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Personalised antiplatelet therapy for patients with narrowing/blocked blood supply to their legs

Submission date
18/10/2023

Recruitment status
No longer recruiting

Registration date
01/11/2023

Overall study status
Completed

Last Edited
13/12/2024

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Peripheral arterial disease (PAD) is a condition where the blood vessels in the legs get blocked. It affects one out of every five adults over the age of 65. As it is the main cause of amputations, the NHS performs over 20,000 operations every year to prevent them. People with PAD benefit from tablets to thin their blood as this improves outcomes after surgery and prevents heart attacks and strokes. The main tablets for this purpose are called aspirin and clopidogrel. These tablets work well in most people, but up to a third of patients do not get any benefit from them, as their bodies cannot process them. This is called resistance to therapy (RT). Because blood thinning is particularly important after operations people with RT may be at higher risk of their operation failing leading to amputation and/or problems such as heart attacks and strokes. Testing for RT has not traditionally been performed because it requires complex laboratory procedures. Recent developments in technology now mean that bedside tests are available for RT. In this study, a simple bedside test for RT will be used to see if patients with severe PAD have RT and whether this affects their risk of complications after an operation. If it is found that RT does affect outcomes for patients with PAD, the information obtained will be used to plan future research to determine if changing blood thinning therapy in people with RT improves their outcomes.

Who can participate?
Adult patients aged 18 years old and over with PAD

What does the study involve?
The study involves a face-to-face baseline appointment where information will be collected about the participants and their medical health. During this appointment, blood samples will be taken to assess any response to the blood thinning medication currently prescribed. Participants will then be contacted in 6 and 12 months via telephone for a 15-minute conversation regarding their medical health.

What are the possible benefits and risks of participating?
Although participants will not receive any extra benefit from taking part, research like this helps

to continually improve the treatment and care provided to all patients now and in the future. There are no extra risks involved in taking part in this research. Participants will not be asked to try any new treatments. Choosing to participate in any of the additional assessments has the main disadvantage of having to give up some time. In addition, bruising may be experienced when blood samples are taken.

Where is the study run from?
University of Leicester (UK)

When is the study starting and how long is it expected to run for?
November 2021 to March 2025

Who is funding the study?
John and Lucille van Geest Foundation (UK)

Who is the main contact?
Sarah Jane Messeder, sjm104@leicester.ac.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
293977

ClinicalTrials.gov number
NCT06047002

Secondary identifying numbers
IRAS 293977, 0829

Study information

Scientific Title
Personalised ANtiplatelet THERapy for patients with symptomatic Peripheral Arterial Disease (PANTHER-PAD)

Acronym
PANTHER-PAD

Study objectives
Identification of patients with peripheral arterial disease with resistance to therapy will allow individualisation of anti-platelet treatment, preventing limb loss and reducing the risk of death

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/12/2021, East Midlands - Nottingham 1 Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8115; nottingham1.rec@hra.nhs.uk), ref: 21/EM/0260

Study design
Prospective observational cohort study

Primary study design
Observational

Secondary study design

Cohort study

Study setting(s)
Hospital, Medical and other records, Telephone

Study type(s)
Diagnostic, Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Resistance to antiplatelet therapy in patients with peripheral arterial disease

Interventions
Peripheral arterial disease (PAD) is a condition where the blood vessels in the legs get blocked. It affects one out of every five adults over the age of 65. As it is the main cause of amputations, the NHS performs over 20,000 operations every year to prevent them. People with PAD benefit from tablets to thin their blood as this improves outcomes after surgery and prevents heart attacks and strokes. The main tablets for this purpose are aspirin and clopidogrel. These work in most people, but up to a third of patients do not get any benefit from them, as their bodies cannot process them. This is called resistance to therapy (RT). Since blood thinning is particularly important after operations, people with RT may be at higher risk of their operation failing leading to amputation and/or problems such as heart attacks and strokes. Testing for RT has not traditionally been performed because it requires complex laboratory procedures. Recent development in technology now means that bedside tests are available for RT. In this study, a simple bedside test for RT will be used to see how many patients with severe PAD have RT and whether this affects their risk of complications after an operation. If RT is found to affect outcomes for patients with PAD, the information obtained will be used to plan future research to determine if changing blood thinning therapy in people with PAD improves their outcomes after surgery.

Primary objective:
To examine the feasibility of using the VerifyNow PRU and Aspirin assays to obtain estimates of the prevalence of resistance to antiplatelet therapy (aspirin & clopidogrel) in patients with symptomatic PAD. [Time Frame: 18 months]

Prevalence of resistance to aspirin and clopidogrel will be calculated as:
Prevalence = (Number of patients resistant/Total study population) * 100

The VerifyNow PRU Test (CPT85576) is reported as P2Y12 Reaction Units (PRU). PRU measures the extent of platelet aggregation in the presence of a P2Y12 inhibitor.
<180 PRU - suggests P2Y12 inhibitor effect
180-376 PRU - suggests lack of P2Y12 inhibitor effect.

The VerifyNow Aspirin (CPT 85576) test is reported as Aspirin Reaction Units (ARU). ARU measures the extent of platelet aggregation in the presence of Arachidonic acid.
</= 549 ARU - Evidence of platelet dysfunction due to aspirin
> 550 ARU - No evidence of aspirin-induced platelet dysfunction.

Secondary objective:
To examine whether resistance to antiplatelet therapy is associated with major adverse cardiac or limb events during the follow-up interval of one year [Time Frame: 18 months]
Risk ratio = Cumulative incidence of major adverse cardiac/limb events in the Resistant Groups /Cumulative Incidence of Major events in the non-Resistant group

Major adverse cardiac events = myocardial infarction, stroke, cardiovascular death Major adverse limb events = major amputation, acute limb ischaemia, re-operation.
Events will be assessed through interrogation of electronic medical records and phone calls with participants at both 6 months and one-year follow up.

Intervention Type
Other

Primary outcome measure
Feasibility of using the VerifyNow PRU and Aspirin assays measured using the obtained estimates of the prevalence of resistance to antiplatelet therapy (aspirin & clopidogrel) in patients with symptomatic peripheral arterial disease at 18 months

Secondary outcome measures
To examine whether resistance to antiplatelet therapy is associated with major adverse cardiac or limb events during the follow-up interval of one year measured using the risk ratios in the resistant and non-resistant groups of cumulative incidence of major adverse cardiac/limb events assessed through interrogation of electronic medical records and phone calls with participants at both 6 months and one year follow up

Overall study start date
20/11/2021

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Aged 18 years old and over
2. Severely symptomatic aorto-iliac and infra-inguinal peripheral arterial disease
3. Ability to provide written informed consent
4. Patients on antiplatelet therapy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
80

Total final enrolment
87

Key exclusion criteria
1. Aged 17 years old and under
2. Unable or unwilling to provide written informed consent
3. Acute limb ischaemia of the lower limb
4. Aneurysmal disease of the arteries of the lower limb
5. Severe diabetic foot sepsis
6. A known history of clotting disorders
7. Inherited bleeding disorders

Date of first enrolment
25/05/2023

Date of final enrolment
14/03/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Glenfield Hospital
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Sponsor information

Organisation
University of Leicester

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Sponsor type
University/education

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ROR
https://ror.org/04h699437

Funder(s)

Funder type
Charity

Funder Name
John and Lucille Van Geest Foundation

Alternative Name(s)
THE JOHN AND LUCILLE VAN GEEST FOUNDATION

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
Planned publication in a high-impact peer-reviewed journal

Intention to publish date

01/12/2025

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?
Participant information sheet	version 1.3	17/05/2023	24/10/2023	No	Yes