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Use of ultrasound lithotripsy to treat calcified peripheral arterial disease

Submission date 26/09/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 28/09/2021	**Overall study status** Completed	
Last Edited 06/08/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Peripheral arterial disease is a common condition where arteries in the leg are blocked or narrowed. It is the main cause of lower-limb amputations. Patients who have peripheral arterial disease often need a procedure to open up their diseased arteries. One of the common reasons why these procedures fail is the presence of calcium on the artery walls. A new treatment called intravascular lithotripsy was recently introduced in the NHS. Intravascular lithotripsy is meant to break down the calcium on diseased artery walls. This study aims to assess what happens to patients in the NHS in different hospitals after they have had intravascular lithotripsy.

Who can participate?
Patients aged over 18 years with peripheral arterial disease who are undergoing intravascular lithotripsy

What does the study involve?
Participants will be observed for 1 year after their intravascular lithotripsy procedure. The researchers will document information about their health and their treated artery (does the treated artery remain open?). They will also ask some patients to have another scan 3 days after the intravascular lithotripsy to see if the artery calcium has broken down.

What are the possible benefits and risks of participating?
This study will not impact the participants' NHS care, which will continue as normal. The main risk of taking part relates to the additional scan that some participants might opt to have, 3 days after the intravascular lithotripsy.

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

When is the study starting and how long is it expected to run for?
March 2021 to June 2023

Who is funding the study?
Shockwave Medical (USA)

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
299307

Central Portfolio Management System (CPMS)
50377

Protocol serial number
1.0

Study information

Scientific Title
Shockwave lithotripsy for calcified plaques in patients with peripheral arterial disease: a pragmatic registry with in-depth automated plaque analysis

Acronym
SHOCC

Study objectives
An angioplasty is a procedure where an artery is opened using wires and balloons. It is the most common procedure offered to patients with peripheral arterial disease (PAD), especially those with limb-threatening ischaemia, and it is recommended by international guidelines. Many factors can affect how long the arteries treated with angioplasty can remain open for. Calcium in the artery is one of the main factors which might cause a new blockage in an artery treated with angioplasty. The presence of a calcified plaque independently predicts restenosis at 1 year after angioplasty.

Intravascular lithotripsy has been developed as an adjunct to plain balloon angioplasty for severely calcified arterial plaques in patients with PAD. This device (produced by Shockwave Medical) shatters the calcium within the atherosclerotic plaque into tiny particles using ultrasound (energy) via a standard angioplasty balloon. The assumption is that applying intravascular lithotripsy makes the plaque more compliant and hence the plaque responds better to angioplasty.

Intravascular lithotripsy has the potential to greatly improve the treatment of patients with calcified atherosclerotic plaques and severe PAD, since it might decrease the need for stenting

(associated with increased costs and complications), decrease the duration of the procedure, limit the need for re-intervention, reduce the possibility of peripheral embolisation, and overall improve long-term clinical results i.e. reduce the chance of amputation.

Before proceeding to a large-scale randomised study across the whole of the NHS, this current study will provide us with valuable information in order to plan such future studies, including: clinical performance of this technology in patients with severe PAD and chronic limb-threatening ischaemia (a group of patients who have very calcified arterial plaques), mechanistic information as to how the plaque responds to intravascular lithotripsy, information about clinicians' equipoise and feasibility of performing a randomised study and the number of eligible patients seen at NHS centres treating patients with PAD. Further, this prospective multi-centre cohort study will provide important clinical information for patients treated with intravascular lithotripsy in the NHS, including: patency after treatment with this technology, additional treatments used with the intravascular lithotripsy, amputation free survival, duration of hospital stay, and number of re-interventions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/09/2021, Wales Research Ethics Committee (REC) 4 Wrexham (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 785738; Wales.REC4@wales.nhs.uk), REC ref: 21/WA/0270

Primary study design
Observational

Study design
Multicentre national prospective cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Peripheral arterial disease

Interventions
Once a participant has consented to take part, the study team will collect information about their medical and surgical history as well as clinical presentation. Further, details regarding their intravascular lithotripsy procedure will be documented and the participant will be observed for 12 months. Major complications and further surgical procedures will be documented. Participants will also be asked if they wish to take part in a sub-study, where the study team will assess the composition of the atheromatic plaque 3 days after the intravascular lithotripsy procedure. This will be done using a computed tomographic scan, limited to the region treated using intravascular lithotripsy.

Intervention Type
Device

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
Intravascular lithotripsy (Shockwave device)

Primary outcome(s)
Patency of the treated arterial atherosclerotic lesion measured using duplex ultrasound at 6 months after the procedure has taken place

Key secondary outcome(s)
Baseline (pre intravascular lithotripsy) data collection:
1. Demographic information (age at time of recruitment, sex)
2. Weight/height, resting BP (anthropometric measurements)
3. Rutherford stage relating to PAD presentation
4. Ankle-brachial pressure index measured using a blood pressure cuff
5. Baseline full blood count results and routine biochemistry, including total cholesterol levels, and lipid profile measured using patients' existing blood tests
6. Baseline serum creatinine and estimated glomerular filtration rate measured using patients' existing blood test
7. Chronic kidney disease status measured using estimated glomerular filtration rate
8. Diabetes status, duration of diabetes history, and current diabetes medication(s) measured using patients' notes
9. History of previous major cardiovascular events measured using patients' notes
10. Results of cross-sectional imaging relating to the arterial vasculature e.g. duplex or computed tomographic angiography*
11. Smoking status
12. WiFi score
13. Previous operations, including a full surgical and vascular history measured using patients' notes
14. All concomitant medications as reported by patients
15. Anonymised minutes from multi-disciplinary team meetings relating to the patient's care

Day of procedure (post intravascular lithotripsy) data collection:
The data collected here will relate to information obtained during the intravascular lithotripsy
1. Exact location of the lesion treated measured using the intra-operative images
2. Number and size(s) of intravascular lithotripsy catheters used measured using the intra-operative images
3. Duration of intravascular lithotripsy application per arterial site in seconds measured using patients' operation notes
4. Exact anatomy (number of occlusions or stenoses) of the arterial lesions present on intra-operative angiography
5. Nature of the additional surgical or endovascular treatments taking place measured using patients' notes
6. Duration of the whole procedure
7. Immediate complications during the procedure and steps taken to address them (e.g. thrombectomy) measured using patients' notes
8. Patency of the treated lesions measured using ultrasound
9. Level of operators performing the procedures
10. Volume of contrast used during the procedure measured using the patient's operation note

Day of discharge data collection:
Where available, the data collected here will relate to the period between the completion of the intravascular lithotripsy procedure and the day of discharge

1. Re-interventions of any nature measured using patients' notes
2. Amputations of any nature measured using patients' notes
3. Ankle brachial pressure index measured using a blood pressure cuff
4. Full blood count results and routine biochemistry
5. Major cardiovascular events during inpatient stay measured using patients' notes
6. Duration of inpatient stay (ward and intensive care where applicable) measured using patients' notes
7. Reason(s) for admission to intensive care if relevant measured using patients' notes
8. Results of cross-sectional imaging relating to the arterial vasculature e.g. duplex or computed tomographic angiography (all of these are routine care)
9. WiFi score
10. All concomitant medications measured using patients' notes

30-day post-discharge data collection:
The data collected here will relate to the time period between the procedure 30 days post discharge.
1. Re-intervention(s) - nature and reasons why this occurred measured using patients' notes
2. Amputation(s) - nature and reasons why this occurred measured using patients' notes
3. Ankle brachial pressure index measured using a blood pressure cuff
4. Major cardiovascular events measured using patients' notes
5. Results of cross-sectional imaging relating to the arterial vasculature e.g. duplex or computed tomographic angiography
6. WiFi score
7. All concomitant medications measured using patients' notes
8. Arterial duplex scan of the affected lower limb (standard of care for patients with severe limb-threatening ischaemia)

6 months post-discharge data collection (final follow-up):
The data collected here will relate to the time period between the procedure 6 months post-discharge.
1. Weight/height, resting BP (anthropometric measurements)
2. Rutherford stage
3. Ankle brachial pressure index measured using a blood pressure cuff
4. Baseline full blood count results and routine biochemistry, including total cholesterol levels, and lipid profile measured using patients' notes
5. Baseline serum creatinine and estimated glomerular filtration rate measured using patients' notes
6. Chronic kidney disease status measured using estimated glomerular filtration rate
7. Diabetes status, duration of diabetes history, and current diabetes medication(s) measured using patients' notes
8. History of previous major cardiovascular events measured using patients' notes
9. Results of cross-sectional imaging relating to the arterial vasculature e.g. duplex or computed tomographic angiography (all of these are routine care)
10. Smoking status
11. Previous operations, including a full surgical and vascular history measured using patients' notes
12. Results of cross-sectional imaging relating to the arterial vasculature e.g. duplex or computed tomographic angiography*
13. WiFi score
14. Quality of life measured using the EuroQol-5D (EQ-5D) questionnaire
15. Recording of all concomitant medications as reported by patients

Completion date
30/06/2023

Eligibility

Key inclusion criteria
Patients:
1. Adults (>18 years of age)
2. Diagnosed with symptomatic PAD (severe incapacitating intermittent claudication or chronic limb-threatening ischaemia - Rutherford stages 4–6)
3. Referred to secondary care to undergo lower limb revascularisation using intravascular lithotripsy
4. Able to understand written and spoken English
5. Willing and able to give written informed consent for participation in the study

Healthcare professionals:
The clinicians who have performed the intravascular lithotripsy procedure on participants included in this research study

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
99

Key exclusion criteria
Patients:
1. Female participants who are pregnant, lactating or planning pregnancy during the course of the study
2. Patients who do not have the capacity to consent for themselves
3. Patients with a life-limiting condition where conservative management is most appropriate
4. Patients with asymptomatic PAD
5. Patients with acute lower limb-threatening lower limb ischaemia
6. Patients not being referred for lower limb revascularisation using intravascular lithotripsy

Date of first enrolment
01/10/2021

Date of final enrolment
01/04/2023

Locations

Countries of recruitment
United Kingdom

England

Wales

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University Hospitals of Leicester
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Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
Shockwave Medical

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		22/05/2024	20/06/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.0	14/09/2021	28/09/2021	No	Yes
Protocol file	version 1.0	14/09/2021	28/09/2021	No	No
Protocol file	version 1.3	19/01/2023	06/08/2024	No	No