Time course of platelet reactivity in the acute phase of STEMI as measured with various platelet function studies

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• To investigate the magnitude and time course of platelet reactivity and platelet activation in patients with a STEMI undergoing primary percutaneous coronary intervention (pPCI).• To investigate the magnitude and time course of thrombin generation…

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

Summary

ID

NL-OMON38015

Source
ToetsingOnline

Brief title
TOPS

Condition

- Coronary artery disorders

Synonym
Platelet reactivity

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: platelet activation, platelet reactivity, STEMI

Outcome measures

Primary outcome

• Platelet function tests, including LTA, VerifyNow P2Y12, TEG, Multiplate, PFA

(see appendix A)

• Percentage platelet bound P-selectin expression (see appendix A)

• Thrombin generation at high tissue factor concentration, at low tissue factor

concentration and with microparticle reagens.

• Coagulation factors: Full length tissue factor pathway inhibitor (FL-TFPI),

total protein S, FVIII, vWF

• Genetic variations associated with response to antiplatelet therapy and

thrombus formation

Secondary outcome

nvt

Study description

Background summary

Platelets play a pivotal role in the pathogenesis of atherosclerosis and thrombus formation, which contributes to the development of acute ischemic coronary events. (1,2) Therefore, dual antiplatelet therapy with aspirin and a thienopyridine drug (clopidogrel or prasugrel) or ticagrelor has become the cornerstone in the management of coronary heart disease. (3,4) However, the individual response to dual antiplatelet therapy is not uniform (5,6) and consistent findings across multiple investigations support the association between a lower degree of platelet inhibition, a high on-treatment platelet reactivity (HPR), and the occurrence of atherothrombotic events. (7-13) These findings have been recently extended to patients with ST-segment elevation

myocardial infarction (STEMI), who experience a high thrombotic burden and a high rate of HPR. (14,15) Increased platelet reactivity as well as pro-thrombotic and pro-inflammatory changes associated with myocardial infarction have been shown to persist up to several months. (16,17) What remains uncertain is to what extent the increased platelet activation observed is due to the disease process itself, i.e. activation of platelets within the abnormal coronary circulation, or to a genetic or environmental propensity for platelets to become activated more easily in response to minimal stimuli. (18) In the former case, one would expect that platelet status would return to normal early after the resolution of the acute event, whereas in the latter case platelet function may remain abnormal for a considerable time or indefinitely. 18 More insights into these processes can result in further optimization of medical treatment for patients with STEMI.

Recently, the new antiplatelet agent ticagrelor was introduced. The PLATO study proved the clinical efficacy of ticagrelor and showed a decrease in atherothrombotic events and mortality during 1 year follow-up compared to clopidogrel.19 The ONSET/OFFSET study 20 showed using platelet function testing in stable coronary artery disease patients that a maximal inhibiting effect on platelet aggregation was achieved within two hours after administration of ticagrelor. However, the onset of action in STEMI patients is unknown. Knowledge about the onset of action of ticagrelor in the first hours after administration will contribute to optimal treatment strategies for STEMI patients.

Study objective

• To investigate the magnitude and time course of platelet reactivity and platelet activation in patients with a STEMI undergoing primary percutaneous coronary intervention (pPCI).
• To investigate the magnitude and time course of thrombin generation, coagulation factors (X and Xa), Tissue factor pathway inhibitor (TFPI), d-dimer-levels, and genetic variations associated with response to antiplatelet therapy and thrombus formation in patients with a STEMI undergoing pPCI.

Study design

This is a non-randomized, open label, multicenter study, designed to investigate the magnitude and time course of platelet activation/reactivity as well as coagulation factors in STEMI-patients undergoing primary PCI.

Study burden and risks

Risk of participation is limited to the possibility of hematomas caused by venapuncture.

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

Patient must meet ALL of the following criteria:
• Males or females > 21 years of age and < 85 years with symptoms of acute myocardial infarction of more than 30 minutes but less than 12 hours.
• ST segment elevation of > 1 mV in 2 adjacent ECG leads, with cumulative ST- segment deviation of 6 mm or more.
• Patients should only be included if there is a reasonable expectation that PCI will be conducted within 1 hour.

Exclusion criteria

1) Patients who are unable to give informed consent or have life expectancy of < 1year

2) Subjects who have received thrombolytic therapy within 24 hours before PCI or GpIIb/IIIa-inhibitors within the last 15 days or during the PCI
3) Subjects with a contra-indication to anticoagulation or at increased bleeding risk
a. Past or present history (<1 year) of bleeding from gastrointestinal (haematemesis) melena, frank bleed in stool or visible haematuria
b. Known platelet count (<100,00/mm3) or coagulopathy or platelet disorder.
c. History of major recent (<30 day) surgery or trauma
4) Known Hb <6.5 mmol/L11g/dl or HCT <33%

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-09-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	12-04-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	15-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	01-10-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL33596.100.10