

# Prognostic Effect of Blood Type on Gastrointestinal Cancer: A Systematic Review and Meta-analysis

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## ABSTRACT

**Introduction:** Although several studies have found an association between ABO blood type and the prognosis of solid tumors, the results are inconsistent. Therefore, we performed a network meta-analysis of ABO blood groups and prognosis in esophageal, gastric, and colorectal cancers.

**Methods:** From January 2007 to December 2021, we searched PubMed for the keyword “cancer, ABO blood type, prognosis” and extracted 206 reports. We selected nine studies involving 12,121 patients. Of these, five papers on esophageal (n = 1), gastric (n = 2), and colorectal (n = 2) cancers, involving 5979 patients, revealed hazard ratios (HRs) by blood group. All reports were retrospective studies conducted at respective medical centers published in China. HRs of overall survival between blood types were the primary basis of our meta-analysis.

**Results:** When type A served as the control group, the HRs of types O, AB, and B were 0.62 [0.46; 0.85], 0.73 [0.53; 0.99], and 0.82 [0.60; 1.11], respectively. Two studies found that type B patients had higher overall survival than non-type B patients. Overall, type O patients had a better prognosis for gastrointestinal cancers than type A patients.

**Conclusions:** On the basis of the findings of the current univariate analysis, the prognosis is favorable in the order of type O, AB, B, and A. Overall, type A has a poor prognosis, but the relationship with prognosis other than type A remains unclear.

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**KEYWORDS:** gastrointestinal cancer, ABO blood type, prognosis, meta-analysis

## Introduction

Karl Landsteiner discovered the ABO blood group in 1900. Human blood is divided into four types, A, B, AB, and

O, based on the presence of A and B antigens on erythrocyte surfaces and A and B antibodies in the serum.<sup>1)</sup> In addition to its expression on the erythrocyte surface, the ABO antigen is highly expressed on the surface of epithe-

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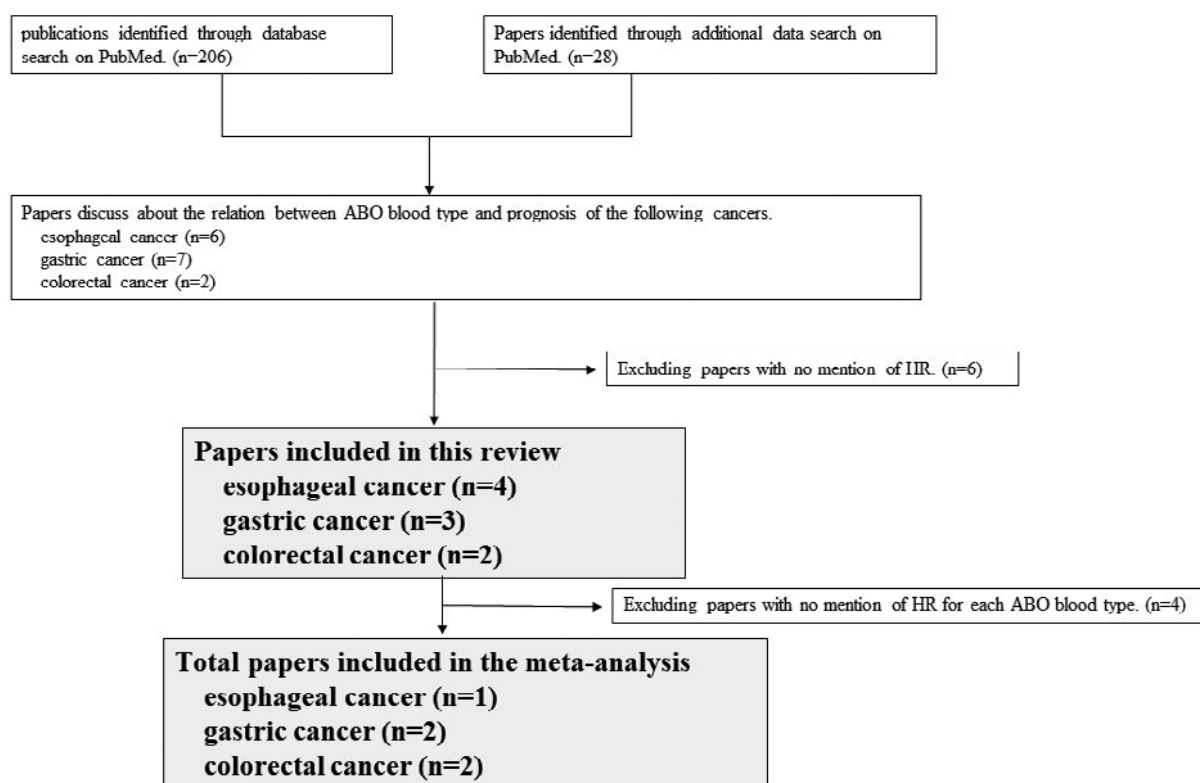


Fig. 1 Flowchart of publication selection.

lial cells in the gastrointestinal tract and bronchopulmonary and urogenital organs.<sup>2)</sup>

There are numerous studies on blood type and carcinogenesis for each cancer type. For example, Brian et al. found that types A, B, and AB have a higher risk of developing pancreatic cancer than type O.<sup>3)</sup> In recent years, an increasing number of studies have found an association between ABO blood type and overall survival (OS) in solid tumors like pancreatic and ovarian cancers.<sup>4, 5)</sup> However, the results are inconsistent. The ABO blood group is a routine preoperative blood test item that is easy to obtain; thus, its utility in predicting prognosis may be significant. Although there are numerous reports on prognostic factors associated with gastrointestinal cancer, no meta-analysis has been conducted on the relationship between blood type and prognosis.

Therefore, we sought to assess the effects of ABO blood type on the OS of patients with gastrointestinal cancers (esophageal, gastric, and colorectal cancers) by conducting a systematic review and meta-analysis.

## Methods

From January 2007 to November 2022, PubMed was searched for literature published in the Ichushi-Web data-

base using the keywords “ABO blood type and cancer and prognosis,” “ABO blood type,” “gastric cancer,” and “prognosis.” We extracted 206 and 28 PubMed reports. No reports were found in the Ichushi-Web database (Fig. 1).

Of these, 15 papers discussed ABO blood groups and prognoses in esophageal, gastric, and colorectal cancers. Nine of the studies mentioned the hazard ratio (HR).<sup>6–14)</sup> Five of these papers<sup>9, 10, 12–14)</sup> described HRs for each blood type (Fig. 1). One was for esophageal cancer, two for gastric cancer, and two for colorectal cancer.

## Statistical analysis

Network meta-analysis of HRs for OS was conducted using the R package netmeta. A random-effects model was used because of the small number of studies and the variability of the results.

Although there are four blood types, none of the studies reported HRs for all six blood type combinations. Point estimates of HRs between blood types that were not listed in each study could be calculated using other combinations; however, the variance and covariance of all HRs were unknown. Therefore, all pairs were treated as independent comparisons, and the unknown variance was replaced by the sum of the variances of the remaining pairs. HRs and

Table 1. Summary of selected articles in this meta-analysis.

Author	Year	[Refs.]	Type of cancer	Country	Period	Number of patients	A	B	O	AB	Male (%)	HR A (95%CI)	HR B (95%CI)	HR O (95%CI)	HR AB (95%CI)
Shuishen Zhang	2020	6	Esophageal	China	2000–2008	2179	617	551	859	152	1682 (77.1)	1.000	1.250 (0.89, 1.77)	1.100 (0.78, 1.55)	1.720 (0.95, 3.10)
Fumiaki Shiratori	2017	7	Esophageal	Japan	2004–2015	181	65	41	60	15	151 (83.4)	2.016 (1.54, 2.65)	2.094 (1.56, 2.81)	1.000	2.373 (1.59, 3.55)
Jian Qin	2015	8	Esophageal	China	2002–2007	548	164	134	202	48	407 (74.2)	3.730 (2.49, 5.57)	2.960 (1.95, 4.48)	2.170 (1.43, 3.30)	1.000
Wei Wang	2015	9	Esophageal	China	2006–2008	406	146	108	109	27	275 (67.7)	1.263 (0.78, 2.05)	0.773 (0.47, 1.27)	0.696 (0.42, 1.15)	1.000
Xiao-Jie Sun	2020	10	Gastric	China	2010–2011	488	133	100	217	38	281 (57.6)	0.832 (0.42, 1.67)	0.368 (0.17, 0.82)	0.299 (0.13, 0.70)	1.000
Shuao Xiao	2017	11	Gastric	China	2008–2015	3234	980	935	988	331	2514 (77.7)	3.040 (1.80, 5.03)	2.650 (1.61, 4.37)	2.470 (1.51, 4.05)	1.000
Ye-Qiong Xu	2016	12	Gastric	China	2005–2010	1412	516	346	407	143	968 (68.6)	1.000	1.955 (1.43, 2.65)	1.433 (1.00, 2.05)	1.000
Jiangpeng Wei	2019	13	Colorectal	China	2011–2016	1613	411	502	545	155	884 (54.8)	0.622 (0.46, 0.85)	0.733 (0.53, 0.99)	0.822 (0.60, 1.11)	1.000
Jiangpeng Wei	2019	13	Colorectal	China	2011–2016	505	142	161	140	62	287 (56.8)	0.622 (0.46, 0.85)	0.733 (0.53, 0.99)	0.822 (0.60, 1.11)	1.000
X Cao	2014	14	Colorectal	China	1995–2002	1555	452 (29.1)	382 (24.6)	598	123	865 (55.6)	0.622 (0.46, 0.85)	0.733 (0.53, 0.99)	0.822 (0.60, 1.11)	1.000

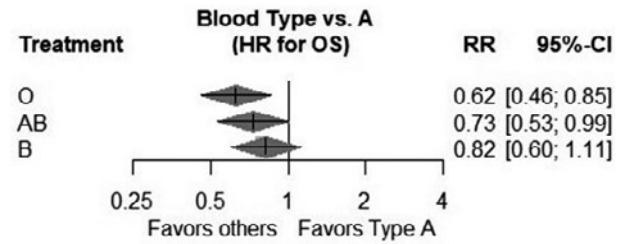


Fig. 2 Forest plot for the relationship of blood groups A, O, AB, and B based on five selected papers.

95% confidence intervals (CIs) for type A are presented. The I-squared ( $I^2$ ) statistics for the heterogeneity measure were computed. P scores, or probability of the lowest risk, were also reported to indicate the rank order of low risk.

## Results

### Summary of the papers

Table 1 displays HRs from nine selected papers on ABO blood type and prognosis in esophageal, gastric, and colorectal cancers. The author, year of publication, type of cancer, country, and number of patients per blood type are also listed (Table 1). Among the nine papers, the current meta-analysis focused on five papers, which included 5979 patients. The five studies included one, two, and two on esophageal, gastric, and colorectal cancers, respectively. One of these contained two studies.<sup>13)</sup> These five reports were released in China between 2014 and 2020. Each study included 406-1555 patients.

### HRs for OS across all blood types

The unadjusted HRs for OS across all blood types were compiled and analyzed. Comparisons between the four blood types were made almost evenly in the extracted articles. In this study, no comparisons between type A and non-type A patients were made.

### Relative risk of OS for each blood group

The relative risk of OS for each blood group is depicted in Fig. 2. The relative risks were 0.62 (95% CI = 0.46; 0.85), 0.73 (95% CI = 0.60; 1.11), and 0.82 (95% CI = 0.53; 0.99) for types O, B, and AB, respectively, using type A as a reference. Types O and AB have significantly better OS than type A.

### P scores by blood type

Fig. 3 shows P scores by blood type. Type O has a 92.8% chance of having the best prognosis, compared with a 4.2% chance of type A. Types B and AB have probabilities that fall somewhere between those of types O and A. Thus, according to the current meta-analysis, the blood types with

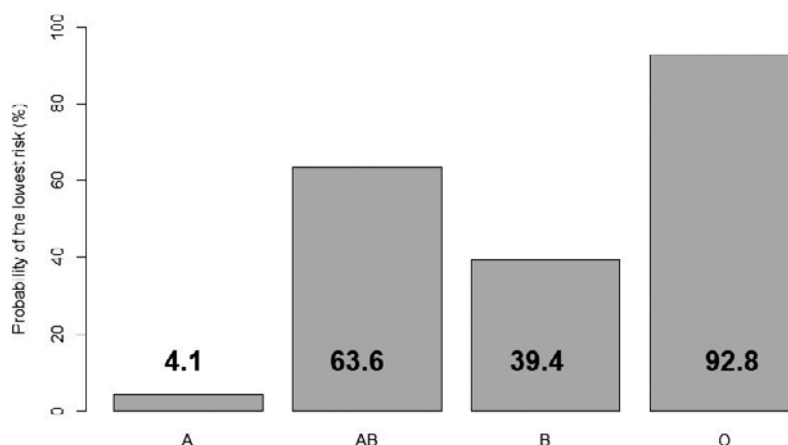


Fig. 3 P scores of various blood types.

the best prognosis are O, AB, B, and A.

## Discussion

For this meta-analysis, five articles were extracted from 234 PubMed papers on ABO blood type and prognosis in gastrointestinal cancer published between 2010 and 2022. A network meta-analysis was performed because there were more than two groups, and we wanted to evaluate all types simultaneously and determine the relative relationship between all types. Conventional meta-analysis is used to show the synthesis of two-group comparisons. They measure the mean extent of certainty that a treatment is better than competing treatments. A meta-analysis of the extracted papers revealed that cancer in type O had a favorable prognosis for all gastrointestinal cancers, whereas cancer in type A had a poor prognosis.

The biological mechanism underlying the association between ABO blood type and malignant tumors, including gastrointestinal cancers, remains unknown. The only hypothesis proposed is an association between blood type and cell adhesion molecule (CAM). Soluble CAMs include sE-selectin, sP-selectin, and soluble intercellular adhesion molecule-1 (sICAM-1), which are inflammatory biomarkers.<sup>15)</sup> The ABO genotype correlates with circulating levels of sE-selectin, sP-selectin, sICAM-1, and tumor necrosis factor- $\alpha$ .<sup>7)</sup> E-selectin has been associated with the metastasis of colon and prostate cancers.<sup>16, 17)</sup> ICAM-1 maintains cell-cell interactions and promotes leukemia and endothelial cell migration. It is a known biomarker in several types of cancer because it promotes cancer metastasis and angiogenesis while potentially weakening the immune response of cancer cells.<sup>18)</sup>

In a healthy Chinese population, type A blood contains significantly lower concentrations of sICAM-1 and sP-selectin than type O blood. This could be because type A has few soluble forms of adhesion molecules and has membrane forms, which may aid in leukocyte migration and adhesion in response to inflammatory stimuli.<sup>19)</sup> The current findings also confirm that type A patients have the worst prognosis.

This study has some limitations. First, many studies excluded HR; therefore, this meta-analysis relied on the findings of a few studies. Second, because the papers are from China, research with raw data from Japan is required. Third, adjusting for confounding factors may be insufficient. Fourth, because there are four blood types, it was preferable to present the findings of six pairwise comparisons. However, only three pairwise comparisons have been reported in the papers. Thus, the CIs and weights were overestimated.

Finally, based on the results of the meta-analysis, the prognosis is favorable in the following order: type O, AB, B, and A. Overall, type A has a poor prognosis, but the relationship with prognosis other than type A remains unclear.

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**Authors' contribution:** H.H., M.O., Y.O., and H.S. designed the study; H.H. and M.O. analyzed the data; H.H., M.O., and H.S. wrote the manuscript.

**Ethics statement:** Ethical approval is not required because all data

in this study were obtained from PubMed.

**Conflicts of interest:** None declared.

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