Switching anticoagulant management from a VKA to a NOAC-based tratment strategy in frail elderly patients with atrial fibrillation

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON55760

Source
ToetsingOnline

Brief title
FRAIL-AF study

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation, heart rhythm disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: ZonMw,Bayer,Boehringer Ingelheim,Pfizer,Sankyo Pharma

Intervention

Keyword: atrial fibrillation, bleeding complications, Frailty elderly, oral anticoagulants

Outcome measures

Primary outcome

Primary outcome: the first occurrence of the composite of at least one major or one clinically relevant non-major bleeding complication during the one-year follow-up period, following definitions from the International Society of Thrombosis and Haemostasis (ISTH).

Secondary outcome

Secondary outcomes include the endpoints of major or clinically relevant non-major bleeding complications separately, minor bleedings (i.e. all other bleeding events nor classified as major of CRNM), thrombo-embolic events, the occurrence of the composite of ischaemic and haemorrhagic stroke, quality of life, cost-effectiveness, and risk factors for bleeding.

Study description

Background summary

For long, vitamin K antagonists (VKAs) were the only therapeutic strategy to reduce stroke risk in patients with atrial fibrillation (AF). Recently, an alternative has entered the clinical domain: non-VKA oral anticoagulants (NOACs). Large randomized controlled trials (RCTs) demonstrated that NOACs are at least as effective as VKAs to reduce the risk of ischaemic stroke, yet with a better safety profile (notably fewer intracranial bleeds). Based upon these trial results, the recent guidelines from the European Society of Cardiology (ESC) have a strong preference of NOACs over VKAs when starting oral anticoagulant treatment in AF patients. Moreover, the ESC guideline considers

switching VKA-treatment to a NOAC appropriate, in particular when the time in therapeutic INR range is low while on a VKA, although this latter recommendation is less strong than the preference of NOACs over VKAs when newly initiating oral anticoagulant treatment. However, frail elderly patients were under-represented in the landmark NOAC RCTs, leaving a knowledge gap on the optimal anticoagulant treatment strategy (VKA or NOAC) in this increasing group of frail AF patients. Both may have advantages as well as risks, and it is yet unknown which type of oral anticoagulant (VKAs or NOACs) should be preferred in this specific population. In particular, it is unknown if switching (chronic) VKA treatment to a NOAC yields fewer bleeding complications in frail elderly AF patients, as may be expected given the current results from RCTs and observational studies that were performed with non-frail AF patients.

Study objective

The primary objective is to evaluate whether the impact of a strategy aimed at switching INR-guided VKA management to a NOAC-based treatment strategy is superior in terms of the occurrence of major or clinically relevant non-major bleeding complications in frail elderly patients with AF. Hereto we will assess the relative risk (hazard ratio) of the randomised groups with respect to the time to first occurrence of a major or clinically relevant non-major bleeding complication (whichever comes first). The total of the two components of this composite outcome, (major or clinically relevant non-major bleeding complications), will also be analysed as separate outcomes secondarily. Other secondary objectives include a comparison of both treatment strategies on the occurrence of all-cause thrombo-embolic events, the composite of ischaemic and haemorrhagic stroke, quality of life and cost-effectiveness, as well as an identification of risk factors for bleeding in frail elderly AF patients treated with either a VKA or a NOAC.

Study design

Multi-centre pragmatic open label registry-based randomized controlled clinical trial.

Intervention

In the index group, the treating physician (general practitioners (GPs) or cardiologists) will be encouraged to switch oral anticoagulant management from INR-guided VKA-management to a NOAC-based management with prescription of one of the available NOACs (dabigatran 150mg twice a day, rivaroxaban 20mg once daily, apixaban 5mg twice a day or edoxaban 60mg once daily) based upon physician and patient preference. Dose adjustments for NOAC treatment will be conform guidelines. The control group continues with current routine-care VKA treatment (either acenocoumarol 1mg or fenprocoumon 3mg), with dose tailoring

based upon regular INR measurements.

Study burden and risks

Both VKAs and NOACs are guideline-recommended treatment options for stroke prevention in AF, and inherently carry a risk of bleeding with possibly an overall lower risk of (notably intracranial) bleeding on NOACs. Nevertheless, the risk of these bleeding complications is not directly related to study participation or study procedures, yet part of routine practice as current guidelines clearly indicate the need to prescribe anticoagulants for stroke prevention in elderly AF patients. Patients in the index group are not being visited at home anymore by the thrombosis service for regular INR measurements and dismissal of these regular home visits could lead to change in quality of life, both in a positive and negative way. Patients in both the index group and the control group are asked baseline characteristics and follow-up questions at respectively 0 and 1, 3, 6, 9 and 12 months. Moreover, patients are asked to fill in quality of life questionnaires at 0, 6 and 12 months.

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

1. Age > 75 years
2. Currently managed on VKA treatment for AF by one of the participating thrombosis services
3. Groningen Frailty Indicator (GFI) 3 or higher
4. Willingness to switch from VKA management to a NOAC-based treatment strategy.

Exclusion criteria

1. Renal impairement, i.e. eGFR below 30 ml/min/1.73m2 (these patients will not be randomized for our main objective, but will be followed observationally in order to evaluate our secondairy objective: risk factors for bleeding)
2. Valvular AF: AF in the presence of a mechanical heart valve, and/ or severe mitral valve stenosis
3. Taking part in other medical scientific research.
4. Unwilling/ unable to provide written informed consent bij the patient.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-01-2018
Enrollment:	2750
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eliquis
Generic name:	apixaban
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lixiana
Generic name:	edoxaban
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Pradaxa
Generic name:	dabigatran
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sintrommitis
Generic name:	acenocoumarol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xarelto
Generic name:	rivaroxaban
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	03-07-2017
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	07-09-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-08-2019
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	30-12-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22182
Source: NTR

Title:

In other registers

Register	ID
EudraCT	EUCTR2017-000393-11-NL
CCMO	NL60426.041.17
OMON	NL-OMON22182