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A randomised controlled trial of the angiotensin converting enzyme (ACE) inhibitor ramipril in asymptomatic aortic stenosis

Submission date
30/09/2004

Recruitment status
No longer recruiting

Registration date
30/09/2004

Overall study status
Completed

Last Edited
24/03/2015

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
For patients with aortic stenosis (a narrowing of the main valve out of the heart), the only effective treatment currently is valve replacement surgery. A group of drugs called ACE inhibitors are of proven benefit in treating heart failure from other causes and reducing increased heart muscle thickness, both of which occur in aortic stenosis. They are however considered to be contraindicated in aortic stenosis, despite a lack of evidence for harm. The aim of our study is to determine whether an ACE inhibitor has any beneficial effects in patients with aortic stenosis.

Who can participate?
Men and women aged over 18 years with aortic stenosis.

What does the study involve?
Participants will be randomly allocated to receive either the ACE inhibitor ramipril or a placebo (dummy) drug.

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

Where is the study run from?
John Radcliffe Hospital (UK).

When is the study starting and how long is it expected to run for?
The study ran from October 2008 to December 2011.

Who is funding the study?
1. Heart Research UK (UK)
2. Oxford Comprehensive NIHR Biomedical Research Centre (UK)
3. Department of Health Technology Platform Grant for Advanced Imaging (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)
2007-005224-32

Protocol serial number
N0176135469 / OCMR 06.01

Study information

Scientific Title
A randomised controlled trial of the angiotensin converting enzyme (ACE) inhibitor ramipril in asymptomatic aortic stenosis

Acronym
RIAS

Study objectives
Patients with narrowed aortic valves (the main valve affecting blood flow out of the heart) sometimes develop symptoms of breathlessness or reduced heart function, and this is often accompanied by a thickened heart muscle. This muscle thickening may actually be detrimental to cardiac function, through increased stiffness, and a reduction of this may be beneficial to the patients. A group of drugs called ACE inhibitors are of proven benefit in reducing heart muscle thickness from other causes, and also improve cardiac function and prolong life in patients with

heart failure. We propose a randomised placebo-controlled trial of one ACE inhibitor, ramipril, in patients with narrowed aortic valves to determine if this can reduce muscle thickness, delay the onset symptoms and the need for valve replacement surgery.

On 21/05/2010 the trial record was updated to add the sources of funding.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire REC C, 06/11/2007, ref: 07/H0606/139

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiovascular: asymptomatic aortic stenosis

Interventions
Factory-prepared randomised packs of identical placebo/ramipril tablets. Initial supply for 2 weeks, then further supply at the second clinic visit, to allow for up-titration of ramipril dose. Randomisation data sealed and unopened until after data analysis at end.

Added 19/05/2010: trial started in 2008 instead of 2002.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ramipril

Primary outcome(s)
1. Safety of administration in this group of patients
2. Changes in left ventricular mass and function

Key secondary outcome(s)
Added 21/05/2010:
1. Change in left ventricular ejection fraction
2. Change in other LV functional parameters assessed by MRI
3. Change in biochemical markers of LV function (BNP)

4. Change in myocardial energetics measured with magnetic resonance spectroscopy
5. Time to symptoms of aortic stenosis or aortic valve replacement
6. Change in distance walked and maximal effort tolerance on exercise treadmill testing

Completion date
31/12/2011

Eligibility

Key inclusion criteria
Added 21/05/2010:
1. Male or female, aged 18 years or above
2. Diagnosed with asymptomatic aortic stenosis of at least moderate degree (peak velocity ≥3.0 m/sec; gradient ≥36 mmHg or valve area <1.5 cm2 by echocardiography) for whom aortic valve replacement surgery is currently not contemplated
3. Left ventricular ejection fraction on echocardiography ≥40% without regional wall motion abnormality suggestive of significant previous myocardial infarction
4. Patient is willing and able to give informed consent for participation in the study
5. Able (in the investigators' opinion) and willing to comply with all study requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Added 21/05/2010:
1. Other significant valve disease
2. Female who is pregnant, lactating or planning pregnancy during the course of the study
3. Significant renal impairment (estimated GFR < 30 ml/min). If moderate renal impairment (GFR 30-59 ml/min) is present, patients may be included in the study, but will not receive gadolinium contrast during the CMR scan
4. Known hepatic impairment (AST/ALT > 2 times the upper limit of normal)
5. Prescription of ACE inhibitors or angiotensin II receptor blockers (ARBs) within the 3 months prior to the start of the study
6. Past history of an allergic reaction or intolerance to ACE inhibitors
7. Sustained systolic blood pressure <100 mmHg or >200 mmHg or diastolic blood pressure <40 mmHg or >110 mmHg at baseline measurement
8. Contraindication to magnetic resonance scanning (pacemaker, cranial aneurysm clips, metallic ocular foreign bodies, severe claustrophobia)

9. Patient is terminally ill
10. Any other significant disease or disorder which, in the opinion of the investigator, may either put the patient at risk because of participation in the study, or may influence the result of the study, or the patient ability to participate in the study
11. Patients who have participated in another research study involving an investigational product in the past 3 months

Date of first enrolment
01/10/2008

Date of final enrolment
31/12/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Cardiovascular Medicine
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research organisation

Funder Name
Heart Research UK (UK)

Alternative Name(s)
HRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Oxford Comprehensive NIHR Biomedical Research Centre (UK)

Funder Name
Department of Health Technology Platform Grant for Advanced Imaging (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2015		Yes	No