Metabolic and renal outcomes in cardiac surgery patients receiving SGLT2 inhibitors

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26563

Source
NTR

Brief title
MERCURI

Health condition

Cardiac surgery associated acute kidney injury

Sponsors and support

Primary sponsor: Amsterdam UMC location AMC
Source(s) of monetary or material Support: The European Research Executive Agency in the form of a Marie Skłodowska-Curie Individual Fellowship awarded to Drs A.H. Hulst

Intervention

Outcome measures

Primary outcome

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

Timing of outcome measurements:
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

Rationale: 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.
Objective: To investigate the potential of empagliflozin 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, randomized clinical trial.
Study population: Patients undergoing cardiac surgery with cardiopulmonary bypass, aged 18-90 years old.
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.

Main study endpoint: The primary outcome of the study is the between group difference of Neutrophil Gelatinase-Associated Lipocalin (NGAL) concentration in plasma measured on day 2 after surgery. Secondary outcomes are the between group differences in kidney injury markers (NGAL, KIM-1), kidney function (eGFR), perioperative glycaemia, the incidence of hypoglycaemia, perioperative ketonemia and the incidence of keto-acidosis.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: For study purposes, an additional 28 ml of blood will be drawn. This will be taken from intravenous or intra-arterial catheters that have been inserted for clinical purposes. Adverse events with empagliflozin treatment are rare. Most often reported are genitourinary infections. While these are most common after prolonged use of SGLT2 inhibitors, for this study, subjects will receive empagliflozin for a period of maximum 10 days. Furthermore, there is a small risk of euglycemic ketoacidosis in the perioperative period related to fasting and surgical stress. Therefore, ketone levels will be measured from admission to the hospital until end of the study. In addition, all patient will receive a glucose-insulin infusion during surgery, to suppress ketone body production. Patient might benefit from this intervention by additional intensive monitoring of metabolic and renal function in the perioperative period. Empagliflozin might reduce the risk of perioperative acute kidney injury. In general, this study will provide more insight in the effect of empagliflozin on parameters of renal function and metabolism in the perioperative setting.

Study objective

We hypothesize that preoperative initiation (7 days before surgery) and perioperative continuation (until day 2 after surgery) of empagliflozin 10 mg daily (10 days total) will reduce the postoperative concentration of NGAL in plasma on postoperative day 2 after cardiac surgery with cardiopulmonary bypass.

Study design

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.

Intervention

Preoperative initiation (7 days before surgery) and perioperative continuation (until day 2

after surgery) of empagliflozin 10 mg daily (10 days total).

Contacts

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Eligibility criteria

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 type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2021
Enrollment:	80
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	20-06-2021
Application type:	First submission

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
NTR-new	NL9561
Other	METC AMC : 2021_162#B2021547

Study results