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Lowering the intensity of anticoagulation is safe and effective for patients with mechanical cardiac valve prosthesis

Submission date
23/05/2008

Registration date
19/06/2008

Last Edited
14/10/2019

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Haematological Disorders

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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
LOWering the INtensity of oral anticoaGulant Therapy in patients with mechanical aortic valve replacement: the LOWING-IT Trial

Acronym
LOWING-IT

Study objectives
The present randomised study tested the hypothesis that a low intensity level oral anticoagulant regime with an international normalised ratio (INR) range between 1.5 to 2.5 is as effective and safe as a higher level of anticoagulant therapy with a recommended INR range of 2.0 to 3.0, in patients with a single aortic mechanical prosthetic valve replacement. In particular, the hypothesised outcome from using a 1.5 to 2.5 INR intensity level (as opposed to the currently recommended INR of 2.0 to 3.0) was a reduction in the incidence of haemorrhagic episodes without affecting the risk of thromboembolic events.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Ethics Committee of the Postgraduate School of Pathophysiology of the Cardiorespiratory System and Associated Biotechnologies, Second University of Naples granted the initial ethics approval for this trial in December 2000. However, our internal regulations have changed to be in line with the international guidelines since the time of initial approval, and this trial was re-submitted and then re-approved by the Ethics Committee of the Monaldi Hospital, Naples on 23 /06/2008 (ref: #15)

Study design
Single-centre, randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Anticoagulant therapy

Interventions
The participants were enrolled from January 2001 to January 2005. They were allocated to the following two arms:
Intervention arm: Low intensity oral anticoagulant regime with an INR range between 1.5 to 2.5
Control arm: Higher level of anticoagulant therapy with a recommended INR range of 2.0 to 3.0

The follow-up of the interventions was 4.3 ± 0.9 years.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Thromboembolic and haemorrhagic events, followed-up for 4.3 ± 0.9 years:
1. Cerebral infarction
2. Coronary and/or peripheral embolism
3. Valve thrombosis
4. Intracranial and spinal bleeding
5. Major extra-cranial bleeding
6. Endocarditis
7. Withdrawal from the oral anticoagulant therapy
8. Death

Cerebral thromboembolic events included the onset of a transient or definitive symptomatic neurological stroke and/or evidence of an ischaemic vascular brain sequela on a computerised tomography (CT) brain scan. Coronary or peripheral embolic events were documented by echo Doppler, angiography, or surgery. Prosthesis thrombosis was defined as impairment of the valve by the deposition of thrombus, demonstrated by echo Doppler or surgery. Haemorrhagic events were considered to be major when blood transfusion, hospitalisation, or a surgical procedure was required. Other haemorrhages were considered to be non-major but were recorded.

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/01/2001

Completion date
01/01/2005

Eligibility

Key inclusion criteria
1. Both male and female patients, aged 20 - 60 years
2. Those presenting for a first single-valve replacement with a bileaflet mechanical prosthesis in the aortic position

3. Those with a low thrombo-embolic risk
4. Valve prosthesis dimension greater than 21 mm
5. Normal ejection fraction (EF)
6. Left atrium diameter less than 47 mm
7. Normal sinus rhythm

Participant type(s)
Patient

Age group
Adult

Sex
Not Specified

Target number of participants
420

Total final enrolment
292

Key exclusion criteria
1. Contraindication to anticoagulant treatment (including pregnant women)
2. Valvular prosthesis on another orifice
3. Dialysed renal failure
4. Hepatic insufficiency
5. Patient or general practitioner refusal to participate in the study
6. Patients with a high risk of thromboembolic events (i.e. atrial fibrillation, history of cardiac thromboembolism, left atrial diameter greater than 47 mm on a time-motion echocardiogram, thrombosis or calcification of the left atrium) (exclusion for ethical reasons)

Date of first enrolment
01/01/2001

Date of final enrolment
01/01/2005

Locations

Countries of recruitment
Italy

Study participating centre
Department of Cardio-Thoracic and Respiratory Sciences
Naples
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Sponsor information

Organisation
Second University of Naples (Seconda Università degli studi di Napoli) (Italy)

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Sponsor type
University/education

Website
http://web.unina2.it

ROR
https://ror.org/05290cv24

Funder(s)

Funder type
University/education

Funder Name
Funded by the PhD Programme in Cardiologic Sciences, Postgraduate School of Medical Surgical Pathophysiology of the Cardiorespiratory System and Associated Biotechnologies, Second University of Naples, Naples (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	01/07/2010		Yes	No
Results article	results	30/05/2018	14/10/2019	Yes	No