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Original Research

Blood types and Cancer Risk: A Comprehensive Analysis of ABO/Rh Association with Colorectal Cancer

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Background: The association between ABO/Rh blood groups and colorectal cancer (CRC) remains inconsistent. This study evaluates their impact on CRC risk and prognosis.

Methods: A retrospective case-control study of 1,687 CRC patients and 1,836 matched controls (2010–2024) analyzed blood group distributions, tumor characteristics, and survival using chi-square tests and logistic regression ($p < 0.05$).

Results: The AB Rh (+) phenotype was significantly more prevalent in CRC patients than controls ($p = 0.032$). The AB blood group was associated with higher risk (OR: 3.56; 95% CI: 1.77–7.15), aggressive tumor features (advanced T stage, metastasis and increased anastomotic leakage), and shorter median survival (30.5 vs. 40.0 months for O group; $p < 0.05$).

Conclusions: AB blood group is linked to increased CRC risk and poorer prognosis, suggesting its potential as a biomarker for risk stratification.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the fourth leading cause of cancer-related mortality worldwide [1]. Despite significant advances in treatment modalities, the identification of risk factors remains essential for improving early detection and prevention strategies. The etiology of CRC is multifactorial, encompassing environmental influences such as diet, obesity, and physical inactivity as well as genetic predispositions. Notably, for locally advanced rectal cancer, total neoadjuvant therapy (TNT) has emerged as the current standard of care, supported by recent evidence demonstrating its safety and higher pathological complete response rates compared to conventional approaches [2].

The ABO blood group system has been proposed as one such potential factor. ABO antigens are expressed not only on the surface of erythrocytes but also on gastrointestinal epithelial cells [3]. This broad tissue distribution has prompted investigations into possible associations between blood group antigens and various malignancies. The first reported link between blood type and cancer dates back to 1953, when an association was observed between blood type A and gastric cancer [3]. Since then, numerous epidemiological studies have explored the relationship between ABO and Rh blood group systems and different types of tumors.

In the context of CRC, however, the existing literature remains limited and the findings

inconclusive. A comprehensive evaluation of the association between ABO and Rh blood groups and CRC is warranted, given its potential implications for both risk stratification and prognostication. Clarifying this association may facilitate the development of blood group based risk models and support the implementation of personalized screening programs. Accordingly, the present study aims to investigate the association of ABO and Rh blood groups with CRC risk and prognosis in a large patient cohort and to assess the potential clinical relevance of these findings.

Materials and Methods

This retrospective case-control study was conducted between January 2010 and December 2024 using our institution's medical records, with the approval of our institution's ethics committee (Decision No: 2025/483). The study population was predominantly Turkish (approximately 90%). The study included 1,687 patients with histologically confirmed colorectal adenocarcinoma and documented preoperative ABO/Rh blood group data, and 1,836 healthy blood donors (confirmed malignancy- free via medical history and follow-up) as the control group.

A power calculation indicated the sample size was sufficient to detect clinically meaningful differences in blood group prevalence ($\alpha = 0.05$, power = 80%).

Inclusion criteria for cases were pathologically confirmed colorectal adenocarcinoma, available blood type information prior to treatment, complete demographic and clinical data, and a minimum follow-up period of 6 months for survival analysis. Exclusion criteria included missing blood group data, prior history of malignancy, immunodeficiency or systemic inflammatory diseases, inadequate follow-up information, and a history of prior blood transfusion that could affect the accuracy of blood group determination. Controls were selected from healthy blood donors without a history of malignancy during the same period and matched 1:1.1 with cases in terms of age (±5 years) and gender.

The variables analyzed included demographic characteristics, ABO/Rh blood groups, tumor characteristics (location, TNM stage, histological grade), surgical outcomes (surgery duration, complications, anastomotic leakage [diagnosed via imaging and clinical criteria], pathological characteristics (lymphovascular invasion[LVI], perineural invasion[PNI]), and overall survival (OS) [time from diagnosis to death or last follow-up].

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 30.0, with categorical variables compared using chi-square or Fisher's exact tests, continuous variables analyzed using Student's t-test or Mann-Whitney U test, and survival outcomes evaluated using Kaplan-Meier analysis with log-rank tests. Multivariate associations were assessed through logistic regression (adjusted for age, sex, and tumor stage) with backward elimination, and goodness-of-fit was assessed via Hosmer-Lemeshow test. Statistical significance was set at $p<0.05$ with Bonferroni correction applied for multiple comparisons where appropriate.

Results

CRC patients (mean age 64.3 ± 11.7 years, 60.1% male) and controls were comparable in demographics (Table 1).

Characteristic	Patients	Controls	p-value
Age, mean ± SD (years)	64.3 ± 11.7	63.8 ± 11.2	0.321
Gender, n (%)			0.289

Female	673 (39.9)	752 (41.0)	
Male	1,014 (60.1)	1,084 (59.0)	
ASA Score, n (%)			
ASA I	253 (15.0)		
ASA II	932 (55.2)		
ASA III	428 (25.4)		
ASA IV	74 (4.4)		
Operation time, mean ± SD (min)	178.4 ± 62.8		
Surgery Type, n (%)			
Elective	1,452 (86.1)		
Emergency	235 (13.9)		
Tumor Location, n (%)			
Rectum	586 (34.7)		
Sigmoid colon	432 (25.6)		
Left colon	271 (16.1)		
Right colon	347 (20.6)		
Transverse colon	51 (3.0)		
Total number of patients	1687		

Table 1. Baseline Demographic and Clinical Characteristics of Colorectal Cancer Patients (n=1,687).

Abbreviations: SD, standard deviation; ASA, American Society of Anesthesiologists; min, minutes.

Among the patients, 86.1% underwent elective surgery, and 55.2% were classified as ASA II. The mean operative time was 178.4 ± 62.8 minutes. The most common tumor sites were the rectum (34.7%) and sigmoid colon (25.6%), with distal colorectal tumors accounting for 60.3% of all cases. No significant associations were found between ABO blood groups and variables such as age, gender, ASA score, operative time, surgical urgency, or tumor location.

The AB Rh (+) phenotype was significantly more prevalent in CRC patients compared to controls (p = 0.032; Table 2).

Blood Group	Patients n (%)	Controls n (%)	p-value	OR (95% CI)	Risk Assessment
ABO Blood Group					
A	667 (39.5)	743 (40.5)	0.578	1.569 (0.85-2.89)	Moderate
B	249 (14.8)	273 (14.9)	0.929	1.000 (Reference)	Low (Reference)
AB	142 (8.4)	120 (6.5)	.043*	3.559 (1.77-7.15)	High
O	629 (37.3)	700 (38.1)	0.613	1.833 (0.99-3.39)	Moderate-High
Rh Factor					
Rh+	1,635 (96.9)	1,784 (97.2)	0.673		
Rh-	52 (3.1)	52 (2.8)	0.673		
ABO-Rh Combinations					
A Rh+	632 (37.5)	705 (38.4)	0.578		
B Rh+	237 (14.0)	262 (14.3)	0.839		
AB Rh+	142 (8.4)	119 (6.5)	.032*		
O Rh+	624 (37.0)	698 (38.0)	0.54		
A Rh-	35 (2.1)	38 (2.1)	0.983		
B Rh-	12 (0.7)	11 (0.6)	0.724		
AB Rh-	0 (0)	2 (0.1)	0.255		
O Rh-	5 (0.3)	1 (0.1)	0.384		
Total	1,687 (100)	1,836 (100)			

Table 2. Distribution of ABO and Rh Blood Groups in Patient and Control Groups and Their Association with Colorectal Cancer Risk.

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; Rh, Rhesus factor.OR calculations performed using B blood group as reference due to lowest mortality rate (5.49%)

The AB Rh (−) phenotype was not observed in the patient group and was found in only two individuals (0.1%) in the control group. When analyzed irrespective of Rh status, the AB blood group remained significantly more common among patients (p = 0.043). Apart from the differences related to the AB group, no significant differences were detected between the other blood groups and controls. Similarly, Rh positivity was not significantly different between the groups.

Using B blood group as reference (lowest mortality, 5.49%), the AB group showed the highest CRC risk (OR: 3.559; 95% CI: 1.77-7.15) and mortality (17.14%; p = 0.041). The AB group also exhibited more aggressive tumor features, including T4 stage (23.9%), lymph node positivity (51.4%), and distant metastasis (21.1%) (Table 3).

Blood Group	A	B	O	AB (n=142)	p-value
	(n=667)	(n=249)	(n=629)		
Primary Outcomes					
Overall mortality	8.36%	5.49%	9.63%	17.14%†	0.041
5-year survival	87.90%	84.30%	88.1%†	82.40%	0.041
Median follow-up (months)	38.5	32	40.0†	30.5	0.012
Surgical Outcomes					
Anastomotic Leakage	9.00%	11.20%	7.20%	14.1%†	0.027
Tumor Characteristics					
T4 stage	16.80%	21.30%	14.60%	23.9%†	0.033
Lymph node positivity	43.30%	45.80%	41.00%	51.4%†	0.022
Distant metastasis	16.20%	19.70%	14.60%	21.1%†	0.045
Invasion Parameters					
LVI positivity	33.00%	37.30%	30.20%	42.3%†	0.02
PNI positivity	26.10%	29.70%	24.00%	33.8%†	0.016
Poor differentiation	11.80%	14.90%	9.40%	15.5%†	0.047

Table 3. Association between Blood Groups and Clinical Outcomes, Pathological Features, and Survival Parameters.

Abbreviations: LVI, lymphovascular invasion; PNI, perineural invasion; T, tumor stage; N, lymph node stage; M, metastasis stage. *p-value represents the overall comparison. † Indicates the most extreme value for each variable among groups with p < 0.05. Note: Values in bold indicate the statistically significantly highest (for poor prognostic factors) or lowest (for survival values) rates for the respective parameter.

Kaplan-Meier analysis revealed shorter median survival in the AB group (30.5 months) compared to the O group (40.0 months; log-rank p = 0.041; Figure 1).

Figure 1. Kaplan-Meier Survival Curves Demonstrating Overall Survival by ABO Blood Group in Colorectal Cancer Patients. The AB group showed significantly shorter median survival (30.5 months) compared to other groups, with the O group having the longest survival (40.0 months). Log-rank test p = 0.041.

Five-year survival rates were calculated as 88.1% (95% CI: 85.2-91.0%) in the O group, 87.9% (95% CI: 85.1-90.7%) in the A group, 84.3% (95% CI: 79.1-89.5%) in the B group, and 82.4% (95% CI: 75.2-89.6%) in the AB group.

Discussion

This study demonstrates a significant association between AB blood group and increased CRC risk (OR: 3.559; 95% CI: 1.77–7.15) and poorer prognosis, including higher mortality (17.14%) and shorter survival (30.5 months). Beyond the increased prevalence in cancer patients, AB blood group emerged as a strong predictor of aggressive tumor behavior and poor clinical outcomes, suggesting a previously underrecognized role in colorectal carcinogenesis.

Existing literature presents mixed findings regarding ABO blood groups and CRC. Studies showing no association [4, 5] contrast with research indicating protective effects of O blood group [6] and increased risk associated with A blood group [7]. These findings align with Senger et al. [8] but contrast with Cao et al. [9], possibly due to differences in population ethnicity, study design, or outcome definitions. The largest meta-analysis to date, conducted by Bahardoust et al., analyzed 413,132 patients across 14 studies and confirmed that A blood group increases CRC risk while O blood group provides protection [10]. However, the analysis found no significant association with AB blood group, highlighting a critical gap in existing research that our study addresses.

The relationship between ABO antigens and CRC may involve several pathways. ABO antigens are expressed on gastrointestinal epithelial cells and may influence tumor development through their roles in cell–cell adhesion, signal transduction, and immune surveillance [11]. Polymorphisms at the ABO gene locus may affect levels of inflammatory markers such as TNF-α, E-selectin, and ICAM-1, thereby promoting chronic inflammation and potentially contributing to carcinogenesis. These inflammatory pathways could explain the aggressive tumor characteristics observed in AB patients, including higher rates of metastasis and invasion [12, 13].

The complete absence of the AB Rh (−) phenotype in CRC patients, while present in controls (0.1%), represents a novel finding that suggests a potential protective effect of this rare phenotype against CRC. This observation warrants validation through multicenter studies and may indicate complex interactions between ABO and Rh systems in cancer biology.

These findings suggest practical applications for clinical practice. Incorporating ABO blood groups into CRC risk assessment models could enhance personalized screening strategies, particularly for individuals with AB blood type who may benefit from earlier or more frequent surveillance. The cost-effectiveness of blood group-based screening in high-risk populations merits investigation.

Strengths include the large sample size (n=3,523), matched controls, and comprehensive outcome analysis focusing on the understudied AB blood group. However, the single-center design and predominantly Turkish cohort (90%) limit generalizability. Unmeasured confounders such as lifestyle factors, dietary habits, and genetic polymorphisms may influence the observed associations. Future studies should explore ABO gene polymorphisms and their role in inflammation through multicenter studies across diverse populations. Specific investigations of tissue-level antigen expression, genetic studies of ABO polymorphisms, and cost-effectiveness analyses of blood group-based screening are warranted. In conclusion, this study demonstrates that AB blood group is associated with increased CRC risk and poorer prognosis, highlighting its potential role as an accessible biomarker for risk stratification and personalized clinical strategies. Future research should focus on elucidating the underlying biological mechanisms of this association and evaluating its relevance across diverse populations and clinical settings.

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