ABO Blood Group Alleles and Prostate Cancer Risk: Results from the Breast and Prostate Cancer Cohort Consortium (BPC3)

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BACKGROUND. ABO blood group has been associated with risk of cancers of the pancreas, stomach, ovary, kidney, and skin, but has not been evaluated in relation to risk of aggressive prostate cancer.

METHODS. We used three single nucleotide polymorphisms (SNPs) (rs8176746, rs505922, and rs8176704) to determine ABO genotype in 2,774 aggressive prostate cancer cases and 4,443 controls from the Breast and Prostate Cancer Cohort Consortium (BPC3). Unconditional logistic regression was used to calculate age and study-adjusted odds ratios and 95% confidence intervals for the association between blood type, genotype, and risk of aggressive prostate cancer (Gleason score ≥ 8 or locally advanced/metastatic disease (stage T3/T4/N1/M1).

RESULTS. We found no association between ABO blood type and risk of aggressive prostate cancer (Type A: OR = 0.97, 95%CI = 0.87–1.08; Type B: OR = 0.92, 95%CI = 0.77–1.09; Type AB: OR = 1.25, 95%CI = 0.98–1.59, compared to Type O, respectively). Similarly, there was no association between “dose” of A or B alleles and aggressive prostate cancer risk.

CONCLUSIONS. ABO blood type was not associated with risk of aggressive prostate cancer. *Prostate* 75:1677–1681, 2015. © 2015 Wiley Periodicals, Inc.

KEY WORDS: ABO; blood type; prostate cancer; genetic epidemiology

INTRODUCTION

Blood group can be traced to a single gene, *ABO*, located on chromosome 9q34. *ABO* encodes a glycosyltransferase that catalyzes the transfer of carbohydrates to red blood cells, thereby forming the distinct antigenic structures of the A and B blood groups. ABO blood group has been associated with several malignancies, including cancers of the pancreas [1], ovary [2], kidney [3], and skin [4]. One study failed to show an association between ABO blood group and overall prostate cancer [5]; however, no studies have

focused on aggressive prostate cancer, which have been shown to be etiologically different from indolent cancer [6]. We used genotype data to investigate the association between ABO blood type (A, B, AB, and O), as well as variation in ABO (OO, AO, AA, AB, BO, and BB) and aggressive prostate cancer risk.

MATERIALS AND METHODS

Data were from the Breast and Prostate Cancer Cohort Consortium (BPC3) aggressive prostate cancer

genome-wide association study (GWAS), described in detail elsewhere [7]. Cases and controls were selected from prospective cohort studies, and were restricted to men of European ancestry. Cases were men with incident prostate cancer with high-histologic grade (Gleason score ≥ 8) or locally advanced/metastatic disease (stage T3/T4/N1/M1); cases were followed for overall and cancer-specific mortality. Controls were men without a diagnosis of prostate cancer. Assessment of ABO blood group alleles was conducted using genotype data from rs505922, rs8176704, and rs8176746 in ABO to infer-phased haplotypes for each participant with $>99\%$ posterior probability, based on an expectation-maximization algorithm [8], similarly to prior studies [1,2]. Briefly, rs8176746 is a marker of the B allele and rs505922 is a proxy ($r^2 = 1$) for rs687289, a marker of the O allele; rs8176704 distinguishes the A¹ and A² alleles [8]. Unconditional logistic regression estimated odds ratios (ORs) and 95% confidence intervals (95% CIs) of the association between ABO blood group and aggressive prostate cancer adjusted for age and study. We further examined dose of A and B alleles by investigating the association between risk of aggressive prostate cancer and ABO genotype (AO, AA, BO, BB, AB, and OO). We also examined study-specific associations between ABO blood group and aggressive prostate cancer. Among cases, we used Cox proportional hazards regression to assess the association between ABO blood group and prostate cancer-specific mortality, adjusted for age at diagnosis and study. *P* values were two sided and analyses were done using SAS statistical packages (SAS Institute).

RESULTS

The study included 2,774 aggressive prostate cancer cases and 4,443 controls. The frequency of ABO blood group is shown in Table I and for each cohort in Supplemental Table SI. When adjusted for age and study, there was no association between ABO blood types and risk of aggressive prostate cancer (Table I). We found no association between Type A or AB, compared to Type O, and risk of aggressive disease.

Similar results were observed when we evaluated ABO genotype (Supplemental Table SII). In the case-only analysis ($n = 2,774$), there was no association between ABO blood group or genotype and prostate cancer-specific mortality ($n = 598$ prostate cancer deaths) (data not shown).

Figure 1 presents study-specific odds ratios for ABO blood group and risk of aggressive disease. There was heterogeneity across studies and no statistically significant associations comparing Type A or B to Type O in any individual study. There was a positive association with aggressive prostate cancer comparing Type AB to O in the Multiethnic Cohort (OR = 3.34, 95%CI = 1.01–11.03) and an inverse association in the Physicians' Health Study (OR = 0.35, 95% CI = 0.15–0.86).

DISCUSSION

In this large nested case-control study, we found no significant association between ABO blood group and aggressive prostate cancer risk or prostate cancer-specific mortality. These data are consistent with a prior study examining prostate cancer risk overall [5].

Previous studies have generally shown an increased risk of cancer, including pancreas, ovarian, and renal, for non-Type O blood group compared to Type O [1–3]. The potential mechanisms linking ABO to risk of cancer are unclear. It has been suggested that ABO antigens interfere with intercellular adhesion and membrane signaling, and may be involved with angiogenesis [3]. In addition, ABO blood group may affect the systemic inflammatory state and immune surveillance for malignant cells [1,3,4].

A strength of this study is the use of genotype-derived blood groups, which reduced the risk of exposure misclassification from self-report blood type and allowed us to specifically assess whether genotypic variation in ABO was associated with aggressive prostate cancer risk. Restricting to men of European ancestry may limit the generalizability of our findings to men of other ethnicities with differing prevalence of blood types and prostate cancer risk. Finally,

TABLE I. Odds Ratios (or) and 95% Confidence Intervals (CI) of the Association Between ABO Blood Type and Aggressive Prostate Cancer* Risk, Breast and Prostate Cancer Cohort Consortium

	Type O	Type A	Type B	Type AB
N (%) cases	1172 (42%)	1182 (43%)	285 (10%)	135 (5%)
N (%) controls	1772 (40%)	1928 (44%)	534 (12%)	209 (5%)
Multivariable adjusted OR (95%CI) ^a	Ref.	0.97 (0.87–1.08)	0.92 (0.77–1.09)	1.25 (0.98–1.59)

*Aggressive prostate cancer defined as Gleason 8+ or locally advanced/metastatic disease.

^aAdjusted for age and study cohort.

Fig. 1. Association between ABO blood type and aggressive prostate cancer risk by study, Breast and Prostate Cancer Cohort Consortium. *Heterogeneity across the cohort was assessed using *P*-value from Cochran's *Q* statistic.

despite a large overall study, the prevalence of type AB was low. Although there is some heterogeneity among studies, overall ABO blood type and ABO genotype do not appear to play a role in the development or progression of prostate cancer.

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