Innovative methodology: The development of a method to measure flow-based thrombin generation

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The objective of this study is to investigate whether thrombin generation is effected by different shear rates and different tissue factor concentrations in plasma, platelet rich plasma and whole blood. Thrombin generation in plasma with/without...

Ethical review	Approved WMO
Status	Pending
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON37888

Source
ToetsingOnline

Brief title
Diagnostic assay to measure secundairy hemostasis

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
clotting, hemostasis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: The Netherlands Heart Foundation

Intervention

Keyword: diagnostic assay, flow, thrombin generation

Outcome measures

Primary outcome

The following parameters will be measured in the blood samples:

• Thrombus generation and coagulation under flow in vitro. Thrombin generation is a dynamical process which includes platelets, coagulation factors and other blood cells. Thrombin generation can be triggered with different concentrations of tissue factor.

• Control experiments need to be carried out per blood sample to check platelet count, quality, plasma quality and quality of whole blood using the standard procedures of our laboratory (flow cytometry, aggregometry, clotting).

The main study parameters are thrombin generation and coagulation under flow conditions in vitro. Four different shear rates will be used to mimic arterial and venous blood flow and results will be compared. Furthermore four different tissue factor concentrations will be used. When no effect of shear rate is found on thrombin generation the study will be cancelled.

Secondary outcome

NA.

Study description

Background summary

Occlusion of a vessel is a dynamic process in which several different systems collaborate in an organized fashion. A too big change in any of these systems (vessel, platelets and coagulation factors) can lead to either a bleeding or thrombotic phenotype. To quantify such changes and thereby detect pathogenic phenotypes several assays can be used. Thrombin generation is a widely used assay to detect a prothrombotic phenotype due to a hyper-active coagulation system. It has repeatedly been shown that increased thrombin generation is associated with myocardial infarction and has prognostic value. A higher potential to generate thrombin is related with thrombosis and a lower one with bleeding. With respect to arterial thrombosis, where platelets and other blood cells play a much larger role than in venous thrombosis, it is an advantage of this assay that it can also measure the interaction between coagulation and platelets as it occurs in platelet-rich-plasma. Recent developments in our laboratory even allow measurement in whole blood.
Furthermore, as soon as platelets are involved flow also starts to play an important role. We have found that in flow platelets need VWF to exert their full prothrombotic character. VWF seems to be a mediator between fibrin and platelets.
Because of the importance of platelets, other blood cells and flow, we would like to expand the current thormbin generation method by measuring hemostasis in whole blood under flow to explore whether we are able to better detect and predict a prothrombotic phenotype thereby its risk on clinical symptoms such as a myocardial infarction.

Study objective

The objective of this study is to investigate whether thrombin generation is effected by different shear rates and different tissue factor concentrations in plasma, platelet rich plasma and whole blood. Thrombin generation in plasma with/without platelets is a well established method for the detection of a prothrombotic or bleeding phenotype. Recently a method was developed to measure thrombin generation in whole blood, thereby taking into account the total cellular compartment of the blood. We would like to expand this assay be including the flow (=shear) that also normally occurs in a blood vessel. Therefore we will test thrombin generation under flow in whole blood, platelet rich plasma and plasma alone. This will be done for 4 different shear rates with 4 different tissue factor concentrations.

Study design

This study is of invasive design. However, the impact on the subjects will be minimal. Blood will be drawn from healthy volunteers (male and female) between the ages of 18 and 65 years. They will be recruited from Maastricht University and Maastricht UMC+. Before blood collection an informed consent will be

signed. For all study objectives described above blood from healthy volunteers is needed. For every study objective an estimated 10 blood donations are needed (in total 120 blood donations over a period of 4 years).

Study burden and risks

The venipunctures will be made by experienced coworkers. Nevertheless, blood sampling causes local bruising, and incidentally a hematoma can be formed. There will be no direct benefit of the subjects.

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

• Healthy men and women aged 18 to 65 years
• Signed written consent to take part in the study

Exclusion criteria

• Use of oral anticoagulants
• Use of oral anti- platelet drugs
• History of thrombosis and/or bleeding

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2012
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO

Date:	28-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL38062.068.11