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How accurate are certain biomarkers in blood detecting silent heart disease in well controlled diabetes?

Submission date
13/11/2015

Recruitment status
No longer recruiting

Registration date
26/11/2015

Overall study status
Completed

Last Edited
10/11/2020

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
A cardiovascular (CV) event refers to an event that causes damage to the heart muscle. This includes any interruption to the blood supply to the heart (such as a blockage of the coronary artery) . People with diabetes are at an high risk of a CV event and it is therefore very important to take steps to prevent them from occurring. This need is highlighted further by the failure of intensive changes to lifestyle and of most oral glucose (blood sugar) lowering treatments (except metformin and recently, Empagliflozin) to reduce CV events. On top of obvious signs of heart disease, a major problem in diabetes is the high number of people with silent but potentially lethal heart disease, i.e. silent ischaemia (inadequate blood supply to the heart but without symptoms), left ventricular hypertrophy (enlargement of the left ventricle of the heart – the part of the heart that pumps blood around the body), left ventricular systolic dysfunction (where the left ventricle does not contract properly), left ventricular diastolic dysfunction (where the left ventricle does not relax normally to let the heart fill with blood before it is pumped around the body) and left atrial enlargement (enlargement of a part of the heart containing blood from the lungs). The purpose of this study is to see how many people with asymptomatic type 2 diabetes (that is, without any symptoms) have multiple silent cardiac abnormalities and whether are there biomarkers (something that can be measured, for example, in the blood) which can identify these silent abnormalities early.

Who can participate?
Patients with type 2 diabetes aged 40 to 85 with no previous known cardiovascular symptoms or events, well controlled blood pressure, well controlled diabetes, no kidney problems and no significant heart disease.

What does the study involve?
After fasting beforehand, blood tests are taken from each participant. They then have a ultrasound scan of their heart (Echo) followed by Dobutamine stress Echo (DSE), a test to assess the hearts function and structures. Should the DSE be contraindicated (that is, if there is any reason why it should not be performed on a patient) or if no conclusions can be drawn from the results, participants have either Myocardial Perfusion Scan (MPS), a procedure where tissues are

examined with the help of a tiny amount of radioactive substance or Computed Tomography Coronary Angiogram (CTCA), a technique for looking at the coronary arteries. 24 hour blood pressure data is also collected. This data is then used to identify participants with silent heart disease and how accurately biomarkers such as High-sensitive troponin T and N-terminal pro-B type natriuretic peptide can detect this disease.

What are the possible benefits and risks of participating?
If data from this study suggests that there are specific tests and markers that may predict heart disease in type 2 diabetes patients who have no symptoms, they can then be given medication to prevent them from developing life threatening events arising from the heart, if this is appropriate. Possible major complications with DSE are heart attack, abnormal heart rhythm and allergic reactions, but these are rare. Minor complications with DSE include palpitations, chest pain, shortness of breath, nausea, vomiting, dizziness and flushing. Participants will receive betablockers to slow down their heart rate for CTCA. The lifetime risk of developing cancer due to this scan would be approximately 1 in 1400 people but this is much smaller than the lifetime risk of developing cancer in the UK, which is 4 in 10 people. On rare occasions, for example if participants have faster heart rate despite betablockers, a slightly larger amount of radiation may be used. There is also a small risk of developing a reaction to the contrast agent. Participants will receive Dipyridamole if necessary for MPS. The lifetime risk of developing cancer due to MPS is approximately 1 in 1700 people. This is much smaller than the lifetime risk of developing cancer in the UK, which is 4 in 10 people. Dipyridamole medicine is safe and tolerable. Some may experience minor side effects such as dizziness, headache, nausea and chest discomfort. These symptoms usually last only a few minutes.

Where is the study run from?
Ninewells Hospital & Medical School, Dundee (UK)

When is the study starting and how long is it expected to run for?
August 2015 to August 2017.

Who is funding the study?
Chief Scientist Office, Scotland (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
2013DM14

Study information

Scientific Title
B-type natriuretic peptide (BNP) for personalised primary prevention in diabetes: a cross-sectional observational study

Acronym
4P

Study objectives
The primary prevention of cardiovascular (CV) events needs to improve because diabetic patients have such a high CV event rate. This need is underscored further by the failure of intensive lifestyle intervention and of most oral glucose lowering agents (except metformin and recently, empagliflozin) to reduce CV events. On top of overt heart disease, a major problem in diabetes is the high incidence of silent but potentially lethal heart disease, i.e. silent ischaemia, left ventricular hypertrophy, left ventricular systolic dysfunction, left ventricular diastolic dysfunction and left atrial enlargement. The purpose of this study is to assess how many people with asymptomatic type 2 diabetes have multiple silent cardiac abnormalities and is there a biomarker(s) which can early identify these silent abnormalities.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service, 07/04/2015, ref: 15/ES/0042

Study design
Single-centre cross-sectional observational study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied

Type 2 diabetes mellitus

Interventions
All patients will undergo a blood test followed by a detailed Echo to assess for left ventricular systolic and diastolic function, left atrial size and left ventricular size. Dobutamine stress Echo (DSE) will be performed to assess for evidence of inducible myocardial ischaemia. In patients whose DSE is inconclusive or DSE is contraindicated, they would then undergo myocardial perfusion scan or CT coronary angiogram. 24 hour blood pressure date will be collected too.

Intervention Type
Other

Primary outcome(s)
Prevalence of silent heart disease in asymptomatic patients with well-controlled diabetes, assessed with Echo (for left ventricular systolic function, left ventricular diastolic function, left ventricular size, left atrial size) and Dobutamine stress Echo (for inducible ischaemia). This is assessed during participant's single visit to study centre.

Key secondary outcome(s))
Accuracy of BNP ± hsTNT as a screening tool for the aforementioned silent heart disease, by assessing correlation of these biomarkers separately and in combination with the silent heart disease. This is further compared with other potential biomarkers in identification of silent heart disease, e.g. uric acid, hs-CRP, neutrophil to lymphocyte count. This is assessed at the end of study, i.e. 18-24 months after commencement of study.

Completion date
01/08/2017

Eligibility

Key inclusion criteria
1. Aged 40-85 years
2. Type 2 diabetes with no previous known cardiovascular symptoms or events
3. Clinic blood pressure (BP) or average 24hour BP ≤140/80mmHg
4. HbA1c value <64 mmol/mol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria

1. Clinic BP and average 24hour BP ≥140/80mmHg
2. Renal impairment (eGFR <60)
3. Atrial fibrillation
4. Significant (defined as more than mild) valvular heart disease either on auscultation or echocardiography
5. Pregnant type 2 diabetics
6. Unable to consent

Date of first enrolment
18/11/2015

Date of final enrolment
01/08/2017

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Ninewells Hospital & Medical School
University of Dundee
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Sponsor information

Organisation
University of Dundee & NHS Tayside

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		10/11/2020	10/11/2020	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes