Anticoagulant treatment after knee arthroscopy or during plaster cast lower leg immobilisation: determining the balance between benefits and risks

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Comparative effectiveness research to determine cost-effectiveness of an existing healthcare policy, i.e. treatment with low molecular weight heparin (LMWH) after knee arthroscopy and lower leg plaster cast immobilization following surgical or…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bone and joint injuries
Study type	Interventional

Summary

ID

NL-OMON41615

Source
ToetsingOnline

Brief title
Pot-(K)Cast

Condition

- Bone and joint injuries
- Fractures
- Embolism and thrombosis

Synonym
blood cloth in vein of the leg, Venous Thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: anticoagulant therapy, knee arthroscopy, lower leg cast immobilisation, Venous Thromboembolism

Outcome measures

Primary outcome

The primary efficacy outcome is symptomatic venous thrombosis, i.e., deep

venous thrombosis (DVT) or fatal or non-fatal pulmonary embolism (PE).

The primary safety outcome is major bleeding, defined according to the

guidelines of the ISTH:

a) fatal bleeding or

b) symptomatic bleeding in a critical area or organ, or

c) extrasurgical site bleeding causing a fall in hemoglobin level of 1.24

mmol/L or more, or leading to transfusion of one or more units of whole blood

or red cells, or

d) surgical site bleeding that requires a second intervention or a hemarthros

interfering with rehabilitation, or surgical site bleeding for which

bloodtransfusion is indicated

Secondary outcome

Other clinically relevant bleeding, defined as overt bleeding not meeting the

criteria for major bleeding but associated with medical intervention,

unscheduled contact with a physician, (temporary) cessation of study treatment,

or associated with discomfort such as pain, or impairment of activities of

daily life.

Economic evaluation: Cost-effectiveness analysis (costs per prevented venous thrombosis and/or pulmonary embolism) and model-based cost-utiltity analysis from a societal perspective (costs per QALY)

Risk factor analysis:

- Genetic variants: rs6025 (F5, Factor V Leiden), rs1799963 (F2, 20210 G>A), ABO blood Group, rs2066865 (FGG 10034 C>T), rs2289252 (F11)

- Plasma levels: factor VIII, factorIX, prothrombin, fibrinogen, Protein C, Protein S, antithrombin.

-Acquired risk factors (cancer, hormone use, etc)

Study description

Background summary

Currently, guidelines and clinical practice differ considerably with respect to use of anticoagulant treatment after arthroscopy of the knee or during cast immobilisation of the lower leg. Trials that have been carried out were aimed at efficacy only, had small sample sizes and therefore mainly used asymptomatic thrombosis as endpoint. From these trials an overall risk benefit-balance could not be established, hence the current controversy exists. In the proposed study we will use relevant symptomatic endpoints in a large cohort of patients. Furthermore we will follow subjects with an adverse event for a longer period, during which we will assess the long term sequelae of these events. Lastly, we will determine high risk groups that will benefit most from anticoagulant treatment.

Study objective

Comparative effectiveness research to determine cost-effectiveness of an existing healthcare policy, i.e. treatment with low molecular weight heparin

(LMWH) after knee arthroscopy and lower leg plaster cast immobilization following surgical or conservative treatment. In addition we will investigate personalized prophylaxis based on genetic and acquired risk factors these groups at high risk of venous thrombosis.

Study design

Two parallel randomised controlled trials comparing a policy with the anticoagulant LMWH to a policy with no anticoagulant in two groups of patients with an increased risk of venous thrombosis: patients who underwent knee arthroscopy and patients with lower leg cast immobilisation.
In both trials determination of genetic and acquired risk factors will be performed at the start of the study. Based on the presence or absence of these factors we will assign a risk profile to each patient.

Intervention

In case of knee arthroscopy: LMWH (nadroparin 2850 IE s.c. once daily, > 100kg 5700IE sc) for 8 days vs no treatment. In case of lower leg plaster cast immobilization: LMWH (nadroparin 2850 IE s.c. once daily, > 100kg 5700IE sc) for the duration of the immobilisation (average 6-8 weeks) vs no treatment.

Blood taken pre- and post-operatively or at the emergency department will be analysed on 5 common single nucleotide polymorphisms (SNPs) known to strongly affect thrombotic risk; on levels of 7 coagulation factors in plasma (of which high or low levels are known to increase the risk). Patients will also be screened on acquired risk factors for thrombosis through a questionnaire.

Study burden and risks

We will compare two standard treatment modes that are currently both given depending on the physician*s or hospital*s preference. The patients in our trial will be subjected to one of these standard treatments. It is therefore not expected that participation will lead to an increased health risk. Nadroparin is not an experimental pharmaceutical. Not participating in the trial may, depending on the physician, still lead to treatment with Nadroparin. All patients will need to undergo one venapuncture for blood sampling for the study. In case of surgical treatment this blood sample will be taken pre-operatively. Another blood sample will be taken post-operatively but does not require an extra venapuncture because it will be taken from the intravenous catheter.In case of cast immobilisation this blood sample will be taken at the first day of immobilisation.
No extra hospital visits are required. Patients who had an arthroscopy of the knee will be, on top of regular follow-up vistis, contacted by telephone after three months, to make sure no complications will be missed. Patients with lower leg cast immobilisation will be contacted by telephone at three weeks and three

months (besides regular follow-up visitis), due to the wide variance in treatment and follow-up.
One questionnaire concerning risk factors for thrombosis, bleeding and patients demographics will be filled in before arthroscopy or at the first day of cast immobilisation.
Only subjects with (serious) adverse events (and a similar random sample of subjects without a (serious) adverse event) will be monitored for a two year period after the event. After six months, one year and two years after the event, patients will be seen for clinical examination and quality of life assessment by means of a questionnaire.

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

Arthroscopy of the knee
Lower leg plaster cast immobilisation.

Exclusion criteria

Contra-indications for LMWH use (recent major bleeding, bleeding disorder, allergy)
Pregnancy
Pre-existent indication for anticoagulation therapy, either LMWH or vitamin K antagonists.
Mental of physical disability to fulfil study requirements.
Insufficient knowledge of the Dutch language.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2012
Enrollment:	3000
Type:	Actual

Ethics review

Approved WMO

Date:	07-07-2011
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	15-11-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-02-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-03-2013
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-07-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-11-2013
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Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	09-03-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
ClinicalTrials.gov	NCT01542762
CCMO	NL35774.058.11