ARIC Manuscript Proposal #3407

PC Reviewed: 6/18/19 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Hematocrit and venous thromboembolism

b. Abbreviated Title (Length 26 characters): Hematocrit and VTE

2. Writing Group:

Writing group members: Aaron Folsom, MD , Wendy Wang, MPH, Romil Parikh, MBBS, Pamela Lutsey, PhD, Mary Cushman, MD

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

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name:
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3. Timeline: Summer 2019

4. Rationale: Patients with markedly elevated hematocrit due to polycythemia vera are at increased risk of arterial thrombosis and venous thromboembolism (VTE). This is most likely from increased blood viscosity (1). Whether more modestly elevated hematocrit may increase VTE risk in the general population is uncertain (10). A large Norwegian population-based epidemiological cohort suggested that a higher hematocrit may increase incidence of venous

thromboembolism generally (2), and a large clinical study reported that elevated hematocrit may increase recurrence of VTE (3). In contrast, a small case-control study also found no independent association of hematocrit with VTE (4) but was potentially under-powered, and we reported no significant association of hematocrit with VTE incidence in early follow-up of the population-based Longitudinal Study of Venous Thromboembolism (LITE) (9).

With longer follow-up of the Atherosclerosis Risk in Communities (ARIC) study component of LITE, we reexamined association of hematocrit with VTE incidence. Because a few research studies have also associated increased leukocyte count, neutrophil to lymphocyte ratio, or platelet count with increased VTE risk (5-8), we also tested whether leukocyte or platelet counts in ARIC also may be associated with VTE.

5. Main Hypothesis/Study Questions:
Is hematocrit associated positively with VTE incidence?

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Design: prospective starting at V1

Exclusions: 48 who were not black or white, 276 with self-reported history of VTE, 852 with a self-reported history of cancer, 69 using anticoagulants, 260 with missing blood counts, and 396 with missing covariate information, leaving 13,891 for analysis.

Outcome: VTE through 2015

Exposure: blood count parameters analyzed continuously and in five groups: four quartiles but with the top quartile split into the 75^{th} to 94^{th} percentile and greater than or equal to the 95^{th} percentile.

Modeling: Cox regression

Covariates: age, race (black, white), sex, BMI, diabetes status (yes, no), current cigarette smoking status (current, former, never), pack-years of smoking, diabetes (yes, no), systolic blood pressure, antihypertensive medication use (yes, no), eGFR, von Willebrand factor, and factor VIII.

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10. Schreijer AJM, Reitsma PH, Cannegieter SC. High hematocrit as a risk factor for venous thrombosis. Cause or innocent bystander? Haematologica. 2010;95(2):182-184. doi:10.3324/haematol.2009.017285.

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 ICTDER03 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 ICTDER 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? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ 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/mantrack/maintain/search/dtSearch.html

_____ 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)?

Ref 9 in the above reference list.

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* ___2001.16_____)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at https://www2.cscc.unc.edu/aric/approved-ancillary-studies

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.