Iron status and outcome in cardiac surgery

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To investigate the relation between a preoperative abnormal iron status and packed red blood cell transfusion, adverse event and change in disability.To investigate the association of the individual preoperative iron status abnormalities (low iron...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Observational invasive

Summary

ID

NL-OMON48045

Source
ToetsingOnline

Brief title
ISOCS

Condition

- Cardiac disorders, signs and symptoms NEC
- Cardiac therapeutic procedures

Synonym
complications, iron status

Research involving
Human

Sponsors and support

Primary sponsor: Amphia Ziekenhuis
Source(s) of monetary or material Support: Amphia Wetenschapsfonds

Intervention

Keyword: anemia, cardiac surgery, iron status, outcome

Outcome measures

Primary outcome

Main study parameters are perioperative levels of haemoglobin, mean corpuscular volume (MCV), reticulocyte count, reticulocyte haemoglobin content, red blood cell count, red cell distribution width (RDW), ferritin, transferrin, transferrin saturation (TSAT), serum iron, vitamin B12, folate, C-reactive protein (CRP), creatinine, eGFR.

Anaemia and iron status are defined as:

- Anaemia: haemoglobin level < 8.1 mmol/l for men and < 7.5 mmol/l for women
- Normal iron status: ferritin 30-300 µg/l, TSAT 20-50% and CRP < 5mg/l
- Abnormal iron status (one of the following): low iron store = ferritin < 100 µg/l, absolute iron deficiency: ferritin < 30 µg/l OR ferritin < 100 µg/l and TSAT < 20% postoperatively (i.e. if CRP > 5 mg/l) OR reticulocyte haemoglobin count < 28 pg, functional iron deficiency: ferritin 100-500 µg/l and TSAT < 20%, iron sequestration: ferritin > 100 µg/l, TSAT <20% and CRP > 5 mg/l

Low levels of erytroid maturation factors are defined as vitamin B12 level < 200 pmol/l and folate level < 9 nmol/l.

Primary study endpoint is 30-day packed red blood cell transfusion-free

survival.

Secondary outcome

30-day adverse event-free survival. Adverse events are (one of the following): postoperative infection (pneumonia (purulent sputum, positive sputum or blood culture and clinical symptoms, e.g. cough, fever or consolidation on chest radiograph), sepsis (qSOFA score *2 in response to an infection: one point for any of the following, glascow coma scale a <15, respiratory rate >21, systolic blood pressure < 100mmHg), surgical site infection:, wound infection (purulent drainage from superficial incision or deliberate opening of superficial incision by surgeon and pain, tenderness, swelling or redness), mediastinitis (an organism isolated from culture of mediastinal tissue or fluid OR evidence of mediastinitis seen during operation OR presence of either chest pain, sternal instability, or fever (>38°C), and purulent drainage from the mediastinum), urinary tract infection (urinary tract symptoms or fever and urine culture with no more than 2 species of organisms identified with at least one of which is a bacterium of *105 CFU/ml), central line associated bloodstream infection (laboratory confirmed bloodstream infection in a patient where the central line was in place for > 2 calender days on the day of the event AND one of the following criteria: 1. patient has a recognized pathogen cultured from one or more blood cultures AND pathogen cultured is not related to an infection at another site 2. At least one of the following signs fever, chills, hypotension AND organism cultured from blood is not related to an infection at another site AND the same matching organism is cultured from two or more blood cultures on separate occasions)

Other

- acute kidney injury (increase in serum creatinine of * 26 µmol/l within 48 hours of surgery or an increase in serum creatinine tot 150% or more within 7 days or urine volume < 0.5ml/kg/h for 6 hours within 7 days)

- renal replacement therapy within 7 days

- stroke (clinical diagnosis of acute transient ischemic attack (TIA) or cerebrovascular accident (CVA))

- myocardial infarction (elevated hs-cTn in combination with clinical symptoms or electrocardiography changes)

- 30-day mortality (+time)

Disability (measured with the World Health Organization Disability Assessment Schedule (WHODAS 2.0, 12-item version) before and 120 days after surgery. Each item is attributed 0 to 4 points (0=none, 1=mild, 2=moderate, 3=severe and 4=extreme). The total score, between 0 and 48, is then divided by 48 and multiplied by 100 to convert it to a percentage of the maximum disability score.

Study description

Background summary

Over one-third of patients undergoing cardiac surgery suffers from preoperative anaemia. Preoperative anaemia is an independent predictor of transfusion of packed red blood cells, which occurs in 30 to 60% of patients. Several observational studies have shown that packed red blood cell transfusion is associated with adverse outcome. For example, transfusion is associated with infection, renal insufficiency, mortality and increased costs.

Functional iron deficiency is the most common cause of preoperative anaemia in cardiac surgical patients. In addition to its essential role in erythropoiesis, iron is vital for cellular energy metabolism and immune function.
A retrospective cohort study in patients undergoing major surgical procedures, including cardiac surgery, suggested that approximately 60% of surgical patients have alterations in iron status, such as low iron stores, absolute iron deficiency, functional iron deficiency or iron sequestration before surgery. This is aggravated in the perioperative period as haemodilution during cardiopulmonary bypass, surgical blood loss and repeated blood sampling lead by definition to some degree of iron depletion. The postoperative iron status, however, is infrequently investigated after cardiac surgery. Commonly used iron store parameters such as ferritin levels are affected by postoperative inflammation, which makes it difficult to distinguish iron deficiency from other causes of anaemia. In a recent international consensus statement specific recommendations were made for diagnosing alterations in iron status even in the presence of inflammation.
Until now, the relationship between iron status abnormalities and outcome after cardiac surgery is unclear. In a pilot study, patients with preoperative iron deficiency received more packed red blood cells units than patients without iron deficiency (2 vs. 0, respectively, $P < 0.05$) and more often reported fatigue. Another exploratory study in cardiac surgical patients showed that iron deficiency was associated with an increased length of hospital stay and fewer days alive and out of the hospital.
If perioperative iron deficiency is associated with transfusion of packed red blood cells or adverse events in cardiac surgical patients, correction of perioperative iron deficiency by iron replacement may reduce the transfusion rate and improve outcome. Currently, limited evidence exists on perioperative iron therapy in patients undergoing cardiac surgery.
The goal of this study is to investigate the association between an abnormal iron status and transfusion of packed red blood cells, adverse events and disability in patients undergoing cardiac surgery.

Study objective

To investigate the relation between a preoperative abnormal iron status and packed red blood cell transfusion, adverse event and change in disability.
To investigate the association of the individual preoperative iron status abnormalities (low iron stores, absolute iron deficiency, functional iron deficiency and iron sequestration) with transfusion of packed red blood cells.
To investigate the association of an abnormal iron status at the day of hospital discharge with change in disability

Study design

Multicenter, prospective, observational study.

Study burden and risks

In each patient two blood samples will be drawn for analysis. The first blood sample is collected during routine preoperative blood sampling the day before surgery or, on the day of surgery, from an arterial line, which is routinely used in patients undergoing cardiac surgery. The second blood sample is collected at hospital discharge and this will often coincidence with routine blood sampling. Patients will be asked to submit a disability questionnaire (average interview time is 5 minutes) before and after surgery. There are no direct risks or benefits for patients included in the study.

Contacts

Public
Amphia Ziekenhuis

Molengracht 21
Breda 4818CK
NL
Scientific
Amphia Ziekenhuis

Molengracht 21
Breda 4818CK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Elective cardiac surgery (CABG, aortic valve replacement, mitral valve replacement, aortic surgery, Maze, or combined surgery)
On-pump surgery
Age * 60 years

Exclusion criteria

Emergent or urgent surgery
Acute infection
Haemochromatosis
Illiteracy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2019
Enrollment:	350
Type:	Actual

Ethics review

Approved WMO

Date:	02-05-2019
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
CCMO	NL68297.100.18