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CASE REPORT
Coronary heart disease

Coronary physiology to guide treatment of coronary artery disease in a patient with severe aortic valve stenosis: friend or foe? A case report

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Background Severe aortic valve stenosis (AS) is the most frequent valve pathology in the developed world requiring intervention. Due to common factors in pathogenesis, patients with AS frequently have concomitant coronary artery disease (CAD). Determining the relative contribution of each component to the disease state is not easy as there is much overlap in complaints. Moreover, severe AS interferes with the haemodynamic assessment of intermediate coronary lesions.

Case summary In this case report we describe the presentation and management of an 84-year-old patient, with a severely degenerated aortic valve bioprosthesis and an intermediate coronary artery lesion, presenting with acute decompensated heart failure and chest pain. Initial invasive haemodynamic assessment of the coronary lesion provided challenging findings and a second catheterization and intervention was needed to free the patient from his chest pain.

Discussion Optimal assessment and treatment of CAD before valve replacement are controversial. Aortic valve stenosis on itself can lead to subendocardial ischaemia with subsequent angina pectoris. Simultaneously, AS can significantly affect coronary haemodynamics, hereby interfering with intra-coronary haemodynamic assessment of co-existing coronary lesions. Currently used coronary physiological indices are not validated in the AS population and valve replacement has variable effects on the fractional flow reserve and commonly used resting indices, such as the resting full-cycle ratio. Further research on this topic is needed and an overview of currently running studies that will advance this field significantly is provided.

Keywords Aortic valve stenosis • Coronary artery disease • Coronary physiology • Microvascular function • Transcatheter aortic valve implantation • Coronary revascularization • Case report

ESC Curriculum 3.4 Coronary angiography • 3.3 Chronic coronary syndrome • 3.1 Coronary artery disease • 4.2 Aortic stenosis • 2.5 Nuclear techniques

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Learning points

- Severe aortic valve stenosis (AS) and coronary artery disease very frequently co-exist and both give rise to dyspnoea and angina.
- Severe AS causes subendocardial ischaemia and interferes with the haemodynamic assessment of coronary lesions, necessitating caution in physiological indices interpretation.
- Transcatheter aortic valve implantation (TAVI) has significant but different effects on coronary indices: where fractional flow reserve (FFR) seems to decrease due to a blunted response to adenosine pre-TAVI, resting full-cycle ratio (RFR) stays stable in most cases.

Introduction

Aortic stenosis (AS) is the most common valve pathology in the developed world. Approximately 60% of patients with severe AS have concomitant CAD, and both pathologies can give rise to shared symptoms.[1] For many years, surgical aortic valve replacement (SAVR) was the gold standard for treating patients with severe AS. Transcatheter aortic valve implantation (TAVI) is now favoured in high surgical risk patients and even in selected low risk patients. However, coronary revascularization recommendations in patients undergoing TAVI are unclear, since randomized controlled trials are lacking.[2] We present a case of a patient with severe AS and concomitant CAD to illustrate the presentation and management of such a patient, highlighting the current diagnostic and therapeutic challenges with a focus on the use of invasive coronary physiology.

Timeline

Timing	Description
10 years before initial emergency department (ED) presentation	Coronary artery bypass grafting (CABG) of the left circumflex artery (LCX) with simultaneous bioprosthetic SAVR for severe aortic valve stenosis
Initial ED presentation	Presentation with acute decompensated heart failure, TTE shows severe degenerated aortic bioprosthesis with high transvalvular gradients, angiography: no signs of acute coronary syndrome, right coronary artery (RCA) stenosis: 70%
1 month after ED presentation	Coronary haemodynamic assessment of RCA lesion: fractional flow reserve (FFR) negative (0.84) and resting full-cycle ratio (RFR) positive (0.80)
2 months after ED presentation	Uncomplicated TAVI
8 months after ED presentation	Because of persistent angina new coronary haemodynamic assessment of RCA lesion: FFR positive (0.72) and RFR positive (0.80). Percutaneous coronary intervention (PCI) with two drug eluting stents
10 months after ED presentation	Outpatient cardiology clinic visit: resolution of angina
20 months after ED presentation, 12 months after PCI	Outpatient cardiology clinic visit: still free from angina

Case presentation

An 84-year-old male presented to the emergency department with sudden onset dyspnoea. He had a history of coronary artery bypass grafting of the LCX with the left internal mammal artery (LIMA) and simultaneous bioprosthetic (21 mm valve) SAVR 10 years before presentation. He also had a history of peripheral vascular disease. On admission, he was taking aspirin (1 × 80 mg/day), ramipril (1 × 2.5 mg/day), and rosuvastatin (1 × 20 mg/day). Laboratory tests showed an elevated NT-pro-BNP {3625 ng/L [normal range (NR): <738 ng/L]} and troponin-T that increased over 4 h from 0.056 to 0.183 ng/L (NR: <0.013 ng/L). The resting ECG showed no signs of ischaemia while the chest X-ray showed signs of pulmonary oedema. Treatment with diuretics was initiated with good effect. Transthoracic echocardiography showed a normal left ventricular (LV) systolic function with a significant gradient over the prosthetic aortic valve (AV) (peak 66 mmHg, mean 42 mmHg, peak velocity 4.1 m/s, AVAV area of 0.9 cm^2). Subsequent coronary angiography showed a patent LIMA–LCX bypass with a moderate-to-severe stenosis in the RCA (*Figure 1A*). The patient's clinical status improved and he was discharged with oral diuretics, appropriate heart failure, and antianginal medications.

Several weeks later, he was admitted for further work-up. His dyspnoea was stable but he also complained of stable angina. An invasive functional assessment of the lesion in the mid-RCA was performed. The FFR was 0.84 (significant: ≤0.80), the RFR was 0.80 (significant: ≤0.89), the coronary flow reserve [CFR was 1.1 (normal ≥2.0) and the index of microvascular resistance (IMR) was 15 (normal <25)] (*Figure 2A*). Since there was still doubt about the ischaemic potential of the coronary stenosis, a myocardial perfusion Single Photon-Emission Computed Tomography with the use of regadenoson was performed. This showed a reversible perfusion defect of 15% in the inferior and inferolateral segments (*Figure 3*).The case was discussed in the heart team meeting and since the valvular stenosis was deemed most important the patient was planned for a valve-in-valve TAVI without coronary revascularization.

The patient's dyspnoea improved significantly, however, 6 months later he still complained of angina under optimal medical therapy. A new invasive functional assessment showed a significant decrease in FFR (0.72), with an increase in CFR (1.4) and a relative stable/slightly increased IMR (20) (*Figure 2B*). The RFR remained positive (0.80).

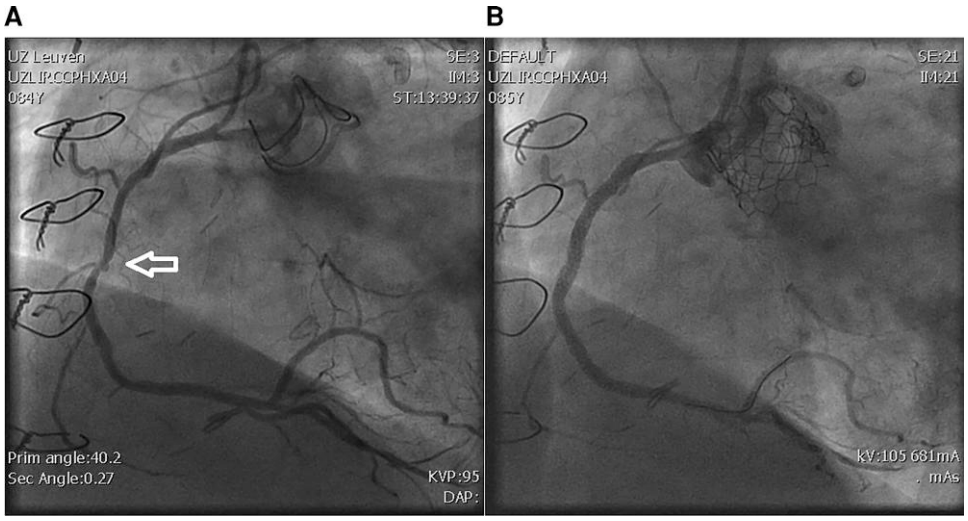

Figure 1 Angiographic image of the coronary stenosis. (*A*) The angiographic image of the right coronary artery stenosis through an left anterior oblique view. The stenosis is marked by the white arrow. (*B*) The angiographic image of the right coronary artery after the placement of two drug eluting stents.

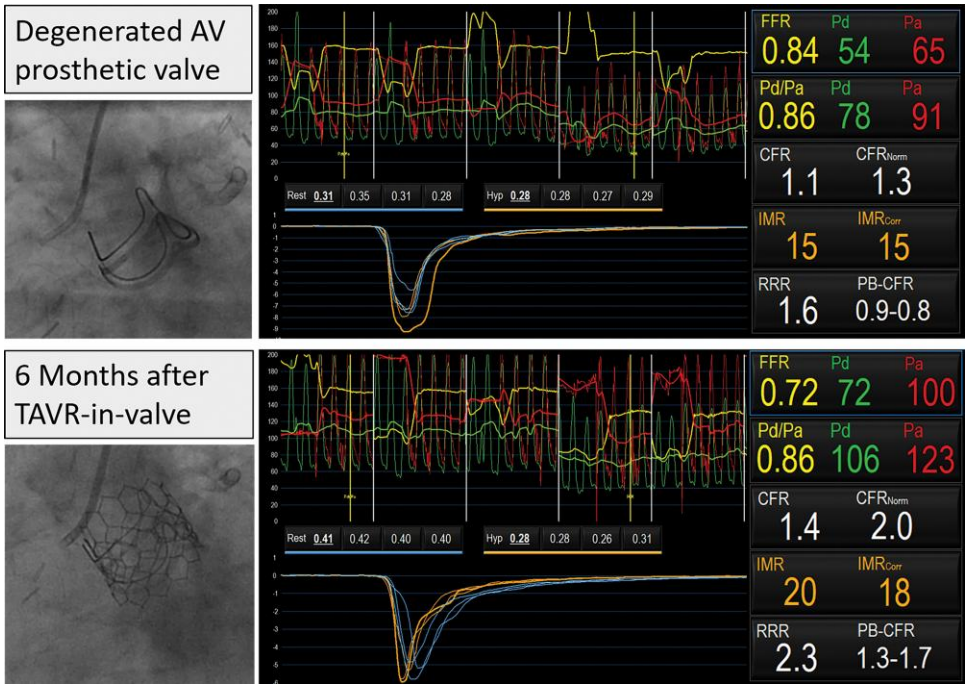

Figure 2 Changes in coronary haemodynamics after transcatheter aortic valve implantation. The top panel shows the angiographic view of the degenerated aortic valve and the coronary haemodynamic measurements during the valve work-up. The lower panel shows the angiographic view of the transcatheter aortic valve implantation prosthesis in the biological valve and the haemodynamic measurements of the same right coronary artery lesion 6 months after the valve procedure. AV, aortic valve; (PB-) CFR (norm), (pressure-bound) coronary flow reserve (normalized); IMR (norm), index of microvascular resistance (normalized); Pa, proximal coronary pressure; Pd, distal coronary pressure; RRR, resistive reserve ratio; TAVI, transcatheter aortic valve implantation.

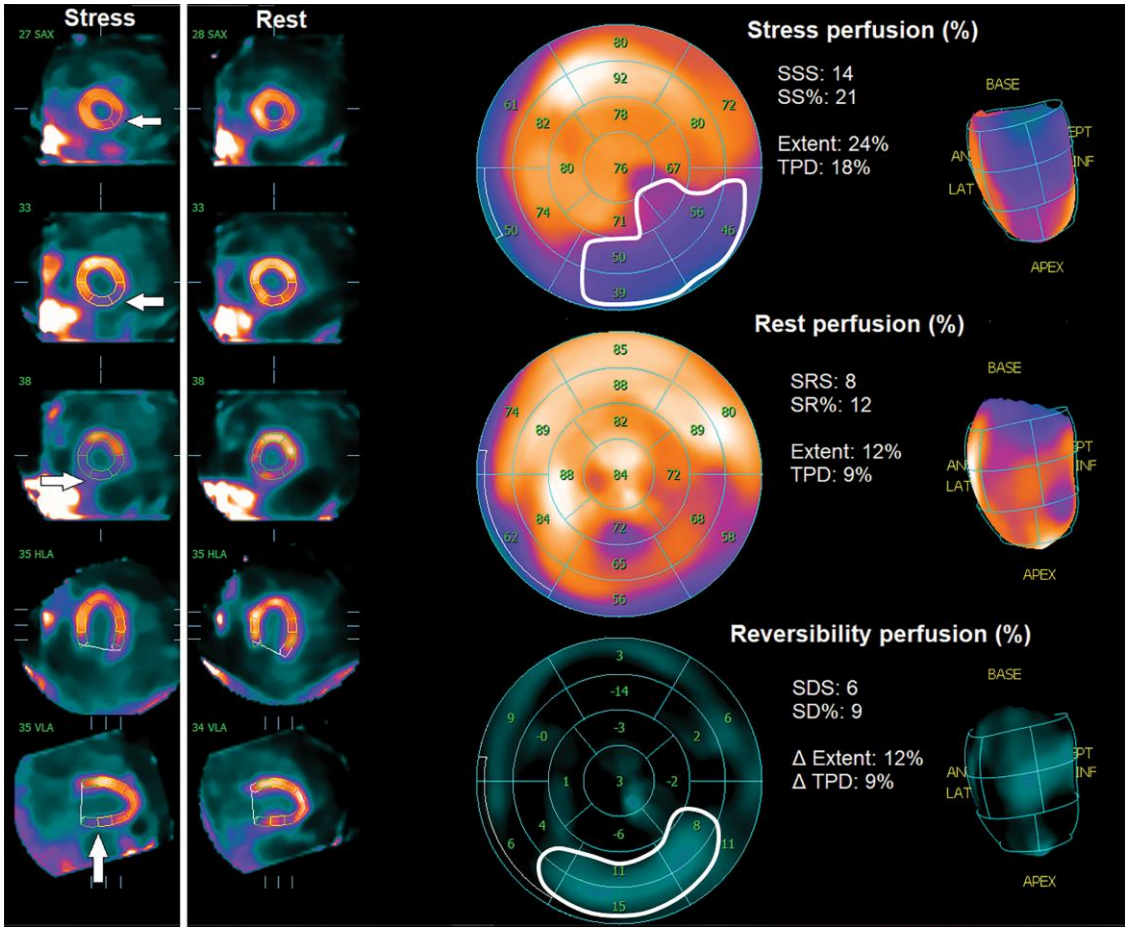

Figure 3 Non-invasive ischaemia testing. The figure shows the results of the myocardial perfusion single photon-emission computed tomography. Regadenoson was used to induce a stress response. A reversible perfusion defect of 15% can be seen in the inferior and inferolateral wall corresponding with the right coronary artery perfusion territory. On the left the perfusion defect is marked with white arrows. On the right the perfusion defect area is traced with white lines. The perfusion defect has an summed stress score of 14 and summed defect score of 6, a delta (Δ) extent of 12% and a delta (Δ) TPD of 9%. SDS, summed defect score; SPECT, single photon-emission computed tomography; SRS, summed rest score; SSS, summed stress score; TPD, total perfusion deficit score.

The lesion was successfully treated with implantation of two drug eluting stents (*Figure 1B*). The patient reported complete resolution of angina 12 months after the PCI procedure.

Discussion

As highlighted in this case, determining the predominant cause of angina in a patient with severe AS and CAD can be challenging. It is known that AS causes a decline in CFR and subendocardial ischaemia due to ventricular hypertrophy, decreased diastolic perfusion time, increased left ventricular end-diastolic pressures, uncoupling of (AV) closure and LV relaxation, and potential microvascular dysfunction.[3,4] The FFR is the gold standard for physiological invasive assessment of coronary lesions, but has not been validated in patients with heart failure or AS.

We report a case demonstrating discrepancy between non-invasive ischaemia testing and resting and hyperaemic invasive indices This is most likely caused by the standard FFR cut-off (0.80) not being valid in our patient with severe AS. With the administration of adenosine, the Pd/Pa (0.86) only dropped to an FFR of 0.84. This small decrease was probably caused by a blunted effect of adenosine to increase coronary flow in AS patients whom are already vasodilated at rest to avoid subendocardial ischaemia caused by the combination of the severe valve stenosis, a hypertrophic myocardium with increased cardiac work and potential microvascular dysfunction. The pressure loss over a coronary lesion increases simultaneous with the maximal flow over that lesion. Studies have shown that coronary flow and CFR increase as LV hypertrophy regresses over time after TAVI.[5] The severely altered CFR that improved after TAVI supports this hypothesis. The increase in coronary flow after TAVI in this case, resulted in the lower and hence appropriately positive FFR. Theoretically, this phenomenon of hyperaemic blunting is not a limitation of non-hyperaemic indices such as RFR. Proof of microvascular dysfunction was not provided by our measurements of IMR, although a vasospastic component was not investigated. These measurements are in line with a study that showed that angina in AS patients is caused by an abnormal cardiac–coronary coupling with reduced diastolic perfusion time rather than intrinsic microvascular dysfunction since AS patients had a normal minimal microvascular resistance.[6,7]

The findings in our case are supported by previous studies that demonstrated a stable coronary flow in the wave-free period of diastole,

Table 1 Active studies investigating coronary physiology in severe aortic stenosis

Study	Description	Participants	Primary outcome	Completion date
COMIC-AS (15) (NCT04420325)	Two-centre observational study in patients with severe AS and CAD	100	Change in FFR and RFR and correlation with myocardial perfusion imaging	2023
TCW (NCT03424941)	Multicentre RCT in patients with AS and multivessel CAD	328	Clinical outcomes 1 year after SAVR + CABG vs. FFR-guided PCR + TAVI	2023
FAITAVI (NCT03360591)	Single centre RCT in patients with AS and CAD	320	Clinical outcomes 1 year after pre-TAVI angiography vs. physiology-guided PCI	2024
NOTION-3 (NCT03058627)	Multicentre RCT in patients with AS and significant CAD	452	Clinical outcomes 1 year after TAVI alone vs. FFR-guided PCI + TAVI	2027
TAVI-PCI (NCT04310046)	Multicentre RCT in patients with AS undergoing TAVI and PCI	986	Clinical outcomes 1 year after iFR guided PCI before vs. after TAVI	2028

CABG, coronary artery bypass grafting; CAD, coronary artery disease; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; RCT, randomized controlled trial; RFR, resting full-cycle ratio; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

and a significant increase in hyperaemic whole cycle flow which resulted in a significant decrease in FFR.[8,9] In contrary, a recent study reported that RFR values did significantly increase and FFR values remained stable at 6 months after TAVR.[10] Although this study had some limitations, it illustrated that even the resting indices, that were proposed to be more stable, can change due to a lower resting coronary flow after TAVI. An argument against the hypothesis of a lower resting coronary blood flow after TAVI, is a study that showed AS patients do have a higher myocardial workload but similar resting coronary blood flows before any valvular intervention.[6] We did not observe a change of RFR in our case, but we should be aware that in some patients the resting indices may increase, making it mainly a useful index to defer revascularization in this population (high negative predictive value).

Since lower-risk and younger patients are more likely to undergo TAVI in the future, identifying and treating haemodynamically significant coronary lesions may become even more relevant. Although there may be no benefit of angiography-guided PCI in older patients,[11] there is some data to support FFR-guided PCI in patients undergoing TAVI.[12] Currently multiple trials on this topic are underway. The COMIC-AS study[13] investigates the acute and long-term effects of AV intervention on intra-coronary indices. Other trials are investigating physiology-guided PCI with CABG The TransCatheter Valve and Vessels Trial (TCW), angiography-guided PCI (FAITAVI), optimal timing of revascularization (TAVI-PCI), or medical management (NOTION-3) of CAD (*Table 1*).

Lead author biography

Lennert Minten was born in Hasselt (Belgium) in 1994 and became an internal medicine resident in 2018. Throughout his training he has done medical internships in the Mayo clinic (Rochester, MN, USA) and Cleveland Clinic (Cleveland, OH, USA) and has worked as a junior doctor in the cardiology department of the Saint-Thomas hospital in London, UK. He recently started a Cardiology fellowship at the University Hospitals Leuven, Belgium and is working as a PhD researcher in the cardiovascular sciences department of the KULeuven. His main interest lies in the field of interventional cardiology and he is a (co)-author of multiple peer-reviewed articles.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written informed consent for the publication of this case report was obtained from the patient in line with Committee on Publication Ethics (COPE) guidelines.

Conflict of interest: None declared.

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