

## RESEARCH ARTICLE

# Association of ABO Blood Group and Risk of Lung Cancer in a Multicenter Study in Turkey

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### Abstract

**Background:** The ABO blood groups and Rh factor may affect the risk of lung cancer. **Materials and Methods:** We analyzed 2,044 lung cancer patients with serologically confirmed ABO/Rh blood group. A group of 3,022,883 healthy blood donors of Turkish Red Crescent was identified as a control group. We compared the distributions of ABO/Rh blood group between them. **Results:** The median age was 62 years (range: 17-90). There was a clear male predominance (84% vs. 16%). Overall distributions of ABO blood groups were significantly different between patients and controls ( $p=0.01$ ). There were also significant differences between patients and controls with respect to Rh positive vs. Rh negative ( $p=0.04$ ) and O vs. non-O ( $p=0.002$ ). There were no statistically significant differences of blood groups with respect to sex, age, or histology. **Conclusions:** In the study population, ABO blood types were associated with the lung cancer. Having non-O blood type and Rh-negative feature increased the risk of lung cancer. However, further prospective studies are necessary to define the mechanisms by which ABO blood type may influence the lung cancer risk.

**Keywords:** ABO blood - group system - lung neoplasms - cancer - risk factors

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### Introduction

Lung cancer is the second most common cancer in both women and men. Although responsible for less than 15% of all cancers, lung cancer is the leading cause of cancer death in the world for both men and women. For the year 2008, about 1.6 million new cases and 1.4 million deaths are estimated worldwide (Jemal et al., 2011). Smoking is the most common risk factor for lung cancer (Dela Cruz et al., 2011). Nonetheless, 10-25% of lung cancer develops in never smokers. Exposure to environmental tobacco smoke, workplace carcinogens, ionizing radiation, and a number of genetic lesions and inherited predisposition are the other suggested potential risk factors for development of the lung cancer (Couraud et al., 2012).

The blood group antigens are actually the first human genetic markers. ABO blood group gene is mapped at the chromosome 9q34, in which the genetic alterations are common (Humphray et al., 2004). The correlation of ABO blood groups with certain disease including infections, vascular, and malignant diseases has been shown (Hakomori, 2001). ABO/Rh blood group was

associated with increased risk of malignancies such as, gastric, pancreatic, ovarian, colorectal and kidney cancer (Wolpin et al., 2009; Edgren et al., 2010; Joh et al., 2012; Poole et al., 2012; Urun et al., 2012). However, the data on the role of ABO blood group and Rh factor in lung cancer is limited and inconsistent (Alvarez-Fernandez and Carretero-Albinana, 1991; Lee et al., 1991; Cerny et al., 1992; Miyake et al., 1992; Gwin et al., 1994; Rice et al., 1995; Graziano et al., 1997; Ulger et al., 2002; Sanchez-Mora et al., 2007; Suadicani et al., 2007; Leon-Atance et al., 2012).

The purpose of this study was to investigate a possible relationship between ABO/Rh blood groups and lung cancer and clinicopathologic features of lung cancer.

### Materials and Methods

All patients who had pathologically confirmed diagnosis of lung cancer between 2000 and 2011 at the involved centers with serologically confirmed ABO/Rh were included in our retrospective reviews of tumor registry records. Volunteer healthy blood donors (ages 18

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**Table 1. ABO Blood Group and Rh Factor by Patient with Lung Cancer and Controls**

		ABO/Rh Blood Group							Total	
		A+	A-	B+	B-	AB+	AB-	O+		O-
Patient	N	784	112	299	55	140	27	539	88	2,044
Group	%	38.40	5.50	14.60	2.70	6.80	1.30	26.40	4.30	100.00
Control	N	1,121,702	154,330	434,143	59,626	200,972	28,582	894,210	129,318	3,022,883
Group	%	37.10	5.10	14.40	2.00	6.60	0.90	29.60	4.30	100.00

\*P=0.016

**Table 2. ABO/Rh Blood Group Distribution**

	Lung cancer n (%)	Control n (%)	p	Odds Ratio
A	896 (43.8)	1,276,032 (42.2)	0.137	1.068
nonA	1,148 (56.2)	1,746,851 (57.8)		(95%CI, 0.979-1.166)
B	354 (17.3)	493,769 (16.3)	0.229	1.073
nonB	1,690 (82.7)	2,529,114 (83.7)		(95%CI, 0.957-1.203)
AB	167 (8.2)	229,554 (7.6)	0.325	1.080
nonAB	1,877 (91.8)	2,793,329 (92.4)		(95% CI, 0.924-1.269)
O	627 (30.7)	1,023,528 (33.9)	0.002	0.864
nonO	1,417 (69.3)	1,999,355 (66.1)		(95%CI, 0.787-0.950)
Rh+	1,762 (86.2)	2,651,027 (87.7)	0.040	0.876
Rh-	282 (13.8)	371,856 (12.3)		(95%CI, 0.773-0.994)

to 65 years old) –similar ancestry with patient's group of Turkish Red Crescent between 2004 and 2011 were identified as a control group.

The relationship of ABO/Rh with clinical features such as age at diagnosis, histological subtype, and sex were evaluated. We compared the distributions of ABO/Rh among 2044 patients and 3,022,883 controls. Among patients, differences between each of aforementioned ABO/Rh groups with respect to various clinical features were explored, respectively.

This study was approved by the Institutional Review Board of Ankara University School of Medicine and conducted according to Helsinki Declaration and good clinical practice.

Statistical analysis was carried out using the computer program Statistical Package for the Social Sciences 11.5 for Windows (SPSS, Inc, Chicago, IL, USA). Frequency (percent) or median (minimum-maximum) were given as descriptive statistics. Chi-square test was used to determine differences in proportions. Mann-Whitney U test was used to compare two independent groups in terms of metric variables. P value of less than 0.05 was considered as statistically significant.

## Results

Of these patients, the median age was 62 years (range: 17-90). Eighty four percent of the patients were male. In control group, 93% (2,818,330) was male and 7% (204,553) was female. There were no significant differences of blood groups regarding age and sex in control group. Overall distributions of ABO blood groups were significantly different between patients (43.8% A, 8.2% AB, 17.3% B, and 30.7% O) and controls (42.2% A, 7.6% AB, 16.3% B, and 33.9% O; p=0.023) (Table 1). In addition, there were significant differences between patients and controls with respect to Rh positive vs. Rh negative (p=0.040) and O vs. nonO (p=0.002). Whereas, the distributions of blood group regarding A vs. nonA,

B vs. nonB, and AB vs. nonAB were not significantly different (Table 2). Likewise, among patients, there were no significant differences of blood groups with respect to sex, age, or histology.

## Discussion

In present study, we showed that ABO blood type was associated with the lung cancer and having blood type other than O and having Rh-negative increase the risk of lung cancer. Overall, O blood group and Rh-positive were associated with a 14% and 13% risk reduction of lung cancer respectively.

There may be some explanations for this association. ABO blood group gene is mapped at the chromosome 9q34 and encodes blood group antigens related glycotransferases (Humphray et al., 2004). Blood group antigens are chemical components on the erythrocyte membrane but they are also expressed in a variety of epithelial cells including respiratory mucosal cells and mucus of bronchial gland mucous cells (Hakomori, 2001). In addition, various cancer cells express blood group antigens on their cell surface. In human lung cancer tissues, alterations of ABO antigen expression have been reported (Alvarez-Fernandez and Carretero-Albinana, 1991; Lee et al., 1991; Cerny et al., 1992; Miyake et al., 1992; Gwin et al., 1994; Rice et al., 1995; Graziano et al., 1997; Ulger et al., 2002; Sanchez-Mora et al., 2007; Leon-Atance et al., 2012).

Cancer and non-O blood group have associated with increased risk of thrombosis (Wu et al., 2008; Cohen et al., 2012). Furthermore, recent studies have reported an association between ABO blood group and the risk of various epithelial cancers. Non-O blood group increases risk of cancer including pancreatic, gastric, ovarian, kidney, colorectal and skin carcinomas (Wolpin et al., 2009; Edgren et al., 2010; Xie et al., 2010; Joh et al., 2012; Poole et al., 2012; Urun et al., 2012). Similarly, the thrombosis was associated with both increased risk of cancer and advanced disease and poor prognosis (Chew et al., 2006; 2007; Ahlbrecht et al., 2012). As well, venous thromboembolism (VTE) was associated with higher risk of death in patients with lung cancer (Chew et al., 2008). Individuals with nonO blood group have higher levels of von Willebrand factor (vWF) factor and VIII plasma levels. ABO blood group carbohydrates on VWF may influence susceptibility to proteolysis by ADAMTS13 (Bowen, 2003). In addition, genome wide association studies showed association between three single nucleotide polymorphisms (SNPs) on chromosome 9q34.2 and VTE (Heit et al., 2012). Likewise, an association between ABO blood group gene and SNP (rs505922) and

pancreatic cancer has been also identified (Amundadottir et al., 2009). For that reason, linkage disequilibrium between ABO blood group gene and cancer related gene might be another explanation.

Although, present study is a multicentric study and all blood group were serologically confirmed and diagnosis of lung cancer was pathologically confirmed there were some limitations. Because of retrospective nature of study, it is subjected to variety of bias including selection and referral bias. In addition, possible confounding factors that related with increased risk of lung cancer were not included.

In conclusion, in the study populations, ABO blood type was associated with increased risk of the lung cancer. Non-O blood group and Rh-negative features increased risk of lung cancer compared with blood group O and Rh-positivity. However, further prospective studies are necessary to define the mechanisms by which ABO blood type may influence the lung cancer risk.

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