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Article:

Functional assessment of coronary artery disease in patients with severe aortic stenosis: a review.

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Abstract

A significant proportion of patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI) have concomitant coronary artery disease. The best way to treat these patients is contentious. Conventional assessments of ischaemia such as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR) are not validated in the context of severe aortic stenosis, despite having a Class I European Society of Cardiology indication in patients with isolated coronary disease. A better understanding of how we assess and interpret coronary physiology in these patients is required to optimise treatment pathways. Only one prospective, randomised trial has investigated the routine use of FFR to guide revascularisation in patients undergoing TAVI, and several observational cohort studies have measured changes in hyperaemic and resting indices in patients with severe AS, as well as before and after TAVI. The purpose of this review article is to provide a summary of the current data regarding the functional assessment of CAD in patients with severe AS and highlight the current best practice in this evolving area.

Key words

Aortic valve stenosis, transcatheter aortic valve replacement, coronary artery disease, percutaneous coronary intervention.

List of acronyms

aCBF	Absolute coronary blood flow
ACTIVATION	Percutaneous Coronary Intervention Prior to Transcatheter Aortic Valve Implantation
AS	Aortic stenosis
BCIS	British Cardiovascular Intervention Society
CABG	Coronary artery bypass Grafting
CAD	Coronary artery disease
CCS	Canadian cardiovascular society
CFR	Coronary flow reserve
CT	Computed tomography
DAPT	Dual antiplatelet therapy
ESC	European Society of Cardiology
EACTS	European Association for Cardiothoracic Surgery
EAPCI	European Association of Percutaneous Cardiovascular Interventions
FAITAVI	Functional Assessment in TAVI
FFR	Fractional flow reserve
iFR	Instantaneous wave-free ratio
IMR	Index of microcirculatory resistance
LV	Left ventricle
LVEDP	Left ventricular end diastolic pressure
LVH	Left ventricular hypertrophy
MACE	Major adverse cardiovascular events
MBF	Myocardial blood flow
MVR	Microvascular resistance
NICOR	National Institute for Cardiovascular Outcomes Research
NOTION-3	Revascularisation in Patients Undergoing Transcatheter Aortic Valve Implantation
PARTNER	Placement of Aortic Transcatheter Valves
PCI	Percutaneous coronary intervention
SAVR	Surgical aortic valve replacement
TAVI	Transcatheter aortic valve implantation

Introduction

Fibrocalcific aortic stenosis (AS) is the commonest form of valvular heart disease in the western world, associated with considerable morbidity and mortality, especially in the elderly.[1] Treatment guidelines for severe AS have been expanded over the last 20 years and transcatheter aortic valve implantation (TAVI) has gained equipoise with the traditional gold-standard treatment with surgical aortic valve replacement (SAVR) in European Society of Cardiology (ESC) and European Association for Cardiothoracic Surgery (EACTS) guidelines.[2] In the UK, TAVI numbers have outstripped SAVR in recent years and are projected to increase further.[3] Many patients with AS also have coronary artery disease (CAD), but despite this, the assessment and treatment of concomitant CAD remains a contentious issue. This is also important, because percutaneous access to the coronary arteries is more challenging after TAVI due to the valve apparatus obstructing catheter access to the coronary ostia.[4] Physiology-guided treatment of isolated CAD is well validated and guideline-based [5]; however, patients with severe AS have been excluded from these trials and therefore, do not feature in the guideline documents. The haemodynamic effects of AS upon coronary physiology and blood flow are complex and require elucidation if we are to understand how best to evaluate and manage CAD in this growing cohort of patients.[6] This review article aims to provide an overview of the current literature in this field and offer practical guidance on safe best clinical practice.

Aortic stenosis and myocardial blood flow

In health, a series of tightly controlled autoregulatory mechanisms augment myocardial oxygen supply at rest and stress.[7] These are primarily driven by changes in proximal coronary perfusion pressure and microvascular resistance (MVR).[7] In AS, several pathophysiological mechanisms impair the capacity of the myocardium to meet rising oxygen demand through exhaustion and impairment of its vasodilatory capacity.[8] Progressive AS results in high LV afterload and end-diastolic pressure (LVEDP) with adaptive concentric LV hypertrophy (LVH) in order to generate enough contractile force to eject blood through a stenotic valve.[9] The hypertrophied myocardium demands more oxygen, creating a supply: demand mismatch at rest. In response, the autoregulatory mechanisms which augment myocardial blood flow (MBF) during stress are up-regulated through vasodilation of intramyocardial arterioles and

capillaries.[9] This results in high resting MBF, recruiting near maximal myocardial vasodilatory capacity, resulting in a supply: demand mismatch during times of physical or pharmacological stress.[9] The haemodynamic conditions of LVH are further compounded by low proximal perfusion pressure, short diastolic filling time, relative capillary paucity and high extravascular compressive forces, which eventually result in systolic flow reversal and a reversal of the endocardial: epicardial MBF ratio, which in health is around 1.2: 1.[8] This reversal leads to subendocardial ischaemia and myocardial fibrosis, exacerbating angina in patients with AS (with or without CAD).[8] Furthermore, in response to these high stress conditions, endothelial cells of the microvasculature become activated and release pro-inflammatory cytokines which impair nitric oxide (NO) production.[10] Falling NO further impairs the capacity of the microvasculature to dilate in response to stress and contributes to impairment of coronary vasodilatory capacity.[10] The net effect of these pathophysiological mechanisms is to create an environment of high resting MBF with exhaustion of vasodilatory capacity and low CFR. Ahn et al provide insights into these dynamics using cardiac-MRI, showing that AS patients experience microvascular dysfunction with ischaemic symptoms despite absence of CAD.[11] Vulnerability to ischaemia becomes even more pertinent in the presence of CAD, emphasising the need to understand indices of coronary physiology in this cohort.

Coronary artery disease in aortic stenosis

The PARTNER-1 trial reported a 74.9% prevalence of significant CAD in high risk patients randomised to TAVI (mean age 83.6±6.8), and PARTNER-2 reported a prevalence of 62.5% in an intermediate risk cohort (mean age 81.5±6.7).[12, 13] The ESC and EACTS guidance regarding the management of valvular heart disease recommend coronary angiography in patients >40 years old undergoing valvular intervention (Class IC).[2] Revascularisation of CAD is recommended based upon >70% diameter stenosis of a "proximal segment" (Class IIaC) and use of fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR) is discouraged.[2] Coronary artery bypass grafting (CABG) is recommended in patients undergoing SAVR with ≥70% stenosis in a major epicardial vessel (Class IC).[2]

TAVI and CAD in the UK

According to a 2021-22 BCIS and NICOR audit, 2.9% of patients undergoing TAVI had elective percutaneous coronary intervention (PCI) during their work-up, a rate which fell from 7% in 2014.[14] The likelihood is that treatment of co-existing CAD is becoming less routine, rather than the prevalence of disease reducing. In a typical tertiary centre (Sheffield Teaching Hospitals, UK), the rate of elective PCI during TAVI work-up has also fallen by >50% since 2017. Only patients with significant proximal CAD and angina undergo PCI, usually at the time of TAVI. Patients >80 years old at the same centre do not have planned angiography prior to TAVI unless they have angina. All patients needing TAVI require a planning CT-scan to guide their procedure.[15] Although these scans are not designed to investigate CAD, they are contrast enhanced and, in many cases, can be retrospectively gated in order to detect significant, proximal CAD.[16] This represents a possible one-stop diagnostic tool which can reduce invasive procedures and TAVI waiting times.

TAVI and CAD in the literature

The recently published NOTION-3 trial randomised 455 patients (mean age 82 years) with severe AS undergoing TAVI with significant CAD (FFR ≤0.8 or stenosis >90%) to revascularisation with PCI or conservative treatment.[17] At a median follow-up of two years, the primary end-point of death and major adverse cardiovascular events (MACE) occurred in 26% in the PCI group compared with 36% in the conservative group (HR 0.71, 95% CI 0.51-0.99, P=0.04) and bleeding in 28% and 20%, respectively (HR 1.51, 95% CI 1.03-2.22). The authors demonstrated that, although patients with CAD undergoing TAVI should have individualised revascularisation decisions, in those deemed suitable, PCI with FFR guidance is safe, feasible and may offer survival benefit.[17] Patients with recent myocardial infarction and left main stem disease were excluded and symptomatology did not form part of the inclusion or exclusion criteria.

The ACTIVATION trial randomised 235 patients listed for TAVI with CAD and Canadian Cardiovascular Society (CCS) class ≤2 angina to angiographically guided PCI or medical therapy. The rates of the composite endpoint of all-cause death and re-hospitalisation at one year were 41.5% for PCI vs 44.0% for medical therapy (P=0.07).[18] The secondary endpoints of major stroke and MACE at 30 days and one year were also similar. Major bleeding events were significantly higher in patients who had PCI, driven by their need for dual antiplatelet

therapy (DAPT). No objective markers of ischaemia were measured, and significant CAD was defined as >70% stenosis in a major epicardial vessel. Patients with left main stem or ostial CAD were excluded from ACTIVATION and represent a vulnerable cohort who may indeed benefit from PCI before TAVI. [18] The mean age was 84 years; and it is not clear whether these findings are applicable to increasingly younger patients being offered TAVI. It should also be noted that isolated AS is known to cause angina without discernible CAD [19]; therefore, attributing angina to visualised CAD alone in the context of AS may over-represent significant CAD. Furthermore, patients without angina who have CAD may not necessarily need PCI. PCI is a proven treatment for angina, but has not been shown to improve survival in patients with stable or asymptomatic CAD.[20, 21]

Aortic stenosis and coronary physiology

The functional assessment of CAD with FFR and iFR in patients without AS improves clinical outcomes with similar economic costs over several years of follow-up.[22, 23] The ESC/EACTS valvular heart disease and revascularisation guidelines discourage physiological assessment of CAD in this cohort despite FFR- and iFR-guided revascularisation gaining a Class IA indication in patients with CAD.[2, 5] The interplay between myocardial blood flow, microvasculature and the complex haemodynamic environment of AS can theoretically affect conventional measures of ischaemia (figure 1).

Aortic Stenosis and Fractional Flow Reserve

FFR is the ratio of the distal (Pd) to proximal (Pa) coronary pressure, considered over the entire cardiac cycle (usually the average of three cardiac cycles), acquired during stable hyperaemia. In AS, Pa may not accurately reflect the true coronary driving pressure due to high transvalvular gradients and low blood volume draining into the coronary ostia.[24] Furthermore, Pd may be artificially high due to high LVEDP, LVH and high extravascular compressive forces affecting distal coronary pressures.[24] The capacity of the microvasculature to respond to pharmacological hyperaemia is also theoretically sub-maximal due to impaired vasodilatory capacity.[11] As such, physiological conditions required to measure FFR may not be reliably achieved and potentially misleading FFR results may be produced which underestimate lesion significance using standard threshold values (≤0.80)

and may lead to 'inappropriate' deferral of significant lesions (figure 1).[6] This is borne out by a meta-analysis of a selection of the studies shown in table 1 by Minten et al.[25] FFR values were seen to decrease by around 0.02±0.07 (P=0.004) when the same lesions were interrogated long-term after TAVI. Therefore, a few borderline cases may be reclassified after TAVI, however this does suggest reliability with strongly positive or negative FFR readings. Pesarini et al demonstrated that when measured immediately pre- and post-TAVI, positive FFR measurements (≤0.80) decreased significantly and negative FFR values (>0.80) improved (see table 1).[26] Table 1 shows results of a number of studies investigating whether FFR values change post-TAVI in patients with untreated CAD. These are small, observational studies, so conclusions can only be limited, but measuring FFR in patients with AS seems to be safe, well tolerated and is the only index to evidence MACE reduction.[17]

Authors	N	Index	Baseline	Immediately Post-TAVI	*P*-value	Long-term	*P*-value	Conclusion
Wiegerinck et al 2015 [27]	27	FFR	0.97±0.05	0.95±0.06	0.042	NA	NA	*Reduction acutely.*
Pesarini et al 2016 [26]	54	FFR	0.89±0.10	0.89±0.13	0.73	NA		*No change acutely in overall analysis.*
Sub-analysis of Pesarini et al 2016			**0.92±0.06**	**0.93±0.07**	**<0.001**	***Increase acutely when FFR >0.80***		
Sub-analysis of Pesarini et al 2016			**0.71±0.11**	**0.66±0.14**	**<0.001**	***Reduction acutely when FFR ≤ 0.80***		
Ahmad et al 2018 [28]	30	FFR	0.87±0.08	0.85±0.09	0.008	NA	NA	*Reduction acutely*
Stoller et al 2018 [29]	40	FFR	0.90±0.08	0.93±0.08	0.0021	NA	NA	*Increase acutely when FFR >0.80*
Scarsini et al 2020 [30]	14	FFR	0.87 (0.85-0.92)	0.88 (0.83-0.92)	0.49	0.88 (0.82-0.92) *(mean-14 months)*	0.33	*No change acutely or long term*

Stundl et al 2020 [31]	12	FFR	0.77±0.04	-	-	0.76±0.08 *(mean 6-8 weeks)*	0.11	*No change medium term*
Vendrik et al 2020 [32]	13	FFR	0.85 (0.76-0.88)	0.79 (0.74-0.83)	<0.001	0.71 (0.65-0.77) *(mean-6 months)*	<0.001	*Reduction acutely and long-term*
Sabbah et al 2022 [33]	40	FFR	0.84 (0.81-0.89)	-	-	0.86 (.78-0.90) *(mean-6 months)*	0.72	*No change long term*
Scarsini et al 2023 [34]	134	FFR	0.9 (0.84-0.94)	0.88 (0.82-0.93)	0.014	NA	NA	*Reduction acutely*
Sabbah et al 2023 [35]	34	FFR	0.90 (0.87-0.92)	NA	NA	0.91 (0.87-0.95)	0.39	*No change long term*

Table 1. *Summary of measurements of FFR pre- and post-TAVI in the literature.*

Aortic Stenosis and Instantaneous Wave-free Ratio

The iFR is a non-hyperaemic surrogate index of coronary flow, derived from the Pd/Pa ratio measured during the 'wave-free' diastolic period when the relationship between coronary pressure and flow is considered to be linear.[36] In AS, increased LVEDP and LVH cause compression of intramyocardial vessels during diastole, raising coronary resistance and potentially decreasing iFR values.[37] Furthermore, iFR is not dependent upon hyperaemia, but the haemodynamic conditions of severe AS mimic hyperaemia in order to meet high demand conditions, and can result in false positive values.[37] However, Yamanaka et al found that iFR may be a more reliable index than FFR in AS patients because it is less influenced by changes in Pa and LV pressure fluctuations seen in AS.[38] They observed that, post-TAVI, iFR correlated better with myocardial perfusion imaging, suggesting that iFR may provide a more consistent reflection of coronary physiology in AS.[38] In a comparative study by Scarsini et al, iFR was shown to have better stability than FFR in AS patients, with values that were more consistent pre- and post-TAVI.[39]

Table 2 demonstrates a number of small observational studies in which iFR values were measured before, acutely post-TAVI and long-term in patients without significant CAD. In all studies, the pre-TAVI iFR value was positive (≤0.89), corroborating the fact that patients with severe AS are already running at a near maximal hyperaemia, making resting indices of coronary physiology difficult to interpret. In a meta-analysis of the studies in table 2 by Minten et al, the iFR was found to increase non-significantly following TAVI (0.016±0.07, P=0.054).[25] This suggests initial overestimation of lesion significance with incomplete regression of the contributing haemodynamic factors post-TAVI.

Authors	N	Index	Baseline	Immediately Post-TAVI	P-value	Long-term	P-value	Conclusion
Ahmad et al 2018 [28]	30	iFR	0.88±0.09	0.88±0.09	0.94	NA	NA	*No change*
Scarsini et al 2018 [39]	66	iFR	0.89±12	0.89±12	0.66	NA	NA	*No change*
Scarsini et al 2020 [30]	14	iFR	0.88 (0.85-0.96)	0.90 (0.83-0.93)	0.30	0.91 (0.86-0.97) *(mean-14 months)*	0.30	*No change*
Vendrik et al 2020 [32]	13	iFR	0.82 (0.80-0.90)	0.83 (0.77-0.88)	0.735	0.83 (0.73-0.90) *(mean-6 months)*	0.735	*No change*

Table 2. *Summary of measurements of iFR pre-and post-TAVI in the literature.*

Aortic Stenosis and Coronary Flow Reserve

Coronary Flow Reserve (CFR) is the ratio of maximal hyperaemic to resting coronary blood flow and is a measure of both epicardial and microvascular function.[40] In severe AS, CFR is typically reduced due to limited vasodilatory capacity, resulting from LVH and increased resting MBF.[41] Patients with AS have reduced coronary flow during hyperaemia because their hypertrophied myocardium demands greater blood flow than the exhausted microvasculature can supply.[41] Impaired CFR reflects microvascular dysfunction associated

with AS, which contributes to angina and ischaemic symptoms even in the absence of CAD.[41] Furthermore, high LVEDP in AS patients compresses the coronary microvasculature, limiting the ability to increase flow during stress. This reduced vasodilatory capacity is exacerbated by the hypertrophied myocardium, which demands oxygen but receives inadequate blood flow due to limited CFR.[42] Steadman et al demonstrated that patients with AS have significantly reduced CFR, particularly those with LVH, and that CFR often improves post-TAVI as aortic and LV pressures normalise.[42] Paolisso et al found that CFR was significantly lower in AS patients due to elevated MVR and reduced vasodilatory reserve.[9] After TAVI, there was a marked improvement in CFR, suggesting that TAVI helps restore microvascular function and improves overall myocardial perfusion.[9] Table 3 lists the studies measuring CFR improvement post-TAVI. These finding emphasise that CFR is a useful index for understanding the full extent of coronary dysfunction in AS patients and its potential reversibility after valve replacement.

Authors	N	Index	Baseline	Immediately Post	*P*-value	Long-term	*P*-value	Conclusion
Camuglia et al 2014 [43]	8	CFR	1.53 (1.27-1.8)	1.58	0.41	2.18 (1.88-2.7) (mean-12 months)	<0.01	*No change acutely. Increase long-term*
Wiegerinck et al 2015 [27]	27	CFR	1.9±0.46	2.1±0.65	0.113	NA	NA	*No change acutely*
Stoller et al 2018 [29]	40	CFR	1.9±0.9	2.0±1.0	0.72	NA	NA	*No change acutely*
Vendrik et al 2020 [32]	13	CFR	1.28 (1.1-1.51)	1.65 (1.47-1.85)	<0.001	1.94 (1.69-2.25) (mean-6 months)	<0.001	*Increase acutely and long-term*
Scarsini et al 2023 [34]	134	CFR	2.0 (1.43-2.67)	2.12 (1.45-2.80)	0.805	NA	NA	*No change acutely*

Sabbah et al 2023 [35]	34	CFR	2.5 (1.5-3.3)	NA	NA	3.1 (2.2-5.1) (mean-6 months)	<0.001	*Increase long-term*

Table 3. *Summary of measurements of CFR pre- and post-TAVI in the literature.*

Aortic Stenosis and absolute coronary blood flow

In severe AS, resting absolute coronary flow (aCBF) is high due to LVH, increased myocardial oxygen demand and elevated LVEDP.[9] Paolisso et al demonstrated that mean resting aCBF in non-diseased LAD of patients with severe AS was significantly higher than in controls (86mL/min vs 67mL/min, P=0.009).[9] CFR was lower in the AS group but hyperaemic flows were similar, thus confirming the mechanism for impaired vasodilatory capacity.[9] Invasive assessment of aCBF has been measured pre- and post-AV treatment for severe AS by Sabbah et al, who measured hyperaemic aCBF in the LAD using the Rayflow™ catheter with continuous thermodilution in 34 patients with no flow-limiting CAD. They showed no change in hyperaemic aCBF in the LAD pre- and post-treatment with either SAVR or TAVI at six months.[35] They did, however, find a significant improvement in CFR (2.5 vs 3.1, P=<0.01), but FFR and MVR did not change.[35] The isolated improvement in CFR suggests a reduction in baseline aCBF (which was not measured) or an increase in hyperaemic MBF when regression of LVH is considered.[35] In either case, these data cannot guide revascularisation, but are hypothesis-generating.

Aortic Stenosis and microvascular assessment

Theoretically, after TAVI, a reduction in LVEDP, LV filling pressures and intra-myocardial pressures should result in reduced MVR. The commonest measure of MVR in practice is the index of microcirculatory resistance (IMR). IMR is measured as the mean Pd multiplied by the thermodilution-derived mean transit time of saline during maximal hyperaemia.[35] Sabbah et al measured IMR pre- and post-TAVI in 34 patients and demonstrated no change at 6 months (13±8 vs 13±7, P=1.0).[35] These results fall in line with studies by Lumley at al [44] and Nishi et al [45] who found patients with severe AS to have similar MVR and IMR to healthy controls. This may be due to capillary rarefaction making the LV more efficient at extracting oxygen, ameliorating the need for capillary proliferation and higher MVR.[35] MVR remains similar and

increased resting myocardial oxygen demand is provided by a reduction in the CFR. The relatively normal IMR measured in these studies suggest that a minimal level of resistance is reached in severe AS which does not fall further, but allows almost maximal recruitment of the capillary bed. Therefore, changes in MBF after treatment of severe AS are not necessarily driven by changes in MVR but through pathophysiological mechanisms of cardiac-coronary coupling already described.[44]

AS and CT-FFR

CT-FFR may provide a unique opportunity to assess coronary physiology and TAVI planning in one investigation. Michail et al recruited 42 patients with severe AS to invasive and CT-based FFR assessment. [46] Mean invasive FFR was 0.83 and mean CT-FFR was 0.77. [46] There was a 76.7% diagnostic accuracy. Although the authors declared the safety and feasibility of CT-FFR in AS, the relatively modest diagnostic accuracy (23.3% of cases were misdiagnosed) does not suggest widespread use is yet applicable. This was a small single-centre study that excluded patients with significant CAD (>90% stenosis or previous revascularisation) and heart failure. Michiels et al measured CT-FFR pre- and post-TAVI or SAVR in 23 patients. [47] Although a statistically significant decrease in LV-mass was noted after treatment of severe AS, CT-FFR values remained unchanged. No invasive FFR were measured for validation and no patients with CAD of >30% were included. Therefore, the real-world validity of assessing coronary physiology using CT-FFR remains a question to be answered.

Discussion and future directions

TAVI has revolutionised the treatment of AS, but the physiological assessment of concomitant CAD is experiencing a "catch-up" period. The studies above highlight the complexities associated with coronary physiology in the context of severe AS, and demonstrate the need for robust randomised data. The evidence for the long-term health benefits of physiologically-assessed CAD in the non-valve-diseased population are clear, whereas the evidence for long-term benefits of PCI with or before TAVI, are less definitive.

Although the studies described in tables 1-3 are insightful, it must be noted that mean values cannot represent individual patient level data. Only Stundl et al [31] and Pesarini et al [26] re-measured FFR if it was ≤0.80 and the rest only studied patients with FFR values >0.8. The

studies in table 2 all demonstrated positive mean iFR values (≤0.89). In all of these studies, FFR was measured in the same lesions, revealing negative mean values (>0.8). These conflicting findings demonstrate the challenges of interpreting data from heterogenous study populations, although Minten et al have produced a helpful meta-analysis of these studies.[25] Furthermore, not all patients with AS live within an identical physiological environment. Patients with extra-valvular LV failure or low-flow AS phenotype may represent a cohort to which revascularisation guidance based on relatively small trials such as NOTION-3 may not be applicable.

Whilst further randomised data are awaited, best practice guidance is offered by Tarantini et al in a clinical consensus statement from the EAPCI and ESC working group on Cardiovascular Surgery.[48] We have suggested a treatment pathway based upon this expert consensus and available data [17] to offer a practical guide to the general cardiologist (figure 2).

Funding

Conflicts of interest

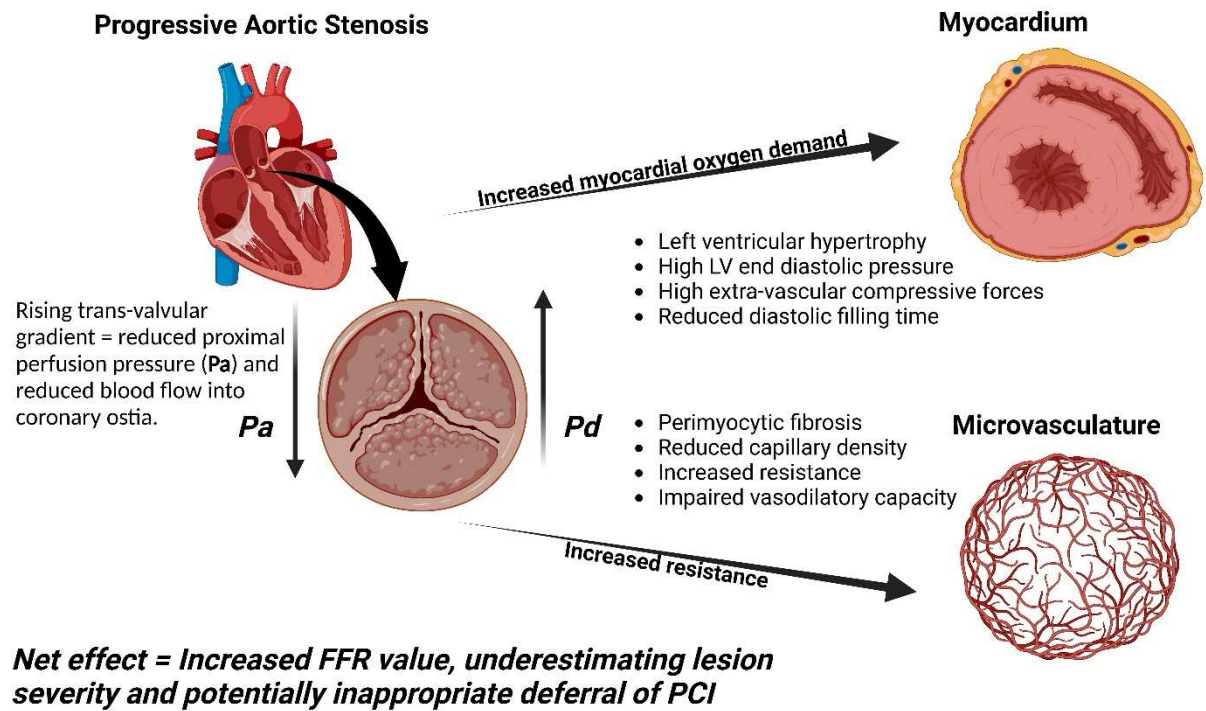The authors have no relevant conflicts of interest.

Figures

Figure 1. The effects of aortic stenosis and its physiological sequalae upon myocardial blood flow and Pd/Pa measurement. FFR is measured as hyperaemic Pd/Pa, with a cut-off value of ≤0.80, as the threshold for physiological significance and intervention. Theoretically, the haemodynamic conditions associated with AS contribute to a lower Pa and an elevated Pd, resulting in a negative FFR measurement and an 'underestimation' (in comparison with normal conditions) of coronary stenosis significance, which can result in deferral of PCI, which may be regarded as inappropriate. Pa; mean proximal aortic pressure. Pd; mean distal coronary pressure. FFR; fractional flow reserve. PCI; percutaneous coronary intervention. Created in BioRender. Yones, E. (2024) https://BioRender.com/ p78m825.
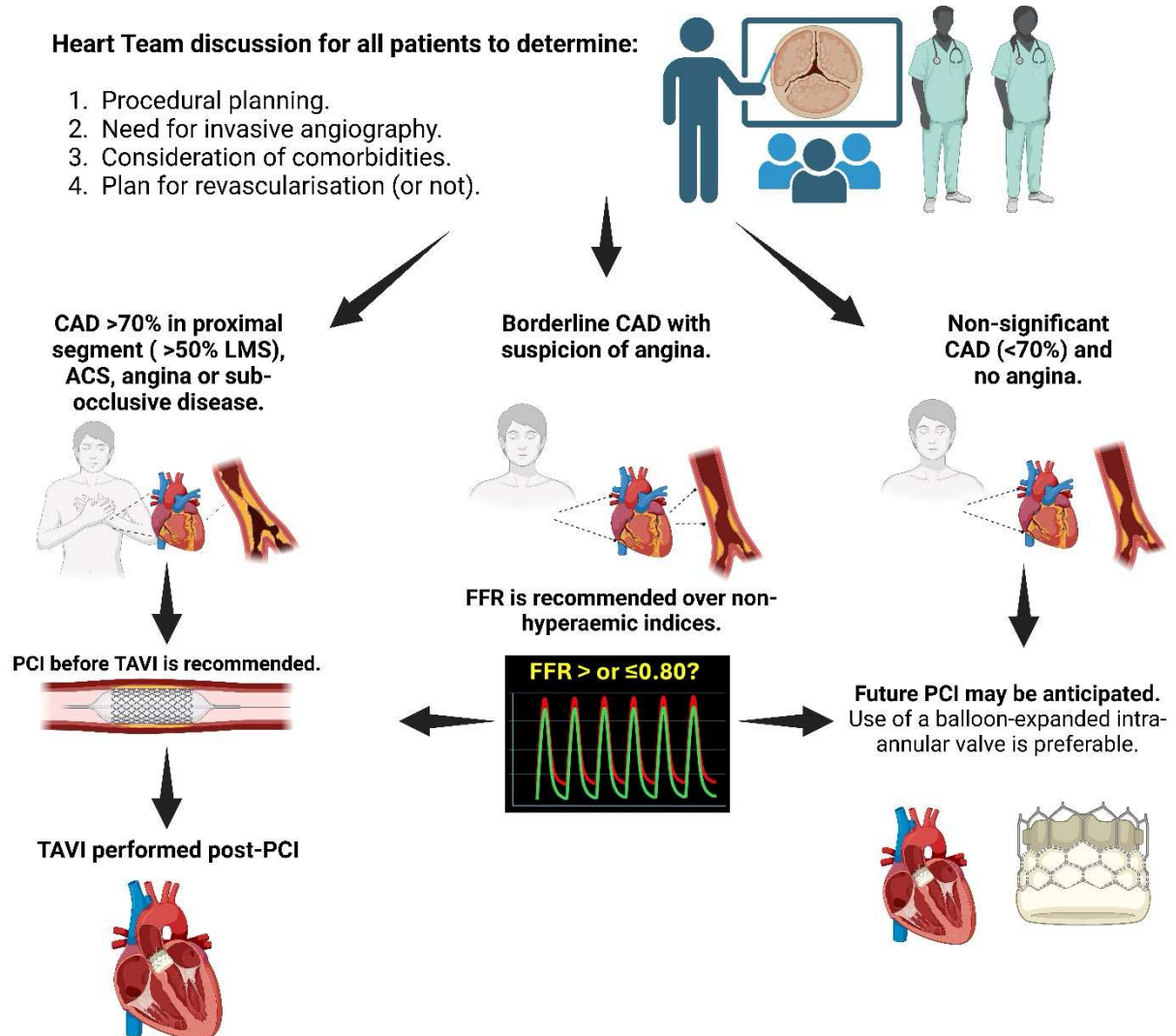
Figure 2. Suggested treatment pathway for patients with severe AS undergoing TAVI who have CAD at angiography (based on Tarantini et al). [48] When angiographically significant CAD is associated with symptoms of angina, recent myocardial infarction or sub-occlusive CAD, it is appropriate to perform PCI prior to TAVI. When there is intermediate CAD and uncertain symptomology, non-invasive imaging suggestive of ischaemia or clinical suspicion of ischaemia, FFR is recommended as the most reliable measure of physiological significance. Note that FFR may slightly underestimate physiological significance in borderline cases by about +0.02 relative to post TAVI measurements.[25] Clearly positive or negative FFR values are likely to be reliable. In cases of angiographically intermediate CAD and absence of symptoms, PCI can be safely deferred; but if future PCI is anticipated, a balloon expanded

intra-annular valve is recommended, associated with easier coronary access post-TAVI. [49]

Created in BioRender. Yones, E. (2024) https://BioRender.com/ g85i548.

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