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How do frailty, muscle strength and multiple health conditions affect outcomes (survival, limb loss and return to normal function) for patients with longstanding circulatory problems in the lower limbs?

Submission date	**Recruitment status**	[_] Prospectively registered
06/09/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/10/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
25/10/2021	Circulatory System	[_] Record updated in last year

Plain English summary of protocol

Background and study aims

In this study the researchers want to find out if there are any routine bedside tests or tests used in everyday care that might suggest that patients are at an increased risk of poorer outcomes. One of the conditions known to influence outcome is frailty. Frailty is a mix of a reduction in function of multiple areas such as muscle strength, movement and other medical problems. These all contribute to less effective recovery and outcome in other areas of medicine and surgery. There may be a similar problem that is not yet fully understood for patients with blood supply issues affecting the lower legs (termed chronic limb-threatening ischaemia [CLTI]). The researchers hope to find out how many patients are affected by frailty and if there are any links with the outcome of their care for the lower limb blood supply.

Who can participate?

Patients aged over 18 years with a leg wound (ulcer), constant pain at rest or gangrene, due to vascular (circulatory) disease

What does the study involve?

The researchers will collect details about the participants (age, sex, weight, height) and the surgery they will receive, as well as carry out routine blood tests. Their current level of frailty will be assessed through a physical test and through routine (CT) medical imaging (if performed). The physical test will involve a grip strength assessment and a five times sit-to-stand test, where participants will be asked to stand up from a chair and sit back down a total of five times (if they can). The medical imaging will involve a CT scan to assess for the muscle mass in the back and the affected limb. The researchers will also use the ultrasound scan images that will routinely be carried out to look at the blood supply in the limbs. The researchers will then observe the participant's recovery following their procedure, taking note of their recovery time and overall progress. Participants will be invited to fill out a questionnaire 90 days after their procedure,

which they can either complete through the telephone or through the post. The questionnaire will be a widely utilised health survey looking at their current wellbeing. The researchers will also see participants back in the clinic as per routine care.

What are the possible benefits and risks of participating?
The information from this study will be useful to improve the overall quality of care for future patients diagnosed with chronic limb-threatening ischaemia. The results are likely to improve care not only in the local area, but also nationally. Being part of a study also means that there is extra healthcare input compared to standard care. There would be no significant disadvantages or risks in taking part in the study. Participants will be receiving the same care as before, and all the data collected will be anonymised.

Where is the study run from?
Freeman Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2019 to September 2022

Who is funding the study?
NIHR Biomedical Research Centre Newcastle (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
294528

Protocol serial number
CPMS 49622, IRAS 294528

Study information

Scientific Title
A multicentre prospective observational study to investigate the prevalence and short-term impact of frailty in chronic limb-threatening ischaemia

Acronym
FraiLTI

Study objectives
Patients with chronic-limb threatening ischaemia (CLTI) are venerable to limb loss and premature death. Due to the nature of vascular disease CLTI patients often have multiple long-term conditions. The interaction of these conditions leaves patients at risk of frailty and deconditioning. It is expected that patients with multiple conditions and/or frailty might have worse clinical outcomes. They may well be more susceptible to limb loss, perhaps death and other complications. Potentially they may too be unable to return to their home environment. The FraiLTI study hopes to understand this interaction and highlight key areas for potential optimisation research.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/07/2021, Health Research Authority (HRA) and Health and Care Research Wales (HCRW, Ground Floor, Temple Quay House, Health Research Authority, BS1 6PN, UK; +44 (0)207 104 8328; approvals@hra.nhs.uk), REC ref: 21/PR/0750

Study design
Observational; Design type: Cross-sectional

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic limb-threatening ischaemia

Interventions
All patients admitted with chronic limb-threatening ischaemia (CLTI) to a dedicated vascular centre will be invited to participate. Confirmation of CLTI diagnosis will be made by the admitting vascular specialist. These will then be screened according to the inclusion and exclusion criteria. Patients meeting the below inclusion criteria will be invited to participate in

the FraiLTI study. Patients will undergo routine care in the hospital. On admission, patients will be first notified about the study by a member of the clinical team. If potential participants are interested and would like more information verbal consent for their details to be shared with the FraiLTI (local site academic or clinical academic team). At this point a member of the FraiLTI study team (on the delegation log and meeting GCP etc) will approach the patient to provide the details of the study, PIS etc. After a period of typically 24 hours a study team member will consent the patient formally for participation. Routine data will be collected that is already part of the admission process (no new blood tests or scans). In addition, the EQ5D Quality of Life assessment will be made at baseline. Two functional assessments will be made: Grip strength and sit/stand test. This will provide data on frailty. Thereafter if the patients undergo a CT (as per their routine care - no additional imaging) these will be used to measure muscle area. After this patients will then continue on their routine care journey. On discharge, their admission length, surgical procedure and outcomes will be recorded. At 90 days patients will be reviewed electronically to record and adverse outcomes in line with the follow-up data. Patients will be invited to complete an EQ5D Quality of life assessment over the telephone.

Intervention Type
Other

Primary outcome(s)
The prevalence of frailty measured using the Fried Frailty Score at baseline

Key secondary outcome(s))
Measured using patient records:
1. Major cardiovascular events (MACE) recorded according to standard international definitions and occurring within 90 days follow-up
2. Major adverse limb events (major amputation, trans-femoral, through knee or trans-tibial) occurring within 90 days
3. Survival measured by record of date of death up to 90 days follow-up
4. Re-interventions defined as the number of times within 90 days that repeat surgery or procedure (open or endovascular) is required
5. Length of stay in days up to 90 days
6. Discharge home or to another care environment within 90 days

Completion date
01/09/2022

Eligibility

Key inclusion criteria
1. All adults aged over 18 years, able to consent and participate with ongoing assessments
2. All chronic limb-threatening ischaemia patients with specifically:
2.1. Tissue loss
2.2. Rest-pain

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Admissions for non CLTI
2. Unable to agree to assessments or participate in study assessments
3. Pregnant women
4. Under 18 years of age

Date of first enrolment
01/10/2021

Date of final enrolment
01/06/2022

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Scotland

Wales

Study participating centre
St Cadoc's Hospital
Lodge Road
Caerleon
Newport
United Kingdom
NP18 3XQ

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
University Hospitals Bristol
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
St Mary's Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston

Birmingham
United Kingdom
B15 2GW

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Belfast Health & Social Care Trust
Knockbracken Healthcare Park
Saintfield Road
Belfast
United Kingdom
BT8 8BH

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Newcastle Biomedical Research Centre

Alternative Name(s)
Newcastle Biomedical Research Centre, Newcastle NIHR Biomedical Research Centre

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.2	01/07/2021	10/09/2021	No	Yes
Protocol file	version 2.0	01/07/2021	10/09/2021	No	No