Diagnostic and prognostic value of intracoronary physiologic indices and need for revascularisation in severe aortic VAlve disease (DIVA)

Published: 26-04-2017
Last updated: 13-04-2024

This study is designed to assess diagnostic and prognostic value of intracoronary flow- and pressure measurements in patients with severe aortic valve stenosis and concomitant coronary artery disease, unravelling the physiological impact on coronary...

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

Summary

ID

NL-OMON49883

Source
ToetsingOnline

Brief title
DIVA

Condition

- Cardiac valve disorders

Synonym
Aortic valve stenosis, stenosis of the aortic valve

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Unrestricted grant via AMR (Academical Medical Research;Amsterdam)

Intervention

Keyword: Coronary hemodynamic, FFR, TAVI

Outcome measures

Primary outcome

- Invasive intracoronary measurements (FFR, CFR, MR, iFR)

Secondary outcome

Secondary study endpoints:

- Standard follow-up criteria (physical examination, ECG, standard laboratory

tests)

- Valve function and left ventricular function parameters and volumes (as

measured with cardiac ultrasonography and cardiac CT)

- Cardiac symptoms (dyspnea (New York Heart Association/ NYHA classification),

angina pectoris (Canadian Cardiologist Society/ CCS score))

- Quality of life (QoL)

Study description

Background summary

Currently, standard therapy for symptomatic severe aortic valve disease is surgical aortic
valve replacement, which relieves symptoms and improves long-term survival. The majority of aortic valve stenosis is degenerative, occurs in the elderly, often involving co-morbidity and leading to (post)-operative morbidity and mortality. In the Euro Heart Survey at least 30% of high-risk patients was rejected or not referred for surgery[1]. Untreated symptomatic aortic valve stenosis has a poor prognosis[2]. Therefore, less invasive transcatheter aortic valve implantation (TAVI) has been developed. The first transcatheter implantation in humans was

performed in 2002[3]. Experience, technical development and careful patient selection have improved the results. The transcatheter treatment of symptomatic patients with severe aortic valve stenosis is a treatment that has been established at the AMC-UVA in 2007 and has been performed under approval by the medical ethical committee (institutional review board).

Since AS is a disease predominantly prevailing in the elderly population and shares a large part of its pathophysiology, risk factors and prevalence with atherosclerotic CAD, both diseases often co-exist in each patient and possibly cause. Prevalence of CAD in patients with severe AS is described being up to 50-65%, depending on definitions used [4-7]. Sharing symptomatology, debate about the need for revascularisation in patients who undergo a TAVI-procedure, regarding treating symptoms, effecting prognosis and influencing costs is ongoing[5, 6, 8, 9].

The left ventricle (LV) of patients with severe aortic valve stenosis shows pathophysiological changes such as hypertrophy and increased stiffness or wall stress, which may lead to diastolic dysfunction and subendocardial ischemia. Ultimately, a severe aortic stenosis can cause a reduction in systolic left ventricular function. By reducing the aortic pressure gradient with aortic valve replacement, LV afterload is reduced. Direct improvements of echocardiographic LV function and reduction in wall strain have been described[10, 11]. Improvement of coronary flow (reserve) measured with transoesophageal echocardiography has been described after both surgical and percutaneous aortic valve replacement[12]. More recently, direct result regarding invasively measured coronary flow (reserve) of transcatheter aortic valve replacement is described in the AMC[13], as well as small cohorts in Canada [14] and London [15]. Recent study shows accurate diagnostic properties of FFR-measurements in patients with AS, concluding that the intra procedural measurements after valve placement are the most reliable to assess lesion severity[16]. However, these results are not described during longer follow-up. The interventional Section Leadership Council of the American College of Cardiology spoke out lately on performance of PCI before TAVI-treatment, but states that the topic has never been profoundly investigated and does not mention the influence of invasive coronary flow- and pressure measurements[17].

The diagnostic and prognostic value of intracoronary flow- and pressure measurements (Fractional Flow Reserve (FFR), Coronary Flow Reserve (CFR), instant Flow Reserve (iFR), MR (Microvascular Resistance)) has been described in patients with stable CAD. In the FAME II cohort, FFR-guided PCI showed a large, significant improved outcome over optimal medical therapy alone [18]. PCI in TAVI patients is described as feasible and safe[19, 20]. In a small case series, FFR shows promise in assessing hemodynamic significance of coronary lesions[21]. However, no data of the diagnostic and prognostic worth of these measurements in patients with AS and LVH have been previously described in a large cohort containing longer term follow-up measurements. The effects of unloading of the left ventricle by TAVI-procedure on coronary hemodynamic (and

its* measurements) is not yet fully understood during longer follow-up [14, 15] and it is reasonable to think this changes significantly after valve replacement regarding left ventricular pressures and function of the coronary microvasculature[13]. We use the combined flow- and pressure wire (Combowire,) to fully understand the expected changes, where most other stated studies namely use one of both measurements.

Following the current trend in treating lower surgical risk patients with TAVI, the question whether to treat CAD in AS patients becomes more important. This study seeks to provide insight in the changes of coronary hemodynamics, probably influencing future clinical decision making.

Study objective

This study is designed to assess diagnostic and prognostic value of intracoronary flow- and pressure measurements in patients with severe aortic valve stenosis and concomitant coronary artery disease, unravelling the physiological impact on coronary hemodynamic of the TAVI-procedure. Answering this physiological question will aid in the question whether CAD needs treatment in patients with concomitant AS.

Study design

Single centre, exploratory study

Intervention

-

Study burden and risks

The added risk of this study, compared to standard clinical care, will be minimal. In different centres performing TAVI, whether or not revascularisation is performed in the work-up or after a TAVI is done by the operators* opinion since no clear data exists until date. This study mimics the current strategy in the AMC, by doing as less as possible coronary revascularisation in the TAVI-workup since the biggest prognostic effect is expected from the TAVI procedure and not from the possible PCI. This study adds safety by adding per procedural and follow-up measurements for monitoring coronary lesions in patients not treated with PCI.

However, patients will be exposed to a minimal extra radiation dose during TAVI-procedure, since placing the wires for measuring flow- and pressure parameters will take imaging and time. However, this radiation will be very minimal, estimated an extra 3-4 minutes of fluoroscopy time, accounting for approximately 2-3 mSV on top of the radiation dose for regular valve placement.

Comparing this to the background radiation in the Netherlands (2-3 mSV), with taking the advanced age of the subjects into account, this risk could be estimated as minimal.
In all patients, there will be a follow-up CAG with coronary measurements. The follow-up CAG including the combined measurements is standard clinical care as in other patients with coronary stenosis of unknown significance. This re-catheterisation adds the (minimal) risks of the invasive procedure and radiation exposure as earlier described once again.

The benefit of this study is a better understanding of mechanisms of LVF improvement after TAVI, as well as identification of dissipating effects of ventricular wall adaptation to aortic valve stenosis on functional parameters of coronary hemodynamic, potentially influencing clinical decision-making. Benefit for included patients will consist of better follow-up and better understanding of the prognostic value (and effect on symptoms) of their existing CAD. All the patients will be closely monitored, especially on symptoms of progressing coronary artery disease and corresponding symptoms after their TAVI-procedure.
This study could not be conducted in another group of patients.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with severe (senile) aortic stenosis (AVA <1,0cm, mean gradient >40mm and maximum jet velocity >4 m/s or or aortic valve area index <=0.6 cm2/m2.)
- Patients are non-eligible for conventional surgical aortic valve replacement due to age, medical history or co-morbidity and thus eligible for T(F)-AVI as decided by the heart-team.
- Patient has coronary artery disease as depicted on screening CAG (defined as >=1 coronary stenosis >50%)
- Patient understands the study requirements and the treatment procedures, and provides written informed consent.
- Patient agrees and is capable of returning to the study hospital for all required scheduled follow up visits

Exclusion criteria

- Patient is able to give informed consent
- Absence of coronary artery disease (defined as >=1 coronary stenosis >50% as depicted on coronary arteriogram during TAVI-screening)
- Subjects with an acute STEMI within 30 days preceding the index procedure (TAVI).
- Significant left main
- Inability to get per procedural reliable, intracoronary measurements (due to place of lesion, unreliable signals, mechanical defects etc.)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-05-2017
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO Date:	26-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-05-2018
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	NL60445.018.17