The perioperative renal and metabolic outcomes after sodium-glucose cotransporter-2 inhibitor in cardiac surgery - an open-label phase IV randomized controlled trial

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To investigate the potential of preoperative initiation (7 days) and perioperative continuation (until day 2 after surgery) of empagliflozin 10 mg daily to reduce the acute kidney injury marker neutrophil gelatinase-associated lipocalin (NGAL) on...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON52118

Source
ToetsingOnline

Brief title
The MERCURI trial

Condition

- Renal disorders (excl nephropathies)

Synonym
acute kidney injury, acute renal failure, cardiac surgery-associated kidney injury

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Research Executive Agency (REA) namens de Europese Unie.

Intervention

Keyword: Acute Kidney Injury, Cardiac Surgery, SGLT2i

Outcome measures

Primary outcome

Neutrophil gelatinase-associated lipocalin (NGAL) concentration in plasma,

measured on the morning of postoperative day 2, between 8:00 and 12:00.

Secondary outcome

• Neutrophil gelatinase-associated lipocalin (NGAL) concentration in plasma.

• Kidney Injury Molecule-1 (KIM-1) in plasma.

• Estimated Glomerular Filtration Rate (eGFR) based on plasma creatinine

measurements.

• Ketones in blood.

• Incidence of keto-acidosis defined as combination of blood ketone

concentration >3mmol/l in combination with high-anion gap acidosis

([Na+]-[Cl-]-[HCO3-]>12).

• Perioperative peak and average blood glucose levels, as measured during usual

care.

• Incidence of hypoglycemia defined as blood glucose measurement < 4 mmol/l at

any time point between start of surgery and end of study.

Moments of measurement:

For NGAL, KIM-1, plasma ketones and incidence of keto-acidosis:

- On day of surgery:

• Before start of surgery (after placement of arterial line)

• At time of start of cardiopulmonary bypass (+/- 20 min)

• At the end of cardiopulmonary bypass (+/- 20 min)

• At time of transport to ICU (+/- 20 min)

- Postoperatively

• Measured daily, in the morning between 8:00 and 12:00 until postoperative day

2.

For eGFR (creatinine)

• Measured daily, in the morning between 8:00 and 12:00 until postoperative day

4.

For peak and average glucose and incidence of hypoglycaemia:

• any measurement occurring between start of surgery and end of study until

postoperative day 4, as part of routine care.

Study description

Background summary

Acute kidney injury is one of the most common complications after cardiac surgery. The new antidiabetic therapy, sodium glucose transport protein 2 inhibitors (SGLT2i) possess renoprotective properties and have been found to reduce acute kidney injury in large cardiovascular outcome trials in patients with diabetes mellitus.

Study objective

To investigate the potential of preoperative initiation (7 days) and perioperative continuation (until day 2 after surgery) of empagliflozin 10 mg

daily to reduce the acute kidney injury marker neutrophil gelatinase-associated lipocalin (NGAL) on day 2 postoperatively in patients undergoing cardiopulmonary bypass surgery.

Study design

Single-center, open-label, parallel-group, balanced (1:1), stratified (diabetes mellitus type 2, 50-50), randomized, controlled (usual care), phase IV clinical trial.

Intervention

The intervention group receives once daily 10 mg empagliflozin starting 7 days before surgery to be continued until two days postoperatively.
The control group will follow usual perioperative care.

Study burden and risks

General trial-related burden:
For this study, additional blood will be drawn to study the effect of the intervention. All blood will be drawn concurring with measurements as part of standard perioperative care. Therefore, no additional venepunctures will occur as part of this study*the total amount of additional blood drawn: 28 ml.

Intervention group related burden:
Patients in the control group will receive standard perioperative care. Patients in the intervention group will take 1 tablet of 10 mg empagliflozin daily from 7 days before surgery until 2 days postoperative (including the day of surgery). Patients in the intervention group run a risk of side effects related to the study drug. These are relatively rare. Potential participants will be informed about the following side effects: genitourinary infections, euglycaemic ketoacidosis, and hypoglycaemia. There is only a risk of hypoglycaemia in patients with diabetes mellitus that are already taking other glucose-lowering drugs.
Regarding potential side-effects:
- genitourinary infections usually occur after longer-term use of SGLT2 inhibitors; in this study, patients will only receive this medication for 10 days. In addition, this side effect's management is straightforward with antimicrobial treatment.
- hypoglycaemia: only patients with diabetes mellitus are at risk, according to previous research. These patients will receive an individualised adaptation of their glucose-lowering medication by the researchers. In addition, blood glucose will be monitored in all patients according to standard perioperative cardiac surgery care.
- euglycaemic ketoacidosis: a lowering of the pH in the blood through the build-up of ketones. This side-effect has been described in patients with

diabetes mellitus and a (relative) insulin deficiency. Patients without diabetes are not at risk, according to previous research. We will monitor perioperative glucose and ketone levels in all patients in the study as well as for the incidence of metabolic acidosis. Should this side-effect occur, we will treat with a glucose-insulin infusion, thereby inhibiting ketone production.

There is solid evidence to support that SGLT2 inhibitors are renoprotective. Acute kidney injury is a common complication after cardiac surgery. Our hypothesis is, therefore, that patients in the intervention group will receive protection from kidney injury. In addition, the results from this trial could lead to the improvement of care and protection of patients undergoing cardiac surgery. The side-effect profile of empagliflozin is mild, and participants will be intensively monitored in this study. Therefore, we estimate that the benefits outweigh the risks for participation in this trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

• 18 to 90 years old (inclusive)
• Undergoing elective cardiac surgery with cardio-pulmonary bypass.
• Providing informed consent

Exclusion criteria

• Current treatment with SGLT2 inhibitors.
• Diabetes Mellitus Type 1
• BMI<25 for people with type 2 diabetes
• Reduced renal function at baseline with eGFR<30 ml/min.
• Systolic blood pressure < 100 mmHg at time of inclusion.
• Emergency surgery, defined as in need of surgery for medical reasons < 7 days, i.e. *S1-4* according to the Amsterdam UMC classification.
• Female of child-bearing potential who is pregnant, breast-feeding or intend to become pregnant or is not using adequate contraceptive methods.
• Known or suspected allergy to trial products or other drugs in the same class.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-03-2022
Enrollment:	80

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jardiance
Generic name:	empagliflozine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-003172-13-NL
CCMO	NL78156.018.21
Other	NL9561