The effect of a high and low protamine-to-heparin dosing on perioperative hemostasis: a randomized clinical trial

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Does a low protamine-to-heparin ratio lead to a reduction in postoperative blood loss and improved postoperative hemostasis when compared to a high protamine-to-heparin ratio in cardiothoracic surgery?

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON36910

Source
ToetsingOnline

Brief title
RATIO-PRO study

Condition

- Coronary artery disorders
- Cardiac therapeutic procedures

Synonym
Antagonising heparin, coagulation disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cardiac surgery, Hemostasis, Heparin, Protamine

Outcome measures

Primary outcome

Postoperative 24-hour blood loss assessed by wound drainage.

Secondary outcome

Hemostatic monitoring:

ROTEM: Intem, Heptem, Extem, Fibtem

* Clotting Time (CT),

* Maximum Clot Firmness (MCF)

* Clot Formation Time (CFT)

Classical coagulation tests:

* aPTT

* PT

Activated Clotting Time (ACT)

Anti-Xa

Heparin concentration

* Patient demographics

* Surgery time, CPB time, cross-clamp time

* Transfusion of blood products

Study description

Background summary

Prior to, and during cardiopulmonary bypass, heparin is transfused in order to avoid massive coagulation activation by the contact surface of the heart-lung-machine. Heparin dosing is commonly based on bodyweight and activated clotting time (ACT). After cardiopulmonary bypass, protamine is transfused to neutralize heparin, thereby reactivating the clotting cascade. Protamine forms a 1:1 salt complex with heparin, but may exhibit an intrinsic anticoagulant activity after overdosing. According to current guidelines, protamine dosing is performed in a 1.0-1.3:1.0 ratio with heparin. However, our own observations and several literature reports suggest that, due to the degrading and loss of heparin during surgery, protamine is usually overdosed. The consequent overdosing of protamine might deteriorate postoperative hemostasis. The present study investigates whether the use of a lower dosing protamine-to-heparin dosing ratio (0.8) is superior as compared to a high protamine-to-heparin dosing ratio (1.3) with respect to postoperative hemostasis, blood loss and transfusion.

Study objective

Does a low protamine-to-heparin ratio lead to a reduction in postoperative blood loss and improved postoperative hemostasis when compared to a high protamine-to-heparin ratio in cardiothoracic surgery?

Study design

Multicenter, randomised, single-blinded clinical study

Intervention

Group A: Low ratio Protamine-to-heparin dosing ratio of 0.8
Group B: High ratio Protamine-to-heparin dosing ratio of 1.3

Study burden and risks

Randomisation into one of the two protamine:heparin dosing groups.
Three extra bloodsample drawings using an existing arterial line during the surgical procedure.

The risk of randomisation and extra blood sampling are estimated as minimal.

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

Patients undergoing low-moderate risk cardiac surgery (coronary artery bypass graft (CABG), and older than 18 years old

Exclusion criteria

Re-operations, emergency operations, patients with a history of hematologic or renal diseases and/or patients with a body mass index (BMI) below 18 kg/m2 or above 35 kg/m2

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-03-2013
Enrollment:	98
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Heparin sodium
Generic name:	Heparin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Protamine hydrochloride
Generic name:	Protamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2015

Application type:	First submission
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
EudraCT	EUCTR2012-003359-12-NL
CCMO	NL40764.029.12
Other	NRT nummer in aanvraag