# RELATIONSHIP ANALYSIS BETWEEN HUMAN ABO BLOOD GROUP AND PANCREATIC DUCTAL ADENOCARCINOMA

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***ABSTRACT***

***Introduction:*** *We aimed to analyze the relationship between human ABO blood group and pancreatic ductal adenocarcinoma (PDAC).*

***Materials and methods:*** *A total of 61 patients with pancreatic ductal adenocarcinoma confirmed by postoperative pathological diagnosis in the Second Affiliated Hospital of Kunming Medical University from January 2003 to December 2017 were enrolled in this retrospective study. Data, including gender, age, ABO blood type, tumor type, tumor differentiation, lymph node metastasis and organ infiltration, were collected and analyzed.*

***Results:*** *Among the 61 patients, there were 21 patients with type A blood, 16 with type B blood, 9 with type AB blood and 15 with type O blood. Moreover, patients with type A blood had a higher degree of tumor differentiation than those with non-A type blood (P=0.023). In patients with type B blood, there were more number of metastatic lymph nodes than the other groups (P<0.05).*

***Conclusion:*** *The patients with type A blood have a higher risk of PDAC than those with other types of blood.*

***Keywords:*** *Pancreatic ductal adenocarcinoma, ABO blood type, pathogenesis, prognosis.*

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## Introduction

In the past few decades, cancer has become one of the most serious challenges to human health, which is the main cause of death in China. It is generally known that pancreatic ductal adenocarcinoma (PDAC) is a common malignant tumor with extremely high malignancy. Due to insensitivity to radiotherapy and chemotherapy, surgery is the main treatment for PDAC[1, 2]. However, early diagnosis of PDAC is difficult. Once diagnosed, most of the patients are in the middle and advanced stage, and only 15% to 20% of patients have the surgical conditions[3]. The patients with PDAC usually have extremely poor prognosis, and the overall five-year survival rate was only about 5%[4, 5]. Therefore, making clear the etiology and risk factors of PDAC, early screening and follow-up for high-risk patients are very important to improve the prognosis. At present, the known risk factors for PDAC include smoking, alcoholism, obesity, type 2 diabetes, chronic pancreatitis, and HP infection[1, 6-8].

Importantly, genetic mutation, including P16, STK11, CETR, APC, KRAS, PALB and BRCA, is also significantly associated with PDAC[9-12]. The ABO blood group, the important blood type system

of human, has the strongest antigen immunity and stable genetic characters. It is widely distributed on the surface of cells, such as red blood cells, platelets, epithelial cells and sensory neurons[13]. It's encoding gene is located at chromosome 9q34.1 - 34.2. The gene product is a glycosyltransferase that controls the biosynthesis of antigens of the ABO blood group[14]. ABO gene seat has three main alleles, namely A, B and O. The alleles coding product specificity and enzyme activity determine the specificity of the surface antigen on red blood cells and antigen intensity. Thus, human ABO blood group can be divided into six different subtypes, including AA, AO, BB, BO, AB, and OO[9].

The ABO blood group antigens may be involved in human immune regulation, leading to programmed cell apoptosis. It also changes inflammation, immune defense, cell adhesion and cellular signaling at the molecular leve[15-17].

It has been reported that the incidence of gastroduodenal ulcer, hepatitis B, cardiovascular diseases, type 2 diabetes and malignant tumor are related to ABO blood type[18, 19]. In 1953, Aird has firstly reported that the ABO blood group is associated with the incidence of gastric cancer[19, 20]. Up to now, it has been found that ABO blood type is associated with the risk of various malignancies, including breast cancer, esophageal cancer, ovarian cancer, etc.[16, 17, 19, 21-23]. Furthermore, several studies have shown that ABO blood group is associated with the onset of pancreatic cancer[20, 24, 25]. However, the results of these studies are controversial, and the effect of the ABO blood type on the prognosis of PDAC is unclear. Therefore, the purpose of this study was to explore the relationship between human ABO blood group and PDAC.

## Patients and methods

### *Patients*

A total of 61 patients with pancreatic ductal adenocarcinoma confirmed by postoperative pathological diagnosis in the Second Affiliated Hospital of Kunming Medical University from January 2003 to December 2017 were enrolled in this retrospective study.

*Inclusive criteria:*

• The diagnosis of pancreatic ductal adenocarcinoma was confirmed by postoperative histopathological examination;

• Patients with the first diagnosis of PDAC;

• Patients who accepted radical operation or palliative operation for pancreatic cancer;

• Patients with complete medical records.

*Exclusion criteria:*

• Patients with acute and chronic pancreatitis;

• Patients with malignant tumor of other organs;

• Patients with heart, lung, kidney and other important organ failure;

• Patients with immune diseases;

• Patients lost to follow-up.

### *Data collection*

Data, including the age, sex, comorbidities, ABO blood group, pathology, tumor size, tumor differentiation degree, frequency distribution, lymph node metastasis and organ infiltration or metastasis, were collected. Date of death was determined through documentation in the electronic medical record or through public obituary records.

### *Statistical analyses*

The statistical analysis was performed using SPSS 24.0 statistical package. Chi-square test was used to compare the differences in gender, tumor location, organ infiltration or metastasis, lymph node metastasis and tumor differentiation degree, and the frequency distribution between patients with different blood types. $P<0.05$ was considered to be statistically significant difference.

## Results

Among the 61 patients with PDAC, there were 44 males and 17 females, with the age of 56.52±21.41. There were 47 cases of tumors located in the pancreatic head and14 cases in the pancreatic body tail. There were 23 patients with distant organ metastasis and 23 with lymph node metastasis. There were 6 patients with highly differentiated adenocarcinoma, 9 with high and middle differentiated adenocarcinoma, 16 with middle differentiated adenocarcinoma, 24 with middle and low differentiated adenocarcinoma, and 6 with low differentiated adenocarcinoma (Table 1).

Among the 61 patients, there were 21 patients (34.43%) with type A blood, 16 (26.23%) with type B blood, 9 (14.75%) with type AB blood and 15 (24.59%) with type O blood. There was no statistically significant differences in the frequency distribution between gender, tumor location and organ infiltration or metastasis among different blood groups ($P>0.05$). Furthermore, the distributions of lymph node metastasis and tumor differentiation were statistically significant differences among the

four groups. There were 21 patients with lymph node metastases and 40 patients without lymph node metastasis. As we can see by the frequency distribution, the number of patients with lymph node metastasis in the B group blood was up to 11, and that in the A group blood was up to 16 (P=0.010). In terms of tumor differentiation degree, patients with middle or low accounted for the largest, with 24.6% and 37.7%, respectively.

Other differentiation levels were evenly distributed. For the frequency distribution, the middle differentiation was the largest number in the patients with AB type blood. In other types of differentiation, the number of patients with A type blood was the largest (P=0.023) (Table 2).

| Items | Type A (%) | Type B (%) | Type AB (%) | Type O (%) |
|---|---|---|---|---|
| Number | 21 (34.43) | 16 (26.23) | 9 (14.75) | 15 (24.59) |
| Average age | 58.29 | 56.24 | 55.08 | 56.34 |
| **Gender** | | | | |
| Male | 18 | 10 | 6 | 10 |
| Female | 3 | 6 | 3 | 5 |
| **Location of tumor** | | | | |
| Head | 18 | 13 | 6 | 10 |
| Body tail | 3 | 3 | 3 | 5 |
| **Organ infiltration or metastasis** | | | | |
| Yes | 9 | 6 | 5 | 3 |
| No | 12 | 10 | 4 | 12 |
| **Lymph node metastasis** | | | | |
| Yes | 5 | 9 | 4 | 5 |
| No | 1 | 7 | 5 | 10 |
| **Degree of differentiation** | | | | |
| Highly | 1 | 3 | 1 | 1 |
| High and middle | 5 | 2 | 2 | 0 |
| Middle | 4 | 3 | 6 | 3 |
| Middle and low | 8 | 6 | 0 | 10 |
| Low | 3 | 2 | 0 | 1 |

**Table 1:** Clinical characteristics of patients with PDAC sorted by ABO blood types.

| Items | $\chi^2$ | df | *P* |
|---|---|---|---|
| Gender | 3.022 | 3 | 0.388 |
| Location of tumor | 2.514 | 3 | 0.473 |
| Organ infiltration or metastasis | 3.460 | 3 | 0.326 |
| Lymph node metastasis | 11.375 | 2 | 0.010 |
| degree of differentiation | 23.572 | 12 | 0.023 |

**Table 2:** The analysis of the association of clinical characteristics and PDAC.

## Discussion

The incidence of PDAC is related to various factors, among which ABO blood group is an important risk factor. Multiple studies have shown that patients with type A blood have a higher risk of PDAC than those with other types of blood[1, 4, 9, 24-29]. In this study, the proportion of patients with type A blood was higher than that of other blood groups. The pathogenesis of the difference in the risk of pancreatic cancer among people with different blood groups are not yet clear. In 1975, Springer et al. have reported that high T antigen expression could be detected in the serum of patients with malignant tumors[30]. T antigen is the direct precursor of the antigen in the MN blood group, which is not expressed in normal tissues and benign lesions except in early embryo expression.

Our study has concluded that T antigen expressed in tumor cells is intersected with type A blood serum, causing the body to mistake the tumor cells for their own cells rather than their immune function. Secondly, T antigen can cause the adhesion between tumor cells to decrease, and the adhesion of tumor cells and normal tissue cells is enhanced, resulting in the proliferation and metastasis of tumor cells[17, 22]. Kupffer cells have adhesion and phagocytic ability to tumor cells, and T antigen can inhibit the adhesion of Kupfer cells through concentration-dependent manner, thereby weakening the immune barrier to tumor cells[31, 32]. Schaffert et al. have suggested that A antigen may be involved in the proliferation of pancreatic cancer cells, which may be a mechanism for pancreatic cancer in patients with type A blood[33]. Moreover, ABO blood group can affect the adhesion process of inflammatory factors to different degrees, thereby regulating the clearance of inflammatory factors and the difference in the risk of different type blood group[28, 34, 35]. Cosmic et al. have detecting all SNPs and found that alleles rs8176741, rs8176746 and rs8176747 could reduce the risk of pancreatic cancer, while rs505922 could increase the risk[29]. According to the study of Naoto, ABO blood group is significantly different in patients with type 2 diabetes[4].

Lymph node metastasis and tumor differentiation are two important predictors for prognosis. In our study, the lymph node metastasis is different in tumor distribution, but the number of lymph node metastasis was the most and in the patients with type B blood. We consider that the results are related to the inadequate samples. In terms of tumor differentiation, the frequency distribution in the patients with type A blood is different from patients with other types of blood. However, it does not indicate that blood type is related to tumor differentiation. The further immunohistochemical analysis and follow-up are necessary. There is no consensus on the effect of different types of blood on the prognosis of patients with pancreatic cancer.

Tugba et al. have showed that the prognosis of patients with type A blood and pancreatic cancer are poorer than the patients with other types of blood[27].

Ben et al. have showed that there are no statistically significant difference between median survival and different blood groups, but the TNM staging of patients with non-O type blood is significantly advanced to the patients with type O blood[9]. In the study of Engin, the survival period of patients with non-O type blood is notably longer than that of patients with type O blood[26]. However, in the study of Bianca, the median survival time of patients with types A, B, AB and O blood is 16, 13. 4, 10.8 and 14.6 months[36].

## Conclusion

PDAC progresses rapidly. The prognosis of the patients is poor, the early condition is hidden, the surgical removal rate is low, and the efficiency of chemoradiotherapy is low. The patients with type A blood have a higher risk of PDAC than those with other types of blood. To study the pathogenesis of ABO blood group and PDAC, it may be possible to develop a more accurate and personalized treatment plan for patients with PDAC in the immunotherapy.

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