



Association of ABO blood group type with cardiovascular events in COVID-19

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Abstract

Cardiovascular complications have been reported in patients with COVID-19. We sought to examine the association of ABO blood group type with cardiovascular complications in COVID-19. We examined 409 individuals enrolled in the COVID-19 Registry to Assess Frequency, Management, and Outcomes of Arterial and Venous Thromboembolic Complications (CORONA-VTE) who had ABO blood group data available. Multiple logistic regression was used to assess the association of ABO blood group types with three primary outcomes: major adverse cardiovascular events (MACE), major arterial and venous thrombosis and all-cause mortality. 201, 121, 61 and 26 individuals had blood group O, A, B and AB, respectively. In multivariable analysis, blood group A was associated with a 2.5-fold higher odds of MACE than blood group O (OR 2.47[1.18–5.18]). There was an effect suggesting a 2-fold higher odds of major thrombotic events in blood group A vs. O that did not reach statistical significance (OR 2.15 [0.89–5.20]). No association between blood group type and all-cause mortality was found. Compared with the other blood group types, blood group A was associated with an increased odds of MACE (OR_{A/non-A} 2.18[1.11–4.29]), while blood group O was associated with lower odds of MACE (OR_{O/non-O} 0.50[0.26–0.97]). In conclusion, blood group A was associated with an increased odds of MACE, whereas blood group O was associated with a reduction in the odds of MACE in patients with COVID-19. These findings may inform risk stratification of COVID-19 patients for cardiovascular complications. Additional studies are needed to validate our findings.

Highlights

- ABO blood group type has been associated with major arterial and venous thrombotic complications in the general population.
- In patients with COVID-19, blood group A was associated with a twofold increase in the odds of major adverse cardiovascular events, whereas blood group O was associated with a 50% reduction in those odds.

- ABO blood group type may inform risk stratification of patients with COVID-19 for cardiovascular complications and inform management.

Introduction

Patients with coronavirus disease 2019 (COVID-19) are at risk of cardiovascular complications [1]. There are conflicting reports in the literature on the association of ABO blood group type with both the susceptibility to COVID-19 and the severity of the ensuing illness [2, 3]. We sought to examine the association of blood group type with cardiovascular complications in COVID-19.

Methods

We analyzed a retrospective observational cohort study using data abstracted through the electronic health record within the Mass General Brigham health network. From March 13 to April 3, 2020, 1114 consecutive adult patients

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with confirmed SARS-CoV-2 infection by polymerase chain reaction testing were enrolled in the COVID-19 Registry to Assess Frequency, Management, and Outcomes of Arterial and Venous Thromboembolic Complications (CORONA-VTE). A subset of this cohort (N = 409) had prior or current blood group laboratory data available within the electronic health record and were included in this study. Thirty-day follow-up was complete for 98% of study participants (N = 401/409). 30-day outcomes were adjudicated by a three-person clinical endpoint committee. Three primary outcomes were examined in this analysis: major adverse cardiovascular events (MACE), major arterial and venous thrombotic events and all-cause mortality. Major adverse cardiovascular event (MACE) was defined as a composite of venous thromboembolism, myocardial infarction, ischemic stroke, transient ischemic attack, systemic embolism, major adverse limb events, heart failure hospitalization, new atrial fibrillation and myocarditis. The study was approved by the Institutional Review Board of Mass General Brigham. Univariable linear and logistic regression were used to compare continuous and categorical variables, respectively, across the different blood group types with blood group O as the reference. Multiple logistic regression with three hierarchical nested models was used to assess the association of ABO blood group types with the three primary outcomes. Covariates in the fully adjusted multivariable model included age, race, sex, cigarette smoking status, body mass index, rhesus antigen status, established atherosclerotic cardiovascular disease, heart failure, atrial fibrillation, chronic therapeutic anticoagulation, chronic antiplatelet therapy and statin therapy. Multivariable analysis results presented below reflect the findings of the fully adjusted multivariable model.

Statistical analyses were performed using STATA 16(Stata Corporation, College Station, TX).

Results

In this cohort, 201 (49.1%), 121 (29.6%), 61 (14.9%) and 26 (6.4%) were blood group O, A, B and AB, respectively (Supplemental Material—Table 1). Individuals with history of cerebrovascular events, cigarette smokers and non-Hispanic Whites were more prevalent in blood group A vs. O (Supplemental Material—Table 1). Hypertension was less common in blood group B vs. O (Supplemental Material—Table 1). The unadjusted incidence proportion of 30-day MACE, major arterial and venous thrombotic events and all-cause mortality was highest for blood groups A and AB and lowest for blood groups O and B (Fig. 1a). In multivariable analysis, blood group A was associated with a 2.5-fold higher odds of MACE than blood group O (OR 2.47, [1.18–5.18]; p-value = 0.02). There was an effect suggesting a twofold higher odds of major thrombotic events in blood group A vs. O that did not reach statistical significance (OR 2.15, [0.89–5.20]; p-value = 0.09). There was no association between blood group type and all-cause mortality (Fig. 1b). Compared with the other blood group types, blood group A was associated with an increased odds of MACE (OR_{A/non-A} 2.18, [1.11–4.29]; p-value = 0.02), while blood group O was associated with lower odds of MACE (OR_{O/non-O} 0.50, [0.26–0.97]; p-value = 0.04). Our findings were consistent across the three hierarchical nested models (Supplemental Material—Table 2).

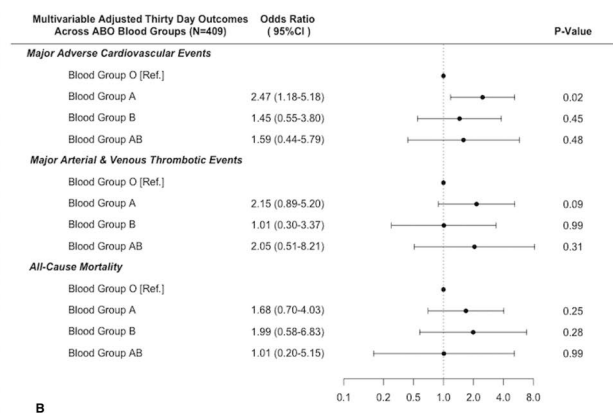
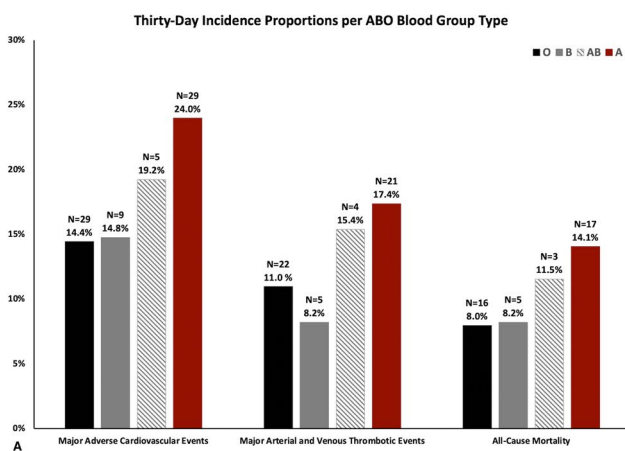


Fig. 1 a 30-day unadjusted incidence proportions of major adverse cardiovascular events, major thrombotic events and all-cause mortality per ABO blood group type (N represents absolute number of events). **b** Forest plot of multivariable association of ABO blood group type with thirty-day major adverse cardiovascular events, major

thrombotic events and all-cause mortality. The multivariable model is adjusted for age, race, sex, cigarette smoking status, body mass index, rhesus antigen status, established atherosclerotic cardiovascular disease, heart failure, atrial fibrillation, chronic therapeutic anticoagulation, chronic antiplatelet therapy and statin therapy

Discussion

We found that blood group A is associated with an increased odds of MACE, whereas blood group O was associated with a reduction in the odds of MACE in patients with COVID-19. A recent genome wide association study found the ABO locus to be associated with respiratory failure in COVID-19 [2]. Furthermore, the authors found blood group A to be associated with increased risk of respiratory failure while blood group O was protective [2]. Our study expands these findings and suggests an association between blood group type and cardiovascular complications in COVID-19. The biological mechanism behind the role of ABO blood groups in COVID-19 remains elusive. Natural anti-glycan ABO antibodies have been shown to inhibit SARS-CoV1 spike protein-angiotensin converting enzyme 2 mediated cellular entry [4, 5]. Furthermore, non-O blood groups have been shown to be associated with increased arterial and venous thrombotic events possibly mediated by increased levels of von Willebrand factor and factor VIII in non-O blood groups [6].

This study has several limitations. Blood group type was available in a subset of patients who overall had more comorbidities (Supplemental Material—Table 3). Thus, we cannot exclude selection bias. Additionally, our sample size was relatively small, which limited the ability to examine the individual components of the composite outcomes and the effect of Rhesus antigen status on outcomes. Our findings suggest an association between ABO blood group types and cardiovascular complications in COVID-19, but no causal relationship should be assumed. Larger studies with longer follow-up are needed to validate our findings.

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Data availability Available on request.

Code availability Available on request.

Compliance with ethical standards

Conflict of interest Dr. Piazza has received research grant support from EKOS, a BTG International Group company, Bayer, the Bristol Myers Squibb/Pfizer Alliance, Portola, and Janssen and consulting fees from Amgen, Pfizer, Boston Scientific Corporation, Agile, and Thrombolex. Dr. Goldhaber has received research support from Boehringer-Ingelheim, Boston Scientific EKOS Division, BMS/Pfizer, Portola, and Janssen, and the NHLBI. He has received consulting fees from Boehringer Ingelheim, Bayer, and Agile. Dr. Nauffal and Mr. Achanta have no conflicts to disclose.

Consent to participate Not applicable.

Consent for publication Not applicable.

Ethical approval Approved by the Institutional Review Board of Mass General Brigham.

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