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Feasibility study of radiofrequency endoscopic ablation, with ultrasound guidance, as a non-surgical, adrenal sparing treatment for aldosterone-producing adenomas

Submission date 03/01/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 12/01/2018	**Overall study status** Completed	
Last Edited 23/06/2022	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
High blood pressure (hypertension) causes strokes and heart attacks. While most patients need long-term treatment with pills, some have a cause which can be removed, curing the hypertension. The commonest curable cause is a benign nodule (adenoma) in one of the hormone glands, the adrenals, causing a condition called primary hyperaldosteronism. About one in 20 patients have such a nodule, but difficulties with diagnosis, and reluctance to undergo surgery for a benign condition, limit the number having adrenal gland surgery to fewer than 300 per year in the UK. A potential, and exciting, solution to this dilemma is to use a momentary electric current to cauterise the nodule (radiofrequency ablation), without affecting the rest of the adrenal gland, and avoiding the need for surgery. Nodules in the left adrenal gland are easily reached under mild sedation using a similar procedure as is standard for investigating stomach ulcers (endoscopy). The aim of this study is to show that this approach (called endoscopic ultrasound guided radiofrequency ablation) is very safe, and to provide initial evidence that the hormone abnormality is cured.

Who can participate?
Patients aged 18 and over with primary hyperaldosteronism

What does the study involve?
A probe is placed under ultrasound guidance by an experienced endoscopist into the identified aldosterone-producing adenoma of the affected left adrenal gland. Ablation is then achieved using electrical energy for a total of up to 25 minutes (10x90 second applications with 60 seconds rest between applications) to remove the aldosterone-producing adenoma. All patients following treatment attend follow up clinic visits as per the study schedule. The total duration for treatment to follow up is 6 months.

What are the possible benefits and risks of participating?
The study is expected to demonstrate that the treatment is safe and offers similar cure rates to

surgical removal of the whole adrenal gland, which is the usual treatment. If ablation is effective, its benefit is transformational, allowing patients to have the benefits of surgery without the side effects, and opening up a potential cure for hypertension to a much larger number of patients. Although the endoscopic route is likely to be lower risk there needs to be a formal assessment of its safety and potential effectiveness for controlling high blood pressure.

Where is the study run from?
St Bartholomew's Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2016 to September 2022

Who is funding the study?
British Heart Foundation (BHF) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03405025

Secondary identifying numbers
34735

Study information

Scientific Title
Feasibility study of RadioFrequency endoscopic ABlation, with ULtrasound guidance, as a non-surgical, Adrenal Sparing treatment for aldosterone-producing adenomas

Acronym
FABULAS

Study objectives
High blood pressure (hypertension) causes strokes and heart attacks. While most patients need long-term treatment with pills, some have a cause which can be removed, curing the hypertension. The commonest curable cause is a benign nodule in one of the hormone glands, the adrenals. About one in 20 patients have such a nodule, but difficulties with diagnosis, and reluctance to proceed to surgery for a begnin condition, limit the number having adrenal gland surgery to fewer than 300 per year in the UK. A potential, and exciting, solution to this dilemma is to use a momentary electric current to cauterise the nodule (radiofrequency ablation), without affecting the rest of the adrenal gland, and avoiding the need for surgery. Nodules in the left adrenal gland are easily reached under mild sedation using a similar procedure as is standard for investigating stomach ulcers (endoscopy). This study is designed to show that this approach (endoscopic ultrasound guided radiofrequency ablation) is very safe, and to provide initial evidence that the hormone abnormality is cured.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Bloomsbury Research Ethics Committee, 17/10/2017, ref: 17/LO/0948, IRAS project ID: 222446

Study design
Non-randomised; Interventional; Design type: Treatment, Management of Care

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied

Aldosterone producing adenoma

Interventions
Treatment is via a single monopolar probe placed under EUS guidance by an experienced endoscopist into the identified aldosterone-producing adenoma of the affected left adrenal gland. Ablation is then achieved using an RFA generator to deliver sequential doses of electrical energy at 10W for a total of up to 25 minutes (10x90 second applications with 60 seconds rest between applications) to ablate the aldosterone producing adenoma. All patients following treatment will undergo surveillance with follow up clinic visits as per study schedule. The total duration for treatment to follow up is 6 months.

Intervention Type
Procedure/Surgery

Primary outcome measure
There will be a hierarchical co-primary endpoint. The first co-primary is whether the recorded patient safety outcome data establishes that perforation, haemorrhage infarction of major organs did not occur. This will be assessed at 48 hours.

The second co-primary endpoint is efficacy, assessed biochemically at 3 months post ablation. This will be achieved by:
1. Accurate adverse event reporting
2. Clinical assessment by history and examination looking for features of blood loss, perforation, or inflammation/infarction of peri-adrenal tissues
3. Blood tests for Hb, WBC, Renal function, amylase, liver function Tests, C Reactive Protein. urinalysis for blood and protein

Secondary outcome measures
The difference from baseline measurements at 3 and 6 months following ablation for biochemical and radiological parameters as follows:
1. Plasma electrolytes
2. Aldosterone and renin ratio at 3 and 6 months
3. 3 month PET CT will be performed post ablation for radiological disappearance, diameter size and SUV measurements
4. The reduced use/or no longer taking supplementary potassium
5. Home BP will be measured 3 reading twice a day for 4 days preceding clinic visit
6. Assessment of cure will be performed at the site not involved in patient care, and subject to ratification by the safety committee, who are not involved in the study
7. Reduction in/or no longer taking antihypertensive medication
8. No/or reduced doses of potassium supplementation

Overall study start date
01/04/2016

Completion date
30/09/2022

Eligibility

Key inclusion criteria

1. Patients aged 18 and above
2. Diagnosis of primary hyperaldosteronism (PHA) based on published Endocrine Society guidelines
3. Positive serum aldosterone renin ratio (ARR) with another local diagnostic confirmatory test (MRI or CT imaging)

There are 3 inclusion subset groups:
Group 1:
1. Left-sided APA proven on either AVS or PET CT
2. Patients wishing to take fewer drugs for their hypertension
3. Patients not usually referred for surgery because the benefit: risk is considered too low
4. Patients aged ≥60 whose BP is at or near target (BP140/90 for most patient groups, BP 130/80 if co-morbidities listed in Hypertension guidelines) on treatment with four or more drugs
5. Patients with identified macroadenomas (APAs >= 1 cm in diameter), who have at least 1 cm of peri-adrenal fat on axial and coronal projections

Group 2:
1. Patients aged 18 years and above with diagnosis of PA and either
2. A definite unilateral left APA, but the patient does not want surgery
3. Probable but not unequivocal evidence of a unilateral left adrenal APA

Group 3:
Patients over 18 years of age meeting criteria for surgery, but consent to undergo endoscopic ablation instead.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Key exclusion criteria
1. Inability to give informed consent
2. Any patients continuing on beta blockers/direct renin blockers
3. Pregnant women or those unable or unwilling to take secure contraceptive precautions
4. Any illness, condition or drug regimen considered a contraindication by the PI/CI

Date of first enrolment
20/01/2018

Date of final enrolment
20/11/2020

Locations

Countries of recruitment
United Kingdom

Study participating centre
St Bartholomew's Hospital
West Smithfield
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Sponsor information

Organisation
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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (BHF); Grant Codes: PG/16/40/32137

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
Following statistical analysis the trialists aim to present results at hypertension and endocrine symposiums/conferences with publications in lead cardiovascular and endocrine journals.

Intention to publish date
30/12/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No