

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

|                                        |                                        |                                                                                                              |
|----------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>22/01/2018   | <b>Recruitment status</b><br>Stopped   | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>23/01/2018 | <b>Overall study status</b><br>Stopped | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>04/01/2021       | <b>Condition category</b><br>Surgery   | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> 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?  
Mia Porteous, Mia.Porteous@york.nhs.uk

## Contact information

### Type(s)

Public

### Contact name

Ms Mia Porteous

### Contact details

Room 147, 3rd Floor  
Junction 8  
York Hospital  
Wigginton Road  
York  
United Kingdom  
YO31 8HE  
+44 (0)1904 725129  
Mia.Porteous@york.nhs.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

2017-002443-15

### Protocol serial number

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/VCO<sub>2</sub> 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

**Primary study design**

Interventional

**Study design**

Prospective proof of concept case series

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Patients with impaired VE/VCO<sub>2</sub> 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(s)**

Ventilator equivalent for CO<sub>2</sub> (VE/VCO<sub>2</sub>), measured at anaerobic threshold or nadir using CO<sub>2</sub> output prior to surgery

**Key secondary outcome(s)**

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 (VO<sub>2</sub>/HR response, VO<sub>2</sub>/Watt response), measured using CPET at baseline and 10 days post IMP commencement

**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/VCO<sub>2</sub> 34 or greater on CPET, as either the value measured at VO<sub>2</sub>@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, VO<sub>2</sub>/HR, panel 2)
    - 6.2.2. Flattened or inflecting oxygen uptake to work rate response (VO<sub>2</sub>/Watt, panel 3)
  - 6.3. Anaerobic threshold <11ml/kg/min

## Participant type(s)

Patient

## Healthy volunteers allowed

No

## Age group

Adult

## Sex

All

## 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**

United Kingdom

England

**Study participating centre**

York Teaching Hospital NHS Foundation Trust

Wigginton Road

York

United Kingdom

YO30 4SR

## **Sponsor information**

**Organisation**

York Teaching Hospital NHS Foundation Trust

**ROR**

<https://ror.org/027e4g787>

## **Funder(s)**

**Funder type**

Charity

### Funder Name

Elsie May Sykes Charitable Research Fund

## Results and Publications

### 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? |
|--------------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">HRA research summary</a> |         |              | 28/06/2023 | No             | No              |