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Graduated compression stockings versus low-molecular-weight heparin for prevention of venous thromboembolism after knee arthroscopy: a prospective randomised trial

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Registration date 22/01/2007	**Overall study status** Completed	
Last Edited 14/08/2008	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title

Acronym
Knee Arthroscopy Nadroparin Thromboprophylaxis (KANT) Study

Study objectives
There is lack of consensus about the need of preventing venous thromboembolism after knee arthroscopy and indeed, in many institutions worldwide, thromboprophylaxis is not an issue. The latest American College of Chest Physicians (ACCP) conference on antithrombotic and thrombolytic therapy guidelines endorsed thromboprophylaxis after knee arthroscopy with low-molecular weight heparins (LMWH) only in patients with pre-existing risk factors or with prolonged or complicated procedures; while suggesting against routine thromboprophylaxis other than early mobilisation in all other patients (both grade 2B recommendations). Conversely, in Italy there is a very high prescription-rate of pharmacological thromboprophylaxis after KA procedures, although with a great heterogeneity in terms of timing and duration.

Added 14/08/2008:
Originally the study had been designed as a triple-arm trial, including a 14-day LMWH course. However, this arm was stopped by the Data and Safety Monitoring Board (DSMB) during a planned interim analysis. Thereafter, the study was continued as a two-arm trial. The previous target number of participants with this third arm was 1950. Details of this stopped third arm can be found in the interventions section below.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Ethics Committee of U.L.S.S. n° 16 - Padua on the 5th February 2002 (ref: 23-S/02)

Study design
Assessor-blind randomised prospective trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet

Health condition(s) or problem(s) studied
Venous thromboembolism

Interventions
Patients with objectively documented VTE were treated according to standard protocols, while patients with a normal diagnostic workup were followed up clinically for three months

Current interventions section as of 14/08/2008:
This is an assessor-blind randomised prospective clinical trial. Patients scheduled for diagnostic arthroscopy or arthroscopy-assisted knee surgery for anterior cruciate ligament reconstruction, partial lateral and/or medial meniscectomy, cartilage shaving or resurfacing, chondroplasty, combined surgical procedures and other surgical procedures (e.g. loose body removal, patella realignment, etc.) were randomised by computerised generated list to wear full-length graduated compression stocking for 7 days or to receive once-daily subcutaneous LMWH (nadroparin, 3800 anti-Xa IU), for 7 or 14 days. All included patients were scheduled for a bilateral whole-leg ultrasound examination at day 7+1 or 14+1. Patients with objectively documented VTE were treated according to standard protocols, while patients with a normal diagnostic workup were followed up clinically for three months.

The DSMB members joined for three planned interim analysis (40%, 65% and 80% of the estimated sample size) to appraise data quality and verify the pre-specified stopping rules (if the efficacy of the more invasive therapeutic protocol or the safety of the less invasive therapeutic protocol was inferior to the others, these arms were stopped: 7-day LMWH versus GCS and 14-day LMWH versus 7-day LMWH or versus GCS). At the second interim analysis the DSMB officially stopped the 14-day LMWH arm, due to concerns about potential safety issues related to a longer LMWH course. Afterwards, the trial continued as a two-arm study (GCS versus 7-day LMWH).

The arthroscopic procedures were performed by a team of 6 experienced orthopaedic surgeons of the Department of Knee Surgery of Abano Terme Clinic. All patients underwent selective subaracnoid anaesthesia. Arthroscopic procedures were performed using a standard two-portal (antero-lateral and antero-medial) technique. All patients were immediately mobilised while in the hospital and were allowed to bear weight on the operated leg, as tolerated on crutches, except for those undergoing chondroplasty who were mobilised non-weight bearing for the first three post-operative weeks. All patients were discharged within 24 hours from the procedure and were invited to immediately start physiotherapy and rehabilitation to resume a full activity as soon as possible.

Previous interventions section:
This is an assessor-blind randomised prospective clinical trial. Patients scheduled for diagnostic arthroscopy or arthroscopy-assisted knee surgery for anterior cruciate ligament reconstruction, partial lateral and/or medial meniscectomy, cartilage shaving or resurfacing, chondroplasty, combined surgical procedures and other surgical procedures (e.g. loose body removal, patella realignment, etc.) were randomised by computerised generated list to wear full-length graduated compression stockings (GCS) (30 - 40 mmHg at the ankle) over the operated leg or to receive once-daily subcutaneous injection of Nadroparin (3.800 anti-Xa IU, equivalent to 0.4 ml subcutaneously), for 7 days. All included patients were scheduled for a bilateral whole-leg ultrasound examination at day 8 (± 1) to assess for the presence of DVT, and were instructed to immediately refer to the coordinating centre if signs or symptoms suggesting venous

thromboembolism (VTE) had become manifest before the scheduled visit. Patients with objectively documented VTE were treated according to standard protocols, while patients with a normal diagnostic workup were followed up clinically for three months.

The arthroscopic procedures were performed by a team of 6 experienced orthopaedic surgeons of the Department of Knee Surgery of Abano Terme Clinic. All patients underwent selective subaracnoid anaesthesia. Arthroscopic procedures were performed using a standard two-portal (antero-lateral and antero-medial) technique. All patients were immediately mobilised while in the hospital and were allowed to bear weight on the operated leg, as tolerated on crutches, except for those undergoing chondroplasty who were mobilised non-weight bearing for the first three post-operative weeks. All patients were discharged within 24 hours from the procedure and were invited to immediately start physiotherapy and rehabilitation to resume a full activity as soon as possible.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Low-molecular-weight heparin

Primary outcome measure
The primary efficacy outcome was the combined incidence of symptomatic PE, symptomatic and asymptomatic proximal DVT and symptomatic isolated calf DVT in both groups.

The primary safety end-point was the incidence of major and clinically relevant bleeding. Major bleedings included:
1. Clinically overt haemorrhages associated with a drop in haemoglobin of at least 20 g/L or with the transfusion of two or more units of packed cells
2. Disabling, retroperitoneal, or intracranial events
3. Bleedings requiring re-intervention
4. Haemarthrosis with a joint drainage of more than 450 millilitres of blood

A clinically relevant bleed was defined as haemarthrosis with a joint drainage of more than 100 and up to 450 millilitres of blood.

Secondary outcome measures
1. Overall incidence of proximal and distal DVT and symptomatic PE
2. Overall incidence of bleeding, including minor episodes (defined as haemarthrosis with a joint drainage of less than 100 millilitres of blood, and all other non-major and non-clinically relevant bleedings)
3. Incidence of superficial thrombophlebitis

Overall study start date
01/03/2002

Completion date
31/12/2005

Eligibility

Key inclusion criteria
All consecutive outpatients scheduled for diagnostic arthroscopy or arthroscopy-assisted knee surgery for anterior cruciate ligament reconstruction, partial lateral and/or medial meniscectomy, cartilage shaving or resurfacing, chondroplasty, combined surgical procedures and other surgical procedures (e.g. loose body removal, patella realignment, etc.)

Participant type(s)
Patient

Age group
Adult

Sex
Not Specified

Target number of participants
1300

Key exclusion criteria
1. Aged less than 18 years
2. Pregnancy
3. Previous deep vein thrombosis (DVT) and/or pulmonary embolism (PE)
4. Active malignancy
5. Known thrombophilia
6. Mandatory anticoagulation
7. Hypersensitivity to low-molecular weight heparins
8. History of recent major bleeding, as described below (less than 4 weeks)
9. Severe renal or hepatic failure
10. Anticipated poor compliance with the study requirements
11. Geographic inaccessibility

Owing to the recommendations of latest ACCP conference, 17 patients with complicated procedures and a tourniquet thigh time longer than 60 minutes were excluded, because they were considered, hypothetically, at higher risk of developing venous thromboembolic complications and pharmacological thromboprophylaxis with fixed-dose of low-molecular weight heparins is suggested (grade 2B).

Date of first enrolment
01/03/2002

Date of final enrolment
31/12/2005

Locations

Countries of recruitment
Italy

Study participating centre
Via Giustiniani, 2
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Sponsor information

Organisation
University Hospital of Padua (Italy)

Sponsor details
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N/A

Sponsor type
University/education

ROR
https://ror.org/04bhk6583

Funder(s)

Funder type
Other

Funder Name
Investigator-funded (Italy)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Results	15/07/2008		Yes	No