

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

Submission date 23/05/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 19/06/2008	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 14/10/2019	Condition category Haematological Disorders	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> 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

Protocol serial number
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

Study type(s)

Treatment

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(s)

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.

Key secondary outcome(s)

No secondary outcome measures

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

Healthy volunteers allowed

No

Age group

Adult

Sex

Not Specified

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

Italy

80060

Sponsor information**Organisation**

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

ROR

<https://ror.org/05290cv24>

Funder(s)**Funder type**

University/education

Funder Name

Funded by the PhD Programme in Cardilogic Sciences, Postgraduate School of Medical Surgical Pathophysiology of the Cardiorespiratory System and Associated Biotechnologies, Second University of Naples, Naples (Italy)

Results and Publications

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