STRESS AORTIC VALVE INDEX FOR ASSESSING RISK IN AORTIC VALVE STENOSIS PATIENTS

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

Summary

ID

NL-OMON55284

Source
ToetsingOnline

Brief title
SAVI-AoS

Condition

- Cardiac valve disorders

Synonym
narrowed heart valve

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Topzorg subsidie

Intervention

Keyword: aortic valve stenosis, stress aortic valve index

Outcome measures

Primary outcome

The primary endpoint is the evaluation of the SAVI metric as a risk predictor compared to standard echocardiographic measurements like AVA and pressure gradient at rest.

Secondary outcome

Secondary endpoints will include correlations between invasive and noninvasive SAVI measurements to explore if stress assessment of the aortic valve can be imaged non-invasively or if it requires invasive hemodynamic measurement. The same will be done with the cardiac CT scans that will be analyzed to see if computational fluid dynamics can simulate invasive SAVI. MRI will provide extra information for cardiac volumes, stroke volume, extracellular volume and grading of hypertrophy.

Study description

Background summary

Aortic stenosis (AS) has been increasing in prevalence in the developed world due to a combination of an aging population and increasing lifespan. Surgical aortic valve replacement (SAVR) and the recent development of transcatheter aortic valve implantation (TAVI) have improved survival and symptoms for these patients, with the exciting potential to help an even wider target population due to advances that reduce procedural risk.

Due to clinical need and an approach based on surgical risk, much of the existing physiologic recommendations for TAVI or SAVR have focused on clearly symptomatic patients with severe AS at rest. Guidelines from the United States

and Europe recommend resting measurements of maximum velocity (Vmax), mean transvalvular gradient (delta P), and aortic valve area (AVA) as well as secondary parameters of AVA indexed to body surface area and the velocity ratio (also called the dimensionless index). Recommendations for a valvular stress test (typically with exercise or dobutamine) focus on a small minority with reduced ventricular function. However, challenges and limitations exist with our current severity classification for AS. For example, because stress-induced symptoms and resting hemodynamic assessment may be discordant, some patients may be inappropriately denied access to SAVR or TAVI.

Therefore, a rational hypothesis asks if routine valvular stress testing beyond current guideline recommendations would identify a wider group of patients who would benefit from TAVI but currently remain undertreated.

Study objective

The goal of this study is to demonstrate the value of SAVI (both non-invasive and invasive) in patients with moderate aortic stenosis. The short-term objective will compare SAVI with standard resting indexes for symptom burden, functional capacity, and biomarkers. The long-term objective will associate SAVI and standard resting indexes with clinical outcomes related to valvular disease. We hypothesize that low SAVI (more marked AS during stress) will track with more symptoms and a worse prognosis.

Study design

Clinical uncertainty exists regarding the need for invasive cardiac catheterization in patients with moderate AS yet symptoms that could be related to the valve. In some centers, such patients undergo coronary angiogram (CAG) to ensure that non-invasive imaging has not underestimated valve severity and to exclude significant coronary artery disease. In other centers, such patients are managed conservatively. This very heterogeneity of practice highlights the need for additional data that will be provided by this protocol. We anticipate that some centers will consider a CAG as 'standard of care' while others will perform it on a research basis. Each MEC/IRB can make this determination given local practice patterns, and indeed it may differ among patients at a single enrolling site.

The study will enroll an observational cohort. Potential subjects will be identified by local investigators or a patient*s cardiologist through screening echocardiography clinics. They will be invited to join the study with review of inclusion/exclusion criteria and informed consent as approved by each local MEC/IRB. After informed consent has been given, visits will be planned for the catheterization with invasive SAVI measurements, non-invasive imaging (baseline and stress echocardiography, cardiac CT scan, MRI scan), quality of life questionnaire, and blood samples. A follow-up visit will be planned 1 year

after enrollment for a cardiac CT scan for valvular calcium scoring, 6-minute walk test, blood samples, quality of life questionnaire, and echocardiography. As a walk test, echocardiography, initial CT scan, MRI scan are routine examinations for a patient with moderate AS, only the CT scan, questionnaire, and blood samples are study investigations. Follow-up will be 5 years. The initial catheterization will contain SAVI measurements that have been investigated in two previous studies and are safe to use.

Study burden and risks

- possible adverse reaction to dobutamine
- allergic reaction to contrast fluid
- standard risks during heart catheterization

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 >= 50 years
2. Moderate aortic stenosis confirmed in the past 3 months by standard echocardiographic evaluation: aortic valve area >1.0 cm2 plus either maximal velocity 2.5-3.9 m/s or mean gradient 15-39 mmHg
3. Ability to undergo exercise stress testing
4. Ability to understand and the willingness to provide written informed consent

Exclusion criteria

1. Severe aortic stenosis
2. Percutaneous coronary intervention or coronary artery bypass grafting in the past three months, or have revascularization planned in the near future
3. Known, unrevascularized, and severe coronary artery disease (for example a 90% diameter stenosis or FFR<0.7 in the proximal left anterior descending artery)
4. Impaired left ventricular function (ejection fraction <50%)
5. Unicuspid, bicuspid, or non-calcified aortic valve observed during echocardiography (note that later cusp fusion noted during study-related cardiac imaging will not exclude a subject)
6. Severe aortic regurgitation, mitral valve disease, tricuspid regurgitation, or a significant intracardiac shunt
7. Co-existing hypertrophic cardiomyopathy or severe septal hypertrophy >15mm
8. Persistent atrial fibrillation with uncontrolled ventricular response
9. Recent (within 6 weeks) acute coronary syndrome
10. Estimated glomerular filtration rate <=30 mL/min or end-stage renal disease on replacement therapy (dialysis)
11. Severe COPD GOLD stage 3 or 4, home oxygen dependence, or >=2 pulmonary inhalers (note that well-treated and stable asthma and GOLD stage 1 or 2 COPD is permitted)
12. Severe comorbid condition with life expectancy <2 years
13. Prior adverse reaction to dobutamine
14. Severe iodine contrast allergy
15. Pregnancy
16. Severe pulmonary hypertension with systolic pulmonary artery pressure greater than 50mmHg or isolated and symptomatic right ventricular failure

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-04-2021
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	10-12-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	30-09-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-12-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-04-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL74875.100.20