Reduced Anticoagulation Targets in Extracorporeal life support

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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...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22774

Bron
Nationaal Trial Register

Verkorte titel
RATE

Aandoening

Heart or lungfailure

Ondersteuning

Primaire sponsor: University Medical Center Groningen (UMCG)
Overige ondersteuning: ZonMw projectnumber 80-84800-98-18009

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

Enrollment will start January 2020

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2020
Aantal proefpersonen:	330
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7969
Ander register	METC UMCG : M19.236755

Resultaten