RESEARCH ARTICLE

Concordance of *KRAS* Mutation in Tumor Tissues and Fecal Samples of Colorectal Carcinoma Patients

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Abstract

BACKGROUND: Colorectal cancer (CRC) is a major global health problem associated with high cancer-related mortality. Profiling of Kirsten rat sarcoma viral oncogene homolog (*KRAS*) mutation status has become a decisive predictive biomarker in the management of CRC. However, *KRAS* mutation testing is commonly performed using tumor tissue obtained through invasive biopsy or surgery; therefore, fecal DNA analysis might offer a promising non-invasive alternative. This study was conducted to evaluate the concordance of *KRAS* mutations between matched tumor tissue and fecal samples and their association with clinicopathological characteristics.

METHODS: This cross-sectional study included 94 patients confirmed of CRC. Tumor tissue specimens were obtained during surgical resection or biopsy, while fecal samples were collected pre-operatively. *KRAS* mutations were analyzed using polymerase chain reaction (PCR) and DNA sequencing, and the associations with clinicopathological variables were statistically evaluated.

RESULTS: *KRAS* mutations were detected in 45.74% of tumor tissue and 26.60% of fecal samples. The overall concordance rate was 65.96%, with a Cohen's Kappa of 0.291 (95% CI: 0.110–0.472), indicating "fair agreement". Notably, allele-specific concordance was 100% among double-positive cases. The fecal assay demonstrated 41.86% sensitivity, 86.27% specificity, 72.00% positive predictive value (PPV), and 63.77% negative predictive value (NPV). Tumor location (colon versus rectum) was significantly associated with fecal *KRAS* detection (p=0.028); other variables showed no significant association (p>0.05).

CONCLUSION: *KRAS* mutations were more frequently detected in tissue than in fecal samples, with fair agreement. High allele-specific concordance suggests fecal DNA accurately reflects the tumor's mutational profile. Tumor location significantly influences DNA detectability, supporting fecal-based KRAS testing as a potential non-invasive approach for CRC molecular assessment.

KEYWORDS: colorectal neoplasms, feces, KRAS protein, human, mutation, neoplasm tissue

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Introduction

Colorectal cancer (CRC) remains a major global health burden. It is the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide, with more than 1.9 million new cases diagnosed each year.(1,2) According to the 2022 GLOBOCAN database, CRC has assumed an alarming trajectory in Indonesia, ranking second among male malignancies with 21,903 new cases (11.6%) and fourth among females with 13,773 cases (6.3%). The cumulative mortality rate of CRC in Indonesia stands at 7.9%, highlighting it as the fourth most lethal malignancy nationwide. This unfavourable

prognosis is heavily tied to delayed clinical identification, as most patients present with advanced or metastatic disease stages.(3)

The pathogenetic framework of CRC is driven by a complex interplay of environmental factors, dietary shifts, and progressive genomic instability.(4–6) Three primary pathogenetic cascades dictate colorectal carcinogenesis: Chromosome Instability (CIN), which accounts for 80–85% of sporadic cases; Microsatellite Instability (MSI); and the CpG Island Methylator Phenotype (CIMP). The classical adenoma-to-carcinoma sequence is characterized by sequential somatic mutations in key oncogenes and tumor suppressor genes, notably adenomatous polyposis coli (*APC*), Kirsten rat sarcoma viral oncogene homolog (*KRAS*), B-rapidly accelerated fibrosarcoma (*BRAF*), and tumor protein 53 (*TP53*).(5,7,8) The *KRAS* oncogene, a component of the small GTPase family, acts as a molecular switch regulating the downstream mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase (PI3K)/Akt signalling cascades.(9,10) Physiologically, wild-type *KRAS* transiently switches from an inactive GDP-bound form to an active GTP-bound form upon upstream activation by the epidermal growth factor receptor (EGFR).(7,11) However, somatic point mutations occurring primarily in hotspot codons 12 and 13 disrupt intrinsic GTPase hydrolysis, permanently stabilizing KRAS in an active GTP-bound state. This constitutive activation drives autonomous cellular proliferation and survival, independent of extracellular EGFR signalling.(7,12)

In contemporary precision oncology, *KRAS* mutation status has become a decisive predictive biomarker in the management of metastatic CRC (mCRC).(13) Patients carrying mutant *KRAS* variants exhibit intrinsic resistance to anti-EGFR monoclonal antibody therapies, such as cetuximab and panitumumab. Consequently, international guidelines mandate testing for *KRAS* mutations prior to prescribing targeted biological agents. Currently, the clinical standard for molecular profiling relies on histopathological tumor tissue specimens retrieved via surgical resection or endoscopic biopsy. However, tissue biopsies are fundamentally limited by their invasive nature, potential for procedure-related complications (such as perforation and haemorrhage), and susceptibility to sampling errors due to intratumoral heterogeneity. Furthermore, repeated tissue sampling to track clonal evolution during therapy is logistically difficult and presents risks for the patient.(7,9)

To address the limitations of tissue diagnostics, non-invasive liquid biopsy alternatives have gained considerable scientific interest. As colorectal tumors grow, rapid cellular turnover, mechanical abrasion by the fecal stream, and inflammation cause malignant cells to desquamate directly into the intestinal lumen. These exfoliated cells release stable mutant tumor DNA into the stool matrix, enabling non-invasive detection. Fecal DNA analysis has therefore emerged as a promising approach for molecular characterization of colorectal cancer.(13) However, the reported concordance between tumor tissue and fecal *KRAS* mutation status remains variable, and the clinicopathological factors that may influence KRAS mutation detection in fecal specimens have not been fully elucidated. Furthermore, evidence from Indonesian populations remains limited. Therefore, this study aimed to evaluate the concordance of *KRAS* mutation status between tumor tissue and fecal specimens and to investigate the association between *KRAS* mutation status and clinicopathological characteristics in Indonesian patients with colorectal cancer.

Methods

Study Design and Setting

This quantitative analytical study employed a cross-sectional design and was conducted at the Polyclinic of Digestive Surgery, Dr. Hasan Sadikin General Hospital (RSHS), Bandung, Indonesia, from May 2025 to April 2026. Matched tumor tissue and fecal samples were collected concurrently from enrolled subjects.

Subject Recruitment

Adult patients with histopathologically confirmed primary CRC scheduled for surgical intervention or diagnostic colonoscopy were consecutively recruited. The inclusion criteria for this study were CRC patients with anatomical pathology confirmation who were over 18 years old and who have agreed to be the subject of this study. CRC patients who have undergone chemotherapy and radiotherapy and have comorbidities such as breast cancer, lung cancer, and pancreatic cancer were excluded from the study. The study protocol received formal approval from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital/ Faculty of Medicine, Universitas Padjadjaran, Bandung. Written informed consent was obtained from all participants prior to specimen collection.

Specimen Collection

The study involved concurrent collection of matched tumor tissue and fecal samples from each enrolled subject to enable parallel molecular comparison between both specimen

types. Tumor tissue specimens were obtained during surgical resection or biopsy procedures and were immediately processed by snap-freezing or fixation in formalin-fixed paraffin-embedded (FFPE) blocks. Preoperative fecal samples were collected in sterile containers, ensuring that samples were free from urine or chemical contamination, and were immediately preserved using specialized stabilization buffers to prevent DNA degradation prior to molecular analysis.

DNA Extraction and *KRAS* Mutation Analysis

Genomic DNA was isolated from approximately 10 mg of fresh tumor tissue preserved in DNA/RNA Shield (Zymo Research, Irvine, CA, USA). The specimens were homogenized in ZR BashingBead Lysis Tubes (Zymo Research) for 40 seconds at 14,000 rpm to obtain a single-cell suspension. DNA extraction was subsequently performed using the Quick-DNA™ Miniprep Kit (Zymo Research) following the manufacturer's protocol, with concentration and purity verified via a NanoDrop™ 2000 Spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA).

Targeted amplification of the *KRAS* exon 2 region was conducted using a polymerase chain reaction (PCR) containing 50–100 ng of genomic DNA and 10 pmol of each primer. The specific primer sequences used were: forward 5'-TTTTTCTTAAGCGTCGATGG-3' and reverse 5'-GGTCCTGCACCAGTAATATGC-3', yielding a 391 bp product. Amplification was performed on a Biorad T100 Thermal Cycler (BioRad, Hercules, CA, USA) using a touchdown PCR protocol. The thermal cycling conditions involved denaturation at 95°C for 30 seconds, followed by 10 cycles of annealing with temperatures decreasing from 60°C to 50°C (1°C reduction per cycle) for 30 seconds, and extension at 72°C for 30 seconds. This was followed by an additional 25 cycles with a constant annealing temperature of 58°C for 30 seconds. PCR products were visualized via 1.5% agarose gel electrophoresis at 90V for 30 minutes and observed under 300 nm UV light using the GelDoc program. Sequencing was executed using the Big Dye Terminator V3.3 kit on an Applied Biosystems 3500 genetic analyzer (Applied Biosystems, Waltham, MA, USA). Functional implications of detected variants were assessed *in silico* using Mutation Taster 2021, PolyPhen-2, and Sorting Intolerant From Tolerant (SIFT).

Clinicopathological Data Collection and Assessment

Clinicopathological data were retrieved from medical and histopathological reports, including patient age, sex, tumor location (colon or rectum), histological differentiation grade (well, moderately, or poorly differentiated), and pathological tumor-node-metastasis (TNM) staging according to the American Joint Committee on Cancer (AJCC) 8th edition. (14) A consecutive sampling technique was used, and all eligible patients during the study period were included until the required sample size was achieved.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics version 26.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used to summarize baseline clinicopathological characteristics and the frequency of KRAS mutations, with continuous variables expressed as mean±SD and categorical variables as percentages. Bivariate analysis to evaluate the association between KRAS mutation status and clinicopathological variables was performed using the Chi-Square test or Fisher's Exact test, as appropriate, with a p-value<0.05 considered statistically significant.

Results

Baseline Clinicopathological Characteristics

A total of 94 patients with histopathologically confirmed colorectal cancer were included in this study. The baseline clinicopathological characteristics of the study population were presented in Table 1. The mean age of patients was 55.0±11.1 years, ranging from 23 to 77 years. The distribution between sexes was relatively balanced, with a slight predominance of female patients.

In terms of the tumor characteristics, rectal tumors were the most frequently observed primary site, followed by colonic subsites including the sigmoid, ascending, transverse, and descending colon. Histopathological evaluation showed that most cases were classified as low-grade tumors. Regarding TNM staging, the majority of patients were in advanced disease stages, particularly stage III and IV, with a high proportion of T3–T4 tumors and significant nodal involvement. Distant metastasis was present in a substantial proportion of patients (Table 1).

***KRAS* Mutation Results**

The distribution of *KRAS* mutation status in tumor tissue and fecal samples was presented in Table 2. *KRAS* mutations were more frequently detected in tumor tissue than in fecal samples, whereas mutation-negative cases predominated in both specimen types. To evaluate the clinical performance

Table 1. Clinicopathological characteristics of subjects.

Clinicopathological Characteristics	n (%)
Gender	
Male	45 (47.87)
Female	49 (52.13)
Tumor Location	
Ascending	15 (15.96)
Transverse	7 (7.45)
Descending	4 (4.26)
Sigmoid	10 (10.64)
Rectum	58 (61.70)
Colon/Rectum	
Colon	36 (38.30)
Rectum	58 (61.70)
Diagnosis Grade	
Low Grade	68 (72.34)
High Grade	10 (10.64)
Mucinous	10 (10.64)
Signet ring cell	6 (6.38)
Histopathological Type	
Well differentiated	44 (46.81)
Moderately differentiated	25 (26.60)
Poor differentiated	17 (18.09)
Specific type	8 (8.51)
T Category	
1	0 (0.00)
2	4 (4.26)
3	50 (53.19)
4	40 (42.55)
N Category	
0	38 (40.43)
1	26 (27.66)
2	30 (31.91)
M Category	
0	67 (71.28)
1	27 (28.72)
Metastasis	
Absent	67 (71.28)
Present	27 (28.72)
Cancer Stage	
I	3 (3.19)
II	31 (32.98)
III	33 (35.11)
IV	27 (28.72)
Total	**94 (100.00)**

of fecal DNA analysis, a direct paired comparison was conducted as shown in the 2×2 contingency matrix in Table 3. *KRAS* mutations were detected in both specimen types for 18 patients (true positives), while 44 patients were negative for mutations in both (true negatives).

Table 2. Distribution of *KRAS* mutation status in tumor tissue and fecal samples.

KRAS Mutation	n (%)
Tumor Tissue	
No	51 (54.26)
Yes	43 (45.74)
Fecal Tissue	
No	69 (73.40)
Yes	25 (26.60)
Total	94 (100.00)

The overall concordance rate between tumor tissue and fecal samples was 65.96%. The calculated Cohen's Kappa coefficient was 0.291 (95% CI: 0.110–0.472), indicating fair agreement between the two specimen types. Furthermore, regarding allele-specific concordance, it was found that 100% of the 18 double-positive cases showed identical *KRAS* variants and base substitutions (*e.g.*, G12D, G12V, G12S) in both tissue and fecal samples. These results suggested that the fecal test might accurately reflects the specific mutational profile of the primary tumor when detected.

Using tumor tissue as the reference standard, the result of fecal *KRAS* mutation assay demonstrated a sensitivity of 41.86%, a specificity of 86.27%, a positive predictive value (PPV) of 72.00%, and a negative predictive value (NPV) of 63.77%. Detailed *KRAS* exon 2 mutation analysis of representative mutation-positive samples was summarized in Table 4. Representative Sanger sequencing chromatograms confirming the identified *KRAS* exon 2 mutations were presented in Figure 1.

Clinicopathological Associations

The association between *KRAS* mutation status in tumor tissue and clinicopathological characteristics was presented in Table 5. There were no statistically significant associations observed between *KRAS* mutation status and any of the evaluated clinicopathological variables, including age, sex, tumor location, histological grade, degree of differentiation, T stage, N stage, metastasis status, and overall stage (all $p>0.05$).

The association between *KRAS* mutation status in fecal samples and clinicopathological characteristics was shown in Table 6. A statistically significant association was observed between KRAS mutation status and tumor location ($p=0.028$). No significant associations were found between *KRAS* mutation status and the other clinicopathological variables (all $p>0.05$).

Table 3. 2×2 Contingency matrix of *KRAS* mutation detection in tumor tissue *vs.* fecal samples.

	Fecal Positive (+)	Fecal Negative (-)	Total Tissue
Tissue Positive (+)	18	25	43
Tissue Negative (-)	7	44	51
Total Fecal	**25**	**69**	**94**

Discussion

This study was conducted to evaluate *KRAS* mutation profiles in tumor tissue and fecal samples and to determine their association with clinicopathological characteristics in patients with colorectal carcinoma. *KRAS* mutations were detected more frequently in tumor tissue than in fecal samples (45.74% vs. 26.60%). To further evaluate the clinical performance of this fecal DNA analysis, we calculated the Cohen's Kappa coefficient, which was found to be 0.291 (95% CI: 0.110–0.472). According to standard interpretation, this represents a "fair agreement" between the two specimen types.

This finding is consistent with the biological characteristics of fecal tumor DNA analysis, in which the detection of *KRAS* mutations depends on the release of tumor-derived DNA into the intestinal lumen, the quantity of DNA reaching the stool, and the preservation of DNA integrity during gastrointestinal transit. A major factor contributing to the observed fair agreement and the relatively low fecal sensitivity (41.86%) is the high limit of detection (LOD) of standard Sanger sequencing, which typically requires a mutant allele fraction of approximately 15–20%. Degradation of tumor DNA, low levels of tumor cell exfoliation, and a low mutant allele fraction may reduce the concentration of target DNA below the detection threshold of molecular assays, resulting in false-negative fecal findings despite the presence of *KRAS* mutations in tumor tissue.(15–18) The fecal *KRAS* mutation frequency observed in the present study was comparable to that reported in a Chinese study (25.93%), although lower than that reported in another Chinese study conducted during the same period (35.8%).(19) These differences may reflect variations in study populations, sample handling procedures, DNA extraction methods, and analytical sensitivity.

Despite the challenges in detection sensitivity, our study achieved 100% allele-specific concordance among the 18 double-positive cases. Every mutation identified in fecal samples, such as G12S, G12D, and G13V, was identical to the specific variant and base substitution found in the corresponding tumor tissue. This indicates that the fecal *KRAS* assay accurately reflects the primary tumor's genetic profile without showing variant heterogeneity in the detected samples, confirming that mismatches are a result of sensitivity limits rather than tumor clonal differences.

The most notable finding of the present study was the significant association between tumor location and *KRAS* mutation detection in fecal samples (p=0.028). Patients with rectal tumors demonstrated higher rates of stool-based *KRAS* mutation detection than those with colonic tumors. One possible explanation is the anatomical proximity of rectal tumors to the site of fecal excretion, which may facilitate the recovery of exfoliated tumor cells and tumor-derived DNA during sample collection.(18,20) Furthermore, the shorter intestinal transit distance may reduce DNA degradation before sample acquisition. These findings suggest that anatomical factors influence the detectability of tumor-

Table 4. Representative *KRAS* exon 2 mutation analysis results.

Sample ID	Specimen	Exon 2 (Codons 12/13)	Base Substitution	Mutation Status
S109	Tumor	G12S	GGT>AGT	Heterozygous
S117	Tumor	G13V	GGC>GTC	Heterozygous
S136	Tumor	G12V	GGT>GTT	Heterozygous
S138	Tumor	G12S	GGT>AGT	Heterozygous
S145	Tumor	G12D	GGT>GAT	Heterozygous
S153	Tumor	G12D	GGT>GAT	Heterozygous
S164	Tumor	G12A	GGT>GCT	Heterozygous
S243	Tumor	G12D	GGT>GAT	Homozygous

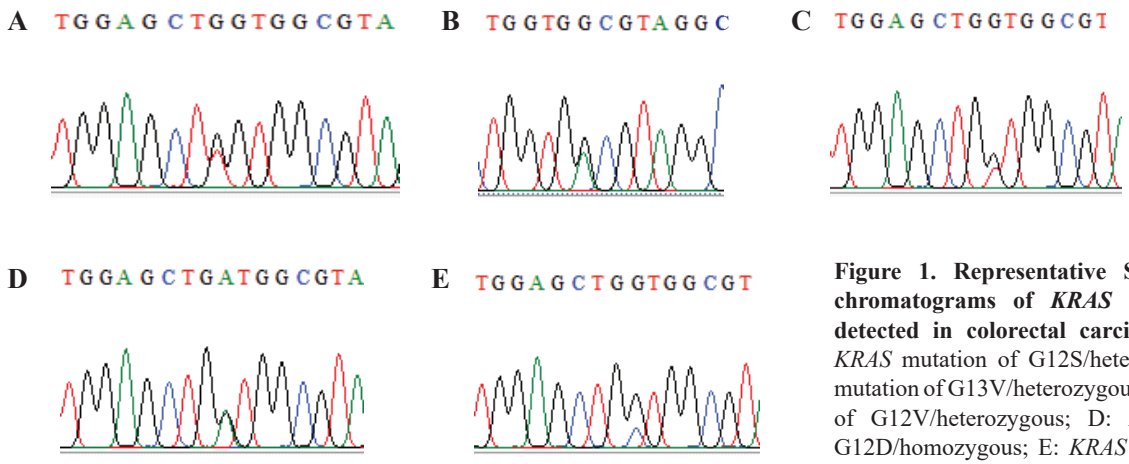

Figure 1. Representative Sanger sequencing chromatograms of *KRAS* exon 2 mutations detected in colorectal carcinoma samples. A: *KRAS* mutation of G12S/heterozygous; B: *KRAS* mutation of G13V/heterozygous; C: *KRAS* mutation of G12V/heterozygous; D: *KRAS* mutation of G12D/homozygous; E: *KRAS* mutation of G12A/heterozygous.

derived genetic material in fecal specimens.(15,16,18) This finding differs from a study conducted in Brazil, which reported no significant association between tumor location and *KRAS* mutation status.(21) The discrepancy may be attributable to differences in study population characteristics, sample size, molecular detection methods, or fecal sample processing protocols. Variations in genetic background and environmental exposures between populations may also contribute to differences in *KRAS* mutation detection patterns. Further studies are needed to clarify the influence of tumor location on fecal *KRAS* detectability across diverse patient populations.

Interestingly, clinicopathological parameters such as tumor differentiation, TNM classification, metastatic status, and overall disease stage were not significantly associated with fecal *KRAS* mutation detection. These findings are consistent with studies conducted in Brazil, Saudi Arabia, and Indonesia, which similarly reported no significant associations between *KRAS* mutation status and clinicopathological characteristics, including tumor grade, cancer stage, metastatic status, age, sex, and tumor location.(22,23) The consistency of these findings across different populations suggests that *KRAS* mutations may occur independently of conventional indicators of tumor progression and disease severity. This observation is biologically plausible because *KRAS* mutation is considered an early event in colorectal carcinogenesis and may occur before the development of advanced clinicopathological features.(11,23) Although advanced tumors are theoretically expected to release greater amounts of tumor-derived DNA into the intestinal lumen, the present findings suggest that anatomical location may exert a greater influence on fecal DNA detectability than tumor burden alone. This observation highlights the importance of considering factors beyond tumor stage when evaluating the performance of stool-based molecular testing. As molecular biomarkers continue to evolve, understanding the factors that influence their detectability and analytical performance remains an important area of colorectal cancer research. Further studies are needed to clarify the relative contributions of tumor burden, anatomical location, and biological factors affecting fecal DNA recovery.(15,16,24)

Several limitations should be acknowledged. This study was conducted at a single center using a cross-sectional design and a relatively small sample size, which may have limited the ability to detect weaker associations. In addition, factors affecting fecal DNA quality, such as sample handling and DNA degradation, were not comprehensively evaluated. Furthermore, this study assessed *KRAS* alterations only at the DNA level using Sanger sequencing. Future multicenter studies with larger cohorts and more sensitive molecular techniques, such as droplet digital PCR (ddPCR) or Next-Generation Sequencing (NGS), are needed to improve the concordance rate and validate these findings.

Conclusion

KRAS mutations were more frequently detected in tumor tissue (45.74%) than in fecal samples (26.60%), with an overall concordance rate of 65.96% and a Cohen's Kappa of 0.291, indicating fair agreement. Notably, 100% allele-specific concordance was observed among double-positive cases, suggesting that fecal DNA accurately reflects the specific types of mutant variants found in the primary tumor. Tumor location significantly influences DNA detectability, supporting fecal-based *KRAS* testing as a potential non-invasive approach for CRC molecular assessment.

Table 5. Association between *KRAS* mutation in tumor tissue and clinicopathological characteristics of colorectal carcinoma patients.

Clinicopathological Characteristics	*KRAS* Mutation		Total [n(%)]	*p*-value
	No [n(%)]	Yes [n(%)]		
Age (years)				0.726[c]
Mean±SD	55.4±11.9	54.46±10.2	55.0±11.1	
Gender				0.317[a]
Male	22 (48.9)	23 (51.1)	45 (100.0)	
Female	29 (59.2)	20 (40.8)	49 (100.0)	
Tumor Location				0.976[b]
Ascending	8 (53.3)	7 (46.7)	15 (100.0)	
Transverse	3 (42.9)	4 (57.1)	7 (100.0)	
Descending	2 (50.0)	2 (50.0)	4 (100.0)	
Sigmoid	6 (60.0)	4 (40.0)	10 (100.0)	
Rectum	32 (55.2)	26 (44.8)	58 (100.0)	
Colon/Rectum				0.821[a]
Colon	19 (52.8)	17 (47.2)	36 (100.0)	
Rectum	32 (55.2)	26 (44.8)	58 (100.0)	
Diagnosis Grade				0.576[b]
Low Grade	36 (52.9)	32 (47.1)	68 (100.0)	
High Grade	5 (50.0)	5 (50.0)	10 (100.0)	
Mucinous	5 (50.0)	5 (50.0)	10 (100.0)	
Signet ring cell	5 (83.3)	1 (16.7)	6 (100.0)	
Histopathological Type				0.487[b]
Well differentiated	24 (54.4)	20 (45.5)	44 (100.0)	
Moderately differentiated	11 (44.0)	14 (56.0)	25 (100.0)	
Poorly differentiated	10 (58.8)	7 (41.2)	17 (100.0)	
Specific	6 (75.0)	2 (25.0)	8 (100.0)	
T Category				0.876[b]
1	0 (0.0)	0 (0.0)	0 (0.0)	
2	2 (50.0)	2 (50.0)	4 (100.0)	
3	26 (52.0)	24 (48.0)	50 (100.0)	
4	23 (57.5)	17 (42.5)	40 (100.0)	
N Category				0.522[a]
0	23 (60.5)	15 (39.5)	38 (100.0)	
1	12 (46.2)	14 (53.8)	26 (100.0)	
2	16 (53.3)	14 (46.7)	30 (100.0)	
M Category				0.767[b]
0	37 (55.2)	30 (44.8)	67 (100.0)	
1	14 (51.9)	13 (48.1)	27 (100.0)	
Metastasis				0.767[b]
Absent	37 (55.2)	30 (44.8)	67 (100.0)	
Present	14 (51.9)	13 (48.1)	27 (100.0)	
Cancer Stage				0.945[b]
I	2 (66.7)	1 (33.3)	3 (100.0)	
II	18 (58.1)	13 (41.9)	31 (100.0)	
III	17 (51.5)	16 (48.5)	33 (100.0)	
IV	14 (51.9)	13 (48.1)	27 (100.0)	
Total	**51 (54.2)**	**43 (45.7)**	**94 (100.0)**	

Tested with [a]Chi-Square; [b]Fisher's Exact Test; [c]Independent t-test. $p<0.05$ is considered significant.

Table 6. Association between KRAS mutation in fecal samples and clinicopathological characteristics of colorectal carcinoma patients.

Clinicopathological Characteristics	*KRAS* Mutation		Total [n(%)]	*p*-value
	No [n(%)]	Yes [n(%)]		
Age (years)				0.669[c]
Mean±SD	54.7±11.1	55.8±11.3	55.0±11.1	
Gender				0.651[a]
Male	34 (75.6)	11 (24.4)	45 (100.0)	
Female	35 (71.4)	14 (28.6)	49 (100.0)	
Tumor Location				0.147[b]
Ascending	12 (80.0)	3 (20.0)	15 (100.0)	
Transverse	6 (85.7)	1 (14.3)	7 (100.0)	
Descending	3 (75.0)	1 (25.0)	4 (100.0)	
Sigmoid	10 (100.0)	0 (0.0)	10 (100.0)	
Rectum	38 (65.5)	20 (34.5)	58 (100.0)	
Colon/Rectum				0.028[a]
Colon	31 (86.1)	5 (13.9)	36 (100.0)	
Rectum	38 (65.5)	20 (34.5)	58 (100.0)	
Diagnosis Grade				0.287[b]
Low Grade	47 (69.1)	21 (30.9)	68 (100.0)	
High Grade	7 (70.0)	3 (30.0)	10 (100.0)	
Mucinous	9 (90.0)	1 (10.0)	10 (100.0)	
Signet ring cell	6 (100.0)	0 (0.0)	6 (100.0)	
Histopathological Type				0.338[b]
Well differentiated	33 (75.0)	11 (25.0)	44 (100.0)	
Moderately differentiated	15 (60.0)	10 (40.0)	25 (100.0)	
Poorly differentiated	14 (82.4)	3 (17.6)	17 (100.0)	
Specific	7 (87.5)	1 (12.5)	8 (100.0)	
T Category				0.920[b]
1	0 (0.0)	0 (0.0)	0 (0.0)	
2	3 (75.0)	1 (25.0)	4 (100.0)	
3	36 (72.0)	14 (28.0)	50 (100.0)	
4	30 (75.0)	10 (25.0)	40 (100.0)	
N Category				0.466[a]
0	28 (73.7)	10 (26.3)	38 (100.0)	
1	17 (65.4)	9 (34.6)	26 (100.0)	
2	24 (80.0)	6 (20.0)	30 (100.0)	
M Category				0.926[a]
0	49 (73.1)	18 (26.9)	67 (100.0)	
1	20 (74.1)	7 (25.9)	27 (100.0)	
Metastasis				0.926[a]
Absent	49 (73.1)	18 (26.9)	67 (100.0)	
Present	20 (74.1)	7 (25.9)	27 (100.0)	
Cancer Stage				0.999[b]
I	2 (66.7)	1 (33.3)	3 (100.0)	
II	23 (74.2)	8 (25.8)	31 (100.0)	
III	24 (72.7)	9 (27.3)	33 (100.0)	
IV	20 (74.1)	7 (25.9)	27 (100.0)	
Total	**69 (73.4)**	**25 (26.6)**	**94 (100.0)**	

Tested with [a]Chi-Square; [b]Fisher's Exact Test; [c]Independent t-test. $p<0.05$ is considered significant.

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Authors Contribution

AB was responsible for conceptualizing and designing the study, conducting data collection, performing data analysis, interpreting the results, and drafting the manuscript. RR, KL, AP, and PN contributed in supervising the study by providing guidance on the study design and methodology, assisting in data interpretation, as well as critically revising the manuscript for important intellectual content. YS contributed to the molecular laboratory procedures, data interpretation, and critical revision of the manuscript. All authors reviewed, approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Ethical Statement

This study adhered to relevant molecular oncology guidelines for colorectal cancer research. Ethical approval was obtained from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital/Faculty of Medicine, Universitas Padjadjaran, Bandung, with approval number DP.04.03/D.XIII.2.3/1226/2026, and written informed consent was obtained from all participants prior to sample collection.

Conflict of Interest

All authors declare that they have no competing interests.

References

1. Hossain MdS, Karuniawati H, Jairoun AA, Urbi Z, Ooi DJ, John A, *et al.* Colorectal cancer: A review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. Cancers. 2022; 14(7): 1732. doi:10.3390/cancers14071732.
2. Wijaya T, Akmal AAM, Herman N, Hasan AA, Hafiz A, Widyastuti H. Apoptotic effects sulfated polysaccharides of Caulerpa racemosa extract on colorectal cancer cells through caspase-3. Mol Cell Biomed Sci. 2025; 9(3): 171–8.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al.* Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021; 71(3): 209–49.
4. Tedjasaputra TR, Hatta M, Massi MN, Natzir R, Patellongi I, Simadibrata M, *et al.* Risk assessment in hereditary colorectal cancer family by using APC and MSH2 mRNA gene expression and bayesian analysis. Indones Biomed J. 2020; 12(4): 368–75.
5. Rianti AM, Cangara MH, Yamin A, Dahlan H, Ilyasa MR, Miskad UA. FGFR2 as a prognostic and predictive marker in colorectal adenocarcinoma based on TILs grade. Indones Biomed J. 2025; 17(2): 188–96.
6. Luminturahardjo W, Soeatmadji DW, Mintaroem K, Rahajoe P, Sandra F. N-cadherin as an important marker in colorectal cancer: An investigation of β-catenin and cadherin expressions of SW-480 and HCT-116 cell lines. Indones Biomed J. 2021; 13(3): 289–94.
7. Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Kao LS, Hunter JG, *et al.* Schwartz's Principles of Surgery. 11th ed. New York: McGraw-Hill Education; 2019.
8. Yamagishi H, Kuroda H, Imai Y, Hiraishi H. Molecular pathogenesis of sporadic colorectal cancers. Chin J Cancer. 2016; 35(1): 4. doi:10.1186/s40880-015-0066-y.
9. Ferretti S, Patriarca S, Carbone A, Zanetti R. TNM classification of malignant tumours, VII edition 2009. Changes and practical effects on cancer epidemiology. Epidemiol Prev. 2010; 34(3): 125–8.
10. Semadhi MP, Prasojo SL, Widarini A. Lung cancer: Biomarkers, tyrosine kinase inhibitors and monoclonal antibodies. Mol Cell Biomed Sci. 2017; 1(2): 41–9.
11. Kumar V, Abbas AK, Aster JC. Robbins & Cotran Pathologic Basis of Disease. 10th ed. Philadelphia: Elsevier; 2021.
12. Porru M, Pompili L, Caruso C, Biroccio A, Leonetti C. Targeting KRAS in metastatic colorectal cancer: Current strategies and emerging opportunities. J Exp Clin Cancer Res. 2018; 37(1): 57. doi: 10.1186/s13046-018-0719-1.
13. Warsinggih, Liliyanto, Marhamah, Kusuma MI, Uwuratuw JA, Syarifuddin E, *et al.* Relationship between BRAF V600E and KRAS mutations in stool for identifying colorectal cancer: A cross-sectional study. Ann Med Surg. 2020; 60: 121–5.
14. The American College of Surgeons [Internet]. AJCC Cancer Staging Form Supplement AJCC Cancer Staging Manual, Eighth Edition [cited 2025 Jan 15]. Available from: https://www.facs.org/quality-programs/cancer-programs/american-joint-committee-on-cancer/cancer-staging-systems/cancer-staging-form-supplement/.
15. Mo S, Wang H, Han L, Xiang W, Dai W, Zhao P, *et al.* Fecal multidimensional assay for non-invasive detection of colorectal cancer: Fecal immunochemical test, stool DNA mutation, methylation, and intestinal bacteria analysis. Front Oncol. 2021; 11: 643136. doi: 10.3389/fonc.2021.643136.

16. Xu H, Chen H, Hu J, Xiong Z, Li D, Wang S, *et al.* Feasibility of quantification based on novel evaluation with stool DNA and fecal immunochemical test for colorectal cancer detection. BMC Gastroenterol. 2022; 22(1): 384. doi:10.1186/s12876-022-02470-z.
17. Wang Z, Shang J, Zhang G, Kong L, Zhang F, Guo Y, *et al.* Evaluating the clinical performance of a dual-target stool DNA test for colorectal cancer detection. J Mol Diagn. 2022; 24(2): 131–43.
18. Sui X, Chen Y, Liu B, Li L, Huang X, Wang M, *et al.* The relationship between KRAS gene mutation and intestinal flora in tumor tissues of colorectal cancer patients. Ann Transl Med. 2020; 8(17): 1085. doi: 10.21037/atm-20-5622.
19. Dong Z, Kong L, Wan Z, Zhu F, Zhong M, Lv Y, *et al.* Somatic mutation profiling and HER2 status in KRAS-positive Chinese colorectal cancer patients. Sci Rep. 2019; 9(1): 16894. doi: 10.1038/s41598-019-53039-y.
20. Moore KL, Agur AMR, Dalley AF II. Clinically Oriented Anatomy. 8th ed. Philadelphia: Wolters Kluwer; 2018.
21. Zanatto RM, Santos G, Oliveira JC, Pracucho EM, Nunes AJF, Lopes-Filho GJ, *et al.* Impact of KRAS mutations in clinical features in colorectal cancer. Arq Bras Cir Dig. 2020; 33(3): e1524. doi: 10.1590/0102-672020200003e1524.
22. Alghamdi M, Alabdullatif N, Al-Rashoud A, Alotaibi J, Alhussaini N, Elsirawani S, *et al.* KRAS mutations in colorectal cancer: Relationship with clinicopathological characteristics and impact on clinical outcomes in Saudi Arabia. Cureus. 2022; 14(3): e23656. doi: 10.7759/cureus.23656.
23. Rudiman R, Alfarisy A, Lukman K, Nugraha P, Setiawan Y, Sribudiani Y. Associations of KRAS mutations and clinical characteristics of colorectal cancer patients in Indonesia. Asian Pac J Cancer Prev. 2024; 25(10): 3457–61.
24. Faroque H, Aria NS, Muzilah NA, Al-Jamal HAN, Rahim MFA, Nakamura Y, *et al*. CHEK1 and GFPT1 as potential blood-based biomarkers for colorectal cancer. Indones Biomed J. 2023; 15(6): 358–65.