

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 30/09/2004	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 24/03/2015	Condition category Circulatory System	<input type="checkbox"/> 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

EudraCT/CTIS number
2007-005224-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Study design

Randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

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

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 measure

1. Safety of administration in this group of patients
2. Changes in left ventricular mass and function

Secondary outcome measures

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

Overall study start date

01/10/2008

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 $\geq 40\%$ 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

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

100 patients

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

England

United Kingdom

Study participating centre

Department of Cardiovascular Medicine

Oxford

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Sponsor information

Organisation

University of Oxford (UK)

Sponsor details

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Sponsor type

Government

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ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

Research organisation

Funder Name

Heart Research UK (UK)

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

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

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

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