The effect of TNF blocking therapy on cardiac function in patients with active rheumatoid arthritis

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Hypothesis - Our hypothesis is that TNF blocking medication improves cardiac function in patients with active RA. Objectives - Primary objective: to investigate the effect of TNF blocking therapy on diastolic left ventricular (LV) function in RA...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational non invasive

Summary

ID

NL-OMON44306

Source
ToetsingOnline

Brief title
Effect of biologicals on cardiac function in active RA patients

Condition

- Heart failures
- Autoimmune disorders

Synonym
heart disease, Rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Jan van Breemen Instituut
Source(s) of monetary or material Support: Jan van Breemeninstitituut en Pfizer,Pfizer

Intervention

Keyword: Cardiomyopathy, Rheumatoid arhritis, TNF blocking therapy, Transthoracic Echography

Outcome measures

Primary outcome

The primary outcome is diastolic LV dysfunction, defined as follows:

mild diastolic LV dysfunction (stage I*impaired relaxation). Characterized by an E/A ratio <1, Em/Am <1, prolonged DT (>240 ms), and IVRT (>110 ms). Em (<8 cm/s) is reduced. E/Em is <10.

Moderate diastolic LV dysfunction (stage II* pseudo normalization). Characterized by an E/A ratio >1, Em/Am <1. Em (<8 cm/s) is reduced and E/Em is >10.

Severe diastolic LV dysfunction (stage III* restrictive filling). This stage is characterized by an overt increased E/A ratio (>2), shortened DT (<150 ms), and IVRT (<60 ms). Em (<8 cm/s) remains at the lowest level. E/Em is >10.

Secondary outcome

Secondary outcomes:

Systolic LV dysfunction will be defined as an ejection fraction of <50%.

NT-proBNP, IL-6, troponin-I, sTNFR1, sTNFR2 and TNF-α. High NT-proBNP is

defined as 125 pg/ml.

Conduction times will be defined as abnormal if PQ time <0.12 or >0.20 seconds,

QRS duration <0.12 seconds and (corrected) QTc interval <450 milliseconds for

men and 460 milliseconds for women.

Study description

Background summary

The mortality rate in patients with rheumatoid arthritis (RA) is increased up to twofold compared with the general population. This predominately caused by an increased cardiovascular (CV) risk, with a significantly enhanced rate of myocardial infarction in comparison to the general population. The systemic inflammatory state in RA patients is deemed responsible for this increased risk by accelerating atherosclerosis and causing endothelial dysfunction. Second after myocardial infarction, congestive heart failure (CHF) is one of the most prevalent causes of death of RA patients. This could be secondary to myocardial infarction as this causes damage and subsequent fibrosis (and thus heart failure) in the heart, or directly by systemic inflammation itself, causing left ventricular (LV) dysfunction.

Anti-inflammatory treatment with tumor necrosis factor (TNF) blocking therapy decreases the CV risk. Therefore, TNF blocking therapy potentially decreases the incidence of CHF by lowering the overall inflammatory state and slowing down the process of atherosclerosis. On the other hand, TNF is also necessary for the cardiac homeostasis. Several trials did not show a detrimental effect of TNF blocking therapy on the incidence of newly onset CHF in RA patients. In addition, echocardiographic parameters seem to improve during TNF blocking therapy. In contrast, some cohort investigations suggested an increased incidence of newly onset CHF in RA patients starting with TNF blocking therapy, particularly in older RA patients. Altogether, it is presently unknown whether or not TNF blocking therapy has a favorable effect on CHF in patients with RA.

Our aim is, first, to determine cardiac function in RA patients with high disease activity at baseline. Second, to investigate the effect of TNF blocking therapy in regular dosage on cardiac function during six months. Third, as RA patients on TNF blocking therapy are followed-up for many years, it is possible to investigate the occurrence of newly onset CHF in RA patients over the

following years.

Study objective

Hypothesis - Our hypothesis is that TNF blocking medication improves cardiac function in patients with active RA.

Objectives - Primary objective: to investigate the effect of TNF blocking therapy on diastolic left ventricular (LV) function in RA patients with active disease.
Secondary objectives - To investigate in RA patients with active disease 1) the effect of TNF blocking therapy on systolic LV function 2) the effect of TNF blocking therapy on NT-proBNP levels 3) the effect of TNF blocking therapy on conduction times and heart rhythm.

Study design

Prospective

Study burden and risks

There are some aspects to this protocol that may cause (some) discomfort to the subjects. First, the subjects have to remain fasted as indicated at the time of blood collection. Second, the collection of blood may cause some discomfort. Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection. Third, during thoracic echography the subject has to stay in a fixed position. Fourth, when measuring blood pressure, the inflation of the cuff may cause transient paraesthesia in the hand.

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

Diagnosis rheumatoid arthritis
Written informed consent
Active disease (DAS28>=3.2) and/or C-reactive protein >10 mg/l and/or Erythrocyte Sedimentation Rate (ESR) > 15 mm/h

Exclusion criteria

Medical history of cardiac disease (i.e. myocardial infarction, heart failure etc)
Use of TNF blocking therapy 3 months prior to start study

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	11-12-2014
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	14-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL49652.048.14