

## ARIC Manuscript Proposal # 1480

PC Reviewed: 03/17/09  
SC Reviewed: \_\_\_\_\_

Status: A  
Status: \_\_\_\_\_

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Cystatin C and venous thromboembolism

**b. Abbreviated Title (Length 26 characters):** Cystatin C and VTE

**2. Writing Group:**

Writing group members: Aaron Folsom, Pam Lutsey, Brad Astor, Susan Heckbert, Mary Cushman

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. AF [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:  
Address:

Phone:  
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**3. Timeline:** Finish by June 09

**4. Rationale:** It is well known that patients with end-stage renal disease are prone to thrombosis but whether lesser degrees of chronic kidney disease is a risk factor for venous thromboembolism (VTE) is uncertain. In a previous LITE paper (1), we found that a creatinine-based measure of GFR was associated inversely with risk of VTE in ARIC and CHS. However, surprisingly Cystatin C, which is a specific kidney disease

marker, was not related to VTE occurrence in CHS. Now that we have Cystatin C in ARIC visit 4, we want to retest this hypothesis using the 263 VTE cases that have occurred since ARIC visit 4, with greater power than we had for CHS previously. We also will examine the association with microalbuminuria measured as the albumin/creatinine ratio, also measured at visit 4.

## **5. Main Hypothesis/Study Questions:**

Cystatin C is associated positively with incidence of VTE

Secondary: albumin/creatinine ratio is associated positively with VTE.

## **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: cohort

Endpoint: VTE incidence

Exposure: visit 4 cystatin C (and cystatin derived GFR) and albumin/creatinine

Astor did a small (n=40) calibration study comparing Baylor cystatin C to the Cleveland Clinic, and found a relatively constant difference, where Cleveland Clinic was 16% higher than Baylor (i.e., Cleveland Clinic =  $1.16 \times$  Baylor). We are using these recalibrated values in our analyses. Then estimated GFR by the Chronic Kidney Disease Epidemiology Collaboration =  $127.7 \times (\text{recalibrated cystatin C in mg/dL})^{-1.17} \times (\text{age in years})^{-0.13} \times (0.91 \text{ if female}) \times (1.06 \text{ if black})$ . (2)

Main covariates: age, race, sex, center, BMI

Analysis: Cox proportional hazards, with exposures modeled as continuous variables and as quartiles. Also look at clinically defined categories.

## **REFERENCES**

1. Wattanakit K, et al. Chronic kidney disease increases risk for venous thromboembolism. J Am Soc Nephrol 2008;19:135-40.
2. Stevens LA, Coresh J, Schmid CH, Feldman HI, Froissart M, Kusek J, Rossert J, Van LF, Bruce RD, III, Zhang YL, Greene T, Levey AS: Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. Am J Kidney Dis 51:395-406, 2008

7.a. Will the data be used for non-CVD analysis in this manuscript? ☐ Yes  
☒ 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 ICTDER03 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  
☒ 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

8.c. If yes, is the author aware that the participants with RES\_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?  
☐ 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.csc.unc.edu/ARIC/search.php>

☒ Yes ☐ No

No overlap other than our previous article cited above.

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)?

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

11.b. If yes, is the proposal

☒ A. primarily the result of an ancillary study (list number\* 1998.03 and 2006.16)

☐ 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 <http://www.csc.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.**