5.9)	10 (35.7)	2 (40.0)	
≥3/4 circumference	35 (62.5)	4 (66.7)	16 (94.1)	13 (46.4)	2 (40.0)	
Morphologic type						0.897
Fungating type	45 (80.4)	5 (83.3)	12 (70.6)	23 (82.1)	5 (100.0)	
Infiltrative	8 (14.3)	1 (16.7)	4 (23.5)	3 (10.7)	0 (0.0)	
Ulcero-infiltrative	2 (3.6)	0 (0.0)	1 (5.9)	1 (3.6)	0 (0.0)	
Ulcero-fungating	1 (1.8)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	
JCCC classification						0.534
Type 1	46 (82.1)	5 (83.3)	12 (70.6)	24 (85.7)	5 (100.0)	
Type 3	1 (1.8)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	
Type 4	9 (16.1)	1 (16.7)	5 (29.4)	3 (10.7)	0 (0.0)	
Histopathological grade						0.857
Grade 1	1 (1.8)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	
Grade 2	51 (91.1)	5 (83.3)	16 (94.1)	25 (89.3)	5 (100.0)	
Grade 3	4 (7.1)	1 (16.7)	1 (5.9)	2 (7.1)	0 (0.0)	

The distribution of *KRAS* exon 2 mutation subtypes identified by Sanger sequencing is illustrated in Figure 1. All detected mutations occurred at codon 12, including G12A (glycine-to-alanine substitution) and G12D (glycine-to-aspartic acid substitution). G12A was the most common mutation subtype.

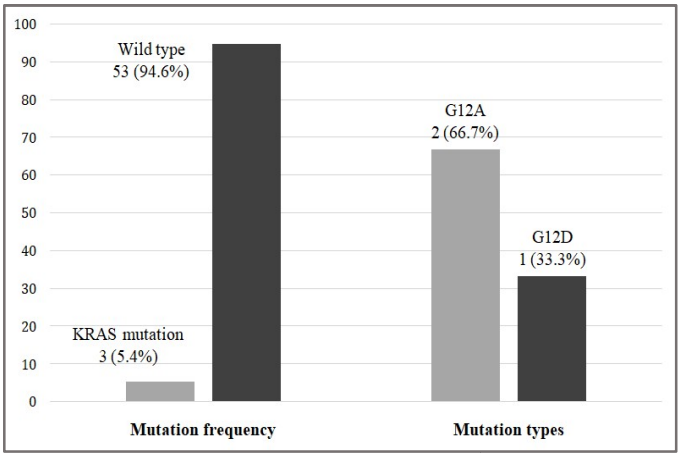

Figure 1. Distribution of *KRAS* exon 2 mutation subtypes in patients with non-polypoid colorectal cancer

Histopathological characteristics and *KRAS* mutation status are presented in Table 3. Grade 2 adenocarcinoma was the predominant histopathological subtype, accounting for 91.1% of cases. *KRAS*mutations were detected in a small proportion of patients, and all mutations were identified at codon 12 of *KRAS* exon 2.

Table 3.Histopathological characteristics and *KRAS* mutation status in patients with non-polypoid colorectal cancer

Characteristics	*KRAS*mutation n (%)	Wild type n (%)	p-value
Tumor location			1.000
Right colon	0 (0.0)	6 (100.0)	
Left colon	1 (5.9)	16 (94.1)	
Rectum	2 (7.1)	26 (92.9)	
Multiple site	0 (0.0)	5 (100.0)	
Tumor size			1.000
<1/4 circumference	0 (0.0)	1 (100.0)	
1/4–<1/2 circumference	0 (0.0)	6 (100.0)	
1/2–<3/4 circumference	1 (7.1)	13 (92.9)	
≥3/4 circumference	2 (5.7)	33 (94.3)	
Morphologic type			0.488
Fungating	2 (4.4)	43 (95.6)	
Infiltrative	1 (12.5)	7 (87.5)	
Ulcero-infiltrativ	0 (0.0)	2 (100.0)	
Ulcero-fungating	0 (0.0)	1 (100.0)	
JCCC classification			0.452
Type 1	2 (4.3)	44 (95.7)	
Type 3	0 (0.0)	1 (100.0)	
Type 4	1 (11.1)	8 (88.9)	
Histopathological grade			0.008
Grade 1	1 (100.0)	0 (0.0)	
Grade 2	1 (2.0)	50 (98.0)	
Grade 3	1 (25.0)	3 (75.0)	

Overall, the results demonstrated that non-polypoid colorectal cancer in this study was characterized by predominant rectal involvement, fungating morphology, and a low frequency of KRAS exon 2 mutations. These findings provide preliminary insights into the clinicopathological and molecular characteristics of non-polypoid colorectal cancer in Vietnamese patients.

DISCUSSION

In the present study, the mean age of patients with non-polypoid colorectal cancer was 60.0 ± 11.37 years, and most patients were aged ≥50 years. This finding is consistent with the epidemiological characteristics of colorectal cancer reported worldwide, in which the incidence increases significantly with age (Bray *et al.,* 2024). Similar results were reported by Dekker *et al.,* (2019), who observed that colorectal cancer is predominantly diagnosed in older adults due to cumulative genetic and environmental exposures. Female patients accounted for 58.9% of cases in our study, which differs slightly from several international reports showing male predominance; however, sex distribution in colorectal cancer may vary among populations and study settings (Yamauchi *et al.,* 2012).

Regarding clinical manifestations, hematochezia and abdominal pain were the most common symptoms. Hematochezia was particularly frequent in rectal tumors, which may be explained by the superficial location and increased vulnerability of rectal lesions to bleeding during bowel movements. Similar observations were described by Aljebreen *et al.,* (2021), who reported rectal bleeding as one of the most common presenting symptoms in colorectal cancer patients with *KRAS* mutation analysis. The significant association between abdominal pain and tumor location in our study suggests that tumor growth pattern and intestinal obstruction may contribute to symptom variability according to anatomical location.

Endoscopic findings showed that most tumors occupied ≥3/4 of the intestinal circumference and predominantly presented as fungating lesions. These findings indicate that many patients were diagnosed at relatively advanced local stages. According to Dekker et al. (2019), non-polypoid colorectal lesions are often difficult to detect during routine colonoscopy because of their flat morphology and subtle mucosal changes, which may delay diagnosis until lesions become large or symptomatic. In the present study, type 1 lesions according to the JCCC accounted for the majority of cases. This predominance may reflect the macroscopic growth characteristics commonly observed in advanced non-polypoid colorectal tumors (Japanese Society for Cancer of the Colon and Rectum, 2019).

Histopathologically, grade 2 adenocarcinoma represented the predominant subtype, accounting for 91.1% of cases. This finding is comparable to previous studies reporting moderately differentiated adenocarcinoma as the most common histological subtype in colorectal cancer patients (Nagtegaal *et al.,* 2020). Only a small proportion of tumors were classified as grade 3, indicating that poorly differentiated tumors were relatively uncommon in our study population.

KRAS mutations were detected in 5.4% of patients, which is considerably lower than mutation frequencies reported in many international studies. Previous reports have demonstrated *KRAS* mutation rates ranging from approximately 30% to 50% in colorectal cancer patients (Prior *et al.,* 2020; Vaughn *et al.,* 2011). Similarly, Rosty *et al.,* (2013) observed frequent *KRAS* mutations in colorectal carcinomas with distinctive clinicopathological features. The relatively low mutation frequency in our study may be related to the limited sample size, the specific subgroup of non-polypoid colorectal cancer, or population-specific genetic characteristics. Another possible explanation is that only *KRAS* exon 2 mutations were analyzed, while mutations in other *KRAS* exons or related genes were not evaluated.
All detected *KRAS* mutations in this study occurred at codon 12 of exon 2, including G12A (glycine-to-alanine substitution) and G12D (glycine-to-aspartic acid substitution). Codon 12 mutations are known to be the most common *KRAS* alterations in colorectal cancer and are

associated with activation of the RAS/MAPK signaling pathway, leading to uncontrolled cell proliferation (Fearon & Vogelstein, 1990). The predominance of G12A mutations in our study differs from several international reports in which G12D or G12V mutations were more common (Prior *et al.,* 2020). This discrepancy may reflect ethnic variation, sample size differences, or the specific characteristics of non-polypoid colorectal cancer.

Although *KRAS* mutations appeared to be more frequently observed in rectal tumors and fungating lesions, no statistically significant association was identified between *KRAS* mutation status and the evaluated clinical or endoscopic characteristics. Similar findings have been reported in previous studies, in which the relationship between *KRAS* mutations and clinicopathological features of colorectal cancer remained inconsistent across different populations and study designs (Yamauchi *et al.,* 2012). The absence of statistically significant associations in the present study may be explained by the relatively low frequency of *KRAS* mutations and the limited number of mutated cases, which reduced the statistical power for subgroup analyses.

Several limitations of this study should be acknowledged. The relatively small sample size, particularly the low number of *KRAS*-mutated cases, may have limited the ability to detect significant associations between *KRAS* mutations and clinicopathological characteristics. In addition, the single-center cross-sectional design may restrict the generalizability of the findings to other populations. The molecular analysis in this study was limited to *KRAS* exon 2 mutations, whereas mutations in other *KRAS* exons or related molecular pathways were not investigated. Furthermore, the study did not evaluate treatment response or long-term clinical outcomes associated with *KRAS* mutation status. Despite these limitations, the present study provides preliminary data regarding the clinical, endoscopic, histopathological, and molecular characteristics of Vietnamese patients with non-polypoid colorectal cancer and may serve as a basis for future studies with larger sample sizes and more comprehensive molecular analyses.

CONCLUSION

Non-polypoid colorectal cancer in this study was predominantly observed in patients aged ≥50 years and was more common in females. Hematochezia and abdominal pain were the most frequent clinical manifestations, while most tumors were located in the rectum and presented as fungating lesions. Histopathologically, grade 2 adenocarcinoma was the predominant subtype. *KRAS* exon 2 mutations were detected in a small proportion of patients, with all mutations occurring at codon 12, predominantly G12A followed by G12D. These findings provide preliminary data regarding the clinicopathological and molecular characteristics of non-polypoid colorectal cancer in Vietnamese patients and may contribute to future studies on molecular biomarkers in colorectal cancer.

ACKNOWLEDGEMENTS

The authors would like to sincerely thank Can Tho University of Medicine and Pharmacy for supporting this study. We are also grateful to all patients who voluntarily participated in this research.

REFERENCES

Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. doi: 10.3322/caac.21834.

Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019 Oct 19;394(10207):1467-1480. doi: 10.1016/S0140-6736(19)32319-0.

Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell. 1990 Jun 1;61(5):759-67. doi: 10.1016/0092-8674(90)90186-i.

Japanese Society for Cancer of the Colon and Rectum. Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma: the 3d English Edition [Secondary Publication]. J Anus Rectum Colon. 2019 Oct 30;3(4):175-195. doi: 10.23922/jarc.2019-018.

Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, Washington KM, Carneiro F, Cree IA; WHO Classification of Tumours Editorial Board. The 2019 WHO classification of tumours of the digestive system. Histopathology. 2020 Jan;76(2):182-188. doi: 10.1111/his.13975.

Prior IA, Hood FE, Hartley JL. The Frequency of Ras Mutations in Cancer. Cancer Res. 2020 Jul 15;80(14):2969-2974. doi: 10.1158/0008-5472.CAN-19-3682.

Pham TNN, Le TV, Hoang DT, Trinh MT, Ngo HT, Nguyen HP, et al. Correlating clinical characteristics of colorectal cancer patients in Vietnam with mutational analysis of exon 2 of KRAS gene. J Southwest Jiaotong Univ. 2023;58(3):1-10. doi:10.35741/issn.0258-2724.58.3.1.

Rosty C, Young JP, Walsh MD, Clendenning M, Walters RJ, Pearson S, Pavluk E, Nagler B, Pakenas D, Jass JR, Jenkins MA, Win AK, Southey MC, Parry S, Hopper JL, Giles GG, Williamson E, English DR, Buchanan DD. Colorectal carcinomas with KRASmutation are associated with distinctive morphological and molecular features. Mod Pathol. 2013 Jun;26(6):825-34. doi: 10.1038/modpathol.2012.240.

Vaughn CP, Zobell SD, Furtado LV, Baker CL, Samowitz WS. Frequency of KRAS, BRAF, and NRAS mutations in colorectal cancer. Genes Chromosomes Cancer. 2011 May;50(5):307-12. doi: 10.1002/gcc.20854.

World Health Organization. Colorectal cancer fact sheet. Geneva: WHO; 2024.

Yamauchi M, Morikawa T, Kuchiba A, Imamura Y, Qian ZR, Nishihara R, Liao X, Waldron L, Hoshida Y, Huttenhower C, Chan AT, Giovannucci E, Fuchs C, Ogino S. Assessment of colorectal cancer molecular features along bowel subsites challenges the conception of distinct dichotomy of proximal versus distal colorectum. Gut. 2012 Jun;61(6):847-54. doi: 10.1136/gutjnl-2011-300865.

****