Does colchicine reduce progression of aortic valve stenosis?

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This study has been transitioned to CTIS with ID 2024-513486-39-00 check the CTIS register for the current data. The main objective of this study is to determine the effect of colchicine on the progression of moderate AS in asymptomatic patients.

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

Summary

ID

NL-OMON51747

Source
ToetsingOnline

Brief title
Colchicine and Inflammation in Aortic Stenosis (CHIANTI)

Condition

- Cardiac valve disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Aortic Stenosis, narrowing of the aortic valve

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: N/A

Intervention

Keyword: Aortic Stenosis, Colchicine, Inflammation

Outcome measures

Primary outcome

The change at 24 months relative to baseline in:

- Aortic valve calcium score measured by computed tomography (Agatston Units).

Secondary outcome

The change at 24 months relative to baseline in:

- 18F-NaF uptake of the aortic valve using positron emission tomography (PET).

- Peak aortic-jet velocity (m/s determined by echocardiography).

Study description

Background summary

Aortic stenosis (AS) is the most common valvular heart disease in the developed world. Once symptomatic, untreated patients have a poor prognosis with five-year survival rate of 25%. Once at an advanced stage, AS will lead to the development of left ventricle hypertrophy, and eventually heart failure and death. At-present, there is no effective medical therapy for aortic stenosis. Current management of patients with AS consists of *watchful waiting*. Valve replacement is needed when these patients (often acutely) become symptomatic. Recent studies have shown that inflammatory processes with similarities to atherosclerosis play an important role in AS. Therefore, we hypothesize that treatment with anti-inflammatory therapy, in the form of colchicine, could reduce the progression of AS. If positive, this trial will be the first to provide a potential therapeutic option for millions of people world-wide with moderate AS.

Study objective

This study has been transitioned to CTIS with ID 2024-513486-39-00 check the CTIS register for the current data.

The main objective of this study is to determine the effect of colchicine on

the progression of moderate AS in asymptomatic patients.

Study design

This study will be a double-blind placebo controlled intervention study, with prior to randomization an open label two-week run-in period.

Intervention

colchicine vs placebo

Study burden and risks

Patients will undergo CCTA, NaF-PET-CT and echocardiography. The CCTA and NaF-PET-CT will be performed at baseline and after 24 months. Echocardiography will be performed at baseline, 12 months and 24 months. Clinical evaluation will be conducted at baseline, 3 months, 6 months and every six months after. Colchicine has been proven to be safe in use. Potential side-effects mostly include gastro-intestinal symptoms. The echocardiographies for this study will replace the echocardiographies needed for usual-care follow-up in AS. This will decrease the burden of participation. We believe that this study has relative low burden for participants with potentially high benefit in a relative vital study group. See also chapter 12 of the study protocol.

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

- Asymptomatic moderate aortic valve stenosis. The severity of AS will be quantified according to current EACVI / ASE guidelines.

Exclusion criteria

• Heavily calcified aortic valve on echocardiography (defined as grade 4 calcification: extensive thickening/calcification of all cusps as described in the articles by Rosenhek et al.).
• Severe mitral valve stenosis (MVA < 1cm2).
• Severe mitral or aortic valve regurgitation.
• Left ventricular dysfunction (LVEF < 35%).
• Bicuspid aortic valve.
• Rheumatic aortic valve disease.
• Valvular disease due to history of chest radiation.
• Patients aged <50 and >80 years.
• Pre-existing chronic gastro-intestinal complaints which may obscure signs of colchicine intolerance.
• The presence of a pacemaker or internal cardiac defibrillator.
• Child-bearing potential without the use of contraception.
• Renal impairment (eGFR <30 ml/min/1.73m2).
• Active or chronic liver disease.
• A planned aortic valve replacement in the next six months.
• Use of CYP3A4 (e.g. verapamil) or P-glycoprotein inhibitors.
• Use of bisphosphonate or denosumab.
• Chronic use of immunosuppressants or anti-inflammatory drugs including colchicine and NSAID*s (excl. acetylsalicylic acid).
• Life expectancy <2 years.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-12-2022
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Colchicine
Generic name:	Colchicine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-01-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-05-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	02-10-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EU-CTR	CTIS2024-513486-39-00
EudraCT	EUCTR2021-005586-40-NL
ClinicalTrials.gov	NCT05162742
CCMO	NL79407.091.21