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• ORIGINAL RESEARCH •

Relationship between ABO blood groups and carcinoma of esophagus and cardia in Chaoshan inhabitants of China

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Abstract

AIM **To study the relationship between ABO blood groups and carcinoma of esophagus and cardia in Chaoshan inhabitants of China, which is a unique Littoral high-risk area of esophageal carcinoma in China. The poor communication and transportation in the past has made Chaoshan a relatively closed area and kept its culture and custure of old China thousand years ago.**

METHODS **Data on age, sex, ABO blood type and X-ray or patholog ical diagnose of the patients with carcinoma of esophagus or cardia were collected from the Tumor Hospital. First Affiliated Hospital, Second Affiliated Hospital of Shantou University Medical College; and the Central Hospital of Shantou and the Central Hospital of Jieyang. A total of 6685 patients with esophageal carcinoma (EC) and 2955 patients with cardiac cancer (CC) in Chaoshan district were retrospectively assessed for their association with ABO blood groups.**

RESULTS **The distribution of ABO blood groups in patients with EC or CC was similar to the normal local population in Chaoshan. However, blood group B in male patients with CC and in the patients with carcinoma in the upper third esophagus was 2.3% and 4.7% higher than the corresponding controls. The relative risk B:O was 1.1415 ($P<0.05$) and 1.2696 ($P<0.05$), respectively. No relationship was found between ABO blood groups and tumor differentiation.**

CONCLUSION **ABO blood group B is associated with the incidence of CC in male individuals and carcinoma in the upper third esophagus. The distri bution of ABO blood groups varies in the different geographical and ethnic groups. As a result, proper controls are very important for such studies.**

Subject headings esophageal neoplasms; stomach neoplasms; ABO blood-group system; Guangdong; human

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INTRODUCTION

Chaoshan is an enclosed littoral region surrounded by mountains located at the boundary between Guangdong Province and Fujian Province of China. Chaoshan residents mostly came from Henan, Shanxi, and Changan thousands years ago, and are a relatively isolated population with a high risk of esophageal carcinoma (EC) and cardiac carcinoma (CC). Within Chaoshan, the Nanao Island has the highest risk[1,2]. According to the report from the Department of Public Health. Guangdong Province in 1993, the mortalities of esophageal carcinoma in the Nana o Island were: 108.68±7.88/100 000 standardized population of China and 145.44±10.49/100 000 standardized world population and 261.16±25.01/100 000 standardized world population aged 35-64 years. The annual average incidence rates of male and female were 132.19/100 000 and 69.20/100 000 in the Nanao Island from 1987 to 1992[3,4]. It has been noticed that EC is a race-related disease. People of Chinese origin living in foreign countries have higher EC frequency than those of non-Chinese origin, and in comparison with the frequency in the people with Chaoshan origin is even higher. The mortality of EC within immigrants of the Nanao Island origin in Meixian County, Guangdong Province is 1.7 times that of the local residents[5]. The poor communication and transportation in the past has made Chaoshan a relatively closed society and formed its unique culture, customs and habits. A preliminary study showed that Chaoshan residents were migrants from central China, and their traditional culture, custom and habits were well kept. This unique society provides us an unparalleled base to study cultural and genetic factors and their interaction in the study of EC.

Since the association between blood group A and gastric cancer was reported in 1953, the relationship with blood groups and incidence[6-16], clinicopathologic parameter[17,18] and prognosis[19-21] had been studied in many cancer and other disease[22,23]. However, there is no consistent result[24-27]. Additionally, ABO genes are distributed differently among socioeconomic groups[28] and we know that socioeconomi c status is one of the risk factors for diseases. Thus, a retrospective assessment of the relation between blood groups and EC, CC was performed with a view to start the study of the genetics of these cancers in Chaoshan district.

MATERIAL AND METHODS

Clinical data

Data about age, sex, ABO blood type and X-ray or pathological diagnosis of the patients with EC and CC were collected from the Tumor Hospital (1978-1998). The First Affiliated Hospital (1989-1998), the Second Affiliated Hospital (1983 - 1998) of Shantou University Medical

College; the Central Hospital of Shantou and the Central Hospital of Jieyang. A total of 6685 patients with EC and 2955 patients with CC in Chaoshan district were retrospectively assessed for the association with ABO blood groups. In these series, histopathological diagnoses were available in 4719 patients with EC and 2120 patients with CC. The differe ntiation of the carcinomas was categorized as grade 1 (well-differentiated tumors) to grade 3 (poorly-differentiated tumors). The remaining cancers were diagnosed by X-ray. In 5638 patients with EC, there is definite information on tumor sites within the esophagus. All patients' medical records, including operative notes and histopathological reports, were reviewed.

Normal control

The ABO blood group distribution of the blood donors from the Central Blood Bank in Shantou city was used as control groups 7276 donors were sampled, of the same ethnic group and from the same native place as the patients.

Statistical analysis

Data were stored in a computer data base (FoxPro, version 2.5b) and analyzed using a computer spread sheet (Microsoft Excel 97) and professional statistical computer software (SPSS, version 6.12 and SAS, version 6.08). The differences of ABO blood group distribution in patient groups and controls were assessed using Chi-square test. The gene frequencies of blood group antigen were calculated by the method of Bernstein and the relative risks were estimated using Woolf's methods. P values <0.05 were regarded as statistically significant.

RESULTS

The distribution of ABO blood groups in the EC group was similar to that of a normal population (Table 1) and so was the gene frequencies (Table 2). Although blood group B in total patients with CC and female patients with CC were 2.3% and 1.5% higher than the corresponding controls, the difference was not significant. In male patients with CC, there was a 1.6% deficiency of blood group A and a 2.3% excess of blood group B as compared with the male controls, and the two groups differ significantly in their ABO distribution ($\chi^2 = 8.518$, $P<0.05$). The gene frequencies of blood group B were 0.196 in male patients with CC, which was higher than that of the male controls (0.175), and the relative risk B:O was 1.14 (95% confidenc e interval 1.01-1.29) with statistical significance (Table 2). This suggests that male individuals with blood group B are more susceptible to CC. With respect to the site of EC, carcinoma in the middle third esophagus is most common (73%), but the prevalence of blood groups in this group and the lower third group were identical to the controls. The blood group B patients with carcinoma in the upper third esophagus was 4.7% higher than the controls, with a higher gene frequency (0.2072), and the difference of the blood group distribution between the two groups was of statistical significance. When blood group B was compared with blood group O, the relative risk was 1.27 (95% confidence interval 1.05-1.54), which was statistically significant by Chi-square test. Although the prevalence of blood group B was a little lower in the poorly differentiated squamous cell carcinoma of the esophagus (ESCC) than expected, the deficiency did not reach significance. No relationship between the tumor differentiation and ABO blood group distribution was found.

Table 1 ABO blood group distribution in EC patients (n, %)

Groups	Total	Blood groups				P value
		A(%)	AB(%)	B(%)	O(%)	
Control						
Male	5447	1468(27.0)	345(6.3)	1398(25.7)	2236(41.0)	
Female	1829	480(26.2)	112(6.1)	477(26.1)	760(41.6)	
Total	7276	1948(26.8)	457(6.3)	1875(25.8)	2996(41.1)	
EC						
Male	4987	1336(26.8)	271(6.0)	1362(27.3)	1990(39.9)	0.260
Female	1698	443(26.1)	102(6.0)	442(26.0)	711(41.9)	0.997
Total	6685	1779(26.6)	401(6.0)	1804(27.0)	2701(40.4)	0.399
CC						
Male	2437	620(25.4)	177(7.3)	683(28.0)	957(39.3)	0.036[a]
Female	518	138(26.7)	27(5.2)	143(27.6)	210(40.5)	0.790
Total	2955	758(25.7)	204(6.9)	826(27.9)	1167(39.5)	0.057
Site of EC						
Upper third	673	164(24.4)	46(6.8)	205(30.5)	258(38.3)	0.045[a]
Middle third	4121	1126(27.3)	243(5.9)	1079(26.2)	1673(40.6)	0.725
Lower third	844	206(24.4)	51(6.1)	245(29.0)	342(40.5)	0.186
Diff. (ESCC)						
Well Diff.	378	106(28.0)	25(6.6)	107(28.3)	140(37.0)	0.444
Moderately Diff.	1290	340(26.4)	75(5.8)	334(25.9)	541(41.9)	0.893
Poorly Diff.	572	160(28.0)	20(3.5)	152(26.6)	240(41.9)	0.064
Diff. (AC)						
Well Diff.	22	6(27.3)	2(9.1)	6(27.3)	8(36.4)	0.936
Moderately Diff.	161	45(28.0)	9(5.6)	43(26.7)	64(39.8)	0.954
Poorly Diff.	311	82(26.4)	24(7.7)	86(27.7)	119(38.3)	0.569

[a]$P<0.05$. EC: Esophagus cancer; CC: Cardiac cancer; AC: Adenocarcinoma; ESCC: Squamous cell carcinoma in esophagus; Diff: Differentiation

Table 2 Gene frequency of abo blood type in EC and CC patients

Group	Gene frequency			A/O			B/O		
	p	*q*	*r*	RR	CI	*P*	RR	CI	*P*
Control	0.1816	0.1754	0.6424						
Total (EC)	0.1758	0.1784	0.6405	1.01	0.93－1.10	NS	1.07	0.98－1.16	NS
Upper (EC)	0.1696	0.2072	0.6210	0.98	0.80－1.20	NS	1.27	1.05－1.54	<0.02
Total (CC)	0.1790	0.1925	0.6285	1.00	0.90－1.11	NS	1.13	1.02－1.26	NS
Male (CC)	0.1794	0.1954	0.6252	0.99	0.88－1.11	NS	1.14	1.01－1.29	<0.03

NS: Not significant; CI: Confidence interval; EC: Esophageal cancer; CC: Cardiac cancer

Table 3 Comparison of ABO blood group distribution in different districts in China

Districts	Blood groups				Characteristics
	A (%)	AB (%)	B (%)	O (%)	
Linxian	2936(24.5)	1254(10.5)	4279(35.6)	3536(29.5)	B>O>A>AB
Shanxi	2908(23.3)	987(7.9)	4120(33.0)	4469(35.8)	O>B>A>AB
Dezhou	994(28.4)	318(9.1)	1064(30.4)	1124(32.1)	O>A>B>AB
Wuhan	10799(33.2)	2970(9.2)	7180(21.9)	11641(35.7)	O>A>B>AB
Hubei	4461(32.5)	1125(8.2)	3376(24.6)	4762(34.7)	O>A>B>AB
Lanzhou	597(33.0)	171(9.4)	512(28.3)	530(29.3)	A>O>B>AB
Yancheng	947(30.3)	299(9.6)	845(27.0)	1037(33.2)	O>A>B>AB
Chaoshan	1948(26.8)	457(6.3)	1875(25.8)	2996(41.2)	O>A>B>AB

DISCUSSION

There seemed to be no association between ABO blood groups and the incidence of EC or CC when the studied patients were not grouped by sex and tumor site. This result is consistent with previous reports. However, in the present study, male individuals with blood group B were more susceptible to CC than those with other blood types, and blood group B was associated with carcinoma of the upper third of the esophagus. It suggested that the susceptibility of male to certain cancer was not the same as female. Thus, further classification by sex may be needed when studying the relation between ABO blood groups and cancer. No relation was found in the current study between blood groups and the histological differentiation of EC or CC. The relationship between ABO blood groups and carcinoma of esophagus and cardia has been controversial[29,30]. Mourant and his colleagues reported that blood groups A and B were both associated with EC and no relation was found between blood groups and CC, based on the data from 31 districts in 13 countries and 7 districts of 6 countries, respectively[31]. But some authors have reported different associations according to geographical locations. Thus, blood group A was associated with EC in the British population of Belfast and blood group B individuals were susceptible to EC in British in Bristol, Bantu in South Africa and Iowa in America. But ABO blood groups have shown no correlation with EC in other districts in these countries[29]. These inconsistent results reflect two fundamental methodological problems with such association studies, the statistical methods and the selection of controls. Since the association between ABO blood groups and different cancers is not the same, associations may be observed if several kinds of carcinoma are analysed together. Small sample size is another possible inconsistency.

The importance of careful selection of controls is illustrated by the comparison of populations from different districts whthin China (Table 3). The distribution of ABO blood groups in different districts differs significantly (χ^2 = 0.141, P<0.01). For instance, there was a 10% excess of blood group A individuals in the population of Wuhan, compared with that of Shanxi, a 13.7% excess of blood group B individuals in Linxian compared with Wuhan, and a difference in the frequency of blood group O in Chaoshan compared to Shanxi, even though Chaoshan residents came from Henan, Shanxi, a thousand years or more ago. This suggests that the frequency of different alleles in immigrants to Chaoshan from Shanxi has drifted, compared with their originating population. The best control is, therefore, the ABO blood group distribution of the healthy population of the same ethnic group and sex and from the same native place as the patients[32]. It is possible that blood group B is just a marker of the ancestral population from Shanxi which is now mixed into the Chaoshan region, Shanxi people are also the population at high risk of EC/CC.

The explanation for the association between ABO blood groups and some special diseases was still unclear. Many reports have shown that blood group antigen expression in tumor is correlated with metastasis[33,34] and prognosis[35,36]. The loss or presence of blood group antigens can increase cellular motility or facilitate the interaction between tumor cells and the endothelium of distant organs[37,38]. ABO(H) blood group genes are map at 9q in which the genetic alteration is common in many cancers[39-44]. Thus, ABO(H) blood group antigen expression may be affected by the genetic change of tumors. On the other hand, it is possible that the observe d associations are not due to the blood group antigens themselves, but to the effects of genes closely associated with them. Additionally, it might have nothing to do with molecular mechanisms or genetics. It is merely the result of population history[45-47], environment[45,48,49], diet[50] and customs[51-55].

In conclusion, the current study shows no association of ABO blood groups with EC and CC, when the patients are not separated by sex and tumor site. If they are so grouped, male individuals with blood group B are found to have increased risk for the development of CC, and blood group B individuals are more likely to get carcinoma in the upper third of the esophagus. These findings may contribute to the genetic or custom study of EC and CC.

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