ARIC Manuscript Proposal # 1132

PC Reviewed: _02/_21_/06	**Status: _____**	**Priority: ____**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Relationship between ABO Blood Group and Venous Thromboembolism (VTE) and its effect modifiers. The Longitudinal Investigation of Tromboembolism Etiology (LITE) study

b. Abbreviated Title (Length 26 characters): ABO Blood Type and VTE

2. Writing Group:

Writing group members: Tetsuya Ohira, MD; Michael Y. Tsai, PhD; Mary Cushman, MD; Wayne D. Rosamond, PhD; Susan R. Heckbert, MD; Aaron R. Folsom, MD.

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _T. O__ **[please confirm with your initials electronically or in writing]**

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3. Timeline: We expect to complete the manuscript by April 2006.

4. Rationale:

An association between ABO blood type and venous thromboembolism (VTE) risk has been reported. Most, but not all, studies reported that the non-O group had a higher risk of VTE

compared with the O blood type. (1-5) However, potential mechanisms or effect modifiers for the association are not established.

Several studies reported that non-O individuals had higher levels of Factor VIII (FVIII) and von Willebrand factor (vWF) than Group O individuals. (6-8) Since our LITE prospective study showed that elevated FVIII and vWF levels predicted future incidence of VTE, (9) altered coagulation factor levels is one of several plausible explanations of how ABO blood type may affect VTE occurrence. However, a case-control study reported that high FVIII levels and non-O blood groups were independent risk factors for VTE. (5)

On the other hand, rates of VTE are markedly lower in Asians than in whites and African Americans, (10, 11) and yet, whites and African Americans have a higher percentage of Group O compared with Asians. (12) Compared with other ethnic groups, Asians tend to have lower prevalences of obesity, (13) diabetes, (14) and factor V Leiden, (15) which are important risk factors of VTE. (16, 17) Therefore, these genetic and lifestyle factors may modify the association between ABO blood type and VTE.

We wish to examine the association between ABO blood group and VTE and its effect modifiers using data from The Longitudinal Investigation of Tromboembolism Etiology (LITE) study.

5. Main Hypothesis/Study Questions:

1. Compared with Group O individuals, non-O individuals have higher incidence of VTE.
2. The association of ABO blood type with VTE is observed in both whites and African Americans and in both men and women.
3. The association between ABO blood type and VTE will be stronger in the presence of obesity, diabetes, factor V Leiden, and high levels of vWF, FVIII, and homocysteine.

6. Data (variables, time window, source, inclusions/exclusions):

Inclusions: LITE nested VTE cases and controls

Exclusions: Subjects with prior history of VTE, warfarin use, and missing lab variables

Dependent variable: Case/control status. Also subdivided by ARIC/CHS, idiopathic/secondary.

Independent variable: ABO blood type

Covariates: Age, race, sex, body mass index, diabetes, FVIII, vWF, homocysteine, factor V Leiden

Analysis:
(1) We will examine associations of covariates with ABO blood type via ANOVA

(2) The odds ratios of VTE and 95% confidence intervals for non-O blood type relative to Group O will be calculated with adjustment for age and other covariates using the logistic regression model. Interactions of obesity, diabetes, factor V Leiden, and high levels of FVIII will be examined using cross-product terms.

7.a. Will the data be used for non-CVD analysis in this manuscript?
____ Yes __X__ No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? ____ Yes ____ No
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?
__X__ Yes ____ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = "No use/storage DNA"? __X__ Yes ____ No

9.The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

Proposal #764: Hemostatic factors and venous thromboembolism incidence: The Longitudinal. Investigation of Thromboembolism Etiology (LITE) Study

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __X__ Yes ____ No

11.b. If yes, is the proposal
__X__ A. primarily the result of an ancillary study (list number* ___25____)
___ B. primiarly based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

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