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Improving cardiac function in high-risk surgical patients: exercise testing, biomarkers and beta-blockade

Submission date 22/01/2018	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 23/01/2018	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 04/01/2021	**Condition category** Surgery	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Major elective abdominal surgery carries a significant risk of mortality (death) and morbidity (illness), a proportion of which is directly due to specific cardiac disease, particularly heart failure. Before people have major surgery they undergo a simple test on a cycle machine, which helps to determine if there are likely to be any particular problems during or after the surgery. These results are used to plan the best way to look after patients around the time of their operation as part of their standard care. For a small number of patients the cycle exercise test shows that the heart function is not as good as expected, with these patients showing a higher risk of developing serious problems after surgery. The aim of this study is to see whether the heart function of surgical patients can be improved using a medication to improve heart function (bisoprolol), thus reducing the risk of mortality and morbidity for these patients.

Who can participate?
Patients aged 55 years or over who are scheduled for major abdominal surgery

What does the study involve?
Participants are prescribed bisoprolol to be taken daily. After 10 days at a follow up appointment their heart function is assessed.

What are the possible benefits and risks of participating?
Taking bisoprolol may improve the performance of the heart and by reduce the risks of having the operation. No additional risks are expected as bisoprolol is fully licensed for use in improving heart performance. There are additional assessments required for the study, which may extend a clinic visit.

Where is the study run from?
York Teaching Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2016 to February 2021

Who is funding the study?
Elsie May Sykes Charitable Research Fund (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2017-002443-15

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
3.0 (08/08/2017)

Study information

Scientific Title
Improving cardiac function in high-risk surgical patients: exercise testing, biomarkers and beta-blockade

Acronym
ICAF-BETA

Study objectives
Administration of Bisoprolol to participants with impaired VE/VCO2 will improve cardiac function.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire & The Humber - Leeds West Research Ethics Committee, 25/08/2017, ref: 17/YH/0222

Study design
Prospective proof of concept case series

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
Patients with impaired VE/VCO2 scheduled for major intra-abdominal surgery

Interventions
Patients aged 55 years or over, scheduled for major abdominal surgery will be eligible. These patients will be sent information about the study prior to their routine pre-assessment appointment. Those patients who consent will undergo screening as part of their appointment; if they meet all inclusion criteria they will be enrolled and prescribed Bisoprolol 2.5mg to be taken daily for a minimum of 7 days prior to surgery. After 10 days a follow up appointment will be required to review heart function.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Ventilator equivalent for CO2 (VE/VCO2), measured at anaerobic threshold or nadir using CO2 output prior to surgery

Secondary outcome measures

1. Beta-natriuretic peptide, measured using blood test at baseline and 10 days post IMP commencement
2. Systolic and diastolic function, measured using ECG at baseline and 10 days post IMP commencement
3. Anaerobic threshold, measured using CPET at baseline and 10 days post IMP commencement
4. Myocardial abnormality (VO2/HR response, VO2/Watt response), measured using CPET at baseline and 10 days post IMP commencement

Overall study start date
28/03/2016

Completion date
01/02/2021

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Aged 55 years or over
2. Scheduled for major intra-abdominal surgery
3. Presenting for routine CPET as part of pre-assessment
4. Not currently taking any BB medication and not taken BB medication within 1 month prior
5. Consent to GP being informed
6. VE/VCO2 34 or greater on CPET, as either the value measured at VO2@AT, or the lowest measured value, plus at least one of the following:
6.1. Presence of a known history of a clinical risk factor for major adverse cardiac events (MACE) after surgery
6.1.1. Ischaemic heart disease
6.1.2. Cerebrovascular disease
6.1.3. Renal insufficiency (creatinine > 170 mol.L-1)
6.1.4. Chronic heart failure
6.2. Evidence of abnormal myocardial response on exercise testing
6.2.1. Flattened or inflecting oxygen uptake to heart rate response (oxygen pulse response, VO2 /HR, panel 2)
6.2.2. Flattened or inflecting oxygen uptake to work rate response (VO2/Watt, panel 3)
6.3. Anaerobic threshold <11ml/kg/min

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
44

Key exclusion criteria
1. Refusal or unable to give informed consent
2. Fewer than 7 days before scheduled surgery at pre-assessment appointment surgery
3. Current beta blocker medication or having taken any beta blocker within 1 month prior
4. Contra-indications to BB medication including:
4.1. Bronchial asthma
4.2. Reversible airways disease
4.3. Decompensated heart failure (NYHA class IV)
4.4. Fluid overloaded
4.5. Hypotensive
4.6. Severe liver impairment
4.7. Second or third degree A-V block (unless pacemaker fitted)
4.8. SA block
4.9. Sick sinus syndrome (unless pacemaker inserted)
4.10. Cardiogenic shock
4.11. Bradycardia (heart rate less than 60 bpm)
4.12. Prinzmetal's angina
4.13. Untreated Phaeochromocytoma
4.14. Metabolic acidosis
4.15. Poor blood circulation in the hands and feet
4.16. Severe peripheral arterial insufficiency
4.17. Known hypersensitivity to bisoprolol or its ingredients (lactose monohydrate, silica colloidal anhydrous, crospovidone (Type A), crospovidone (Type B), povidone 30, sucrose, magnesium stearate)
4.18. Co-prescription with negative chronotropic agents such as digoxin, diltiazem, verapamil, amiodarone
4.19. Co-prescription with medications that affect the plasma concentrations of bisoprolol such as rifampin, cimetidine, quinidine, fluoxetine, paroxetine, propafenone, digoxin, reserpine, monoamine oxidase inhibitors, clonidine

Date of first enrolment
01/02/2018

Date of final enrolment
01/01/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
York Teaching Hospital NHS Foundation Trust
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Sponsor information

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/027e4g787

Funder(s)

Funder type
Charity

Funder Name
Elsie May Sykes Charitable Research Fund

Results and Publications

Publication and dissemination plan
Details are not yet finalised but results will be published in appropriate journals.

Intention to publish date
31/12/2020

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