BMJ Open

Impact of transcatheter aortic valve implantation on left ventricular function recovery, mass regression and outcome in patients with aortic stenosis: protocol of the TAVI-NOR prospective study

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To cite: Mohamed Ali A, Wasim D, Løland KH, *et al*. Impact of transcatheter aortic valve implantation on left ventricular function recovery, mass regression and outcome in patients with aortic stenosis: protocol of the TAVI-NOR prospective study. *BMJ Open* 2021;**11**:e039961. doi:10.1136/bmjopen-2020-039961

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-039961).

Received 01 May 2020
Revised 25 December 2020
Accepted 07 January 2021

Check for updates

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ABSTRACT

Introduction Transcatheter aortic valve implantation (TAVI) is a widely used treatment option as an alternative to surgical aortic valve replacement in patients with severe aortic stenosis (AS) at high or intermediate surgical risk. TAVI improves symptoms, induces reverse left ventricular (LV) remodelling and increases overall survival. However, a careful patient selection is essential to achieve better outcome. Evidence on LV functional recovery and LV mass regression after TAVI based on contemporary registry data is scarce. The impact of TAVI on the arterial vasculature is also less explored.

Method and analyses This is a study of 600 consecutive patients with AS who underwent a TAVI at Haukeland University Hospital, Bergen, Norway. Demographics, clinical data, arterial haemodynamics and echocardiographic parameters were prospectively collected. In the present paper, we describe the design, major scientific objectives and echocardiography imaging protocol of the TAVI-NOR (TAVI in western NORway) study. The main objectives are: To explore the impact of TAVI on cardiac structure and function in patients with severe AS, identify the echocardiographic predictors of reverse LV remodelling, assess survival benefits according to baseline risk profile, evaluate long-term therapeutic success as reflected by reduction in valvular-arterial impedance and to investigate the impact of various types of blood pressure response immediately after TAVI on clinical outcome.

Ethics and dissemination The study was approved by the Regional Committees forMedical and Health Research Ethics (REK vest, ref. number 33814) and theInstitutional Data Protection Services. Patients' consent was waived. The study findings will be disseminated via peer-reviewed publications and presentation in national and international scientific meetings and conferences.

Trail registration number The study was registered in the international database: ClinicalTrials.gov, Identifier: NCT04417829.

Strengths and limitations of this study

- This is a large prospective study of patients with severe aortic stenosis who underwent transcatheter aortic valve implantation in western Norway.
- Clinical and echocardiographic assessment will be performed at 6–12 months follow-up visit in a real-world context.
- Long-term outcome data in terms of cardiovascular and all-cause mortality will be available.
- The limitations are that there is no control arm for comparison and this is a single-centre registry study.

INTRODUCTION

Degenerative aortic stenosis (AS) is the most common heart valve disease requiring valve intervention, and the prevalence is increasing in developed countries as a result of the ageing population. The development of symptoms (angina, syncope or dyspnoea) or a drop in left ventricular ejection fraction (LVEF) <50% are class I indications for valve intervention (transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR)) in patients with haemodynamically severe AS.[1 2] Without valve replacement, patients with severe AS are at substantially high risk of cardiovascular complications and death.[1 2] In AS, LV remodelling (LV hypertrophy (LVH) or concentric remodelling) initially reflects an adaptive response to normalise wall stress and maintain LV systolic function.[3] However, during the disease progression, afterload and consequently LV wall stress will increase and the contractile function will decline. Such a maladaptive response will typically lead to systolic and diastolic LV dysfunction, subendocardial ischaemia, fibrosis, increased end-diastolic pressure, pulmonary hypertension, symptoms and death.[3] The reduction in LVEF in patients with AS may be either: (1) due to afterload-contractility mismatch: a condition in which LV has preserved intrinsic

contractile function, but an increase in afterload causes reduction in stroke volume (SV) and decline in LVEF[4 5] or (2) due to irreversible myocardial damage related to fibrosis or concomitant coronary artery disease.[6–8] The reduction in LVEF due to afterload mismatch may be reversible if valve stenosis is removed by TAVI or SAVR. TAVI has become an established therapeutic option for patients with symptomatic severe AS who are ineligible for SAVR. The overall expected clinical benefits following TAVI are reduction in mean pressure gradient, improvement in LV systolic function, normalisation of SV, regression of LV mass, relief of symptoms and increased survival. LV mass regression after TAVI is achievable and associated with improved outcome.[9 10] However, the level of baseline cardiovascular comorbidity may affect clinical outcome and survival. Furthermore, the evidence on LV functional recovery and LV mass regression after TAVI based on contemporary registry data is scarce. Similarly, the impact of residual risk of hypertension following TAVI on the arterial vasculature is less explored. In the present paper, we will describe the study design, major scientific objectives and echocardiography imaging protocol of the TAVI-NOR (TAVI in western NORway) registry.

Box 1 Procedure and device-related complications

Intraprocedural complications
- Coronary artery occlusion.
- Aortic dissection.
- Cardiac tamponade.
- Annular rupture.
- Device migration (embolisation).
- Valve thrombosis.
- Re-intervention.
- Need for acute open heart surgery.
- Conversion to alternative access.
- Access site/vascular complications.

In-hospital complications.
- Significant paravalvular leak.
- Implantation of permanent pacemaker.
- Stroke/transient ischaemic attack.
- Major vascular complications.
- Acute renal failure and need for dialysis.
- Major bleeding and need for transfusion.
- Cardiac arrest.

Late complications
- Prosthetic valve endocarditis.
- Subclinical leaflet thrombosis.
- Structural valve deterioration.
- Patient–prosthesis mismatch.

METHODS

Study design

Between January 2012 and July 2019, a total of 600 patients with AS were treated with TAVI at the Department of Heart Disease, Haukeland University Hospital, Bergen in Western Norway. All patients were symptomatic and had clinically significant AS. The indication for TAVI was based on a joint decision taken by the heart valve team according to guidelines and technical suitability for the procedure. During the initial phase of the study, each patient was assessed by an experienced cardiologist within the TAVI-team for informal frailty testing. During the late phase of study, particularly following the 2017 European Society of Cardiology guidelines,[2] we included formal frailty testing (Short Physical Performance Battery, the Mini-Mental State Examination, nutrition status) in cooperation with a geriatrician in our team. Patients with substantial comorbidities, high grade of frailty, life expectancy <1–2 years, severely reduced cognitive function or technically not suited for TAVI were not treated and thereby excluded from this registry (table 1).

Demographic, clinical and echocardiographic data at baseline were prospectively collected (box 1), and entered into the Norwegian Registry of Invasive Cardiology (NORIC), a national mandatory healthcare and quality improvement registry established in 2012. NORIC includes data on virtually all invasive cardiology procedures (coronary angiography, percutaneous coronary interventions and TAVI). In the present dataset, all patients had at least three transthoracic echocardiograms: Baseline echocardiography immediate before TAVI, first follow-up within approximately 1-month and second follow-up at 6–12 months clinical visit following TAVI.

Table 1 Eligibility criteria for TAVI-NOR (TAVI in western NORway) registry

Inclusion criteria	Patients with symptoms and clinically significant aortic stenosis.
	Anticipated life expectancy >1–2 years.
	Patients undergoing TAVI according to guidelines.
Exclusion criteria	Patients with substantial comorbidities.
	High grade of frailty.
	Severely reduced cognitive function.
	Technically not suited for TAVI.

TAVI, transcatheter aortic valve implantation.

Objectives

The main objectives of the TAVI-NOR registry are:

1. To explore the impact of TAVI on cardiac structure and function in patients with AS.
2. To identify the echocardiographic predictors of reverse LV remodelling.
3. To assess survival benefits according to baseline risk profile.
4. To evaluate long-term therapeutic success as reflected by reduction in valvular-arterial impedance.
5. To assess the impact of various types of blood pressure (BP) response immediately after TAVI on cardiac structure, function and clinical outcome.

End-points

The primary outcome is all-cause mortality. Date and cause of death will be verified by the linkage between NORIC and The Norwegian Cardiovascular Disease Registry. The secondary end-points of interest are LV mass regression and functional recovery at 6–12 months follow-up and clinical events such as cardiac-related hospitalisations during follow-up. Follow-up time will be calculated from the baseline echo immediately before TAVI until censoring or death.

Measurement and data collection

Cardiovascular risk factors and BP measurements

At study entry, anthropometric measures (height, weight, body mass index, body surface area), severity of symptoms by New York Heart Association classification and/or Canadian Cardiovascular Society angina score, cardiovascular risk factors and comorbidities (smoking, hypertension, diabetes, hypercholesterolaemia, previous stroke/transient ischaemic attack, coronary artery disease, chronic kidney disease, atrial fibrillation, pacemaker or implantable cardioverter defibrillator, type and frequencies of previous valve interventions, chronic obstructive pulmonary disease), type of antihypertensive treatment, use of statin, antiplatelets and direct oral anticoagulants were collected. The procedure and device-related complications according to the Valve Academic Research Consortium were entered into NORIC registry (box 1).[11]

Brachial BP was measured prior to each echocardiogram according to the standard methodology after an initial 5 min rest in the sitting position. An average of all BP measurements obtained during hospitalisation after TAVI (measured at least 3–4 times a day) will be carefully calculated and used as post-TAVI BP to assess the types BP response after TAVI.

Hypertension was defined as a history of hypertension, use of antihypertensive medications or elevated brachial BP (≥140/90 mm Hg) at study entry. Hypercholesterolaemia was defined as use of statin. Coronary artery disease was defined as previous myocardial infarction, coronary artery bypass grafting or percutaneous coronary intervention or angiographic evidence of significant stenosis in the epicardial coronary arteries defined by diameter stenosis ≥50%, or by invasive pressure measurements.

Electrocardiogram

Standard ECGs were recorded prior to each echocardiogram to assess rhythm, LVH, QRS duration and LV strain (≥0.1 mV (≥1 mm) convex downsloping ST segment depression with asymmetrical T-wave inversion in leads V5–V6).

Echocardiography

All echocardiograms were performed using commercially available ultrasound machines (Acuson Sequoia C512, Siemens, Mountain View, California, USA; Philips iE33; Philips Medical Systems, Eindhoven, The Netherlands; Philips 'Epiq 7'; Philips Medical Systems, Bothell, Washington, USA; and Vivid E9 GE Vingmed Ultrasound, Horten, Norway). Studies were acquired and stored digitally, and transferred to a secure server. Studies performed by certified echotechnicians were reviewed and quality assured by imaging cardiologists.

Image acquisition

ECG leads were placed on the patient before imaging. A particular emphasis was put on adequate ECG signal. For patients in atrial fibrillation or atrial flutter, the sonographer was instructed to obtain 3–5 cardiac cycle acquisitions per view. Colour Doppler imaging was optimised with appropriate Nyquist limit. Special attention was directed to obtain optimal spectral Doppler signals through the aortic valve with best alignment between ultrasound beams and direction of the blood flow. Sector depth, sample volume size and spatial and temporal resolution were optimised.

Measurement protocol

Echocardiographic parameters will be measured offline in an Echopac work station for research purpose according to international guidelines (box 2).[1 2 12–14]

Aortic dimensions were measured at the levels of aortic root, sinotubular junction and ascending aorta from a dedicated parasternal long-axis view. Right ventricular free wall thickness, LV wall thicknesses and cavity dimensions, left atrial anterior–posterior diameter were measured from a parasternal long axis view.[13] Right ventricular basal diameter was measured from an apical four-chamber view.[14] LV volumes and LVEF were derived from the biplane Simpson method. LV mass in grams was calculated according to the Devereux formula,[15] and indexed for body surface area:

$$\text{LVMi} = 0.8\left\{1.04[([\text{LVEDd} + \text{IVSd} + \text{PWd}]^3 - \text{LVEDd}^3)]\right\} + 0.6\ \text{g/m}^2\ \text{body surface area}$$

LVEDd is the end-diastolic dimension and LVEDs the end-systolic dimension of LV, IVSd interventricular septum thickness in diastole and PWd is posterior wall thickness in diastole. Normal LV mass index was defined as ≤95 g/m^2 in women and ≤115 g/m^2 in men.[13] Relative wall thickness was calculated as: 2x LV posterior wall thickness/LV internal diameter at end-diastole and considered normal if ≤0.42. Transmitral flow (E and A wave velocities, and E

Box 2 Echocardiographic data and arterial haemodynamics

- Heart rate (beat per minute).
- Aortic annulus diameter (cm).
- Aortic root diameter (cm).
- Ascending aorta diameter (cm).
- Left atrial anterior–posterior diameter at end-systole (cm).
- Right ventricular free wall thickness in end-diastole (cm).
- Right ventricular basal diameter (cm).
- LV end-diastolic and end-systolic diameter (cm).
- Septum and posterior wall thickness at end-diastole and end-systole (cm).
- LV mass (g).
- Peak aortic jet velocity (m/s).
- Peak and mean aortic pressure gradients (mm Hg).
- Aortic valve area (cm^2).
- Doppler stroke volume index (mL/m^2).
- Trans-aortic flow rate (mL/s).
- Peak LVOT velocity (cm/s).
- Mitral flow (E and A wave velocities, E/A ratio, E-deceleration time).
- Isovolumic relaxation time (ms).
- E/e' ratio.
- Septal and lateral mitral annulus S' (cm/s).
- LV ejection fraction (%).
- Mid-wall fractional shortening (%).
- Circumferential end-systolic stress ($kdynes/cm^2$).
- The severity grade of tricuspid, mitral and aortic regurgitation.
- The severity grade of mitral stenosis.
- Systemic vascular resistance ($dynes \times s/cm^5$).
- Systemic arterial compliance (stroke volume was indexed/pulse pressure) ($mL/m^2/mm$ Hg).
- Valvular-arterial impedance (Zva) (mm Hg/mL/m^2).

LV, left ventricular; LVOT, LV outflow tract.

deceleration time) was measured by pulsed-wave Doppler from the apical 4-chamber view with the sample volume positioned between the tips of mitral leaflets. Peak tissue Doppler velocities (S' and e') were measured at lateral and septal levels. LV filling pressure was assessed by E/e' ratio. The severity of AS was defined according to the joint European Association of Cardiovascular Imaging and American Society of Cardiology guidelines[1 2 12] using a standard three-step approach: (1) measurement of LV outflow tract (LVOT) diameter in mid-systole at the aortic annulus level; (2) Pulsed-waved Doppler in the LVOT to derive velocity time integral (VTI), peak LVOT velocity and SV (LVOT VTI x LVOT area); (3) Transaortic VTI by continuous-waved Doppler from different windows by imaging and non-imaging transducers to measure peak aortic jet velocity (Vmax), peak and mean pressure gradients and aortic valve area (AVA) (figure 1). Moderate AS was defined as AVA 1.0–1.5 cm^2 and severe as AVA <1.0 cm^2.[1 2] SV was indexed to body surface area (SVi). Systolic ejection time and time to peak (acceleration time) will be measured retrospectively from transaortic continuous wave Doppler signal through the aortic valve to derive flow rate (SV divided by systolic ejection time) (figure 1).[16] Patient–prosthesis mismatch was defined on the basis of the prosthetic valve effective orifice area (EOA) indexed to the patient's BSA: absent or not clinically significant if indexed EOA was >0.85 cm^2/m^2, moderate when it was between 0.65 and 0.85 cm^2/m^2, and severe when<0.65 cm^2/m^2.[17] The preprocedural haemodynamic classification of AS severity grade was assessed according to flow-gradient subtypes (figure 2). Subendocardial and mid-wall fractional shortening (MWFS) were calculated according to the standard methodology,[18 19] and contractility-afterload mismatch by MWFS in relation to end-systolic stress.

Low-dose dobutamine stress echocardiography

Low-dose dobutamine stress echocardiography was performed in selective patients with classical low flow (SVi <35 mL/m^2), low gradient (mean pressure gradient

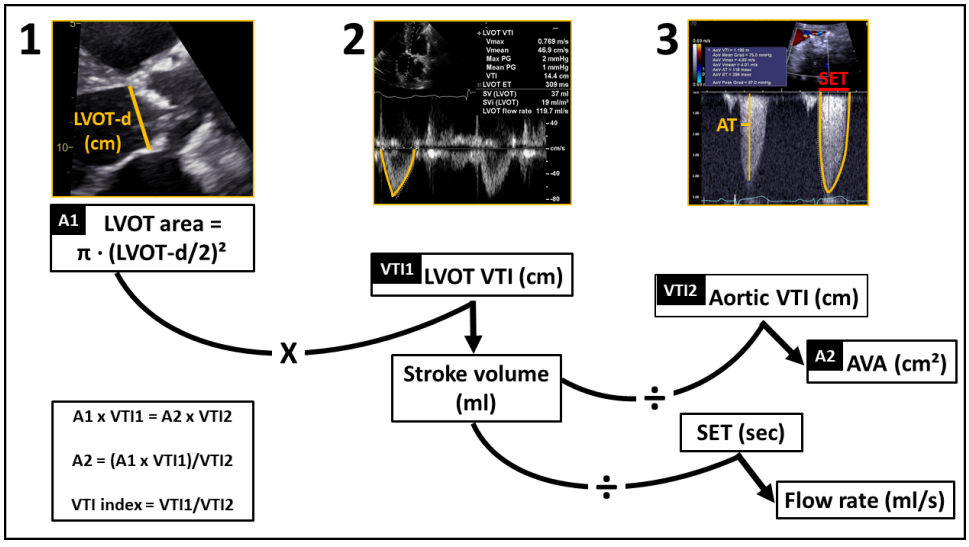
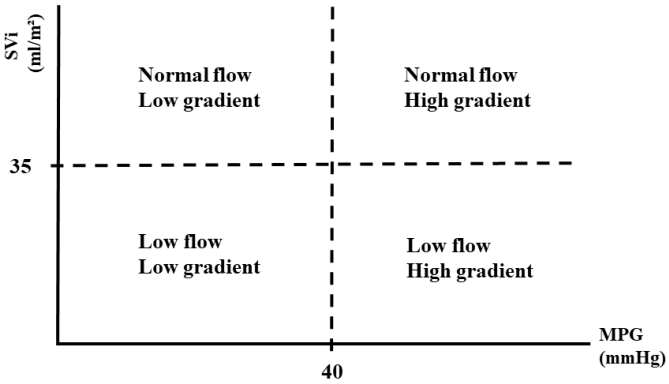


Figure 1 Measurement of LVOT diameter,[1] VTI and stroke volume[2] and peak aortic jet velocity, VTI, pressure gradients and AVA.[3] AT, acceleration time; AVA, aortic valve area; LVOT, left ventricular outflow tract; SET, systolic ejection time; VTI, velocity time integral.



	Normal flow High gradient	Normal flow Low gradient	Low flow High gradient	Low flow Low gradient	
				EF <50%	EF ≥50%
SVi	≥35	≥35	<35	<35	<35
MPG	≥40	<40	≥40	<40	<40
AVA	<1.0	<1.0	<1.0	<1.0	<1.0

Figure 2 The subtypes of severe aortic stenosis by flow gradient. AVA, aortic valve area; EF, ejection fraction; MPG, mean pressure gradient; SVi, stroke volume index.

<40 mmHg) severe AS and LV dysfunction (LVEF <50%) to assess: (1) myocardial contractile reserve; (2) to differentiate true severe AS from pseudosevere (moderate) AS.[20] A standard protocol of low dose dobutamine stress echocardiography was used, starting with 5 µg/kg/min, increasing the infusion to 10, 15 and 20 µg/kg/min in 3 min stages).[20] ECG was continuously monitored and BP and heart rate were measured in each stage. In case of symptoms, BP fall or development of any arrhythmias, the infusion was terminated. Low flow low gradient AS was considered true severe if mean pressure gradient exceeded ≥40 mm Hg and AVA remained <1.0 cm^2. Contractile reserve was defined as an increase in SV >20%. Symptomatic coronary artery disease (unstable angina), recent myocardial infarction, previous ventricular tachycardia, significant LVOT obstruction at rest and severely uncontrolled hypertension were considered contraindications for dobutamine stress echocardiography.

Afterload assessment

Valvular-arterial impedance (Z_{va}), a measure of global LV afterload, will be retrospectively calculated as: (systolic BP+mean aortic pressure gradient)/SVi.[21] Systemic arterial distensibility, a measure of pulsatile arterial load, will be calculated from the ratio of SVi divided by central pulse pressure (PP) (SVi/PP) (mL/m^2/mm Hg),[22] where central PP is calculated as: brachial PP x 0.49+ age x 0.30+7.11. Systemic vascular resistance, a measure of non-pulsatile vascular load, will be calculated as: 80×mean BP÷cardiac output (dyne×s×cm−5).

Statistical analysis

The latest version of SPSS (IBM) and R (The R Foundation for Statistical Computing, Vienna, Austria) will be used for data management and statistical analyses. All variable distribution will be inspected visually including Q-Q plots and presented as mean (±SD) for normally distributed data and median (IQR) for skewed distributions. Comparison between two groups will be performed using the two-sided Student's t-test and χ^2 test or Fisher's exact test, as appropriate. When sex and age adjustment is warranted, logistical or median quantile regression will be applied. Subgroup analyses will be performed in an exploratory fashion. Analysis of variance and generalised linear or additive models will be used as appropriate. If substantially different patient characteristics are associated with specific subgroups implying selection bias, propensity score adjustment or matching will be applied. The predictors of functional recovery, LV mass regression and afterload mismatch will be identified in univariable and multivariable regression analyses. Survival will be evaluated by using the Kaplan-Meier method and Cox proportional hazard modelling to adjust for confounders and produce estimates. A two-sided p<0.05 will be considered statistical significant.

Patient and public involvement

Patients were not invited to comment on the conception of study or research questions, outcome measures, study design, recruitment or conduct, or dissemination plans of our research. Patients were not asked to contribute to the writing or editing of this protocol paper.

Ethics and dissemination

All patients were treated with TAVI as clinically indicated and followed according to hospital routines. The study was approved by the Regional Committees for Medical and Health Research Ethics (REK vest, ref. number 33814) and the Institutional Data Protection Services. Patients' consent was waived. The study findings will be disseminated via peer-reviewed publications and presentation in national and international scientific meetings and conferences.

DISCUSSION

The prevalence of AS is expected to increase due to increasing life expectancy and changing demographic of our Western populations. Aortic valve calcification and systemic atherosclerosis share the same cardiovascular risk factors. Although systemic atherosclerosis can be modified by statin and antiplatelet treatment, no medical treatment has so far been proven to stop or delay the progression of aortic valve calcification.[23–25] The development of symptoms in patients with severe AS is associated with a poor prognosis. Thus, TAVI or SAVR are the only proven treatment options to reduce morbidity and mortality. TAVI has emerged as a relatively safe and effective treatment, initially for elderly frail patients with severe AS at high risk for conventional surgery,[26] but later also for intermediate[27] and low-risk patients.[28 29] However, it is crucial to undertake a careful selection of patients who will benefit from TAVI as it may also carry a high risk of periprocedural complications as well as being a huge economic burden for the society. The present TAVI-NOR

study is a prospective cohort study of 600 patients with predominantly severe AS which aims to explore the impact of TAVI on LV function and structure, and prognosis. A comprehensive echocardiographic assessment was performed at baseline, 1 month and 6–12 months after TAVI. The main echocardiographic characteristics of interest are aortic flow, LV and right ventricular dimensions, and systolic and diastolic function (box 2). Vascular haemodynamics in terms of brachial BP, systemic arterial compliance, and valvular-arterial impedance (Zva) are other outcome measures.

The impact of TAVI on functional recovery and LV mass regression

Patients treated with TAVI show improvement in symptoms, quality of life and systolic LV function, and regression of LV mass. A subset of patients with severe AS (AVA <1.0 cm^2) and EF <50% may not have impaired LV systolic function and the ventricle is demonstrating a normal response to high afterload (AS and increased arterial load). In afterload mismatch even if LVEF is severely reduced, LV may recover and return to normal after valve intervention. By contrast, in the presence of irreversible myocardial damage due to infarct/scar tissue or fibrosis, functional recovery of the LV and regression of LVH may not be feasible. These patients often carry a markedly increased procedural risk.[30] In a study by Kamperidis *et al*[31] functional recovery of the LV as reflected by improvement in global longitudinal strain occurred during the first 6 months after TAVI and remained stable for the next 6 months. In other studies, improvement in LVEF was more likely in women,[32 33] which may partly be explained by the lower burden of myocardial fibrosis in women.[34] In our study, in addition to LVEF and systolic tissue Doppler velocities (S'), the measurements of LV wall thicknesses and dimensions enable us to examine MWFS, a robust marker of systolic LV function, as well as examine afterload/wall stress. In early TAVI studies, patients were typically elderly with prohibitively high surgical risk.[3] In recent TAVI studies, however, patients are younger and have lower-risk profile.[3] Hence, the rate and extent of reverse LV remodelling may differ according to the baseline cardiovascular risk profile.

Furthermore, assessment of right ventricle in AS is somehow neglected. In our study, right ventricular free wall thickness and basal diameter may provide useful insights on the impact of TAVI on RV structure. Finally, it is important to compare the echocardiographic features of the various biological TAVI prosthesis (eg, the CoreValve prosthesis compared with the Edwards Sapien) which may affect the rate and severity of residual paravalvular leak and its relation with functional recovery and prognosis.

Arterial haemodynamics and bp response to TAVI

Valvular-arterial impedance

In AS, LV is exposed to increased afterload due to valvular stenosis, systemic hypertension and increased aortic stiffness.[3] After TAVI, LV is partially unloaded and the normalisation of mean pressure gradient and flow (SVi) is normally used to evaluate short-term therapeutic success. However, reduction in ZVa which incorporates the markers of valvular and arterial load (global LV load), and is associated with adverse LV remodelling and impaired outcome in AS,[3] may be a better marker of long-term therapeutic success. Reduction in Zva is only possible if hypertension is optimally treated.

Excessive bp rise immediate after TAVI

Some patients may exhibit an excessive BP rise immediately after TAVI, which is believed to be caused by a sudden rise in SV and increase in LVEF, particularly in patients with afterload mismatch. These patients often require intravenous infusion of alpha- and beta-blocker drugs such as Labetalol with careful BP monitoring. However, the optimal BP target in acute setting is not clear. Furthermore, the clinical significance and prognostic value of excessive BP rise immediately after TAVI is not fully explored, and the results are conflicting.[35 36] In our study, BP was carefully measured during hospitalisation for TAVI, and an average BP (post-TAVI BP) will be calculated from all valid measurements. Hence, TAVI-NOR has the potential to examine the clinical significance and prognostic value of an exaggerated BP rise, as well as other patterns of BP response immediately after TAVI.

Limitations

First, global longitudinal strain measured by speckle tracking echocardiography has been shown to predict survival in patients with AS. Strain imaging was not a part of the study protocol. Second, in the earlier period of the study the patient selection criteria were somehow strict and mainly restricted to elderly patients with severe AS who had prohibitively high risk for conventional surgery. These patients had often degenerative stenosis of a tricuspid aortic valve. By contrast, patients with a bicuspid aortic valve are often <65 years and normally assigned for a conventional AVR in combination with coronary bypass grafting. Therefore, in the present study we may to some extent have underestimated the true prevalence of bicuspid aortic valve. Furthermore, we do not have any registration or follow-up data on patients rejected for TAVI. The information on the change in antihypertensive treatment during follow-up (posthospitalisation) was not a part of the study protocol and may affect study outcome. Finally, there is some uncertainty on the proportion of patients who completed 6–12 months echocardiographic follow-up.

In conclusion, TAVI-NOR study is a large prospective cohort study of patients with severe AS that will provide important clinical insights on the effect of TAVI on cardiac structure and function. It will help to determine the echocardiographic predictors of reverse LV remodelling as well as identify patients who are at high risk of procedure-related complications. TAVI-NOR will also assess the association of various types of abnormal BP response immediately after TAVI with cardiac structure and function, vascular haemodynamics and prognosis.

Collaborators John B. Chambers.

Contributors SS and ØB contributed to the study design and planning. AMA, DW, ØB and SS drafted the manuscript protocol. KHL and SR revised the manuscript. SS, AMA and DW collected the echo data. All authors approved the publication of the protocol.

Funding The authors would like to thank the Grieg Foundation, Bergen, Norway for financial support.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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