A Cross-over Randomized Controlled Trial; Pulmonary edema detection after fluid loading with blood versus saline in patients after CABG

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Cardiac surgery patients are often exposed to blood products perioperatively (18). Due to their underlying cardiac condition and ventricular dysfunction these patients are at an increased risk for TACO.(19) In a *proof of principle* approach we will...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON47009

Source
ToetsingOnline

Brief title
TACO crossover TRIAL

Condition

- Heart failures
- Pulmonary vascular disorders

Synonym
Transfusion Associated Cardiac Overload, Volume-overload

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cardiac Overload, Fluid loading, Pulmonary Edema, Transfusion

Outcome measures

Primary outcome

Hydrostatic pressure overload defined as * PCWP

Secondary outcome

Capillary leakage defined as * EVLWI

Volume overload measured by

Pulmonary artery catheter CO

Arterial line / PICCO MAP, PPV, SVV, CO, CI, EVLWI, SVR

Colloid osmotic pressure COP

by membrane colloid osmometer

Estimated circulating volume * PV, * BV

Microcirculation measured by

CytoCam microscope system TVD, PVD, PPV, MFI, Øbv

Fluid responsiveness defined by PLR * CO > 10%

TACO criteria 6 hours after infusion of autologous blood transfusion

Study description

Background summary

Transfusion associated cardiac overload (TACO) is now considered the leading cause of transfusion*related mortality in Europe. TACO is defined in terms of clinical characteristics. The International Society of Blood Transfusion defined TACO as the onset of any four of the following symptoms which occur within six hours of transfusion: acute respiratory distress, tachycardia, increased blood pressure, acute or worsening pulmonary edema and or evidence of positive fluid balance. Other definitions use similar markers such as bilateral infiltrates, ultrasound of the heart, pulmonary wedge pressure or a history of cardiac decompensation.

The pathophysiology of TACO is poorly understood; current literature describes TACO as hydrostatic pulmonary edema due to volume overload. This seems unlikely, since 20% of TACO occurs after only one transfused unit. Moreover, differences in the incidences of TACO after red blood cell (RBC) compared to plasma transfusion cannot be explained. Our hypothesis is that the pathogenesis is a *two hit**entity: the *first hit* is an underlying condition (e.g. cardiac failure or acute kidney injury) resulting in poor compliance to fluid loading * the *second hit* being a transfusion. This may explain why especially critically ill patients are at risk. Furthermore, we hypothesize that TACO is a combination of hydrostatic pulmonary edema (overload) and pulmonary edema by protein leakage following exposure to mediators in different types of blood products (a mechanism similar to transfusion related acute lung injury).

It is paramount to understand the pathophysiology of TACO, as currently no evidence-based therapy exists for this life-threatening syndrome.

Study objective

Cardiac surgery patients are often exposed to blood products perioperatively (18). Due to their underlying cardiac condition and ventricular dysfunction these patients are at an increased risk for TACO.(19) In a *proof of principle* approach we will determine whether TACO is solely volume overload or arises from a combination of volume overload and capillary leakage, by investigating the difference in change in volume parameters and capillary leakage after autologous transfusion or saline infusion. Furthermore, we will investigate the effect of fluid loading on the microcirculation.

Study design

Open-label, prospective cross-over randomized controlled trial.

Intervention

Patients will be allocated to either infusion of 300mL saline with a subsequent autologous RBC (cell saver) transfusion of 300 mL at a rate of 10mL/min, or the same in the reversed order. Prior to start of the intervention, 15 minutes following start of infusion and a the end of infusion, we will measure wedge pressure (PCWP), as well as extravascular lung water index (EVLWI) and CO estimation through PICCO® and Pulmonary Artery Catheter. We will identify fluid responsiveness by performing a passive leg raise test (PLR). We aim to measure total vessel density (TVD), perfused vessel density (PVD), proportion of perfused vessels (PPV), microvascular flow index (MFI), and blood vessel diameters (Øbv) from the oral microcirculation by CytoCam microscope system. We will estimate the effective circulating blood and plasma volume through dilutional infusion of indocyanine green prior to initial infusion, between and at the end of subsequent infusion. In total 6 times measurements will be performed.

Study burden and risks

The study provides no benefits for the participants. The study will include placement of a Swan Ganz catheter. Central line placement is part of standard care in cardiac surgery. The placement of a Swan Ganz Catheter depends on patient category, anaesthesiologist and hospital settings. The application of a Swan Ganz Catheter may result in a better read out of cardiac function. On the other hand, some studies find a small increase in catheter related side effects.

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

1. Age >18 years
2. Elective (non-redo) coronary arterial bypass grafting surgery
3. Reduced left ventricular ejection fraction (<55%)
4. Transfusion of autologous blood (cell saver blood, 300ml, HCT60%, 30min)
5. Informed consent

Exclusion criteria

1. Patients with no indication for autologous RBC transfusion
2. Patients with pulmonary hypertension, congenital heart disease, mitral or tricuspid valve disease.
3. Contraindications for PAC placement; coagulopathy, bundle branch block, defibrillator or pacemaker (risk of displacement). External pacemaker placed during surgery is no exclusion criterium.
4. Patients for acute, non-elective surgery
5. Chronic kidney disease stage 4 or higher (eGFR < 30)
6. Massive transfusion
7. Previous randomization in the current trial
8. Postoperative ongoing bleeding
9. Bypass duration > 2 hours
10. Infusion of high dose corticosteroids
11. Hemodynamic instability with a mean arterial pressure (MAP) < 60 mmHg, central venous pressure > 20 mmHg or dependence on high dosages of inotropic drugs after admittance to the ICU
12. Severe arrhythmias
13. Development of severe pulmonary edema during infusion of autologous blood or saline.
14. Elevated liver enzymes

15. Iodine allergy

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-08-2017
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	06-02-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL59191.018.16