

ARIC Manuscript Proposal # 847r

PC Reviewed: 11/29/01

Status: A

Priority: 1

SC Reviewed: 12/03/01

Status: A

Priority: 1

1.a. Full Title: Platelet, endothelial and fibrinolytic proteins in MRI-detected cerebral infarction

b. Abbreviated Title (Length 26 characters): MRI and hemostasis

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:

8 weeks- Data analysis and manuscript preparation

4. Rationale

Population based and clinical prospective studies have shown independent association of several hemostatic factors with CHD and stroke (1-3). There are very few reports on the association of hemostatic factors with subclinical brain infarct-like lesions detected by MRI. These lesions, because of their relation to disease of very small arteries and arterioles, may be particularly susceptible to a hypercoagulable state of the blood. The ARIC study previously showed that increased levels of fibrinogen and von Willebrand factor and reduced level of protein C were associated with cerebral infarction identified by MRI (4). The ARIC study measured more hemostatic factors in Visit 3, including platelet activation markers beta-thromboglobulin, fibrinolytic factors and inhibitors plasminogen, t-PA, PAI-1 and D-dimer. In addition, the vasoprotective endothelial molecule thrombomodulin was measured as well as TMA455V polymorphism. Several studies of patients with cerebrovascular disease have used plasma B-TG concentrations as an indicator for the activation of platelets, suggesting

that the platelets participate in the development of most ischemic strokes (5-7). There is little information about the relationship of endothelial, fibrinolytic or platelet markers in MRI-detected small brain infarcts.

- 1 Catto AJ, Grant PJ. Risk factors for cerebrovascular disease and the role of coagulation and fibrinolysis. Blood Coagul Fibrinolysis 1995;6:497-510.
2. Smith et al. Hemostatic factors as predictors of ischemic heart disease and stroke in the Edinburgh Artery Study. Arterioscler Thromb Vasc Biol 1997;17:3312-3325.
3. Folsom AR et al. Prospective study of markers of hemostatic function with risk of ischemic stroke. Circulation 1999;100:736-742.
4. Knuiman MW et al. Association of hemostatic variables with MRI-detected cerebral abnormalities: the ARIC study. Neuroepidemiology 2001;20:96-104.
5. Taomoto K et al. Usefulness of the measurement of plasma BTG in cerebrovascular disease. Stroke 1983;14:518-524.
6. Shah AB et al. Enhanced in vivo platelet activation in subjects of ischemic stroke. Stroke 1985;16:643-647.
7. Woo E et al. Beta-thromboglobulin in cerebral infarction. J Neurol Neurosurg Psychiatry. 1988;51:557-562.

5. Main Hypothesis/Study Questions: a) Higher plasma levels of B-TG, DD, and lower plasma levels of plasminogen and thrombomodulin are associated with excess intravascular thrombogenesis in subjects with MRI infarcts.

6. Data (variables, time window, source, inclusions/exclusions): Visit 3 MRI data will be related to visit 3 measures of BTG, t-PA, Plasminogen, PAI-1, D-dimer, soluble thrombomodulin, TMA455V, vWf and CRP. Major risk factors will be adjusted for using logistic regression.

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://bios.unc.edu/units/csc/ARIC/stdy/studymem.html>

X Yes No