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Clinicopathological Features and Prognostic Factors in Colorectal Cancer

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ABSTRACT

Background: Colorectal Cancer (CRC) remains a major global health burden. This retrospective study aimed to analyze clinicopathological features, treatment outcomes, and prognostic factors in CRC patients.

Methods: Data from 480 CRC patients treated at a tertiary center (2021–2023) were retrospectively analyzed. Patient demographics, tumor characteristics, treatment modalities, and survival data were evaluated. Survival was assessed using Kaplan-Meier method, and prognostic factors were identified via Cox regression.

Results: The median age was 62 years (IQR: 55–70), with 58% male patients. Right-sided CRC (42%) showed more advanced stages (III/IV: 65%) compared to left-sided (52%, p=0.023). Surgical resection improved overall survival (OS) vs. non-surgical treatment (median OS: 62 vs. 28 months, p<0.001). Multivariate analysis identified tumor stage (HR=3.89, 95% CI: 2.71–5.61, p<0.001), lymph node metastasis (HR=2.17, 95% CI: 1.45–3.24, p=0.001), and KRAS mutation (HR=1.68, 95% CI: 1.12–2.52, p=0.013) as independent risk factors.

Conclusion: Right-sided CRC exhibits more aggressive features. Surgical resection and molecular profiling (e.g., KRAS) are critical for prognosis. These findings inform personalized CRC management.

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Introduction

Colorectal Cancer (CRC) is the third most common cancer globally, with an estimated 2.2 million new cases in 2023 [1]. Despite advancements in treatment, prognosis varies widely due to tumor heterogeneity and molecular diversity. Right-sided CRC (RSCRC) and left-sided CRC (LSCRC) exhibit distinct clinicopathological features, with RSCRC often associated with poor prognosis [2]. Molecular markers like KRAS and NRAS mutations influence treatment response to anti-EGFR therapy [3]. However, the interplay between tumor location, molecular profile, and survival in real-world settings remains understudied.

This retrospective study aimed to characterize clinicopathological features, evaluate treatment outcomes, and identify independent prognostic factors in CRC patients, with a focus on tumor laterality and molecular markers.

Materials and Methods

Patient Cohort

Data from 480 CRC patients (pathologically confirmed adenocarcinoma) treated at a tertiary center between January 2021 and December 2023 were analyzed. Exclusion criteria: incomplete clinical data, metastatic disease at diagnosis (stage IV), or prior neoadjuvant therapy. Tumor laterality was defined as right-sided (cecum to transverse colon) vs. left-sided (descending colon to rectum).

Data Collection

Clinical data included age, sex, tumor location, TNM stage (AJCC 8th edition), KRAS/NRAS mutation status, treatment modality (surgical resection vs. non-surgical), and survival outcomes (overall survival, OS). OS was defined as time from diagnosis to death or last follow-up (median follow-up: 36 months).

Statistical Analysis

Categorical variables were compared using chi-square/Fisher's exact tests. Survival analysis used Kaplan-Meier method with log-rank test. Univariate and multivariate Cox proportional hazards models identified independent prognostic factors. All analyses were performed in SPSS 28.0 (IBM), with p<0.05 considered significant.

Results

Baseline Characteristics

The cohort included 280 male (58%) and 200 female (42%) patients, median age 62 years (IQR: 55–70). RSCRC comprised 42% (202/480) and LSCRC 58% (278/480). RSCRC patients had more advanced stages (III/IV: 65% vs. 52%, p=0.023) and higher rates of mucinous histology (18% vs. 10%, p=0.015) (Table 1).

Table 1: Clinicopathological Features by Tumor Laterality

Characteristic	Right-sided (n=202)	Left-sided (n=278)	*p*-value
Median age (years)	63 (56–71)	61 (54–69)	0.12
Male sex (%)	59% (119/202)	58% (161/278)	0.89
TNM stage III/IV (%)	65% (131/202)	52% (145/278)	0.023
Mucinous histology (%)	18% (36/202)	10% (28/278)	0.015
KRAS mutation (%)	45% (91/202)	32% (89/278)	0.003
NRAS mutation (%)	8% (16/202)	5% (14/278)	0.28

Treatment Outcomes

Surgical resection was performed in 75% (360/480) of patients, with higher rates in LSCRC (82%) vs. RSCRC (65%, $p<0.001$). Median OS was significantly longer in resected vs. non-resected patients (62 vs. 28 months, $p<0.001$). Among stage III patients, adjuvant chemotherapy improved OS (median OS: 58 vs. 42 months, $p=0.007$) (Table 2).

Table 2: Survival Outcomes by Treatment Modality

Treatment	n	Median OS (months)	3-year OS (%)	p-value
Surgical resection	360	62	68%	<0.001
- Stage I/II	180	72	79%	–
- Stage III	180	58	61%	–
Non-surgical treatment	120	28	32%	<0.001
- Chemotherapy alone	90	30	35%	0.12
- Best supportive care	30	22	25%	–

Prognostic Factors Analysis

Univariate analysis identified tumor stage (HR=5.21, 95% CI: 3.89–6.98), lymph node metastasis (HR=2.89, 95% CI: 2.01–4.16), KRAS mutation (HR=1.92, 95% CI: 1.35–2.73), and RSCRC (HR=1.65, 95% CI: 1.12–2.43) as risk factors for poor OS. Multivariate analysis confirmed tumor stage (HR=3.89, 95% CI: 2.71–5.61, $p<0.001$), lymph node metastasis (HR=2.17, 95% CI: 1.45–3.24, $p=0.001$), and KRAS mutation (HR=1.68, 95% CI: 1.12–2.52, $p=0.013$) as independent predictors (Table 3).

Table 3: Univariate and Multivariate Cox Regression for OS

Variable	Univariate HR (95% CI)	*p*-value	Multivariate HR (95% CI)	*p*-value
Tumor stage (III vs. I/II)	5.21 (3.89–6.98)	<0.001	3.89 (2.71–5.61)	<0.001
Lymph node metastasis (+)	2.89 (2.01–4.16)	<0.001	2.17 (1.45–3.24)	0.001
KRAS mutation (+)	1.92 (1.35–2.73)	0.001	1.68 (1.12–2.52)	0.013
RSCRC (+)	1.65 (1.12–2.43)	0.013	1.32 (0.89–1.96)	0.16
Age (>65 years)	1.28 (0.95–1.73)	0.11	–	–

Discussion

This retrospective analysis of 480 CRC patients highlights key findings: RSCRC was associated with advanced stages, mucinous histology, and higher KRAS mutation rates, consistent with prior studies [2,4]. These features may explain poorer outcomes in RSCRC, as mucinous tumors are often chemoresistant and KRAS mutations predict resistance to anti-EGFR therapy [3]. Surgical resection significantly improved OS, underscoring its role as curative intent therapy. However, RSCRC had lower resection rates, possibly due to more advanced presentation or technical challenges, leading to worse survival [5]. Tumor stage and lymph node metastasis were strong predictors, aligning with AJCC guidelines. KRAS mutation emerged as an independent risk factor, consistent with its role in oncogenic signaling and immune evasion [6]. Notably, RSCRC lost significance in multivariate analysis, suggesting its impact is mediated by stage and molecular features. Single-center design, potential selection bias in treatment allocation, and lack of data on newer therapies (e.g., immunotherapy). Routine molecular profiling (e.g., KRAS/NRAS) and aggressive surgical approaches for resectable tumors are critical. Future studies should explore immunotherapy responses in KRAS-mutant CRC and address disparities in RSCRC management. Tumor laterality, stage, and KRAS status influence CRC prognosis. Surgical resection remains pivotal, while molecular testing guides targeted therapy. These findings support personalized treatment strategies to improve outcomes in CRC [7-8].

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