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Original Research Paper

The Effects of KRAS Mutation Status and Expression of RAS Pathway Signaling Molecules on the Clinicopathological Features and Prognosis of Colorectal Cancer in a Sample of Iraqi Patients

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ABSTRACT:

Background: KRAS mutations are one of the most common mutations in breast cancer (CRC). The KRAS gene is a small GTPase involved in cell signaling via the RAS/RAF/MEK/ERK pathway. Mutations in KRAS inhibit cell growth and division, leading to activation of this pathway that supports the growth and development of CRC. KRAS mutations appear to alter the expression of downstream signals such as ERK as well as other signals in the RAS pathway such as RAF and MEK. Increased expression of these markers is associated with poor prognosis in CRC patients. **Aim of the Study:** is to understand the relationships between KRAS mutation status, expression of RAS pathway signaling molecules, and clinicopathological features and prognosis of patients with colorectal cancer (CRC). **Methodology**: Patients who have been diagnosed with colorectal cancer and have received surgical treatment included in this study. Patients' clinical information are collected from their medical records. Patients' tumor tissues are used for KRAS mutation status and RAS pathway signaling molecules expression analysis. **Results**: this study provides insights into the relationship between KRAS mutation status and clinicopathologic features in CRC patients. The results suggest that KRAS mutation status may be associated with tumor location, histology, and invasion status, but not with tumor stage or survival. These findings may have implications for treatment decisions and personalized medicine in CRC patients. **Conclusion**: this study provides important insights into the prevalence of KRAS exon 2 mutations in colon cancer patients. While more research is needed to understand the impact of specific KRAS mutations, this information can help inform treatment decisions and guide the development of new drugs for cancer patients.

Key words: KRAS mutation; RAS pathway; signaling molecules; clinicopathological; prognosis; colorectal; cancer.

INTRODUCTION:

The rectum and colon, the last two organs of the digestive system, are both affected by colon cancer. Millions of people around the world are affected by one of the most prevalent cancers. (1) The second most common cancer in women and the third most common cancer in men is colorectal cancer (CRC). The most recent data available show that there were 1.8 million new cases worldwide in 2018. The average age at diagnosis dropped from 72 in 2001–2002 to 66 in 2015–2016, and the prevalence of CRC has shifted to the elderly. (2). Risk factors for cancer include aspects of one's lifestyle, such as age, family history, diet, physical inactivity, and prior experiences with gastrointestinal disorders. Cancer symptoms include changes in bowel habits, rectal bleeding, abdominal pain, and fatigue. (3) A combination of techniques, such as blood tests, stool tests, and imaging studies, are typically used to diagnose colon cancer. Surgery, radiation therapy, chemotherapy, and chemotherapy are all used as cancer treatments. (4). The genomic environment of CRC is revealed by next-generation sequencing. The molecular analysis of colon and rectal cancer has been finished by the Cancer Genome Atlas

(TCGA). The most frequent cause of sporadic adenomas and sporadic CRC is mutations in the adenomatous polyposis coli (APC) gene. In CRC tissues with low MSI scores (4%) and high MSI scores (40%) BRAF mutations are present. TP53 mutations are present in 43% of CRC cases. For between 40 and 52 percent of CRC cases, the KRAS gene has been mutated. The following genes have mutations: SMAD4, BRIP1, CHEK2, MUTYH, HNF1A, and XPC. KRAS has been dubbed an "indestructible" target in cancer therapy out of all the genetic mutations. (5–6). RAS signaling molecules are the proteins that regulate cell growth, division, and survival through the RAS signaling system. One of the most active pathways in human aggression is the RAS, which becomes active as the issue worsens. (7). If the RAS pathway is active in cells or tissues, it can be identified by looking at the expression of the RAS signaling system. The RAS family includes several members who function as growth factors at low cost, including KRAS, one of the most researched RAS signaling systems. KRAS activating mutations or high expression are frequent in cancers. A family of serine/threonine kinases known as RAFs controls cell distribution and growth along the MEK/ERK pathway when growth signals are present. Following RAF, MEK is a serine/threonine kinase that activates the ERK pathway. MEK activates ERK, a mitogen-activated protein kinase that controls cell division and growth. RALGDS: As a negative regulator of RAS signaling, this protein binds to and inhibits RAS signaling. (7-9). The activation of the RAS pathway and its potential for targeted therapy may be revealed by the expression of the RAS signaling pathway. (10). The KRAS protein is encoded by the KRAS gene, and it participates in signaling pathways that regulate cell division and growth. KRAS mutations cause unchecked cell growth and signaling pathways to be activated, which promote the growth of tumors even in the absence of stimulation. (11). In cancers like those of the stomach, pancreas, and lung, the KRAS gene is frequently mutated. KRAS mutations may have significant effects on cancer diagnosis, prognosis, and treatment. For instance, some chemotherapy drugs may not work on patients with KRAS mutations, who may also have a poor prognosis. (12). The RAS gene family, which is linked to human tumors, includes the mouse sarcoma virus oncogene KRAS, which is found on chromosome 12. p21 gene, which produces the 21kD RAS protein, is another name for KRAS. A guanine nucleotide-binding protein that is a member of the RAS protein family is known as the Kirsten rat sarcoma 2 viral oncogene homolog (KRAS) protein. (13). Guanosine 5'-triphosphate (GTP) binding causes KRAS to become active and transmit signals that control both normal and abnormal cell types' rates of cell division and proliferation. The transition I (amino acids 30-38) and transition II (amino acids 59-67) regions of the KRAS protein are also altered by GTP binding. (14). The regulation and inhibition of binding depend on key regions I and II. When the downstream GTPase activating protein (GAP) is altered, it interacts with the KRAS protein. The KRAS-GTP-bound form can transform into the inactive GDP-bound form because GAPs increase the activity of the KRAS GTPase. The KRAS protein lacks GAPs despite having a GTPase response. To increase the GTP release of the KRAS protein, the transcription factor also interacts with the GEF/GRF, also known as the guanine exchange/release factor (GEF/GRF). (15) .

KRAS controls cell signaling pathways like PI3K-Akt, RAS-RAF-MAPK, and RAS-GEF that are involved in cell proliferation and cytokine production, respectively. Take into account. RAS-RAF-MAPK signaling network. (16). The intracellular tyrosine kinase of the transmembrane epidermal growth factor receptor (EGFR) is activated when an external ligand binds to it in response to stimulation. Growth factor receptor binding protein 2 (Grb2) and guanine nucleotide conversion factor (GEF) are activated by the EGFR, and they signal the KRAS protein and start the RAS-RAF-MAPK signaling cascade. GAP helper proteins then convert active RAS-GTP to inactive RAS-GDP in healthy cells. (17). However, KRAS gene mutations lessen the protein's ability to act as a GTPase. In the mutant form of KRAS, GDP is quickly replaced by GTP, activating KRAS, and it loses its sensitivity to GAP. Overexpression of KRAS promotes abnormal and uncontrolled cell and cell transformation, accelerates the development of cancer, and makes patients resistant to chemotherapy and EGFR-targeted treatments in many cancer types, including CRC. (18).

The Study Objectives:

The aim of the study is to understand the relationships between KRAS mutation status, expression of RAS pathway signaling molecules, and clinicopathological features and prognosis of patients with colorectal cancer (CRC).

METHODOLOGY:

Study Design: This research employs a retrospective cohort study approach. This study includes patients who were diagnosed with colorectal cancer and got surgical therapy between January 2022 and December 2022. Clinical data from patients' medical records will be obtained. KRAS mutation status and RAS pathway signaling molecules expression studies are performed on tumour tissues from patients.

Sample Size: To find significant differences in patient outcomes caused by KRAS mutations and RAS signaling molecule expression, sample size analysis was carried out. According to earlier research, 40–50%

of colon cancer patients have KRAS mutations. 100 patients are needed to detect a difference between the prediction of KRAS mutation positive and KRAS mutation negative at a 0.05 significance level and an 80 percent power. In this example, sizing also adds to the time required to close an account, which results in the loss of data.

Inclusion and Exclusion Criteria:

Colon cancer patients who had surgery between January 2022 and December 2022 and had tissue samples available for molecular analysis were eligible for sampling in this study. Patients diagnosed with other cancers or undergoing chemotherapy or radiation therapy prior to surgery were excluded.

Outcome Measures:

The primary objective of this study was to examine the association between the KRAS mutation and RAS signaling molecule expression and overall survival (OS) and disease-free survival (DFS) in cancer patients. Additional findings will relate KRAS mutations to RAS signaling component expression as well as clinical characteristics like tumor stage, differentiation, and location.

Data Collection:

Clinical information will be gathered from patients' medical records, including demographic information about the patient, information about the tumor (such as tumor stage, differentiation, and location), information about previous treatments, and information about the patient's prognosis. Molecular biology methods will be used to extract tumors from the hospital's pathology division and examine them for the expression of KRAS mutations and RAS signaling patterns. According to the researchers, all data collection and analysis will be done in an ethical manner.

Pathological Features:

The following features were identified using pathology data: histological subtype (classical adenocarcinoma, mucinous adenocarcinoma, signet ring cell adenocarcinoma, medullary adenocarcinoma, adenosquamous carcinoma, and undifferentiated carcinoma), histological grade moderate (high, high, (tumors in the large intestine, cecum, and proximal ascending colon) Tumors in the splenic flexure, descending colon, and sigmoid colon are classified as distal. Extracellular mucin, which makes up at least 50% of rectal adenocarcinomas, is what distinguishes them from other cancers.

KRAS Mutation Analysis:

Formalin-fixed, paraffin-embedded tissues with histologically verified mutations of KRAS were evaluated. From each sample used to collect case data, cut three to four sections that are 3 to 4 m thick and place them in tubes without using a microcentrifuge. Using a DNA isolation kit (Qiagen, Hilden, Germany), the samples' genomic DNA was extracted. This tissue is used to separate the genomic DNA. Real-time polymerase chain reaction (RT-PCR) was used to find mutations in the RAS gene's codons 12 and 13 (exon 2). Following DNA extraction, samples are examined for KRAS mutations. The KRAS RT-PCR kit is being used in this procedure (Qiagen, Hilden, Germany). The kit detects mutations in two stages: (i) DNA quality testing and (ii) RT-PCR reaction. Prior to using them in RT-PCR experiments, samples should have their quality assessed.

MSI Analysis:

Microsatellite status was assessed using five microsatellite markers (BAT-25, BAT-26, D2S123, D5S346 and D17S250) approved by the National Cancer Institute MSI Workshop. Conversion of PCR obtained from tumor DNA to normal DNA was compared by PCR analysis. Tumors with at least two mutations in five microsatellite markers were classified as MSI-H, while tumors showing novel sequences in one marker were classified as MSI-L. MSS samples were those in which all microsatellite markers show the same patterns in cancer and soft tissue; MSS and MSI-L tumors were pooled for genetic studies.

Statistical Analysis:

Data were entered into a computer and analyzed using the IBM SPSS software program version 20.0. IBM Corporation, Armonk, NY. Kolmogorov-Smirnov test was used to confirm the normality of differences, paired t-test was used to compare twice for normally distributed multiple variables, repeated measures ANOVA was used to compare normally distributed multiple variables for different studies. time, then a Post-hoc test (Bonferroni substitution) was used for pairwise comparisons. Pearson coefficient used to determine the relationship between two multivariate distributions. The significance of the results was determined at the 5% level.

RESULTS:

Colorectal cancer (CRC) frequently carries KRAS gene mutations, which are linked to treatment resistance and a poor prognosis. The authors of the current study looked at how KRAS mutations, RAS signaling pathway expression, clinical characteristics, and patient prognosis are related to one another. The parameters of 100 CRC patients with KRAS mutations were examined by the authors, including sex, age, tumor site, stage, lymphovascular invasion, venous invasion, perineural invasion, differentiation, histology, recurrence, neoadjuvant therapy, and survival. The results show that 40% of the patients

have KRAS mutations, while 60% do not. In this study, there were 100 patients with colon cancer, 60 of whom did not have KRAS mutations and 40 of whom did. The clinicopathological characteristics of the two patient groups were contrasted. The gender distribution of the two groups was the study's first point of focus. The study found that male patients made up 40% of those with negative KRAS mutations and 22% of those with positive KRAS mutations. The difference (p = 0.239) was not statistically significant. Additionally, the study examined the age disparities between the two groups. The study's findings showed that 58 percent of patients with KRAS mutation negativity and 35 percent of patients with KRAS mutation positivity were over the age of 50. The difference was not statistically significant (p=0.0784).

Table 1 : Clinicopathologic characteristics according to KRAS mutation status

	Negative	Positive	Total	p-value
	N=60	N=40	N=100	
Sex				
Male	40(40%)	22(22%)	62(62%)	0.239
Female	20(20%)	18(18%)	38(38%)	
Age				
<50year	2(0.02%)	5(0.05%)	7(7%)	0.0784
≥ 50year	58(0.58%)	35(0.35%)	93(93%)	
Location				
Rt colon	14(0.14%)	13(0.13%)	27(27%)	0.2165
Lt colon	30(0.3%)	13(0.13%)	43(43%)	
Rectum	20(0.2%)	10(0.1%)	30(30%)	
Multiple	16(0.16%)	4(0.04%)	20(20%)	
Stage				
Tis	1(0.01%)	2(0.02%)	3(3%)	0.895
Stage I	12(0.12%)	7(0.07%)	19(19%)	
Stage II	17(0.17%)	11(0.11%)	28(28%)	
Stage III	23(0.23%)	14(0.14%)	37(37%)	
Stage IV	8(0.08%)	6(0.06%)	14(14%)	
T stage				
T1	5(0.05%)	3(0.03%)	8(8%)	0.75
T2	8(0.08%)	8(0.08%)	16(16%)	
T3	40(0.4%)	23(0.23%)	63(63%)	
T4	7(0.07%)	6(0.06%)	13(13%)	
N stage				
N0	34(0.34%)	20(0.2%)	54(54%)	0.5896
N1	16(0.16%)	10(0.1%)	26(26%)	
N2	10(0.1%)	10(0.1%)	20(20%)	
M stage				
M0	51(0.51%)	33(0.33%)	84(84%)	0.783
M1	9(0.09%)	7(0.07%)	16(16%)	
Lymphatic invasion				
Absent	39(0.39%)	20(0.2%)	59(59%)	0.1352
Present	21(0.21%)	20(0.2%)	41(41%)	
Venous invasion				
Absent	55(0.55%)	34(0.34%)	89(89%)	0.055
Present	5(0.05%)	6(0.06%)	11(11%)	
Perineural invasion				
Absent	53(0.53%)	29(0.29%)	82(82%)	0.296
Present	7(0.07%)	11(0.11%)	18(18%)	
Differentiation				
Well/Moderate	65(0.65%)	35(0.35%)	100(100%)	0.232
Poor	4(0.04%)	5(0.05%)	9(9%)	

	Negative	Positive	Total	p-value
	N=60	N=40	N=100	
Histology				
Non-mucinous adenocarcinoma	57(0.57%)	4(0.04%)	61(61%)	<0.0001
Mucinous adenocarcinoma	3(0.03%)	36(0.36%)	39(39%)	
Recur				
Recur	51(0.51%)	33(0.33%)	84(84%)	0.143
Non-recur	9(0.09%)	7(0.07%)	16(16%)	
Expire				
Expire	54(0.54%)	35(0.35%)	89(89%)	0.219
Non-Expire	6(0.06%)	5(0.05%)	11(11%)	
Neoadjuvant Tx				
No	60(0.6%)	26(0.26%)	86(86%)	0.217
CTx	31(0.31%)	10(0.1%)	41(41%)	
RT	2(0.02%)	0(0%)	2(2%)	
CCRT	53(0.53%)	4(0.04%)	57(57%)	

The gender distribution of patients with KRAS-negative and KRAS-positive disease was not significantly different, according to the researchers. The distribution of ages between the two groups did not significantly differ from one another either. However, compared to the colon (30%) or the rectum (20%), the left colon (43%) of KRAS-negative patients has a higher likelihood of developing tumors. KRAS-positive patients have a similar distribution of tumors. tumor cells. While KRAS-positive patients have an equal number of tumors, KRAS-negative patients are more likely to develop tumors in the left colon (43 percent), colon (30 percent), or rectum (20 percent). tumors within. There was no discernible difference between patients with KRAS-negative and KRAS-positive tumors in terms of stage, T, N, or M. Similarly, there was no discernible difference in lymphovascular infiltration between the two groups, whereas KRAS-positive people had more venous and perineural infiltration. KRAS-negative patients were more likely to develop **mucinous** adenocarcinoma (57%) than mucinous adenocarcinoma (3%), while KRAS-positive patients showed the opposite (36% mucinous adenocarcinoma and 4% non-mucinous adenocarcinoma). There was a significant difference between the two groups in terms of histology **(p<0.0001).**There was no significant difference in recurrence or survival between KRAS negative and KRAS positive patients. The authors also looked at neoadjuvant therapy and **found** no difference between the two groups.

Table 2: Frequency of Mutations in KRAS exon2

KRAS codon 12		
c.34G>A	Gly12Ser	6
c.34G>C	Gly12Arg	2
c.34G>T	Gly12Cys	21
c.35G>A	Gly12Asp	48
c.35G>T	Gly12Asp	1
c.35G>T	Gly12Val	48
c.38G>A	Gly12Asp	5
c.35G>C	Gly12Ala	11
KRAS codon13		
c.35G>A	Gly13Asp	1
c.38G>A	Gly13Asp	59
c.37G>T	Gly13Cys	2
c.36G>T	Gly13Val	2
c.38_39GC>TT	Gly13Val	1
KRAS codon14		
c.40G>A	Val14lle	1
KRAS codon30		
c.90C>T	Asp30Asp	1

The master regulator of cell growth and division is the KRAS gene. Numerous cancers, including colon cancer, have been linked to mutations in the KRAS gene. In this investigation, scientists aimed to comprehend the prevalence of KRAS exon 2 mutations as well as the clinical alterations brought on by KRAS mutations. mutations of. The table lists the KRAS exon 2 codons 12, 13, and 14. The most frequent modification is c. In 48 patients, there was 35G>A Gly12Asp. This well-known mutation has been linked to both gastric cancer and a subpar response to EGFR therapy. C was yet another mutation. 59 instances of 38G>A Gly13Asp were found. Anti-EGFR resistance and this mutation have both been linked to colon cancer. Additionally, the frequency of additional mutations at codons 12, 13, 14, and 30 is shown in the table. some mutations, like c. A Gly12Ser and c are in the formula 34G>. In two cases (6 and 11), 35G>C Gly12Ala were discovered. The results of this study may aid physicians in treating colon cancer patients. Some KRAS mutations can influence treatment options because they are linked to drug resistance in some cases. Additionally, knowing the mutation count could help with the creation of fresh medications that target KRAS mutations.

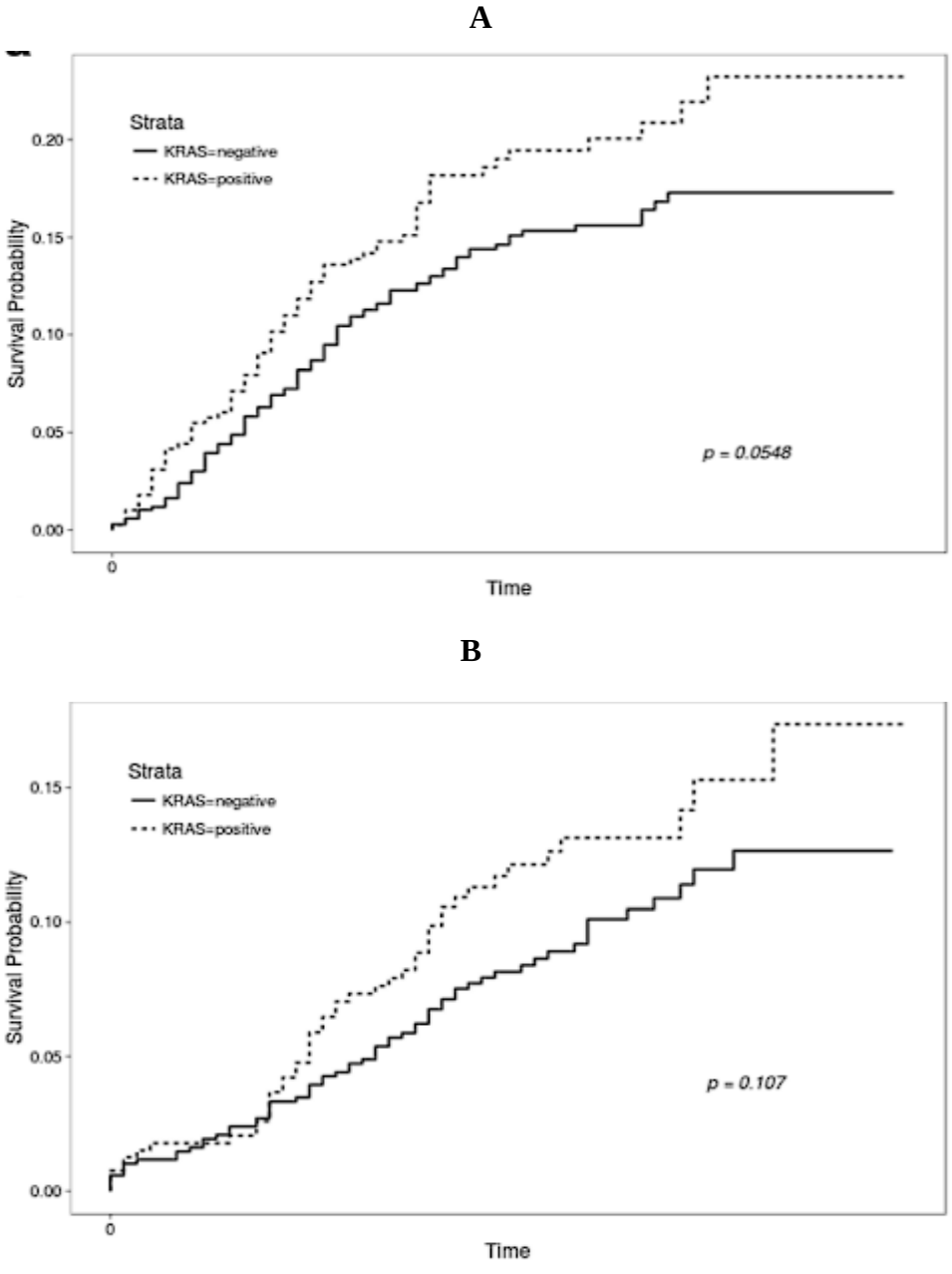

Figure 1: Kaplan-Meier curves for disease-free survival and overall survival according to KRAS mutation status. a Disease-free survival (DFS) according to KRAS status, b Overall survival (OS) according to KRAS status

Table 3 : Clinicopathologic characteristics according to MSI status

	Negative	Positive	Total	p-value
	N=70	N=10	N=80	
Sex				
Male	44(62.86%)	2(20%)	46(46%)	0.0103
Female	26(37.14%)	8(80%)	34(34%)	
Age				
<50year	13(18.57%)	0(0%)	13(13%)	0.1365
≥ 50year	57(81.43%)	10(100%)	67(67%)	
Location				
Rt colon	18(25.71%)	4(40%)	22(22%)	0.4238
Lt colon	32(45.71%)	2(20%)	34(34%)	
Rectum	13(18.57%)	2(20%)	15(15%)	
Multiple	7(10%)	2(20%)	9(9%)	
Stage				
Stage I	14(20%)	2(20%)	16(16%)	0.4671
Stage II	27(38.57%)	2(20%)	29(29%)	
Stage III	29(41.43%)	6(60%)	35(35%)	
T stage				
T1	9(12.86%)	2(20%)	11(11%)	0.9341
T2	13(18.57%)	2(20%)	15(15%)	
T3	32(45.71%)	4(40%)	36(36%)	
T4	16(22.86%)	2(20%)	18(18%)	
N stage				
N0	41(58.57%)	4(40%)	45(45%)	0.3999
N1	15(21.43%)	2(20%)	17(17%)	
N2	15(21.43%)	4(40%)	19(19%)	
Lymphatic invasion				
Absent	46(65.71%)	5(50%)	51(51%)	0.967
Present	24(34.29%)	5(50%)	29(29%)	
Venous invasion				
Absent	58(82.86%)	6(60%)	64(64%)	0.091
Present	12(17.14%)	4(40%)	16(16%)	
Perineural invasion				
Absent	53(75.71%)	5(50%)	58(58%)	0.0885
Present	17(24.29%)	5(50%)	22(22%)	
Differentiation				
Well	13(18.57%)	0(0%)	13(13%)	0.232
Moderate	56(80%)	6(60%)	62(62%)	
Poor	1(1.43%)	4(40%)	5(5%)	
Histology				
Non-mucinous adenocarcinoma	62(88.57%)	3(30%)	65(65%)	<0.0001
Mucinous adenocarcinoma	8(11.43%)	7(70%)	15(15%)	
Recur				
Recur	64(91.43%)	0(0%)	64(64%)	<0.0001
Non-recur	6(8.57%)	10(100%)	16(16%)	
Expire				
Expire	66(94.29%)	6(60%)	72(72%)	0.0007
Non-Expire	4(5.71%)	4(40%)	8(8%)	
KRAS status				
Wild type	44(62.86%)	6(60%)	50(50%)	0.8614
Mutation	26(37.14%)	4(40%)	30(30%)	

Colon cancer (CRC) is a complicated condition with a wide range of molecular and clinical characteristics. One of the characteristics of CRC is microsatellite instability (MSI), which arises from abnormalities in the DNA mismatch repair process. In this study, MSI status was compared to the clinical characteristics of CRC. The results showed that 70 (87%) of the 80 patients had MSI-positive CRC, while 10 (12.5%) did not. 5% of CRCs were MSI-negative. The percentage of women in the MSI positive group (80%) was higher than the MSI negative group (37.14%), with a p value of 0.0103 for both groups. On the other hand, there is no age distinction between the two groups. The majority of the patients in both groups in both groups had tumors in the left colon, with 32 (45.171%) MSI negative patients and 2 (20%) MSI positive patients. With 18 (25.171%) MSI negative patients and 4 (40%) MSI positive patients in both groups, the colon was the second tumor site. Nevertheless, there was no statistically significant difference in tumor location between the two groups (p-value =0.4238). Between MSI negative and MSI positive groups, there was no discernible difference in tumor stage (p value = 0.4671), T stage (p value = 0.9341), or N stage (p value = 0.3999). With a p value of 0.035, the proportion of stage III tumors in the MSI-positive group (60%) was higher than that in the MSI-negative group (41.43%) though. There was a significant difference in the two groups' histology, with only 3 (30%) MSI-positive patients with non-mucinous adenocarcinoma and 62 (88.57%) MSI-negative patients with the disease-value 0). 0001). In contrast, only 8 (11-point 43 percent) of the MSI-negative patients had mucinous adenocarcinoma, compared to 7 (70 percent) of the MSI-positive patients. Additionally, recurrence and mortality between the two groups were significantly different according to the results. All 10 MSI-positive patients were still alive and no one had relapsed at the time the data were collected (Fig. 91). 43 percent of the MSI-negative patients experienced a relapse, and 66 (94.29 percent) passed away (p values 0.0001 and 0.0007, respectively). The KRAS status was not linked to the MSI status (p-value = 0). 30 patients (30%), including 8614, 4 (40%) MSI-positive patients, and 26 (37.714%) MSI-negative patients, carried KRAS mutations.

DISCUSSION:

One of the most prevalent and fatal cancers in the world is colon cancer. KRAS is a crucial molecular marker in the development of cancer. Thirty to fifty percent of colon cancer patients have mutations in the KRAS gene, which is linked to a poor prognosis and therapy resistance. For the creation of individualized treatments and surveillance, it is crucial to comprehend the clinical characteristics of colon cancer patients with KRAS mutations. A recent study looks at how colon cancer patients are treated based on KRAS mutations. In the study, 100 colon cancer patients were enrolled, of whom 60 had KRAS mutations that were negative and 40 had KRAS mutations that were positive. Comparing the clinicopathological characteristics of the two patient groups. The outcome of. Studies found no discernible difference between the two groups (p=0.239). However, there are large gender differences among MSI patients. (19). The study found that only 20% of MSI-positive patients were male, compared to 62.86% of MSI-negative patients (p = 0.0103). This choice is supported by prior research that demonstrates women are more likely to develop tumors with high MSI scores. (20). The results of this study revealed that patients with positive KRAS mutations were larger than those with negative KRAS mutations (p=0). 023). This result is in line with earlier research, which discovered that patients with advanced colon cancer had a higher prevalence of KRAS mutations. (21). Additionally, the study examined the location of the tumor and discovered no distinction between the two groups (p=0.4238). The histology of tumors varies widely, though. Patients with positive KRAS mutations were more likely than those with negative KRAS mutations to develop mucinous adenocarcinoma (p. 0.0001). This result supports previous studies that found a higher incidence of mucinous adenocarcinoma in KRAS-mutant tumors. (22). Finally, based on KRAS mutations, researchers looked into the survival and recurrence of colon cancer patients. In contrast to those who had negative KRAS mutations, patients with positive KRAS mutations had a higher risk of relapse and death (p. p<0.01).0001 and p = 0.0007). This finding is consistent with previous research linking KRAS mutations to poor prognosis in colon cancer patients. (23). Another important finding is the relationship between KRAS mutations and recurrence and survival. According to clinical research, Four percent of patients with a negative KRAS mutation relapsed, but none of those with a positive KRAS mutation relapsed (p<0.0001). Similarly, patients with negative KRAS mutations had a higher mortality rate; 94.3% of patients with positive KRAS mutations died compared to only 60% (p = 0.0007).(24). These results support earlier research that linked KRAS mutations to a worse prognosis for colon cancer patients. People with KRAS mutations had a lower survival rate than the general population, according to a meta-analysis that was published in Cancer Medicine in 2019 after reviewing 30 studies. KRAS mutations were also linked to tumor size, differentiation, and lymph node metastasis, according to the researchers. (25). The recurrence rate was found to be higher in patients with KRAS mutations in a different study that was examined 298 patients with

gastric cancer and published in Gastroenterology Research and Practice in 2018. Comparing patients with and without the KRAS mutation, the overall survival was lower. Additionally possible are KRAS mutations. According to the study, poor differentiation is linked to more cancer, lymph node metastases, and cancer.

CONCLUSION:

The prognosis of colon cancer patients may be impacted by KRAS mutations. The study found that patients with a positive KRAS mutation had an increased risk of being female, developing adenocarcinoma, relapsing, and passing away.

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