The residual heparin concentration in the autotransfusion system product in cardiothoracic surgery: A pilot study

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Primary Objective: What is the residual heparin concentration in autotransfusion system product in cardiothoracic surgery? Secondary Objective(s): 1. What is the outcome of the anti Xa determination? 2. How much residual heparin concentration does...

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56644

Source
ToetsingOnline

Brief title
The residual heparin concentration in the autotransfusion system product

Condition

- Other condition
- Coronary artery disorders

Synonym
Aortic valve disease, coronary artery disease

Health condition

aandoeningen met hartklep

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Leeuwarden
Source(s) of monetary or material Support: verrichter van het onderzoek

Intervention

Keyword: Autotransfusion, coagulation, heparin, wash quantities

Outcome measures

Primary outcome

The aim of this pilot study is to understand more about possible residual heparin concentration in the ATS product. In addition, the relationship between wash quantity and residual fraction of heparin will be examined. The primary outcome of this study is the residual heparin fraction in the ATS product.

Secondary outcome

Secondary study parameters are the ROTEM values (coagulation management: INTEM, EXTEM, FIBTEM and HEPTEM), APTT values, ACT values, blood loss and blood transfusion. Study information will be obtained from each patient, represented in a form in the Appendix.

Study description

Background summary

The clinical perfusionist in the MCL is responsible for the use of the ATS during CTS. Sometimes, a potential detrimental effect on hemostasis is seen after retransfusion of the ATS product. Possible residual heparin concentration after washing is considered. This pilot study aims to explore the residual heparin concentration in ATS product.

Besides, the optimal intraoperative washing regimen (Popt) is defined by the perfusion protocol in the MCL. However, variation in practice exists causing uncertainty regarding the extent (efficiency) to which heparin is eliminated

during the ATS washing process. Therefore, also the relationship between the washing quantity and the residual heparin concentration in the ATS product will be examined.

Sometimes, after washing around 700 ml, a message is displayed: minimum quality reached. This message is based on the transparency of the waste liquid and the contaminant removal algorithm. The Xtra ATS indicates that at a wash volume of 700 ml, the wash quality may possibly be acceptable. The transparence is detected by the waste line color indicator, an optical sensor. However, the wash out of heparin is not mentioned in the Xtra manual or literature (Sorin, 2021). Administration of an ATS product containing heparin could potentially result in increased bleeding tendency and transfusion requirements.

1.3 Hypothesis

The ATS is very often used during CTS procedures, but only sometimes additional measures of coagulation are necessary. Besides the experience, the residual heparin in washed blood in the study of Vieira et al. is <0.1 IU/ml (Vieira et al., 2021). The study of Overdevest et al. reported the elimination rate of heparin in the ATS product (98.8%) for the Popt regimen (Overdevest et al., 2012). In this pilot study, a residual heparin concentration <0.5 IU/ml is expected with the standard washing quantities (1000 ml), as required by the AABB guidelines (American Association of Blood Banks, 2013; Buys et al., 2017; Vieira et al., 2021) .

Sometimes, the Xtra ATS indicates that at a wash volume of 700 ml, the wash quality may possibly be acceptable. However, the wash out of heparin is not mentioned in the Xtra manual or literature (Sorin, 2021). For comparison, the aim is to examine whether there is a difference in residual fraction of heparin in the ATS product in case of more than the standard volume washing (1000 ml). Therefore, besides the wash quantity of 700 ml, also 1300 ml is added.

The study of Overdevest et al. compared the Popt and Pstd_P regimens of the Xtra with regard to residual heparin concentration (Overdevest et al., 2012). The Pstd_P regimen used a wash quantity of 600, compared with the 1000 ml of the Popt regimen of the Xtra. Besides the wash quantity in Pstd_P, other parameters also varied in the study of Overdevest et al. such as prime speed, wash speed and empty speed (Overdevest et al., 2012). These other parameters were detrimental to the residual fraction of heparin. Nevertheless, the Popt and Pstd_P were almost equal in the elimination rate of heparin: 98.8% and 99%, respectively (Overdevest et al., 2012).

Based on these data and the experience of perfusionists, the null hypothesis is expected as an outcome, showing no difference in residual concentration of heparin in the ATS product at the various washing quantities.

The ACT, APTT and anti-Xa determination are all measurements to monitor the efficacy of UFH (Eikenboom, 2021; Hoffmann et al., 2007; Nguyen et al., 2021).

The ACT is measured on the intrinsic pathway in whole blood and has a higher measurement range than APTT. Besides UFH, the ACT is prolonged by multiple factors, such as thrombocytopenia. The APTT is prolonged when there is a deficiency of at least one CF from the intrinsic pathway, such as UFH (Eikenboom, 2021; Hammami & Staros, 2021; Hoffmann et al., 2007; Winter et al., 2017). The current gold standard to measure UFH in citrated human plasma is the chromogenic anti-Xa assay. Color development is inversely proportional to the amount of heparin or anti-Xa activity. Hyperbilirubinemia, hyperlipidemia and hemolysis due to the free hemoglobin can be interfering factors for this test (Eikenboom, 2021). Therefore, the research hypothesis is that higher residual heparin concentration (anti-Xa) in the ATS product leads to prolonged APTT and ACT measurements.

Study objective

Primary Objective: What is the residual heparin concentration in autotransfusion system product in cardiothoracic surgery?

Secondary Objective(s):
1. What is the outcome of the anti Xa determination?
2. How much residual heparin concentration does autotransfusion system product contain after washing with different wash quantities (700 ml, 1000 ml and 1300 ml)?
3. What is the correlation between the APTT and ACT and the concentration of residual heparin (=anti-Xa) in the autotransfusion system product?

Study design

A prospective, single-center, pilot clinical study is performed, with the primary outcome assessing the residual heparin fraction in the erythrocyte concentrate obtained by the ATS. The study is executed at the CTS of the MCL.

Intervention

3.4.1 Collection and processing blood
The study population can be divided into three groups of 15 patients. This sub population has a certain wash volume of the ATS (700 ml, 1000 ml and 1300 ml). The standard setting of 1000 ml washing quantity in Popt will be compared with 700 ml and 1300 ml washing quantity. The researcher decides the washing quantity of the ATS prior to the procedure by randomization. A container contains 15 tickets with 700 ml, 15 tickets with 1000 ml and 15 tickets with 1300 ml. If the ATS is not used during the procedure, the corresponding ticket will be returned to the container. The examiner will adjust this quantity on the ATS. The washing quantity will be taped during the procedure. The randomization is blind to the surgeon and anesthesiologist.

All measurements will be performed with an ATS from the company LivaNova: Xtra®. The ATS will be performed according to the program Popt. This regimen includes two different filling flow rates (400ml/min and 250ml/min) and an automatic standby mode. This does not require any adjustments to the settings of the ATS for the measurements, except for the different washing volumes. The Xtra bowl (225ml) is used for measurements (LivaNova, 2020).

3.4.2 CTS procedure

During the CTS procedure, the Xtra ATS system is connected via a drip chamber (Aspiration and Anticoagulation line - AAL) with one liter of saline including 50 000 IU heparin. The filter (40µm) of the reservoir (Xres T) is wetted with saline containing heparin (approximately 100 ml), after which the liquid is administered dropwise (approximately 1 drop per second) into the reservoir. The ATS is set to the Popt regimen and Xvac is set to -100 mmHg.

The perioperative heparin administration was standardized. The perfusionist routinely added 7500 IU of heparin to the CPB circuit prime. The cardio-anesthesiologist administers 300-350 units/kg of unfractionated heparin (UFH) as the initial dose at the start CPB, as outlined in the CTS anesthesia protocol of the MCL (Loos, 2021). Dripping heparinizing saline is stopped by the perfusionist at complete heparinization (ACT>480 seconds). During the CTS procedure, ACT values are recorded on the appendix form. The ATS is initiated when the collection reservoir contains sufficient blood from which approximately 225 ml of ATS product can be obtained (approximately 500 ml blood loss excluding saline, depending on the patient*s Hct). During CPB, the perfusion protocol of the MCL will be followed (Broek, 2021). Study information will be obtained from each patient, represented in a form in the Appendix. The ATS washing quantity is filled in later.

After weaning CPB, the ATS is connected to the 3L saline for washing. Then the ATS product is formed from the aspirated blood in the ATS reservoir. The perfusionist restarts the dripping heparinizing saline when protamine sulfate is initiated by the cardio-anesthesiologist (1:1 with initial heparin dose). After 10 minutes the protamine is administered 2.7 mL of blood will be collected in a citrate tube for ROTEM measurement and an ACT measurement is initiated. This ACT value may deviate no more than 10% from the ACT value before heparin was administered. In case the ACT varies, further correction is made with protamine. Before the ATS product is infused to the patient, a sample (4ml) is taken to determine the residual fraction of heparin. Again, after administering the ATS product, 2.7 ml of blood is collected in a citrate tube for a ROTEM measurement. Close monitoring of the coagulation and possible correction with blood products reduces the impact of the possible coagulation problem. Blood products may be administered even if the patient does not participate in this study. When a sample is taken from the patient in the ICU, an APTT value will also be determined in the laboratory.

3.4.3 Anti Xa assay

The MCL Certe will perform the chromogenic anti-Xa test. The results of the residual heparin fraction will not be displayed in the electronic patient record (EPD). The measurement will be performed in research setting, with patient approval.

3.4.4 Standard of care and research
Waste blood, e.g. from wound area, is collected and processed by the ATS. This allows to produce an erythrocyte concentrate, also called ATS product. This study differs slightly compared to standard care, because a 4 ml sample of the ATS product is taken for the anti-Xa test. After the sample is taken, the ATS product is administered to the patient. In other words, patients receive 4 ml less ATS product that has collected and processed the waste blood. In addition, the ATS does not use a standard wash volume of 1000 ml. Patients are randomly assigned to a wash volume of 700, 1000 or 1300 ml.

Study burden and risks

Blood (4ml) from the erythrocyte concentrate is sampled during the operation. The surgical procedure will not take longer when the patient participates in the study. In addition, the patient does not need to visit the MCL additionally for this study.

The blood sample (4 ml) of erythrocyte concentrate (minimum 225 ml) does not cause any side effects. Another wash volume set of the cellsaver may not cause any urgent side effects. Blood (products) might be administered after surgery to correct the coagulation. This may be administered even if the patient does not participate in this study.

Coagulation factors may not be returned to the patient due to centrifugation of the ATS. Due to the fact that the patient only receives erythrocytes back from the wasted blood, it is thought that the ATS may affect coagulation after surgery. Blood (products) might be needed postoperatively because heparin might still have been present in the erythrocyte concentrate.

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

The study population involves 45 patients undergoing on-pump CABG or/and AVR procedure in the MCL, where ATS has been used. Male or female patients aged 18 years or older who were in a non-emergency situation are eligible.

Exclusion criteria

Exclusion criteria includes patients who were using anticoagulant medication prior to surgery, patients with preoperative known coagulation problems and liver problems (increased APTT/ALAT/ASAT values in Electronic Health Record (EHR)). Also, patients in which hypothermia (<34 degrees Celsius) is used during cardiopulmonary bypass (CPB) are excluded from this study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	45
Type:	Anticipated

Ethics review

Not approved

Date:	14-03-2024
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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	NL85865.099.23