

## RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND COLORECTAL CANCER

IRENA MIHIĆ LASAN, MARIJA SKOKO, JELENA CULEJ, TIHA VUČEMILO and DEANA ŠTURM

“Sestre milosrdnice” University Hospital Center, University Hospital for Tumors, Zagreb, Croatia

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### Summary

The distribution of the ABO blood group system (A, B, O or AB) and Rhesus type (Rh-positive or Rh-negative Rh+ or Rh-) was studied retrospectively in 981 patients with colorectal cancer. The distribution of ABO and Rh blood groups among the observed patients was similar to the distribution among the normal population in Croatia. No specific relationship has been established between the blood group type and colorectal cancer. There were significant differences in the proportions of the various ABO blood groups in Rh-positive and Rh-negative patients (chi-square = 15.18;  $p = 0.0017$ ), with the A/O ratio of 1.15 and 0.75 in Rh-positive and Rh-negative patients, respectively. Further analysis confirmed that these significant differences were due to the O Rh-negative blood group. No significant difference could be found in the ABO distributions with regard to tumor stage.

KEYWORDS: *ABO blood group, Rhesus type, colorectal cancer, tumor stage*

### POJAVNOST KOLOREKTALNOG KARCINOMA I ABO SUSTAV KRVNIH GRUPA

#### Sažetak

U ovoj studiji retrospektivno je proučavana raširenost ABO i Rh krvnih grupa u 981 bolesnika oboljelih od kolorektalnog karcinoma. Raširenost ABO i Rh krvnih grupa u bolesnika bila je slična raširenosti krvnih grupa u zdravoj populaciji u Hrvatskoj. Nije utvrđena posebna povezanost između krvnih grupa i kolorektalnog karcinoma. Značajne razlike pronađene su u udjelima različitih ABO krvnih skupina u Rh-pozitivnih i Rh-negativnih bolesnika (hi-kvadrat = 15,18,  $p = 0,0017$ ) s A/O omjerom 1,15 u Rh+ i 0,75 u Rh- bolesnika. Daljnja analiza potvrdila je da je uzrok značajnim razlikama O Rh-negativna krvna grupa. Nije se mogla utvrditi povezanost između krvnih grupa i stadija bolesti.

KLJUČNE RIJEČI: *ABO krvna grupa, Rhesus tip, kolorektalni karcinom, stadij bolesti*

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### INTRODUCTION

Numerous studies have been carried out in order to support correlation between risk factors and colorectal cancer. In 1953, Aird et al. (1) reported an excess of blood group A patients among those with cancer of the stomach. Since then, some authors have questioned the relationship between blood groups and cancer risk (2, 3). Colorectal cancer remains one of the leading causes of cancer-related morbidity and mortality in all parts of the Western world (4). In Croatia, colorectal cancer is the second leading cause of death related

with cancer for both sexes. The incidence in male patients was 75.4, while in female patients it was 52.9 per 100000 population (5). In the current study, the distribution of the ABO blood groups and Rh types was studied retrospectively in 981 patients with colorectal cancer, with special attention to the tumor site and stage of the disease.

### MATERIALS AND METHODS

The charts of all patients diagnosed with adenocarcinoma of the colorectum and treated at the

'Sestre milosrdnice' University Hospital Center, University Hospital for Tumors, Zagreb, Croatia (operated patients, patients undergoing chemotherapy or radiotherapy) between January 2006 and May 2012 were reviewed. Patients with polypoid and planocellular carcinoma of the anus were excluded from this study. The main type (A, B, O or AB) of the ABO blood group system and the Rhesus type (Rh + or Rh -) were noted for each patient at the Department of Transfusion Medicine. In the present study, data obtained from the clinical records include ABO blood group, Rhesus type, sex, tumor site and stage of the disease. The tumors were categorized into the following four locations: right colon (cecum + ascending colon), transverse colon (hepatic flexure, transverse colon, splenic flexure), left colon (descending colon + sigmoid) and rectum (rectosigmoid + rectum). The stage of the tumor was classified according to the modified Dukes' staging system: A - limited to the bowel wall; B - extending through all layers of the bowel wall; C - regional lymph node involvement; and D - metastatic spread. The statistical method used to estimate the significance of differences between the ABO group system was a chi-square test. A value of  $p < 0.05$  was considered statistically significant. *It is important to point out that in this study not a random sample of patients, but all of the patients recorded at our Department of Transfusion Medicine were analyzed during the study period.*

## RESULTS

The results of this study are presented in five tables: in percentages and the chi-square statistic. The distribution of ABO blood group, Rh type, tumor stage and tumor site are shown in Table 1 for the group of 981 patients. A comparison of male and female patients shows that male patients are represented by a ratio 623/358 or 1.74. No significant differences could be found in tumor site and stage distributions between male and female patients. The overall distribution of ABO and Rh blood groups in the patients was similar to the distribution in the normal population of Croatia. Therefore, A and O are the most common blood group types. The A/O ratio of the patients was 1.1 (375:353).

In both sexes, it is evident that 56% of the patients had a rectal tumor with the A/O ratio 1.01, i.e. evenly spaced blood groups A and O among the patients. Also, the occurrence rate of stage D in

both sexes was 57%. There were no significant differences in the distribution of the ABO blood groups with regard to tumor sites. In all blood groups the most common localization was the rectum (Table 2), but there were no statistically significant differences between the groups (chi-square = 8.362,  $p = 0.502$ ). According to the chi-square test, no significant differences could be found in the ABO distributions with regard to tumor stage (chi-square = 9.84,  $p = 0.364$ ).

Table 3 shows that, in stage A, the most common blood group is O. *If we look at A/O ratios by the stage of the disease, only in stage A the A/O ratio is significantly lower than in our population (1.1) and amounts to 0.62, which indicates a higher prevalence of the blood group O in the initial stage of the disease. However, with respect to only 6.5% of patients in stage A, we cannot conclude that patients with the blood group O have a better prognosis.*

Table 4 shows the relationship between ABO and Rh in our 981 patients. There were significant differences in the proportions of the various ABO blood groups in Rh+ and Rh- patients (chi-square = 15.18;  $p = 0.0017$ ), with the A/O ratios of 1.15

Table 1.

ABO BLOOD GROUP, RH TYPE, TUMOR STAGE AND SITE OF THE DISEASE IN 981 PATIENTS WITH COLORECTAL ADENOCARCINOMAS

	Men n=623	Women n=358	All n=981
ABO blood groups			
Group A	233(37)*	142(40)	375(38)
Group B	133(21)	55(15)	188(19)
Group O	215(35)	138(39)	353(36)
Group AB	42(7)	23(6)	65(7)
Rhesus type			
Rh+	515(83)	301(84)	816(83)
Rh-	108(17)	57(16)	165(17)
Tumor stage			
Stage A	41(7)	23(6)	64(7)
Stage B	119(19)	75(21)	194(20)
Stage C	98(16)	61(17)	159(16)
Stage D	365(59)	199(56)	564(57)
Tumor site			
Right colon	73(12)	51(14)	124(13)
Transverse colon	48(8)	33(9)	81(8)
Left colon	141(23)	88(25)	229(23)
Rectum	361(58)	186(52)	547(56)
Total	623	358	981

\* Figures in parentheses refer to column-wise percentages

Table 2.

ABO BLOOD GROUPS BY TUMOR SITE IN 981 PATIENTS WITH COLORECTAL CANCER

	Tumor site		
	Right colon	Transverse colon	Left colon Rectum
ABO blood groups			
Group A	47(38)*	27(33)	96(42) 205(37)
Group B	27(22)	15(19)	41(18) 105(19)
Group O	37(30)	35(43)	78(34) 203(37)
Group AB	13(10)	4(5)	14(6) 34(6)
Total	124	81	229 547

\* Figures in parentheses refer to column-wise percentages

Table 3.

ABO BLOOD GROUPS BY TUMOR STAGE IN 981 PATIENTS WITH COLORECTAL ADENOCARCINOMAS

	Tumor stage		
	A	B	C D
ABO blood groups			
Group A	18(28)*	71(37)	68(43) 218(39)
Group B	12(19)	43(22)	28(18) 105(19)
Group O	29(45)	62(32)	53(33) 209(37)
Group AB	5(8)	18(9)	10(6) 32(6)
Total	64	194	159 564

\* Figures in parentheses refer to column-wise percentages

Table 4.

ABO BLOOD GROUPS BY RHESUS TYPE IN 981 PATIENTS WITH COLORECTAL ADENOCARCINOMAS

	Rhesus type	
	Rh-	Rh+
ABO blood groups		
Group A	59(36)*	316(39)
Group B	19(12)	169(21)
Group O	79(48)	274(34)
Group AB	8(8)	57(7)
Total	165	816

\* Figures in parentheses refer to column-wise percentages

Table 5.

TUMOR SITES BY RHESUS TYPE IN 981 PATIENTS WITH COLORECTAL ADENOCARCINOMAS

Tumor site	Rhesus type	
	Rh -	Rh +
Right colon	M 16(22)* F 8(16)	M 57(78) F 43(84)
Transverse colon	M 8(17) F 8(24)	M 40(83) F 25(76)
Left colon	M 22(16) F 13(15)	M 119(84) F 75(85)
Rectum	M 62(17) F 28(15)	M 299(83) F 158(85)
Total	165	816

\* Figures in parentheses refer to row-wise percentages in men (M) and women (F)

and 0.75 in Rh+ and Rh- patients, respectively. Further analysis confirmed that those significant differences were due to the O blood group and Rh-. Comparing the ratios of rectal cancer occurrence in male and female patients, with regard to the Rh type, a higher occurrence of rectal cancer in Rh- compared to Rh+ males (2.33 – 1.89) is visible (Table 5).

## DISCUSSION

The results of the present study are in agreement with earlier observations in which the risk of colorectal cancer has repeatedly been found to be independent of the ABO blood groups (6, 7). The total distribution of the ABO and Rh blood groups in the study patients was similar as in the normal population in Croatia. In our study, we found that 56% of patients had a rectal tumor with the A/O ratio of 1.01, i.e. evenly spaced blood groups A and O among patients. For rectal cancer, however, women and men had the same A/O ratio (1.01). Comparing the ratios of occurrence of rectal cancer in men and women with regard to the Rh type, a higher occurrence of rectal cancer in Rh- than Rh+ is evident in men (2.33-1.89). There were no significant differences in the distribution of ABO blood groups in regard to the tumor sites. On the other hand, some significant differences were found in the proportions of the various ABO blood groups in Rh+ and Rh- patients (chi-square = 15.18; p = 0.0017) with A/O ratios of 1.15 and 0.75 in Rh+ and Rh- patients, respectively. Further analysis confirmed that those significant differences were due to the

O Rh-negative blood group. No relationship between blood groups and colorectal cancer has been well defined so far. Vogel (8) reported an A/O relative incidence of 1.11 in patients with colorectal cancer based on a study of the world's literature. Recently, Halvorsen (9) published a study about blood group and rhesus factor distribution in colorectal cancer in Norway. He found that patients with the Rh-negative type had a more favorable stage distribution. Further, Halvorsen speculated that the Rh-negative status might be associated with improved immunologic defense mechanisms since a previous report had shown that both Rh-negative normal population and melanoma patients had higher natural killer cell activity (10). A recent report by Lee et al. (11) showed that the expression of the blood group antigen A on tumor cells in non-small-cell lung cancer is associated with a favorable prognosis. The authors felt that the loss of the blood group antigen A was a possible marker of tumor progression. The finding by Slater et al. (12) showed that all multiple cancers were found in Rh+ patients. There have been no previous reports of any relationship between these two variables. In two large prospective cohorts, Khalili et al. (13) did not find a consistent association between blood group serotypes and overall risk of colorectal cancer. They did observe a borderline significant association between the blood group B and overall risk of colon cancer. However, there is no clear biological mechanism that would explain the differential association of the group B compared with the group A antigen with cancer. Taken together with the lack of similar associations observed with the blood group AB and overall risk of colon cancer, these findings for the blood group B are likely due to chance. And what is furthermore interesting and shown by Itzkowski (14) in his study - during the progression to malignancy of colonic cancer cells, the blood group antigens A, B, H and Le(b), which are normally expressed only in the proximal colon, can be re-expressed in distal colon cancers or deleted in proximal colon cancers.

## CONCLUSION

Further studies are needed to search even deeper into the relationship between blood group antigens and colorectal cancer.

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*Author's address: Irena Mihić Lasan M.D., 'Sestre milosrdnice' University Hospital Center, University Hospital for Tumors, Zagreb, Ilica 197, Croatia, e-mail: irenalasan@net.hr*