TRICS-III: Transfusion Requirements in Cardiac Surgery. An international, multi-centre, randomized controlled trial to assess transfusion thresholds in patients undergoing cardiac surgery

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A lower hemoglobin concentration for red cell transfusion (restrictive transfusion strategy) will be non-inferior to a liberal strategy in terms of vital organ function (heart, brain and kidney) and mortality.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Cardiac therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON43759

Source
ToetsingOnline

Brief title
TRICS-III

Condition

- Cardiac therapeutic procedures

Synonym
Anemia

Research involving
Human

Sponsors and support

Primary sponsor: St. Michael's Hospital
Source(s) of monetary or material Support: funded by Canadian Institutes of Health Research and Canadian Blood Services

Intervention

Keyword: blood transfusion, cardiac surgery, Hemoglobin concentration

Outcome measures

Primary outcome

The primary outcome is a composite score of any one of the following events occurring during the index hospitalization (from the start of surgery until hospital discharge or postoperative day 28, whichever comes first): (1) all-cause mortality; (2) myocardial infarction; (3) new renal failure requiring dialysis; and (4) new focal neurological deficit.

Secondary outcome

The secondary endpoints are as follows; see section 8.12 for definitions and details: 1. Incidence of each individual component of the primary outcome: in-hospital all-cause mortality, myocardial infarction, new renal failure requiring dialysis, and new focal neurological deficit (index hospitalization) 2. Length of stay in the ICU and hospital (index hospitalization) 3. Prolonged low output state defined as the need for two or more inotropes for 24 hours or more, intra-aortic balloon pump postoperatively or ventricular assist device (index hospitalization) 4. Duration of mechanical ventilation (index hospitalization) 5. Infection; infection will be defined as septic shock with positive blood cultures, pneumonia defined as roentgenographic infiltrate and two of three criteria: fever, leukocytosis, and positive sputum culture, and/or

deep sternal or leg wound infection requiring intravenous antibiotics and/or surgical debridement108 (index hospitalization) 6. Acute kidney injury (defined by the Kidney Disease Improving Clinical Outcomes practice guideline,110) (index hospitalization) 7. Gut infarction confirmed by imaging (e.g. angiography), autopsy, or through surgical means (index hospitalization) 8. The proportion of patients transfused and the number of blood products and hemostatic products utilized (e.g. red cells, plasma, platelets, cryoprecipitate, factor VII) (index hospitalization) 9. Death (within 6 months of index surgery) 10. New onset dialysis (since incident surgery) status (6 months after index surgery) 11. Stroke (within 6 months of index surgery) 12. Coronary revascularization (within 6 months of index surgery) 13. MI (within 6 months of index surgery) 14. Health Care Utilization (within 6 months of index surgery) * Canadian data only

Study description

Background summary

Acute anemia is associated with increased mortality likely due to impaired oxygen delivery and tissue hypoxia. Since hemoglobin contributes to more than 99% of blood oxygen content, severe anemia leads to inadequate tissue oxygen delivery, resulting in tissue hypoxia, organ failure, and death. In acute anemia the increase in mortality is proportional to the reduction in hemoglobin. During cardiopulmonary bypass (CPB), the acute hemodilution that occurs has been shown to reduce oxygenation in the brain, heart, kidney, intestine, and muscle, although the critical hemoglobin concentration that would lead to inadequate oxygen delivery during CPB has not been determined. There are a number of complications related to transfusion that are associated with considerable morbidity and mortality. Non-infectious risks from transfusion such as TRALI, which tends to occur more frequently in patients having cardiac surgery,has a high case fatality rate, 5 to 13%. Additionally, administrative errors resulting in hemolytic transfusion reactions can be

life-threatening. Pulmonary edema, due to the volume of red cells transfused, has also been shown to occur more frequently in patients with critical illness and cardiovascular disease who were transfused at a hemoglobin concentration of 100 g/L compared to a hemoglobin concentration of 70 g/L. Although the risk of acquiring the human immune deficiency virus and hepatitis C virus is low, new emerging pathogens constantly threaten the blood supply. Unnecessary transfusions also have an impact on the care of patients. Optimum utilization of blood components is essential as there is a continuous strain on blood systems because of increased blood utilization. Additionally, increased blood utilization results in increased resource utilization and cost of blood is increasing. In an era where there are new emerging pathogens and blood shortages, it is essential that these patients be transfused appropriately. There is a critical need to determine the appropriate threshold for red cell transfusion in patients undergoing cardiac surgery. While restrictive transfusion strategies have been shown to reduce transfusion in other patient populations, it may be inappropriate and unsafe to extrapolate these findings to cardiac surgery. This clinical uncertainty is reflected in the tremendous inter-physician and inter-hospital variability in transfusion practice, which are unrelated to patient risk factors. This has prompted the recommendation by the expert panel of the NHLBI to classify a trial such as this as one of the most important trials required. If our trial demonstrates the safety of a restrictive strategy, the risks and costs attributable to unnecessary transfusions will be reduced. Alternatively, if restrictive transfusion is found to be inferior, risks of complications related to untreated perioperative anemia will be reduced. Our multicentre international study will thus provide high-quality generalizable data to guide transfusion practice worldwide, regardless of its eventual results.

Study objective

A lower hemoglobin concentration for red cell transfusion (restrictive transfusion strategy) will be non-inferior to a liberal strategy in terms of vital organ function (heart, brain and kidney) and mortality.

Study design

An international, multi-centre, open-label, randomized controlled trial of two commonly used transfusion strategies, using a non-inferiority trial design.

Intervention

Study participants will be randomized to one of the following transfusion strategies in a 1:1 manner: * Restrictive transfusion strategy: patients will receive a red cell transfusion if their hemoglobin is <75 g/L (<7.5 g/dL; <4.7 mmol/L) intraoperatively and/or postoperatively * Liberal transfusion strategy: patients will receive a red cell transfusion if their hemoglobin concentration

is <95 g/L (<9.5 g/dL; <5.9 mmol/L) intraoperatively or postoperatively in the intensive care unit; or <85 g/L (<8.5 g/dL; <5.3 mmol/L) on the ward. When the appropriate hemoglobin trigger is reached, patients in each group will have one unit of red cells administered at a time followed by repeat determination of the hemoglobin concentration. Each group will be transfused only if their hemoglobin concentration falls below the transfusion threshold.

Study burden and risks

It is an obligation of the site Investigator to obtain informed consent from every study patient by means of a dated and signed informed consent form before any study related procedure is performed. *Informed consent* also implies individual discussion with the patient about the nature of study interventions to be conducted in a language that is easy to comprehend, which will take about 10 to 15 minutes. At 6 months, a telephone follow-up will occur and the following clinical outcomes will be collected based on patient or caregiver report, since hospital discharge/postoperative day 28: * Death (and reason for death) * MI * Stroke * Surgical or non-surgical coronary revascularization * New renal dialysis status at 6 months which will take about 5 to 10 minutes. risks: There are a number of complications related to transfusion that are associated with considerable morbidity and mortality and on the other hand acute anemia is associated with increased mortality.

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

Age 18 or older
* Planned cardiac surgery using cardiopulmonary bypass
* Informed consent obtained
* Preoperative European System for Cardiac Operative Risk Evaluation (EuroSCORE I) of 6 or more (using the standard additive EuroSCORE I available at www.euroscore.org/calcold.html or refer to the study Manual of Operations)

Exclusion criteria

Age 18 or older * Planned cardiac surgery using cardiopulmonary bypass * Informed consent obtained * Preoperative European System for Cardiac Operative Risk Evaluation (EuroSCORE I) of 6 or more (using the standard additive EuroSCORE I available at www.euroscore.org/calcold.html or refer to the study Manual of Operations)

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	150
Type:	Anticipated

Ethics review

Approved WMO Date:	26-07-2016
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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
ClinicalTrials.gov	NCT02042898
CCMO	NL55146.015.15