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Research Paper

Feasibility and utility of anatomical and physiological evaluation of coronary artery disease with cardiac CT in severe aortic stenosis (FUTURE-AS registry)

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ABSTRACT

Background: Coronary artery disease (CAD) is common in patients with severe aortic stenosis (AS) and may impact transcatheter aortic valve replacement (TAVR) procedural and long-term outcomes. CT coronary angiography (CTA) and CT-derived fractional flow reserve (FFR_{CT}) are tools used to assess CAD. However, adoption in the TAVR population is hindered by safety concerns with nitroglycerin and beta-blockers. The safety, accuracy, and utility of CTA and FFR_{CT} optimised with these medications for TAVR have not been established.
Methods: This international, multi-center, prospective registry included severe AS patients referred for TAVR, assessed for CAD with CTA and FFR_{CT}. Patients all received nitroglycerin and beta-blockers as needed to optimise image quality. Severe ventricular dysfunction, recent syncope/heart failure, critical hemodynamics, or prior revascularization were excluded. Significant CAD was defined as CTA stenosis ≥50 % and FFR_{CT}≤0.75. Primary endpoint was per-patient sensitivity and negative predictive value (NPV) of CTA compared to invasive coronary angiography (ICA). Secondary endpoints included specificity and positive predictive value (PPV) of CTA and

Abbreviations: AS, Aortic Stenosis; AVR, Aortic Valve Replacement; CAD, Coronary Artery Disease; CAD-RADS, Coronary Artery Disease–Reporting and Data System; CTA, Computed Tomography Angiography; FFR, Fractional Flow Reserve; FFRCT, CT-Derived Fractional Flow Reserve; GTN, Glyceryl Trinitrate (Nitroglycerin); ICA, Invasive Coronary Angiography; LV, Left Ventricle; LVEF, Left Ventricular Ejection Fraction; NYHA, New York Heart Association; PCI, Percutaneous Coronary Intervention; SCCT, Society of Cardiovascular Computed Tomography; TAVR, Transcatheter Aortic Valve Replacement.

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FFR_{CT}, safety, feasibility (non-evaluable rate), and the modelled potential of CTA + FFR_{CT} to reduce pre-TAVR ICA.

Results: 327 patients (75.9 ± 9.7 years, 53 % male) underwent CTA. CTA was safe and well tolerated in nearly all patients, with transient hypotension in 4 (1.2 %). CTA was evaluable in 326 patients (99.7 %), with 9 (2.8 %) having a non-evaluable vessel. FFR_{CT} and ICA were performed in 110 (33.6 %) and 133 (40.7 %) patients, respectively. Per-patient sensitivity, specificity, NPV, and PPV of CTA were 100 %, 71.4 %, 100 %, and 75.9 % and per-vessel 82.7 %, 78.9 %, 92.3 %, and 59.9 %. FFR_{CT} improved specificity and PPV to 88.9 % and 88.0 % for per-patient and 95.1 % and 81.8 % for per-vessel analysis. Using a simulated triage model deferring ICA in patients with CTA <50 % or ≥50 % stenosis with FFR_{CT} >0.75, 267 patients (81.7 %) could potentially have avoided ICA.

Conclusion: Coronary CTA performed with nitroglycerin and selective use of beta-blockers is safe and effective for assessing CAD in stable severe AS patients. Combining CTA and FFR_{CT} enhances diagnostic accuracy, potentially reducing the need for invasive angiography and streamlining TAVR workup.

1. Introduction

Transcatheter aortic valve replacement (TAVR) is a well-established alternative to surgical aortic valve replacement (SAVR) with comparable or superior outcomes.[1–4] Coronary artery disease (CAD) frequently co-exists in patients with severe aortic stenosis, necessitating preprocedural assessment to inform treatment strategies for both the underlying coronary and valvular heart disease.[5,6] Despite uncertainties surrounding the prognostic value of revascularization in patients undergoing TAVR, preprocedural invasive coronary angiography (ICA) remains the standard diagnostic approach.[6,7]

Cardiac computed angiography has been central to TAVR planning, providing accurate and reproducible means for annular sizing, assessing risk of complications and guiding the procedural strategy.[8] Coronary CT Angiography (CTA) extends the role of cardiac CT as an established safe, cost-effective tool for identifying the presence of CAD and is increasingly utilised as a first-line non-invasive modality for evaluation of stable CAD.[9] However, the adoption of coronary CTA in severe AS has been limited by safety concerns related to the optimization of image quality with nitroglycerin and β-blockers and coronary calcification in an elderly population.[8,10] Furthermore, as the TAVR population shifts toward younger, lower-risk patients, comprehensive CAD evaluation is increasingly important, particularly to address challenges in post-TAVR coronary access and lifetime planning.[6]

Fractional flow reserve (FFR) is superior to anatomical stenosis alone in identifying CAD that warrants revascularization.[11,12] Advances in computational technology have enabled the derivation of non-invasive FFR from coronary CTA (FFR_{CT}), demonstrating diagnostic accuracy and prognostic value across various populations.[13–15] However, its clinical utility in patients with severe AS—a population with a high burden of coronary calcification—remains inadequately explored.[16]

The FUTURE-AS Registry was designed to evaluate the safety, accuracy and clinical utility of integrating coronary CTA and FFR_{CT} for preprocedural CAD assessment in patients with severe AS referred for TAVR. This study aims to determine whether coronary CTA with FFR_{CT} can optimise CAD evaluation and reduce the need for unnecessary ICA in this population.

2. Methods

2.1. Study population

This was a prospective observational registry performed in 8 sites in the United States, Canada, United Kingdom and Australia between November 2020 and June 2024. Relevant institutional ethics committees approved the study according to national guidelines and according to institutional practice. Informed consent was obtained in line with the principals of Good Clinical Practice (GCP).

Stable patients with severe AS being considered for aortic valve replacement (AVR) were screened for inclusion in the study. Exclusion criteria were (1) severe left ventricular dysfunction (ejection fraction <30 %) (2) critical AS (aortic valve area <0.6 cm^2, indexed aortic valve area <0.4 cm^2/m2, peak velocity >5 m/s, mean pressure gradient >60 mm Hg, or dimensionless index <0.20), (3) recent decompensated heart failure or syncope within the past 90 days, (4) renal impairment with an estimated glomerular filtration rate ≤30 mL/min/1.73 m^2, and (5) history of coronary revascularization.

2.1.1. Cardiac CTA imaging protocol and analysis

Imaging was performed using third-generation or more recent CT scanners as per the recommendations of the Society of Cardiovascular Computed Tomography.[8] Coronary CTA was acquired in the same setting as the routine electrocardiogram-gated, multiphasic, contrast-enhanced chest, abdomen, pelvis CT used for planning TAVR procedures. Coronary CTA acquired in isolation was permitted if it was performed prior to AVR. Patients all received sublingual nitroglycerin (0.3–0.8 mg) to optimise image quality according to local institutional protocol and rate control medications were recommended to achieve a pre-scan heart rate of <70 beats/min. While SCCT guidelines recommend a target heart rate of <60 bpm, a threshold of <70 bpm was used to reflect historical safety concerns surrounding beta-blocker use in patients with severe AS[17]. This approach was chosen to assess real-world feasibility in a population where rate control has traditionally been avoided. Sites were provided with a protocol to guide the safe administration of these medications, and any adverse events were recorded (Supplemental Fig. 1). Prospective electrocardiogram-gated acquisition was encouraged to minimize radiation dose and contrast bolus delivery was as per local acquisition protocols. For annular assessment, systolic phases (typically 20–40 % of the R–R interval) were reconstructed in accordance with SCCT TAVR imaging recommendations.[18] For coronary assessment the best quality phase usually mid-diastole, was selected for analysis.[17] Non-contrast gated cardiac CT images were also acquired for coronary artery calcium scoring. Coronary CTA images were analysed from either diastolic or systolic phases depending on image quality.

Coronary CTA was analysed by experienced local readers linded to ICA results. All vessels >2 mm across the 18 coronary segment model were analysed.[17] Stenosis severity was graded according to CAD-RADS criteria with normal (0 %), minimal (1–24 %), mild (25–49 %), moderate (50–69 %), severe (70–99 %) and occluded (100 %).[19] A vessel was considered to have significant disease if there was ≥1 segment with ≥50 % stenosis. A non-evaluable segment due to imaging artifact or significant calcification was defined as a moderate stenosis.

2.1.2. FFR_{CT} analysis

FFR_{CT} analysis was performed by an independent core laboratory (HeartFlow Inc, Redwood City, CA). FFR_{CT} was recommended for stenoses in the 50 %–90 % range in vessels >2 mm in diameter[20]; however, application of FFR_{CT} was at the discretion of local sites, and in some cases extended beyond this range. In line with the updated CAD-RADS 2.0 guidelines and given the threshold for revascularization is typically higher in patients considered for AVR, a positive FFR_{CT} was defined as ≤0.75.[19] FFR_{CT} was measured in a lesion-specific manner 20–30 mm distal to the stenosis for each coronary artery >2 mm. This lesion-specific approach aligns with CAD-RADS 2.0 guidance, which recommends interpreting FFR_{CT} at a physiologically meaningful location distal to the lesion. Vessel-level classification was based on this lesion-specific value, and the lowest per-vessel FFR_{CT} was taken as the per-patient FFR_{CT} value. No routine invasive FFR measurements were collected as part of the study protocol.

2.1.3. Invasive coronary angiography

Decision to perform ICA (either pre-TAVR or at the time of TAVR) was at the discretion of institutional heart teams (Figs. 2 and 3). ICA before TAVR was encouraged for patients with coronary CTA indicating significant anatomical or physiological CAD and for uninterpretable proximal or mid-vessel segments (Supplementary Fig. 2). For other patients with non-significant disease, ICA at the time of the TAVR procedure was encouraged. Revascularization and management decisions were at the discretion of local physicians. Invasive coronary angiograms were interpreted by experienced interventional cardiologists at each site as per routine clinical practice. ICA served as the reference standard for diagnostic accuracy analyses. A lesion was classified as significant if visually estimated stenosis was ≥50 %. For per-patient analyses, the ICA result was considered positive if any epicardial vessel >2 mm had ≥50 % stenosis. Coronary CTA and FFR_{CT} analyses were conducted independently and were linded to ICA results.

2.1.4. Statistical analysis

The study endpoints assessed the accuracy, safety and feasibility of optimizing coronary CTA with nitroglycerin ± beta-blockers in patients with severe AS prior to AVR. The primary end point was the per-patient sensitivity and negative predictive value of coronary CTA compared to ICA. Secondary endpoints included a) per-patient specificity and positive predictive value of coronary CTA and FFR_{CT} compared with ICA, b) per-vessel diagnostic performance, c) Incidence of symptomatic hypotension or bradycardia requiring intervention following nitroglycerin or beta-blocker administration prior to coronary CTA, d) incidence of non-interpretable coronary CTA or non-evaluable FFR_{CT} and e) the modelled clinical utility of combining coronary CTA with FFR_{CT} to potentially reduce pre-TAVR ICA.

Continuous variables were expressed as mean±SD or median ± interquartile range, and categorical variables were expressed as frequency (percentage). Diagnostic accuracy of coronary CTA (≥50 % stenosis) or FFR_{CT} (≤0.75) in assessing significant CAD identified on ICA (≥50 % stenosis) was calculated via diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Sensitivity and NPV for FFR_{CT} were not assessed as FFR_{CT} was used to guide ICA referrals, introducing selection bias and precluding unbiased evaluation of these metrics.

To model the potential impact of coronary CTA and FFR_{CT} on pre-TAVR ICA utilisation, we simulated a decision-making pathway in which ICA would be deferred in patients with coronary CTA <50 % or, for those with ≥50 % stenosis and FFR_{CT} >0.75. While some patients in these categories did undergo ICA in the registry, our model assumes that these cases could have been managed non-invasively. For patients with coronary CTA ≥50 % who did not undergo FFR_{CT}, we applied the observed rate of physiologically non-significant disease (FFR_{CT} >0.75) from the tested subgroup to estimate the number who could have been similarly deferred. This approach allowed a simulation-based estimate of the total potential ICA deferral, assuming broader FFR_{CT} utilisation.

3. Results

3.1. Baseline demographics

A total of 368 patients with severe aortic stenosis being considered for AVR were enrolled in the study (Fig. 1). A total of 41 patients were excluded for either meeting pre-specified exclusion criteria or not receiving pre-coronary CTA nitroglycerin. Therefore, the final study cohort included 327 patients.

Baseline characteristics are shown in Table 1. The mean age of the patients was 75.9 ± 9.7 years and 47.4 % were female. The mean BMI was 29.2 ± 7.2 and nearly all patients (86.8 %) were symptomatic. Median aortic valve gradient, aortic valve area and left ventricular

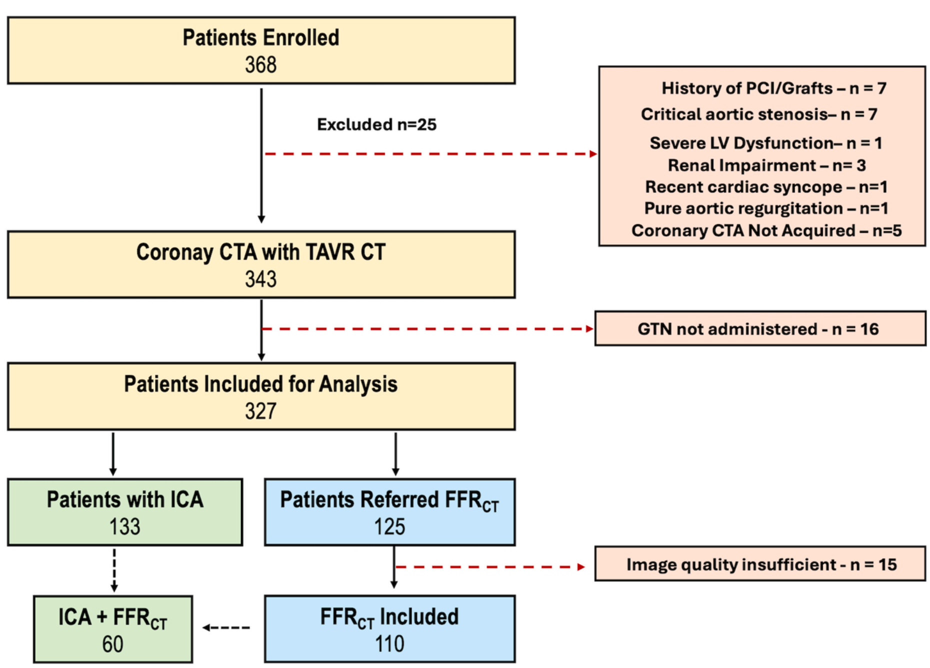

Fig. 1. - Study Flow Chart
FFR_{CT} = CT-Derived Fractional Flow Reserve; ICA = Invasive coronary angiography; PCI = percutaneous coronary intervention; LV = left ventricular dysfunction. GTN = glyceryl trinitrate (nitroglycerin).

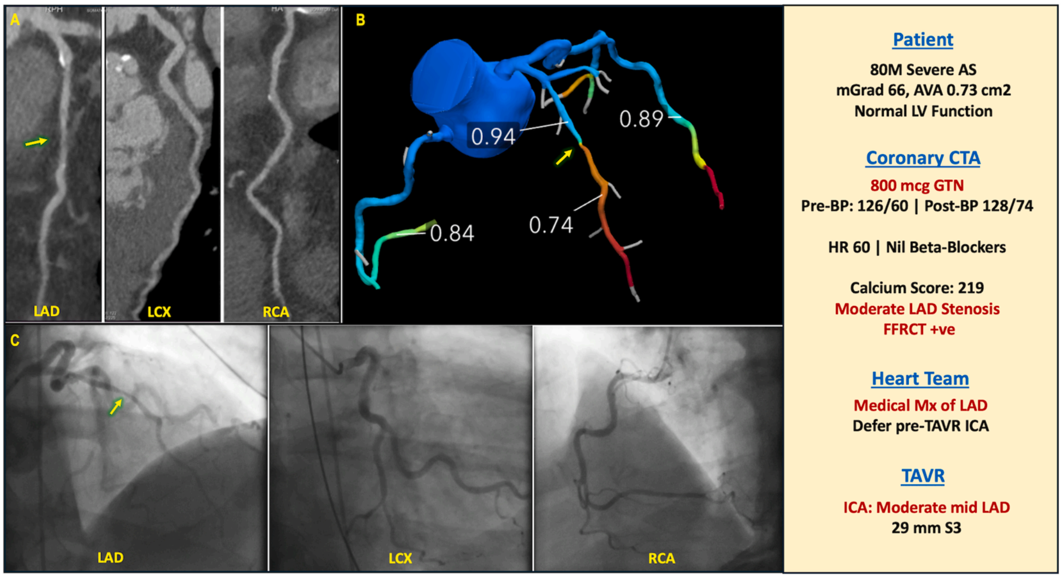

Fig. 2. – Case Example 1 of FUTURE-AS Pathway
80-year-old male with severe aortic stenosis and normal left ventricular function. TAVR CT optimised with 2 sprays (800 mcg) of GTN. CT acquired at 60 bpm with no complications. Calcium score 219 and moderate stenosis of mid LAD. FFR_{CT} was positive in the LAD at 0.74. Heart Team decision to medically manage CAD and defer pre-TAVR ICA. ICA at time of TAVR confirmed mid LAD stenosis and patient successfully treated with SAPIEN-3 TAVR device.
TAVR = transcatheter aortic valve replacement; GTN = glyceryltrinitrate; CAD = coronary artery disease; ICA = invasive coronary angiogram; LAD = left anterior descending artery.

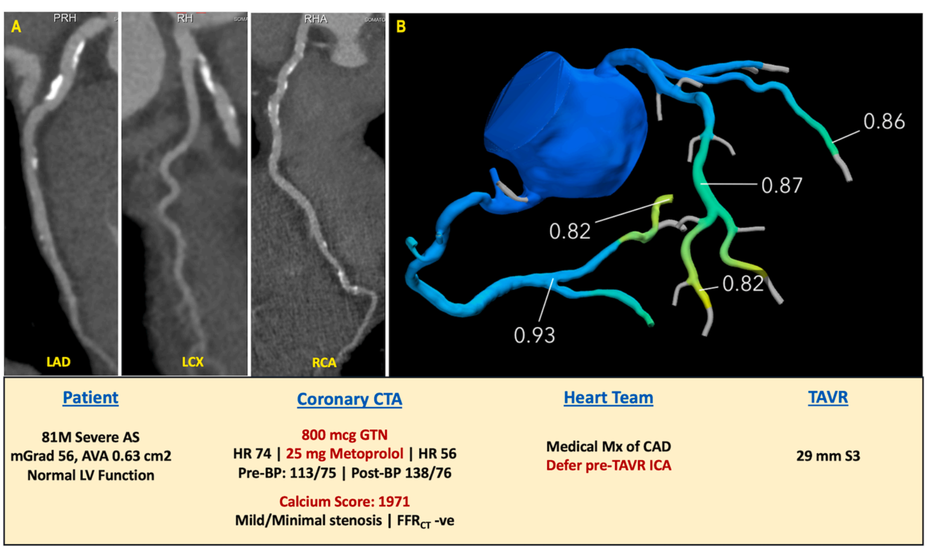

Fig. 3. – Case Example 2 of FUTURE-AS Pathway
81-year-old male with severe aortic stenosis and normal left ventricular function. TAVR CT optimised with 2 sprays (800 mcg) of GTN and 25 mg of metoprolol. CT acquired at 56 bpm with no complications. Calcium score of 1971 with minimal to mild stenosis throughout. FFR_{CT} negative across major vascular territories. Heart Team decision to defer pre-TAVR ICA and patient treated with SAPIEN-3 TAVR device.
TAVR = transcatheter aortic valve replacement; GTN = glyceryltrinitrate; CAD = coronary artery disease; ICA = invasive coronary angiogram.

ejection fraction were 40 mmHg (34–47), 0.82 cm^2 (0.70–0.98) and 60 % (55–60) respectively.

3.2. Coronary CTA/FFR_{CT} characteristics and patient safety

Coronary CTA acquisition characteristics and safety of nitroglycerin are summarised in Table 2. Nitroglycerin was administered in all patients with most common dose being 400 mcg (67.2 %), although 800 mcg was administered in 31.4 %. Beta-blockers were administered in 21.7 % with average oral and IV dose being 54.5 ± 31.1 mg and 9.4 ± 6.7 mg, respectively. Mean acquisition heart rate was 68.1 ± 13.2 bpm. Nitroglycerin and beta-blockers were tolerated in nearly all patients with mild, self-limiting hypotension in 4 patients (1.2 %) and no incidence of shock, vasopressor requirement or hospital admission. Further details can be found in Supplementary Table 1.

Coronary CTA disease burden is summarised in Table 3. The mean coronary artery calcium score was 754 ± 910 and median was 445 [108–1035] Agatston units, respectively. The mean and median calcium score in those who underwent FFR_{CT} was 932 ± 967 and 647 [239–1191] Agatston units, respectively.

The entire coronary CTA was non-evaluable in only 1 patient (0.3 %) with 9 patients (2.8 %) having a vessel that was entirely non-evaluable (Fig. 4A). A non-evaluable segment was present in 26 patients (8.0 %), the majority of which were side-branches (5.2 %) or distal main vessel segments (7.4 %) (Fig. 4B). The left main coronary artery (LMCA) or proximal main vessel segment were evaluable 99.7 % and 98.2 % of

Table 1
Patient and echocardiographic characteristics.

	N = 327
Age, years (SD)	75.9 (9.7)
Gender (male), n (%)	172 (52.6)
BMI, kg/m2 (SD)	29.2 (7.2)
Hypertension, n (%)	242 (74.0)
Diabetes mellitus, n (%)	86 (26.3)
Coronary artery disease, n (%)	72 (22.0)
Previous myocardial infarction, n (%)	6 (1.8)
Hyperlipidemia, n (%)	212 (64.8)
Atrial fibrillation, n (%)	78 (23.9)
Previous stroke/TIA, n (%)	47 (14.4)
Peripheral arterial disease, n (%)	13 (4.0)
COPD, n (%)	44 (13.5)
Prior PPM or AICD, n (%)	31 (9.5)
Prior AVR, n (%)	14 (4.3)
Congestive cardiac failure, n (%)	61 (18.7)
NYHA class, n (%)	
I	43 (13.1)
II	158 (48.3)
III	123 (37.6)
IV	3 (0.9)
Prior RBBB, n (%)	32 (9.8)
Prior LBBB, n (%)	26 (8.0)
Echocardiographic parameters (IQR)	
LVEF, %	60 (55–60)
Aortic mean gradient, mmHg	40 (34–47)
AVA, cm^2	0.82 (0.70–0.98)
eGFR, ml/min/1.73m^2 (SD)	70.6 (20.2)

BMI = body mass index; TIA = transient ischaemic attack, COPD = chronic obstructive pulmonary disease; PPM = permanent pacemaker insertion; AICD = automated implantable cardiac defibrillator; LBBB = left bundle branch block; RBBB = right bundle branch block; LVEF = left ventricular ejection fraction; AVA = aortic valve area; eGFR = estimated glomerular filtration rate.

Table 2
Cardiac CT acquisition and medication characteristics.

	N = 327
GTN administered, n (%)	327 (100)
GTN mode of administration, n (%)	
Oral	113 (34.6)
Sublingual	213 (65.1)
GTN dose, n (%)	
300 mcg	4 (1.2)
400 mcg	220 (67.2)
800 mcg	103 (31.4)
Beta blocker use, n (%)	71 (21.7)
Oral administration	38 (11.6)
IV Administration	35 (10.7)
Beta block dose, mg (SD)	
Oral	54.5 (31.1)
IV	9.4 (6.7)
Adverse reactions, n (%)	
Hypotension	4 (1.2)
Symptomatic bradycardia	0
Cardiogenic shock	0
Pulmonary oedema	0
Hospital admission	0
Acquisition heart rate, bpm (SD)	68.1 (13.2)
Contrast volume, ml (SD)	96.7 (26.6)
kV[a], n (%)	
80	2 (0.6)
90	61 (18.7)
100	96 (29.4)
110	55 (16.8)
120	99 (30.3)

GTN = glyceryl trinitrate; IV = intravenous kV = kilovoltage.
[a] Data available in 313 patients.

patients, respectively. Significant CAD (≥50 %) was present on coronary CTA in 45.8 % of patients (Fig. 5A) and 38.1 % of vessels.

Supplementary Table 2 summarises the characteristics of FFR_{CT} in this cohort. FFR_{CT} was requested in 125 patients (38.2 % of cohort), with 110 having sufficient image quality for analysis, resulting in overall feasibility rate of 88 % (Fig. 4B). Non-evaluability in the remaining cases was due to inadequate image quality for FFR_{CT} analysis. The median FFR_{CT} was 0.82 (0.74–0.89) with 29.1 % of patients having a positive FFR_{CT}. (Fig. 5B).

Significant (≥50 %) stenosis in the left main or proximal LAD was identified on CCTA in 50 patients (15.3 %). Among these, 26 underwent FFR_{CT} analysis and 11 had a positive FFR_{CT}.

Table 3
Coronary CTA feasibility and disease burden.

	N = 327
Calcium score, AU*	
Mean (SD)	756 (912)
Median (IQR)	445 (108–1035)
CAD-RADS, n (%)	
0	33 (10.1)
1	67 (20.5)
2	77 (23.5)
3	90 (27.5)
4/5	60 (18.3)
Non-evaluable, n (%)	
Entire coronary CTA	1 (0.3)
Entire vessel territory	9 (2.8)
Segment(s)	26 (8.0)
LMCA	1 (0.3)
Proximal segment LAD/LCX/RCA	6 (1.8)
RCA	2 (0.6)
LAD	3 (0.92)
LCX	3 (0.92)
Side-branch	17 (5.2)
PDA	10 (3.1)
PLV	10 (3.1)
Diagonal	6 (1.8)
OM	10 (3.1)
Distal main vessel	24 (7.4)
FFR_{CT} n (%)	110 (33.6)
FFR_{CT} ≤0.75, n (%)	32 (29.1)
FFR_{CT} 0.76–0.80, n (%)	12 (10.9)
FFR_{CT} > 0.80, n (%)	66 (60.0)
ICA (stenosis severity), n (%)	133 (40.6)
ICA ≥50 % stenosis, n (%)	63 (47.4)
ICA <50 % stenosis, n (%)	70 (52.6)

LMCA = left main coronary artery; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; PDA = posterior descending artery; PLV = posterior left ventricular artery; OM = obtuse marginal artery; FFR_{CT} = CT-Derived Fractional Flow Reserve; ICA = invasive coronary angiography; AU = Agatston units.

3.3. Diagnostic performance of coronary CTA and FFR_{CT}

The per-patient and per-vessel diagnostic performance of coronary CTA and FFR_{CT} with 95 % confidence intervals is summarised in Table 4. Invasive coronary angiography was performed in 133 patients (40.6 %). Significant CAD (≥50 %) was present in 47.4 % of these patients and 27.6 % of vessels. The per-patient sensitivity, specificity, PPV and NPV for coronary CTA were 100 %, 71.4 %, 75.9 %, 100 % respectively with overall diagnostic accuracy of 84.9 %. The per-vessel performance was 82.7 %, 78.9 %, 59.9 % and 92.3 % respectively with an overall diagnostic accuracy of 79.9 %. FFR_{CT} improved the per-patient specificity and PPV to 88.9 % and 88.0 % respectively with a similar improvement for per-vessel analysis to 95.1 % and 81.8 %, respectively.

3.4. Baseline differences between ICA and Non-ICA groups

Compared with patients managed non-invasively with only coronary CTA±FFR_{CT}, those subsequently referred for ICA were older (77.3 vs. 74.9 years, $p = 0.026$), less likely to be male (45.1 % vs. 65.1 %, $p = 0.025$), had higher aortic valve gradients on echocardiography (42 vs. 39 mmHg, $p = 0.019$), more likely to be prescribed beta-blockers at time

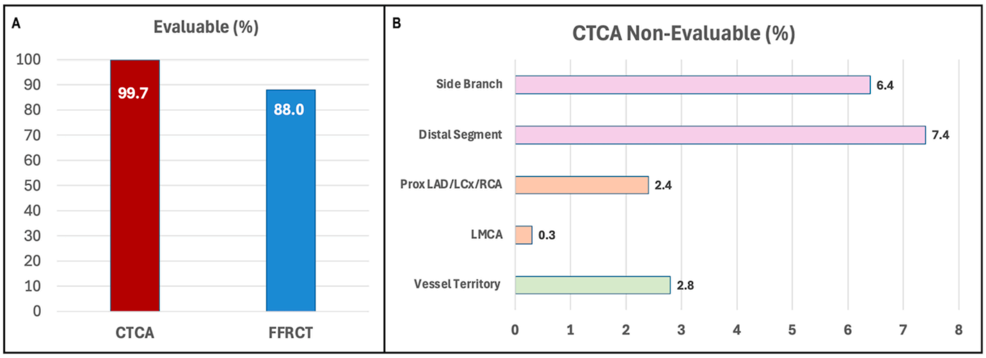

Fig. 4. – Coronary CTA and FFR_{CT} Feasibility and Non-Evaluable Segments
A) Patients (%) with Coronary CTA or FFR_{CT} being non-evaluable B) Patients (%) with a non-evaluable segment or vessel territory
FFR_{CT} = CT-Derived Fractional Flow Reserve.

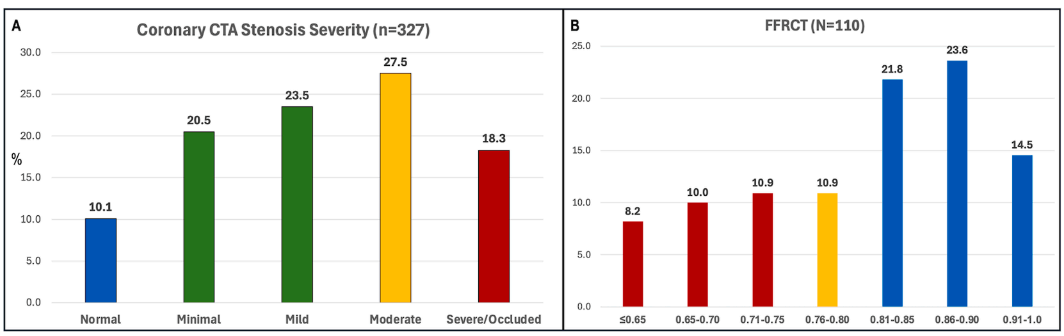

Fig. 5. Coronary CTA and FFR_{CT} Disease Burden
CTA = CT angiography, FFR_{CT} = CT-Derived Fractional Flow Reserve.

Table 4
- Coronary CTA and FFR_{CT} diagnostic performance.

	Per Patient Analysis		Per Vessel Analysis	
	CTCA >50 %	FFRCT <0.75	CTCA >50 %	FFRCT <0.75
n	133	60		
True positive	63	22	91	27
False positive	20	3	61	6
True negative	50	24	228	116
False negative	0	*11*[a]	19	*26*[a]
Sensitivity % (95 % CI)	100.0 (94.3–100.0)	*Not reported*[a]	82.7 (74.6–88.7)	*Not reported*
Specificity % (95 % CI)	71.4 (59.9–80.7)	88.9 (71.9–96.1)	78.9 (73.8–83.2)	95.1 (89.7–97.7)
PPV % (95 % CI)	75.9 (65.7–83.8)	88.0 (70.0–95.8)	59.9 (51.9–67.3)	81.8 (65.6–91.4)
NPV % (95 % CI)	100.0 (92.9–100.0)	*Not reported*	92.3 (88.3–95.0)	*Not reported*
ROC AUC	0.86	*Not reported*	79.9	*Not reported*
Accuracy (%)	85.0	*Not reported*	0.81	*Not reported*

CTCA = CT coronary angiography; AUC = area under the receiver operator curve; PPV = positive predictive value; NPV = negative predictive value.
[a] FFR_{CT} was performed in a non-random, selected subset of patients, introducing work-up bias. As such, sensitivity, NPV, and accuracy are not reported, as these metrics may be biased due to the differential likelihood of undergoing ICA based on CT findings.

of coronary CTA acquisition (41.0 % vs. 14.0 %, $p < 0.001$) and undergo FFR_{CT} analysis (45.1 % vs 25.8 %; $p < 0.001$). Patients referred for ICA also had higher coronary artery calcium scores (median 762 vs. 289 Agatston units, $p < 0.001$), more severe coronary disease on CTA (CAD-RADS 4/5: 32.3 % vs. 8.8 %, $p < 0.001$) and a greater proportion with abnormal FFR_{CT} values ≤ 0.75 (41.7 % vs. 14.0 %, $p = 0.001$). In contrast, a history of clinical heart failure was more common in the non-ICA group (22.2 % vs. 13.5 %, $p = 0.049$) (Supplementary Table 3).

3.5. Clinical utility of coronary CTA and FFRCT

To investigate the potential impact of a coronary CTA-guided referral strategy, we modelled a decision-making approach in which referral to ICA would be based on coronary CTA and FFR_{CT} findings. Under this simulated model, ICA would be deferred in patients with CTA <50 % stenosis, or in those with CTA ≥50 % and FFR_{CT} >0.75. Applying these criteria to the study cohort, 177 patients (54.1 %) had CTA <50 % and would be deferred from ICA. Among the remaining 150 patients with CTA ≥50 % stenosis, 77 underwent FFR_{CT}; of these, 46 (59.7 %) had physiologically non-significant disease (FFR_{CT} >0.75) and would also be deferred (Supplementary Table 2). For the 73 patients with CTA ≥50 % who did not undergo FFR_{CT}, we applied the same proportion of physiologically non-significant disease observed in the tested group, estimating that an additional 44 patients could have been deferred. Based on this simulation, a total of 267 out of 327 patients (81.7 %) could potentially have avoided ICA using a coronary CTA and FFR_{CT} guided approach (Fig. 6).

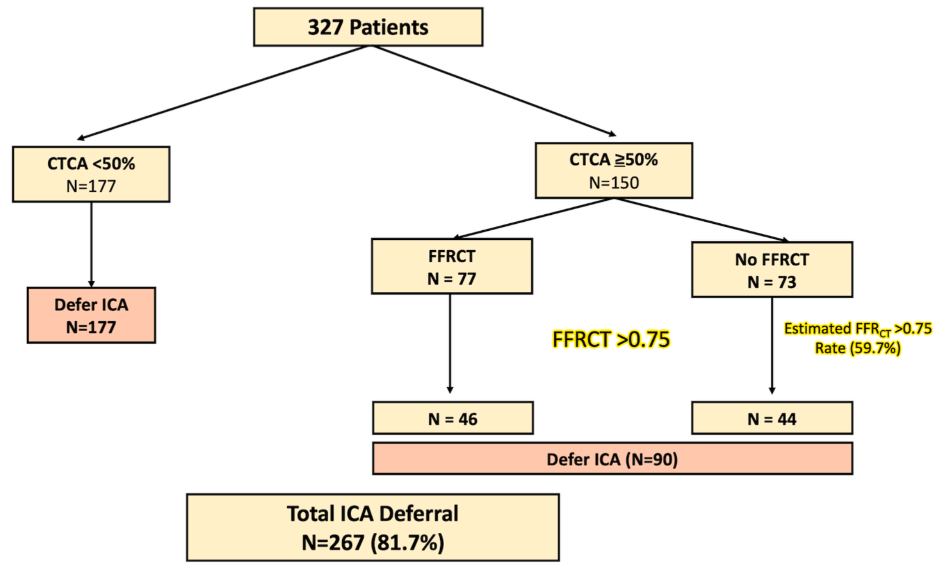

Fig. 6. Simulated Model of ICA Deferral based on Coronary CTA±FFR_{CT}.
CTCA = CT coronary angiogram FFR_{CT} = CT-Derived Fractional Flow Reserve; ICA = invasive coronary angiogram.

4. Discussion

The FUTURE-AS Registry is the first large, multicenter study to evaluate the feasibility, accuracy, and clinical utility of integrating coronary CTA and FFR_{CT} for the assessment of CAD in patients with severe AS undergoing evaluation for TAVR. Our findings demonstrate that coronary CTA, when optimised with nitroglycerin and selective use of beta-blockers, is seemingly safe and an accurate modality for identifying significant CAD in this population. The addition of FFR_{CT} significantly improves specificity and PPV, and in a simulated triage model, could have allowed ICA to be deferred in up to 81.7 % of patients. These results have important implications for refining guidelines on TAVR CT imaging protocols, streamlining preprocedural workflows, reducing procedural risks and optimizing resource utilisation.

Our findings build on previous work evaluating the accuracy and utility of coronary CTA in severe AS populations. A meta-analysis of 14 studies and 2533 patients reported a pooled per-patient sensitivity of 97 % and specificity of 68 % compared to ICA.[21] In another study of 338 patients undergoing CT-FFR for coronary assessment as part of work-up for TAVR had a sensitivity of 77 % and specificity of 65 %, with low sensitivity likely secondary low disease prevalence in the patient cohort.[22] Despite these promising results, the adoption of coronary CTA in severe AS has been limited by concerns regarding image quality, particularly from blooming artifact from coronary calcification thereby reducing specificity and motion artifact from inadequately controlled heart rates which limit overall diagnostic accuracy.[10] Given the safety concerns of vasodilatation in severe AS, previous studies have all avoided administering nitroglycerin and have had limited use of beta-blockers.[8,10]

Our study addresses these concerns by demonstrating that these medications are well-tolerated in select stable patients with severe AS, with only 1.2 % experiencing mild, transient hypotension and no cases of severe adverse events. We achieved a high feasibility for coronary CTA assessment, with only 1 scan (0.3 %) completely non-evaluable due to motion artifact. Additionally, our study provides the first insight into coronary CTA feasibility for the entire 18-segment model, demonstrating that most patients with non-evaluable segments were limited to side-branches (6.4 %) and distal segments (7.4 %). The LMCA and proximal main vessel segments were evaluable in 99.7 % and 98.2 % of patients respectively, highlighting that coronary CTA optimised with nitroglycerin and beta-blockers can provide a reliable and comprehensive coronary assessment in most patients with severe AS.

Despite the optimization of image quality in our study, coronary CTA demonstrated modest specificity (71.4 %), which could still lead to unnecessary referral for ICA. FFR_{CT} is a well-established tool that has high diagnostic accuracy in stable CAD populations and improves appropriate ICA referrals compared to coronary CTA alone in both the stable and acute setting. However, concerns have been raised regarding its accuracy in severe AS due to left ventricular hypertrophy and abnormal coronary physiology, which may affect hyperaemic response to adenosine.[6] Our initial pilot work by Michail et al. demonstrated high per-vessel accuracy of FFR_{CT} in severe AS when compared with invasive FFR measurements.[16] Additionally, a small study by Sasaki et al. reported no significant difference in diagnostic performance of FFR_{CT} before and after TAVR, suggesting that post-valve haemodynamic changes do not significantly impact FFR_{CT} accuracy.[23]

Our study is the first real-world, prospective study to demonstrate that a clinically available FFR_{CT} technique significantly improves specificity and PPV to 88.9 % and 88.0 %, respectively. The feasibility of FFR_{CT} in this cohort was high, with 88 % of cases being analyzable despite a mean calcium score of 932 ± 967 Agatston units. While true diagnostic performance in this cohort remains incompletely defined due to the lack of invasive FFR comparison, our results are broadly consistent with prior studies using alternative FFR_{CT} approaches, which have reported specificity between 70 and 90 %, albeit largely in retrospective settings and using platforms not commercially available.[24]

Recent data highlight the ongoing challenge of managing CAD in patients undergoing TAVR. A registry of 1911 patients reported that TAVR in the presence of untreated severe CAD was safe and associated with low rates of clinical events at 2 years.[25] In contrast, the NOTION-3 randomized trial demonstrated that pre-TAVR PCI, guided by severe (>90 %) anatomical stenosis or FFR, significantly reduced the incidence of myocardial infarction and urgent revascularization at a median follow-up of 2 years.[26] The high evaluability of the left main and proximal coronary segments in our cohort is particularly relevant, as contemporary guidelines recommend considering PCI before TAVR in patients with severe proximal or left main coronary stenoses.[27,28] Despite the lack of consensus on the optimal management of CAD prior to TAVR, current guidelines continue to recommend preprocedural CAD assessment as an essential component of patient evaluation.[7,29] In routine practice, CAD assessment is typically conducted separately from TAVR planning, with CT used for aortic root assessment and procedural planning and ICA performed to evaluate CAD.[6]

This study suggests that integrating coronary CTA with FFR_{CT} could, in a simulated model, allow deferral of ICA in over 80 % of patients, significantly streamlining the pre-TAVR workup. This approach has the potential to reduce patient discomfort, minimize costs, and eliminate delays to definitive valve treatment. The landmark DISCHARGE trial demonstrated that a CT-first diagnostic pathway significantly improved clinical outcomes compared to an ICA-first approach, primarily through a reduction in major procedural-related complications.[30] Recent data from Hussain et al. also support a CT-first strategy in the TAVR population, demonstrating that a CTA-based pathway with selective use of CT-FFR safely reduced the need for ICA without adversely affecting outcomes.[31] With TAVR indications also expanding to include asymptomatic and moderate AS patients, optimizing the diagnostic pathway is important to ensuring timely and cost-effective treatment.[32] Furthermore, as TAVR is increasingly performed in younger patients, the cumulative lifetime risk of CAD and acute coronary syndromes becomes more relevant. Coronary CTA offers a readily available and accurate tool for evaluating both stenosis severity and plaque composition, making it an attractive alternative to routine ICA. Unlike CTA strategies in severe AS that focus solely on reporting proximal coronary segments,[33] this dataset demonstrates that optimised coronary CTA provides a more comprehensive assessment of the entire coronary tree, thereby better addressing the needs of younger TAVR patients who require more personalised lifetime management of both their valvular and coronary disease.

This study had several limitations. First, given its real-world nature, FFR_{CT} was used to guide referrals for ICA, introducing selection bias and precluding an unbiased assessment of its sensitivity and NPV. Because ICA was performed at clinician discretion rather than in a prespecified verification subset, verification bias is possible and diagnostic performance metrics, particularly sensitivity and NPV, may be overestimated. Since patients with positive FFR_{CT} values were preferentially referred for ICA, those with negative results often did not undergo invasive evaluation, limiting the ability to fully assess all measures of diagnostic performance including accuracy overall. As a result, only specificity and PPV were reported for FFR_{CT} in this analysis. Patients referred for ICA also differed in baseline characteristics, including higher coronary calcium burden, more severe coronary disease, and less frequent clinical heart failure, further reinforcing this selection bias. Second, while this was a multicenter study, variability in local CTA acquisition protocols and ICA referral practices may have influenced diagnostic performance. Interpretation of coronary CTA, FFR_{CT}, and ICA was conducted at the site level without core laboratory adjudication, which may introduce inter-operator variability but reflects real-world practice. Third, patients with prior coronary revascularization were excluded, which may impact the generalizability of our findings, particularly in older or higher-risk TAVR candidates where previous PCI or CABG is more common. Additionally, this study only included stable AS patients without critical hemodynamics or severe LV dysfunction, limiting the applicability of our findings, particularly the safety of nitroglycerin to this excluded cohort. Fourth, despite a high overall evaluability rate for coronary CTA and FFR_{CT}, approximately one in ten patients had a non-evaluable segment, reflecting the challenges of maintaining adequate image quality in this patient population. In our cohort beta-blockers were used selectively, with 22 % of patients receiving rate-control therapy to achieve a pragmatic heart-rate target of <70 bpm. This lenient target reflected long-standing caution around beta-blocker use in severe AS rather than protocol non-adherence. Importantly, despite modest beta-blocker use, coronary CTA evaluability remained very high. While beta-blockers were well tolerated when administered, the study was not designed to test stricter heart-rate thresholds recommended by SCCT guidelines and routine beta-blocker administration cannot be inferred from these data. Their use should remain individualised based on haemodynamic stability and local practice. In our cohort, nitroglycerin was administered in only stable patients with a systolic blood pressure >100 mmHg, using 400 mcg dose in most cases (67 %), and 800 mcg in smaller proportion (31 %) according to site preference. Prior studies have shown that nitrates have a greater effect on the feasibility of FFR_{CT} analysis than on the anatomical evaluability of coronary CTA, which may partly account for the small proportion of non-evaluable FFR_{CT} studies observed in our cohort.[34,35] Lastly, this study focused on preprocedural CAD assessment, and long-term outcomes related to CTA + FFR_{CT} guided ICA deferral, revascularization decisions, and post-TAVR CAD events require investigation in future studies.

5. Conclusion

Coronary CTA, when performed with nitroglycerin and selective use of beta-blockers, may be a safe, feasible and accurate modality for CAD assessment in stable severe AS patients undergoing TAVR evaluation. The addition of FFR_{CT} improves diagnostic specificity and PPV, with the potential to reduce unnecessary invasive angiography and streamline the pre-TAVR workup.

Disclosures

SS: Grants paid to institution from Edwards Lifesciences, Medtronic, HeartFlow; consulting fees from Edwards Lifesciences, Anteris Technologies, and Medtronic; equipment loan agreement from ViVitro Labs. **JL:** Grants from GE HealthCare; consulting fees and stock options from HeartFlow and Circle Cardiovascular Imaging; personal core lab services from Arineta **ARI:** has received consultancy fees from Abbott Medical, Edwards Lifesciences and Artrya (including stock options). JS is an employee of Boston Scientific. MA is consultant to Edwards Lifesciences, Medtronic and Abbott. MA is consultant to Edwards Lifesciences, Medtronic and Abbott.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

SS: Grants paid to institution from Edwards Lifesciences, Medtronic, HeartFlow; consulting fees from Edwards Lifesciences, Anteris Technologies, and Medtronic; equipment loan agreement from ViVitro Labs. **JL:** Grants from GE HealthCare; consulting fees and stock options from HeartFlow and Circle Cardiovascular Imaging; personal core lab services from Arineta **ARI:** has received consultancy fees from Abbott Medical, Edwards Lifesciences and Artrya (including stock options). **JS** is an employee of Boston Scientific. **MA** is consultant to Edwards Lifesciences, Medtronic and Abbott. **MA** is consultant to Edwards Lifesciences, Medtronic and Abbott.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcct.2025.12.012.

References

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363(17): 1597–1607. https://doi.org/10.1056/nejmoa1008232.
2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 364(23):2187-2198. doi:10.1056/nejmoa1103510.
3. Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet*. 2016;387(10034):2218–2225. https://doi.org/10.1016/s0140-6736(16)30073-3.
4. Blankenberg S, Seiffert M, Vonthein R, et al. Transcatheter or surgical treatment of aortic-valve stenosis. *N Engl J Med*. 2024;390(17):1572–1583. https://doi.org/10.1056/nejmoa2400685.

5. Faroux L, Guimaraes L, Wintzer-Wehekind J, et al. Coronary artery disease and transcatheter aortic valve replacement JACC state-of-the-art review. *J Am Coll Cardiol*. 2019;74(3):362–372. https://doi.org/10.1016/j.jacc.2019.06.012.
6. Tomii D, Pilgrim T, Borger MA, et al. Aortic stenosis and coronary artery disease: decision-making between surgical and transcatheter management. *Circulation*. 2024; 150(25):2046–2069. https://doi.org/10.1161/circulationaha.124.070502.
7. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2021;43(7):561–632. https://doi.org/10.1093/eurheartj/ehab395.
8. Blanke P, Weir-McCall JR, Achenbach S, et al. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/Transcatheter aortic valve replacement (TAVR) an expert consensus document of the society of cardiovascular computed tomography. *JACC, Cardiovasc Imaging*. 2019;12(1):1–24. https://doi.org/10.1016/j.jcmg.2018.12.003.
9. Haase R, Schlattmann P, Gueret P, et al. Diagnosis of obstructive coronary artery disease using computed tomography angiography in patients with stable chest pain depending on clinical probability and in clinically important subgroups: meta-analysis of individual patient data. *BMJ*. 2019;365:l1945. https://doi.org/10.1136/bmj.l1945.
10. Boogert TPW van den, Vendrik J, Claessen BEPM, et al. CTCA for detection of significant coronary artery disease in routine TAVI work-up. *Neth Heart J*. 2018;26 (12):591–599. https://doi.org/10.1007/s12471-018-1149-6.
11. Xaplanteris P, Fournier S, Pijls NHJ, et al. Five-year outcomes with PCI guided by fractional flow reserve. *N Engl J Med*. 2018;379(3):250–259. https://doi.org/10.1056/nejmoa1803538.
12. Zimmermann FM, Ferrara A, Johnson NP, et al. Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial. *Eur Heart J*. 2015;36(45):3182–3188. https://doi.org/10.1093/eurheartj/ehv452.
13. Nørgaard BL, Terkelsen CJ, Mathiassen ON, et al. Coronary CT angiographic and flow reserve-guided management of patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2018;72(18):2123–2134. https://doi.org/10.1016/j.jacc.2018.07.043.
14. Nørgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease the NXT trial (analysis of coronary blood flow using CT angiography: next steps). *J Am Coll Cardiol*. 2014;63(12):1145–1155. https://doi.org/10.1016/j.jacc.2013.11.043.
15. Min JK, Taylor CA, Achenbach S, et al. Noninvasive fractional flow reserve derived from coronary CT angiography clinical data and scientific principles. *JACC, Cardiovasc Imaging*. 2015;8(10):1209–1222. https://doi.org/10.1016/j.jcmg.2015.08.006.
16. Michail M, Ihdayhid AR, Comella A, et al. Feasibility and validity of computed tomography-derived fractional flow reserve in patients with severe aortic stenosis. *Circ: Cardiovasc Interv*. 2021;14(1):e009586. https://doi.org/10.1161/circinterventions.120.009586.
17. Leipsic J, Abbara S, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of cardiovascular computed tomography guidelines committee. *J Cardiovasc Comput Tomogr*. 2014;8 (5):342–358. https://doi.org/10.1016/j.jcct.2014.07.003.
18. Blanke P, Weir-McCall JR, Achenbach S, et al. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): an expert consensus document of the society of cardiovascular computed tomography. *J Cardiovasc Comput Tomogr*. 2019;13(1):1–20. https://doi.org/10.1016/j.jcct.2018.11.008.
19. Cury RC, Leipsic J, Abbara S, et al. CAD-RADS™ 2.0 - 2022 coronary artery disease-reporting and data system an expert consensus document of the society of cardiovascular computed tomography (SCCT), the American college of Cardiology (ACC), the American college of radiology (ACR), and the North America Society of cardiovascular imaging (NASCI). *J Cardiovasc Comput Tomogr*. 2022;16(6):536–557. https://doi.org/10.1016/j.jcct.2022.07.002.
20. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the evaluation and diagnosis of chest pain: a report of the American college of Cardiology/American Heart Association Joint Committee on clinical practice Guidelines. *Circulation*. 2021;144(22):e368–e454. https://doi.org/10.1161/cir.0000000000001029.
21. Gatti M, Gallone G, Poggi V, et al. Diagnostic accuracy of coronary computed tomography angiography for the evaluation of obstructive coronary artery disease in patients referred for transcatheter aortic valve implantation: a systematic review and meta-analysis. *Eur Radiol*. 2022;32(8):5189–5200. https://doi.org/10.1007/s00330-022-08603-y.
22. Peper J, Becker LM, Berg H van den, et al. Diagnostic performance of CCTA and CT-FFR for the detection of CAD in TAVR Work-Up. *JACC Cardiovasc Interv*. 2022;15 (11):1140–1149. https://doi.org/10.1016/j.jcin.2022.03.025.
23. Sasaki S, Kawamori H, Toba T, et al. Diagnostic accuracy of pre-transcatheter aortic valve replacement nitroglycerin-free fractional flow reserve-computed tomography-based physiological assessment in patients with severe aortic stenosis for predicting post-transcatheter aortic valve replacement ischemia. *Circ J*. 2024;88(4):501–509. https://doi.org/10.1253/circj.cj-23-0312.
24. Becker LM, Peper J, Ginkel DJ van, et al. Coronary CTA and CT-FFR in trans-catheter aortic valve implantation candidates: a systematic review and meta-analysis. *Eur Radiol*. 2024:1–18. https://doi.org/10.1007/s00330-024-11211-7. Published online.
25. Persits I, Layoun H, Kondoleon NP, et al. Impact of untreated chronic obstructive coronary artery disease on outcomes after transcatheter aortic valve replacement. *Eur Heart J*. 2024;45(21):1890–1900. https://doi.org/10.1093/eurheartj/ehae019.
26. Lønborg J, Jabbari R, Sabbah M, et al. PCI in patients undergoing transcatheter aortic-valve implantation. *N Engl J Med*. 2024;391(23):2189–2200. https://doi.org/10.1056/nejmoa2401513.
27. Praz F, Borger MA, Lanz J, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2025;46(44):4635–4736. https://doi.org/10.1093/eurheartj/ehaf194.
28. Tarantini G, Tang G, Fovino LN, et al. Management of coronary artery disease in patients undergoing transcatheter aortic valve implantation. A clinical consensus statement from the European Association of percutaneous cardiovascular interventions in collaboration with the ESC working group on cardiovascular surgery. *EuroIntervention*. 2023;19(1):37–52. https://doi.org/10.4244/eij-d-22-00958.
29. Members WC, Otto CM, Nishimura RA, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease A report of the American college of Cardiology/American heart association joint committee on clinical practice Guidelines. *J Am Coll Cardiol*. 2020;77:e25–e197. https://doi.org/10.1016/j.jacc.2020.11.018. J Am Coll Cardiol 63 2014.
30. Group TDT, Maurovich-Horvat P, Bosserdt M, et al. CT or invasive coronary angiography in stable chest pain. *N Engl J Med*. 2022;386(17):1591–1602. https://doi.org/10.1056/nejmoa2200963.
31. Hussain K, Lee K, Minga I, et al. Real-world application of CCTA with CT-FFR for coronary assessment pre-TAVI: the CT2TAVI study. *Int J Cardiovasc Imag*. 2025;41 (3):523–535. https://doi.org/10.1007/s10554-025-03333-w.
32. Généreux P, Schwartz A, Oldemeyer JB, et al. Transcatheter aortic-valve replacement for asymptomatic severe aortic stenosis. *N Engl J Med*. 2025;392(3): 217–227. https://doi.org/10.1056/nejmoa2405880.
33. Boogert TPW van den, Claessen BEPM, Opolski MP, et al. DEtection of ProxImal Coronary stenosis in the work-up for Transcatheter aortic valve implantation using CTA (from the DEPICT CTA collaboration). *Eur Radiol*. 2022;32(1):143–151. https://doi.org/10.1007/s00330-021-08095-2.
34. Andreini D, Belmonte M, Penicka M, et al. Impact of coronary CT image quality on the accuracy of the FFRCT planner. *Eur Radiol*. 2024;34(4):2677–2688. https://doi.org/10.1007/s00330-023-10228-8.
35. Holmes KR, Fonte TA, Weir-McCall J, et al. Impact of sublingual nitroglycerin dosage on FFRCT assessment and coronary luminal volume–to–myocardial mass ratio. *Eur Radiol*. 2019;29(12):6829–6836. https://doi.org/10.1007/s00330-019-06293-7.