# Platelet receptor glycoprotein VI in thrombus formation and growth in atrial fibrillation and venous thromboembolism

Submission date	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered		
11/06/2016		[X] Protocol		
<b>Registration date</b>	Overall study status	Statistical analysis plan		
02/08/2016	Completed	[] Results		
Last Edited	Condition category	[_] Individual participant data		
17/08/2022	Circulatory System	[] Record updated in last year		

## Plain English summary of protocol

## Background and study aims

Platelets are small blood cells that help wounds to heal and help to stop bleeding by forming blood clots. However, if these blood clots form inside blood vessels (thrombosis) they can cause heart attacks, stroke or peripheral vascular disease. Atrial fibrillation (AF) is the term used to refer to common cardiac (or heart) condition which causes an irregular and often abnormally fast heart rate, in some cases faster than 100 beats per minute. The risk of developing the condition increases with age and anyone with the condition is up to 7 times more likely to have a stroke. This is due to the 'fibrillating' movement of the heart chambers causing a build-up of a blood clot in the heart which can then migrate (travel to) to the brain causing a stroke. Similar blood clots can also develop in blood vessels such as veins. People that have blood clots in the veins (for example a deep vein thrombosis) are sad to suffer from venous thromboembolic disease. Venous thromboembolism (VTE) can occur in patients that are hospitalised and are relatively immobile due to the disease that caused their admittance to hospital. It is believed that the way clots formation due to atrial fibrillation and venous thromboembolism is similar, but the involvement of platelets is not fully understood as yet. Cholesterol plaques develop in blood vessels in, for example, older people, people with high blood cholesterol, smokers, people with high blood pressure and people with diabetes. These plaques can rupture, exposing collagen to the blood stream which, in turn, leads to the formation of blood clots. Again, these blood clots can migrate to other places in the body to cause heart attack and stroke. There is currently a mass of evidence which points to glycoprotein VI (GPVI) as the main platelet receptor (a protein involved in platelets adhering, or getting stuck to, collagen) involved in the early stages of blood clot formation due to its interaction with exposed collagen at the sites of plaque rupture. What is not known, however, is its role in blood clot formation in AF and VTE where the platelet clumping and blood clot formation is independent of collagen and plague rupture. There is recent emerging evidence that fibrin, a compound that which acts to stabilise a blood clot interacts with GPVI and activates platelets. If so this would be a common mechanism for blood clot formation and growth in both AF and venous thromboembolic disease. The GRAFITE (Glycoprotein six Receptor in Atrial FIbrillaiton and ThromboEmbolism) study will investigate the involvement of platelets in blood clot formation. The research team will specifically look at any genetic variances that cause blood clot formation, as well as doing some investigation of the

platelet receptor (glycoprotein VI dimer) and its role in blood clot formation. The research will be carried out in patients admitted to hospital with either atrial fibrillation or venous thromboembolism (for example, deep vein thrombosis), and the role of the Glycoprotein VI receptor plays in the formation of blood clots will be further investigated.

Who can participate? Adults who have been admitted to hospital with AF or confirmed venous thromboembolic disease.

## What does the study involve?

This study involves taking blood samples taken from patients for genetic analysis, platelet activation and glycoprotein VI dimer levels using a method called flow cytometry. This is carried out by laboratory testing on blood samples (from one blood sample per patient). The blood samples are taken on day two of admission, after consent is obtained. Laboratory measurements are then carried out the day the blood is taken, and within 8 hours of collection.

What are the possible benefits and risks of participating? Not provided at time of registration

Where is the study run from? Cambridge University NHS Foundation Trust and the University of Cambridge (UK)

When is the study starting and how long is it expected to run for? June 2016 to October 2017

Who is funding the study? British Heart Foundation

Who is the main contact? Dr Isuru Induruwa ii231@cam.ac.uk

#### Study website

http://www.neurology.cam.ac.uk/

## **Contact information**

#### **Type(s)** Public

**Contact name** Dr Isuru Induruwa

## **Contact details**

Clinical Neurosciences Box 83 Cambridge University Hospitals NHS Foundation Trust Cambridge United Kingdom CB2 0QQ +44 1223 245151 ii231@cam.ac.uk

# Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

Secondary identifying numbers N/A

# Study information

**Scientific Title** Glycoprotein six Receptor in Atrial FIbrillation and ThromboEmbolism

## Acronym GRAFITE

## Study objectives

Levels of platelet glycoprotein VI receptor are higher in blood samples of patients with atrial fibrillation and venous thromboembolism compared to healthy normals.

**Ethics approval required** Old ethics approval format

**Ethics approval(s)** Cambridge East Ethics, 29/11/2016, ref: 16/EE/0436

**Study design** Observational cross-sectional cohort study

**Primary study design** Observational

**Secondary study design** Cohort study

**Study setting(s)** Hospital

**Study type(s)** Not Specified

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied

Atrial fibrillation and venous thromboembolism

## Interventions

This study involves taking blood samples taken from patients for genetic analysis, platelet activation and glycoprotein VI dimer levels via flow cytometry. This will be carried out by laboratory testing on blood samples (one single blood draw) collected from patients who have atrial fibrillation (either a new diagnosis or known) or venous thromboembolic disease, who are admitted to hospital. The blood samples will be taken on day two of admission, after consent is obtained. Laboratory measurements will be carried out the day of blood draw, within 8h of collection. Measurements will include total glycoprotein VI and dimer levels on platelets, genetic analysis, and blood measurements of known biomarkers of thrombus formation, atrial fibrillation and coagulation.

## Intervention Type

Other

## Primary outcome measure

Measuring platelet glycoprotein VI dimer levels from blood taken when patients are admitted to hospital with atrial fibrillation or venous thromboembolism, as measured by mean fluorescence on flow cytometry

## Secondary outcome measures

1. Measure the correlation between glycoprotein VI dimer mean florescence intensity on flow cytometry with levels of known common blood biomarkers for atrial fibrillation, coagulation and stroke (d-dimer, hs-CRP, BNP)

2. Measure the correlation between glycoprotein VI dimer levels as measured by mean fluorescence on flow cytometry and estimated risk of stroke as stratified by the CHADS2-VASC2 score calculated at the time of participant involvement

3. Determine the genetic basis for atrial fibrillation and venous thromboembolism and a therefore look for a genetic basis for possible pre-disposition to stroke

## Overall study start date

15/06/2016

# Completion date 30/09/2019

# Eligibility

## Key inclusion criteria

1. Patients with a new diagnosis of AF and those with persistent or paroxysmal AF, whether they are on anticoagulation or not

- 2. Patients with confirmed venous thromboembolic disease
- 3. Admitted under a medical team to Cambridge University Hospitals

## Participant type(s)

## Patient

## Age group

Adult

Sex

Both

**Target number of participants** 150

Total final enrolment

79

## Key exclusion criteria

1. No clear confirmation of the presence of atrial fibrillation in medical notes or ECG (for AF patients)

2. No confirmed venous thromboembolic disease on any imaging modality (only for those with suspected VTE)

- 3. Age less than 18 years
- 4. Pregnancy
- 5. Active and known malignancy
- 6. Known platelet disorder
- 7. Known HIV/AIDS
- 8. Known hepatitis B or hepatitis C infection
- 9. Admitted with a transient ischaemic attack or stroke ischaemic or haemorrhagic

10.Patients who lack capacity

## Date of first enrolment

01/10/2016

Date of final enrolment 01/10/2017

# Locations

**Countries of recruitment** England

United Kingdom

**Study participating centre Cambridge University NHS Foundation Trust** Hills Road Cambridge United Kingdom CB2 0QQ **Study participating centre Department of Biochemistry, University of Cambridge** Downing Site Cambridge United Kingdom CB2 1QJ

# Sponsor information

**Organisation** British Heart Foundation

## **Sponsor details**

Division of Cardiovascular Medicine ACCI, Level 6, Box 110 Addenbrooke's Hospital Hills Road Cambridge United Kingdom CB2 0QQ

**Sponsor type** Charity

ROR https://ror.org/02wdwnk04

# Funder(s)

## Funder type

Charity

**Funder Name** British Heart Foundation

**Alternative Name(s)** the bhf, The British Heart Foundation, BHF

**Funding Body Type** Private sector organisation

**Funding Body Subtype** Trusts, charities, foundations (both public and private) **Location** United Kingdom

# **Results and Publications**

## Publication and dissemination plan

Not provided at time of registration

Intention to publish date 01/02/2023

# Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

## IPD sharing plan summary

Published as a supplement to the results publication

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<u>Protocol file</u>	version 2	10/11/2016	15/08/2022	No	No
HRA research summary			28/06/2023	No	No