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Optimising cardiac surgery outcomes in people with diabetes

Submission date	Recruitment status	[X] Prospectively registered
10/05/2018	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
07/06/2018	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
04/02/2022	Nutritional, Metabolic, Endocrine	[_] Record updated in last year

Plain English summary of protocol

The study is open to external sites. If you are interested in participating please contact octopus@soton.ac.uk.

Background and study aims
Diabetes is particularly common in people having heart surgery. People with diabetes whose blood sugar levels are too high tend to have a slower recovery after surgery. They are more likely to get infections (both chest infections and in their surgical wounds). They cannot go home as quickly after surgery as those with well-controlled diabetes. Their risk of death is higher. A team at Bournemouth hospital has developed an outpatient-based approach to improve blood sugar levels in the weeks before surgery. They have shown that in patients receiving joint replacements, this approach can reduce the time they have to stay in hospital. This study will adapt the Bournemouth approach so that it can be used for people undergoing heart surgery. It will first be tested in Southampton to assess whether people undergoing cardiac surgery and their healthcare team find the approach acceptable and easy to follow. The approach will be changed according to their feedback and will then be tested in up to 15 UK NHS hospitals.

Who can participate?
Patients aged over 18 with poorly controlled type 1 or type 2 diabetes who are awaiting elective cardiac surgery

What does the study involve?
Participants are randomly allocated to the intervention group or the usual care group. Participants in the intervention group are seen by the OCTOPuS practitioner immediately following the outpatient clinic appointment at which the decision to proceed to cardiac surgery is made. The OCTOPuS practitioner is a clinically qualified health care worker with expertise in diabetes. They are most likely to be a diabetes nurse specialist, but might, for example, be a pharmacist, dietitian or physician. During this session, the OCTOPuS practitioner assesses a number of factors known to be associated with poor surgical outcomes in people with diabetes. Although the focus of the intervention is to improve glucose control, the intervention also includes the management of other aspects of diabetes, such as weight, smoking, blood pressure and lipid profile, which are known to affect surgical outcomes. Based on this assessment, the OCTOPuS practitioner and participant agree a tailored plan of actions to improve their diabetes

control over the 3 months before surgery. Treatment options are likely to include a graded exercise regimen, dietary advice, smoking cessation advice, medication review and specific advice about managing expectations. After the initial consultation, the OCTOPuS practitioner contacts the patient every 2 weeks, either face-to-face or by telephone to oversee medication regimens, signpost patients to local services, and to advocate on the patient's behalf. Participants in the usual care group receive treatment as usual as per local practice in the cardiothoracic centre attended by the patient. This is likely to include brief advice from the patient's surgeon to pay attention to their diabetes in the run up to surgery. Some patients may act on this advice, either on their own or in conjunction with their GP. 'Usual care' at all recruiting centres is documented. All patients then receive their cardiac surgery. Time in hospital varies for each patient. Patients are followed up at the time when the surgeon determines they are fit for discharge, and 7 days and 30 days after surgery. Patients do not need to attend for a trial visit after 30 days after surgery. After the first 100 patients in the study have had their surgery it is tested to see if the intervention has an effect on their diabetes control by seeing if their HbA1c, which is a measure of average blood sugar levels, has improved. If it has not changed, the trial is stopped, as it will be unlikely that the intervention works as hoped. If the blood sugar levels have improved, a further 326 people with diabetes are invited to take part. The trialists look to see if patients are ready to leave hospital earlier, and also what is the effect on infections and deaths. They also discuss with patients their experience of the intervention, to make sure that if patients do recover more quickly they think the effort involved in the intervention is worth it. They also assess the cost of introducing the intervention into NHS care.

What are the possible benefits and risks of participating?
It is expected that patients in the intervention group will benefit from the diabetes management review resulting in a better surgical experience. There is the potential to increase the risk of low sugar levels, although the intervention will largely advocate the use of drugs that are not associated with this side effect. Participants will be warned of this risk and advised how to recognise and treat low glucose values. It is possible that encouraging exercise in people with heart problems may worsen angina. Cardiac patients awaiting surgery may exacerbate ischaemic events. All OCTOPuS practitioners are health professionals and are fully trained in delivering the intervention and will be advised to only recommend gentle exercise that does not lead to symptoms.

Where is the study run from?
University Southampton Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2018 to November 2024

Who is funding the study?
NIHR Health Technology Assessment Programme (HTA) (UK)

Who is the main contact?
1. Mrs Liz Dixon
e.dixon@soton.ac.uk
2. Dr Giorgos Dritsakis
g.dritsakis@soton.ac.uk

Study website
https://www.journalslibrary.nihr.ac.uk/programmes/hta/162512/#/

Contact information

Type(s)
Public

Contact name
Mrs Liz Dixon

ORCID ID
http://orcid.org/0000-0002-9876-9533

Contact details
Southampton Clinical Trials Unit
MP131
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 (0)2381205331
e.dixon@soton.ac.uk

Type(s)
Public

Contact name
Dr Giorgos Dritsakis

Contact details
Trial Manager
Southampton Clinical Trials Unit
MP131, Southampton General Hospital, Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 (0)23 8120 5588
g.dritsakis@soton.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 16/25/12

Study information

Scientific Title
A multicentre, parallel group, single-masked, individually randomised trial incorporating a pre-planned futility analysis comparing time from surgery until clinically fit for discharge in adults with poorly controlled type 1 or 2 diabetes undergoing elective cardiothoracic surgery between the OCTOPuS intervention and usual care

Acronym
OCTOPuS

Study objectives
To develop an outpatient intervention to be delivered to adults with poorly controlled diabetes in need of elective cardiac surgery to assess whether the intervention can improve glycaemic control and reduce the length of stay of the surgical admission.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Hampshire A Research Ethics Committee, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, Tel: +44 (0)207 104 8241, Email: nrescommittee.southcentral-hampshirea@nhs.net, date of original approval: 12/11/2018, date of 1st Substantial Amendment approval: 09/01/2019, ref: 18/SC/0508

Study design
A multicentre, parallel group, single-masked, individually randomised trial incorporating a pre-planned futility analysis comparing time from surgery until clinically fit for discharge in adults with poorly controlled type 1 or 2 diabetes undergoing elective cardiothoracic surgery between the OCTOPuS intervention and usual care

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

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
People who require elective major cardiac surgery and who have poorly controlled diabetes

Interventions

A manualised out-patient intervention to be delivered by a trained health professional to people with poorly controlled diabetes to improve cardiac surgical outcomes compared to treatment as usual.

Patients will be randomised using an online randomisation system in a 1:1 ratio between arms and stratified by centre, using pre-generated permuted blocks to prevent clinicians anticipating the allocation.

The trialists will develop a manualised outpatient intervention to be delivered to adults with poorly controlled diabetes in need of elective cardiac surgery to assess whether the intervention can improve glycaemic control in the pre-operative period and reduce the length of stay of the surgical admission compared to treatment as usual.

Arm A: OCTOPuS Intervention
The OCTOPuS intervention comprises several elements, which are brought together in a systematic way. Participants who receive the intervention arm will be seen by the OCTOPuS practitioner immediately following the outpatient clinic appointment at which the decision to proceed to cardiac surgery is made. The OCTOPuS practitioner is a clinically qualified health care worker with expertise in diabetes. They are most likely to be a diabetes nurse specialist, but might, for example, be a pharmacist, dietitian or physician.
During this session, the OCTOPuS practitioner will assess a number of factors known to be associated with poor surgical outcomes in people with diabetes. Although the focus of the intervention is to improve glucose control, the intervention also includes the management of other aspects of diabetes, such as weight, smoking, blood pressure and lipid profile, which are known to affect surgical outcomes. Based on this assessment, the OCTOPuS practitioner and participant will agree a tailored plan of actions to improve their diabetes control over the approx. 3 months prior to surgery.
Treatment options are likely to include a graded exercise regimen, dietary advice, smoking cessation advice, medication review and specific advice about managing expectations.
After the initial consultation, The OCTOPuS practitioner will contact the patient every 2 weeks, either face-to-face or by telephone. They need to oversee medication regimens, signpost patients to local services, and to advocate on patient's behalf.

Arm B: Usual care
Patients will receive treatment as usual as per local practice in the cardiothoracic centre attended by the patient. This is likely to contain brief advice from the patient's surgeon to pay attention to their diabetes in the run up to surgery. Some patients may act on this advice, either on their own or in conjunction with their GP. 'Usual care' at all recruiting centres will be documented.

All patients will then receive their cardiac surgery. Time in hospital will vary for each patient. The total duration of intervention will be from the point of listing for surgery until surgery. For most participants this will be approximately 3-4 months based on current waiting list times for elective cardiac surgery. Participants will be followed up at the time when the surgeon determines they are fit for discharge, 7 days and 30 days post-surgery. The trialists will also collect HbA1c at 90-180 days post-surgery from standard care tests during this period. Patients will not need to attend for a trial visit after 30 days post-surgery.

After the first 100 patients in the study have had their surgery the trialists will test to see if the intervention has an effect on their diabetes control, by seeing if their HbA1c, which is a measure

of average blood sugar levels, has improved. If it has not changed, they will stop the trial, as it will be unlikely that the intervention works as hoped. If the blood sugar levels have improved, they will then invite a further 326 people with diabetes to take part.

The trialists will look to see if patients are ready to leave hospital earlier, and also what is the effect on infections and deaths. They will also discuss with patients their experience of the intervention, to make sure that if patients do recover more quickly they think the effort involved in the intervention is worth it. They will also assess the cost of implementing the intervention into NHS care.

Intervention Type
Behavioural

Primary outcome measure
Time from surgery until clinically fit for discharge, as judged by the surgical team, measured using medical notes at 7 and 30 days post-surgery

Secondary outcome measures
Current secondary outcome measures as of 19/03/2021:
1. Time from surgery to actual discharge from hospital – this recognises that discharge can be delayed for non-clinical reasons
2. Days alive between surgery and either out of hospital or judged as clinically fit for discharge
3. Pre-operative mortality; 30-day mortality; 90-day mortality
4. Time on ITU
5. Time on a ventilator
6. Sternal Wound Infections, defined according to the NICE guidance and the CDC criteria
7. Leg wound infections, in those who provide donor veins; graded according to the Centers for Disease Control and Prevention definitions of surgical site infections
8. Chest infections, defined as a change in typical chest symptoms (cough, increased respiratory rate, shortness of breath) in conjunction with a fever or inflammatory markers
9. Urinary tract infections, defined as "clinically-diagnosed and treated, whether or not results from a urine culture are available"
10. Acute Coronary Syndrome
11. Change in weight between randomisation and surgery
12. Effect on postoperative renal function and incidence of acute kidney injury as assessed by measurement of serum creatinine and calculation of estimated glomerular filtration rates
13. HbA1c immediately preoperative, and at between 90 and 180 days post-operation
14. Change in HbA1c between baseline and immediately preoperative, and change from preoperative to between 90 and 180 days post-operation
15. Operations cancelled for sub-optimal glycaemic management
16. Frequency and severity of self-reported overall, minor, severe and nocturnal hypoglycaemia assessed at Baseline, during the Support Contact and Pre-surgery
17. EQ-5D at baseline, 7, 30 and 90 days post-surgery
18. Qualitative interviews and psychosocial questionnaires at baseline and 90 days post-surgery to explore participants' experiences and perceived benefits of the intervention and any changes to their diabetes self-management.
19. Cost-effectiveness of the intervention, including: use of NHS lifestyle improvement programs and diabetes services; use of medication, time spent by practitioners for training, delivering the intervention and liaising with local services; HbA1c point-of-care and blood glucose monitoring costs

Previous secondary outcome measures:
1. Time from surgery to actual discharge from hospital, measured using medical notes at 7, 30 and 90-180 days post-surgery
2. Mortality, measured using medical notes on admission for surgery and at 7, 30 and 90-180 days post-surgery
3. Sternal infections, measured using medical notes at 7, 30 and 90-180 days post-surgery
4. Leg wound infections in participants who provide donor vein, measured using medical notes at 7, 30 and 90-180 days post-surgery
5. Chest infections, measured using medical notes at 7, 30 and 90-180 days post-surgery
6. Weight, measured using scales at baseline, on admission for surgery and at 7, 30 and 90-180 days post-surgery
7. Renal function, measured using laboratory tests at baseline, on admission for surgery and at 7, 30 and 90-180 days post-surgery
8. HbA1c, measured using laboratory tests at baseline, on admission for surgery and at 90-180 days post-surgery
9. Number of operations cancelled because of poor glycaemic control, measured using medical notes on admission for surgery
10. Quality of life, measured using EQ-5D at baseline, on admission for surgery, and 90-180 days post-surgery (In the first phase the trialists will also explore the utility of collecting EQ-5D at 30 days post-surgery. This has the potential for providing an extra data point, but the increased participant burden may risk the loss of completeness of days at 90 days)
11. Patient experience, measured using qualitative interviews at baseline, on admission for surgery, and at 3, 6 and 12 months post-surgery

Overall study start date
01/01/2018

Completion date
30/11/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 19/03/2021:
1. Aged ≥ 18 years old with type 1 diabetes or type 2 diabetes
2. Sub-optimally managed diabetes defined as an HbA1c >53 mmol/mol (7%) for those ≤75 years old and an HbA1c >64 mmol/mol (8%) for those >75 years old. The higher HbA1c criterion for older people is to minimise the risk of iatrogenic hypoglycaemia. This will be measured using a near patient test at the cardiothoracic surgery outpatient appointment where the decision to proceed to surgery is made
3. Awaiting elective open-heart cardiac surgery
4. Anticipated delay before surgery of at least 2 months
5. Surgery will take place at a hospital participating in the trial
6. Ability to give informed consent.
7. Ability to interact with the study documentation and processes.

Previous inclusion criteria:
1. Adults (aged >18 years) with poorly controlled type 1 or type 2 diabetes. Poor control is defined as an HbA1c > 53 mmol/mol using a near-patient test at the cardiothoracic outpatients appointment where the decision to proceed to surgery is made
2. Awaiting elective cardiac surgery, where it is anticipated the delay before surgery will be at

least 3 months (updated 13/02/2019 to ‘2 months’)
3. Ability to give informed consent
4. Ability to interact with the study documentation and processes

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Intervention Pilot: approx. 20; Main Trial: 426

Key exclusion criteria
Current exclusion criteria as of 19/03/2021:
1. Active malignancy, where the malignancy is currently being treated by chemotherapy, surgery or radiotherapy or is likely to cause death within 6 months
2. Pregnancy
3. Previous cardiac surgery
4. Known haemoglobinopathies that affect the measurement of HbA1c
5. Other illnesses or conditions that would preclude engagement with the OCTOPuS intervention
6. Surgery taking place outside the participating hospitals, e.g. at a private hospital

Previous exclusion criteria:
1. Malignancy (updated 13/02/2019 to ‘Active malignancy’)
2. Pregnancy
3. Previous cardiac surgery
4. Other illnesses or conditions that would preclude engagement with the OCTOPuS intervention

Date of first enrolment
01/03/2022

Date of final enrolment
30/11/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

University Southampton Hospital NHS Foundation Trust
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

Sponsor details
R&D Department
University Hospital Southampton NHS Foundation Trust
SGH, Level E, Laboratory & Pathology Block, SCBR, MP 138
Tremona Road
Southampton
England
United Kingdom
SO16 6YD
+44 (0)23 8120 4989
researchmanagement@uhs.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trialists plan to publish the protocol once finalised and following ethics approval. This will include details of the statistical analysis. Prior to this, study protocol and statistical analysis plan will be made available to the trial steering committee and data monitoring and ethics committee. The manual and all patient facing information will be made available after the trial's completion.

The trialists plan to publish the results in Health Technology Assessment and other high impact peer reviewed journals. If the intervention is shown to be superior to standard care, then they will undertake further action to disseminate the work. They will discuss their findings with organisations such as NICE, the Joint British Diabetes Societies, and the Society for Cardiothoracic Surgery in Great Britain and Ireland with a view to integrating the intervention into guidelines and professional practice.

Intention to publish date
30/11/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Liz Dixon (octopus@soton.ac.uk). Further details on data will be added once the main trial is finalised.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		09/06/2021	11/06/2021	Yes	No
Interim results article	Pilot study results	17/08/2021	19/08/2021	Yes	No
HRA research summary			28/06/2023	No	No