

Reduced Anticoagulation Targets in Extracorporeal life support

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22774

Source

Nationaal Trial Register

Brief title

RATE

Health condition

Heart or lungfailure

Sponsors and support

Primary sponsor: University Medical Center Groningen (UMCG)

Source(s) of monetary or material Support: ZonMw projectnumber 80-84800-98-18009

Intervention

Outcome measures

Primary outcome

The primary outcome parameter is a composite endpoint consisting of: 1) severe hemorrhagic complications according to the ELSO definitions (see below); 2) severe thromboembolic complication defined as ischemic stroke, limb ischemia, or acute pump failure; 3) mortality at 6 months.

This composite outcome was designed to capture the net clinical effect of reduced anticoagulation targets, e.g. a reduction of major bleeding not counteracted by an increase in thromboembolic complications. Mortality is part of the composite outcome to capture unknown or unmeasured effects of reduced anticoagulation.

Severe hemorrhagic complications will be registered according to the Extracorporeal Life Support Organization (ELSO) definitions for major bleeding and is defined as clinically overt bleeding with a decrease in hemoglobin of at least 1,24 mmol/L (2 g/dl)/24 hours, or a transfusion requirement of ≥ 3 EH RBC over that same time period. Bleeding that is retroperitoneal, pulmonary or involves the central nervous system, or bleeding that requires surgical intervention is also considered major bleeding.

Secondary outcome

Secondary outcome parameters are: 1) blood transfusions; 2) quality of life (HR-QoL) at 6 months; 3) exchange of the membrane oxygenator (ECMO); 4) vessel thrombosis after ECLS removal detected by echography (see below); 5) pulmonary embolism; 6) costs; 7) the individual components of the composite outcome; 8) all thromboembolic complications combined; and 9) all hemorrhagic complications combined.

Study description

Background summary

Rationale:

ECLS treatment has a mortality of 38%, for a large part treatment related due to complications. The most feared complication is ischemic stroke for which heparin is administered with an aPTT target 2.0-2.5 times baseline (approximately 60-75 sec). However, there is no relation between aPTT and the occurrence of stroke (1.2%), but there is a relation with the much more frequent occurrence of bleeding complications (55%) and blood transfusion. Both are strongly related to outcome.

Objective:

Our objective is to study if reduced anticoagulation targets diminish bleeding complications without an increase in thromboembolic complications or a negative impact on outcome.

Study design:

Three-arm non-inferiority RCT.

Study population:

All adult Dutch patients treated with ECLS during the 30 months of the study.

Intervention:

Randomization between a target of 2-2.5 times baseline aPTT (usual care, about 60-75 sec.), 1.5-2.0 times (45-60 sec.) or LMWH guided by weight and renal function.

Main study parameters/endpoints:

The primary outcome parameter is a combined endpoint consisting of: 1) major bleeding including hemorrhagic stroke according to the ELSO definitions; 2) severe thromboembolic complication defined as ischemic stroke, limb ischemia, or acute pump failure; 3) mortality at 6 months.

Secondary outcome parameters are: 1) blood transfusions; 2) quality of life (HR-QoL) at 6 months; 3) exchange of the membrane oxygenator (ECMO); 4) vessel thrombosis after ECLS removal detected by echography; 5) pulmonary embolism; 6) costs; 7) the individual components of the composite outcome; 8) all thromboembolic complications combined; and 9) all hemorrhagic complications combined.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

We estimate that with an aPTT target of 45-60 sec. or with use of LMWH the primary endpoint will be met in 60% of patients compared to 70% with usual care. To show non-inferiority 91 patients per group are needed. To compensate for a lower effect and drop-outs 330 patients will be enrolled. Results will be analyzed by intention to treat.

Apart from anticoagulation targets, treatment will be as usual so study participation will not lead to a burden for the patient, e.g. no extra blood sampling, tests or visits. After 6 months the patients will be contacted for a questionnaire to measure health-related quality of life. A risk may be that reduced anticoagulation target or anticoagulation with LMWH is inferior to standard practice. A benefit may be that reduced anticoagulation target or anticoagulation with LMWH is superior to standard practice.

Study objective

We expect that with a target of 1.5-2.0x baseline aPTT or with LMWH the primary composite endpoint will be reached in 60% of patients compared to 70% in usual care. To show non-inferiority with a significance level (alpha) of 5%, power of 80% and a non-inferiority limit (delta) of 7.5% the corresponding sample size is 91 patients per group. In other words, if there is a true difference in favor of the experimental treatment of 10%, then 91 patients per group are required to be 80% sure that the upper limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) will exclude a difference in favor of the standard group of more than 7.5%. To compensate for a lower effect and drop-outs 330 patients will be enrolled.

Study design

Enrollment will start January 2020

Intervention

Randomization between a target of 2-2.5x baseline aPTT (usual care, about 60-75 sec.), 1.5-2.0x (45-60 sec.) and therapeutic LMWH guided by weight and renal function.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- ECLS treatment during the study period in one the participating centers
- (deferred) informed consent
- Age above 18

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Patients in whom the ECLS is only used to bridge a procedure like a high risk percutaneous coronary intervention or during surgery
- No (deferred) informed consent
- Vital indication for anticoagulation (e.g. mechanic mitral valve, pulmonary embolism)
- Heparin induced thrombocytopenia (HIT)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-01-2020
Enrollment:	330
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Ethics review

Not applicable	
Application type:	Not applicable

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

NTR-new

Other

ID

NL7969

METC UMCG : M19.236755

Study results