ARIC Manuscript Proposal # 3182

PC Reviewed: 6/12/18 SC Reviewed:	Status: Status:	Priority: 2 Priority:
1.a. Full Title: Migraine and	l Venous Thromboembolisn	n (VTE)
b. Abbreviated Title (Leng	gth 26 characters): Migrain	ne and VTE
2. Writing Group: Writing group members:	Aaron Folsom, Pam Lutsey	, Mary Cushman
I, the first author, confirm tha proposal [please confi		en their approval for this manuscript tronically or in writing]
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ARIC author to be contacted does not respond or cannot be Name: Address:	-	t the manuscript and the first author RIC investigator).
Phone: E-mail:	Fax:	
3. Timeline: Fall 2018		

4. Rationale:

A recent, large, record-based prospective study (Adelborg K et al. BMJ 2018;360:k96) showed positive associations of migraine with multiple cardiovascular outcomes, including venous thromboembolism (VTE) (RR=1.59). A Chinese prospective clinical study found an increased risk of VTE for migraine with aura but not without aura (Peng KP et al. Headache 2016;56:1290-9). A cross-sectional German Study showed a 2-fold higher history of VTE in migraineurs than

in non-migraineurs (Schwaiger J et al. Neurology 2008;71:937-43). In a large, population based sample of pregnant women, VTE discharge codes during pregnancy were 3 fold more common in those with peripartum migraine vs. no migraine (Bushnell CD et al. BMJ. 2009;338:b664).

Although many reports relate cerebral venous thrombosis with migraine-like headaches, the relation of migraine with deep vein thrombosis and pulmonary embolism seems surprising and unexplained. Of course, an association of migraine with stroke is well established (PMIDs 24057117, 28885052, 8864251).

Migraine was self-reported in ARIC by questionnaire at visit 3, which included information on aura. Additionally, the LITE study has validated VTE events, and recently updated VTE occurrence in ARIC through 2015. Therefore using LITE data we can examine the association of migraine with VTE prospectively with better outcome validation than most previous studies on this topic.

5. Main Hypothesis/Study Questions:

Main hypothesis: compared with those free of migraine, participants with migraine have greater VTE incidence in ARIC.

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).

Main design: Prospective

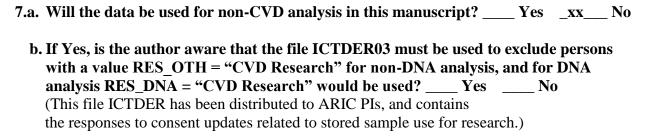
Exposure: migraine assessed at Visit 3; migraine with and without aura

Outcome: time to VTE occurrence **Exclusions**: VTE and anticoagulant use

Potential confounders: sex, race, age, BMI, CKD, cancer diagnosis

Analysis: Calculate age and sex-adjusted incidence rates using Poisson and multivariably adjusted HRs for migraine diagnosis (yes, no) and Cox models. Similar analyses will be done looking at a 3 level exposure (migraine with aura, migraine without aura, no migraine). Subgroup analyses will examine PE/DVT and provoked/unprovoked VTE individually.

If we find an association, in secondary analyses we will try to understand possible explanations by exploring whether biomarkers related to VTE are related to migraine



8.a.	Will the DNA data be used in this manuscript? Yesxx_ 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
	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
-	xxYesNo
,	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)?
	None
	a. Is this manuscript proposal associated with any ARIC ancillary studies or use any illary study data? _xx Yes No
	o. If yes, is the proposalxx A. primarily the result of an ancillary study (list number*2001.16
LIT	TE) B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)*
*an	cillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/
120	Manuscript propagation is expected to be completed in one to three years. If a

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://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.