ISRCTN96975795 https://doi.org/10.1186/ISRCTN96975795

Cardiometabolic Early Intervention Study

Submission date
10/10/2023

Recruitment status
No longer recruiting

Registration date
20/03/2024

Overall study status
Completed

Last Edited
18/12/2024

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
People with diabetes are at increased risk of major complications such as heart and kidney damage, which are responsible for the majority of deaths in patients with this disorder. Additionally, patients with diabetes who have had a heart attack have a 2-3-fold increased risk of mortality compared to those without diabetes, not only during the acute event but long after surviving the initial event. Sodium-glucose co-transporter-2 inhibitors (SGLT2i), are prescribed to help control blood sugar levels in type-2 diabetes mellitus (T2DM). These drugs, which are safe and well tolerated, have also shown significant cardiovascular benefits reducing mortality, heart failure, heart attack, and strokes in T2DM patients. However the optimal starting time in patients with T2DM in the context of acute myocardial infarction (AMI) is unclear. As a result, there is variability in the practice of starting these medications following a heart attack, with some being started prior to discharge or at 3 months (early-intervention), or much later at 6-12 months (late-intervention) but in reality many were missed altogether (missed-intervention). This was the fundamental reason that led to the formation of the cardio-metabolic program at the Lincolnshire Heart Centre. Determining any benefit from an early start (before discharge or at 6 months) would potentially reduce further events and hospitalisations which would improve the quality of life for patients, as well as reduce the burden on our health care system. This study will assess whether there is any benefit of an early start of SGLT2i in T2DM patients with AMI.

Who can participate?
Patients aged 18 years old and over with T2DM and Type 1 acute AMI

What does the study involve?
This study will assess whether there are cardiovascular outcomes, mortality, and safety benefits for T2DM patients with AMI who had an early start on SGLT2i compared with T2DM patients who started late or missed the intervention. Retrospective data, previously collected from patients' medical notes (including electronic) and investigations, as part of our audit databases, will be studied for these analyses. This will be a "real-world" descriptive, retrospective, registry-based, cohort-matched, and observational study.

What are the possible benefits and risks of participating?
Benefits and risks not provided at the time of registration

Where is the study run from?
Lincoln County Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2023 to December 2024

Who is funding the study?
Lincolnshire Heart Centre (UK)

Who is the main contact?
Dr Muhammad Usman Shah, muhammadusman.shah@ulh.nhs.uk (UK)

Contact information

Type(s)
Principal investigator

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Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
320151

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
23012 V2.0, IRAS 320151

Study information

Scientific Title
Early versus delayed use of sodium-glucose co-transporter-2 inhibitors (SGLT2i) in patients with type 2 diabetes mellitus and acute myocardial infarction and impact on cardiovascular outcomes and mortality: The Cardio Metabolic early-Intervention Study (CAMIS), an observational registry study

Acronym
CAMIS

Study objectives
Sodium-glucose co-transporter-2 inhibitors (SGLT2i) were initially developed as glucose-lowering medications for use in patients with type-2 diabetes as a second-line agent. The Phase III randomised controlled trials (RCTs) for SGLT2i established the safety profile and characteristics for the use of SGLT2i and also the clinical benefits, efficacy, and clinical indications for use in type 2 diabetes mellitus (T2DM) with atherosclerotic cardiovascular disease (ASCVD) or cardiovascular (CV) risk, in heart failure (HF) and chronic kidney disease (CKD). These landmark trials formed the basis of the change in practice and recent international guidelines on diabetes and cardiovascular disease. Developed in collaboration with the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD), the National Institute for Health and Care Excellence (NICE) guidelines now recommend the use of SGLT2i in patients with T2DM and have stable ischaemic heart disease (IHD) or high risk of ASCVD, defined as having additional co-morbid conditions including hypertension, hyperlipidaemia or on treatment with lipid-lowering medications or active smoking. However, there is limited data on the use of SGLT2i in patients with T2DM with early initiation of SGLT2i soon after acute myocardial infarction (AMI). In the context of the current evidence, limited to small retrospective observational and surrogate marker studies, there is no clear guidance on when SGLT2i should be commenced in patients with T2DM and admitted with AMI. As a result, although clinically indicated and licenced for use, there is significant variation in prescribing practice amongst health care practitioners, with some initiating SGLT2i before discharge or within 6 months, whilst other patients are either prescribed at a much later stage or in reality have been found to not be prescribed an SGLT2i despite being eligible and were missed entirely.

This study will assess whether there is any benefit of an early start of SGLT2i in T2DM patients with AMI in comparison to those that were started late or missed, to cardiovascular outcomes, mortality and safety. This study may help inform us of the optimal timing of SGLT2i therapy in T2DM patients in the context of an AMI, of the potential clinically meaningful benefits or of any

potential side effects or harm. This will help guide future clinical practice in the management of acute coronary syndromes of patients with diabetes in the UK.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/09/2023, HRA and Health and Care Research Wales (HCRW) (-, -, -, United Kingdom; None available; approvals@hra.nhs.uk), ref: 23/HRA/3597

HRA and Health and Care Research Wales (HCRW) (UK) confirmed that Research Ethics Committee approval was not required as this is an observational retrospective registry study.

Study design
Descriptive retrospective registry-based observational study

Primary study design
Observational

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Type 2 diabetes mellitus, ischaemic heart disease, acute coronary syndrome.

Interventions
Patient-related clinical information as stated in the protocol, is collected as part of the local cardiodiabetic database, which is regularly updated from the local MINAP database and electronic health records. Retrospective information for patients admitted to the service and who meet the eligibility criteria from 1st July 2018 to 31st December 2023 will then be acquired from the cardiodiabetic database at the end of December 2024.

Intervention Type
Other

Primary outcome(s)
A combined outcome of cardiovascular death, non-fatal MI, non-fatal stroke, and hospitalisation of heart failure in patients with type 2 diabetes mellitus and acute myocardial infarction and early (before discharge to 6 months) versus late (6-12 months) or missed initiation (>12months /never) of SGLT2i

Key secondary outcome(s))
The following secondary outcome measures will be measured using from patient's medical notes at one timepoint:
1. Time to all-cause death
2. Time to CV death
3. Time to first nonfatal MI or nonfatal cerebrovascular accident (CVA)
4. Time to first unplanned coronary revascularisation
5. Time to the first episode of hospitalisation for heart failure
6. Composite Renal outcomes including doubling of serum creatinine, or eGFR ≤ 15 mL/min/1.73m2, or the initiation of permanent renal replacement therapy or death due to renal disease

7. SGLT2i Safety Profile as a composite of reported hypoglycaemia, postural hypotension, diabetic ketoacidosis, acute kidney injury, urinary tract infection, mycotic genital infections, diabetic foot emergencies, amputations (digital/limb) or Fournier's gangrene
8. Net overall benefit as an assessment of overall benefit versus overall harm observed

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. 18 years and older (no upper age limit)
2. Male or female
3. Type 1 acute myocardial infarction (AMI) (both ST elevation and Non-ST elevation MI) as per the 4th Universal definition of myocardial infarction
4. Known or newly diagnosed type 2 Diabetes Mellitus
5. Successful discharge from the hospital after the index event

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
969

Key exclusion criteria
1. Type 1 DM (as the safety of SGLT2i in this group is still not known and therefore, not recommended currently)
2. Non-diabetics
3. Prediabetics
4. Current pregnancy (contraindication for SGLT2i use)
5. Breastfeeding (contraindication for SGLT2i use)
6. End-stage kidney with a life expectancy of fewer than 6 months, including GFR,15 ml/min/1.73 m2 (making SGLT2i contraindicated)
7. End-stage liver disease life expectancy of less than 6 months
8. Death in hospital at index event (First heart attack for the duration of the study)

9. Non-cardiovascular conditions, such as advanced malignancy, that will result in a life expectancy of less than 6 months

Date of first enrolment
18/09/2023

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
United Lincolnshire Hospitals NHS Trust
Lincoln County Hospital
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Sponsor information

Organisation
University of Lincoln

ROR
https://ror.org/03yeq9x20

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Lincolnshire Heart Centre

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Prof Lee (kelvin.lee@ulh.nhs.uk).

Pseudonymised data in Excel format will be available for sharing at variable times. This is a retrospective, observational study with pseudonymisation, therefore no formal consent was obtained or required from individual patients. HRA approval is in place. All participant data will be pseudonymised prior to any study analysis. No patient-identifiable data will be distributed.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes