Journal of the Society for Cardiovascular Angiography & Interventions 4 (2025) 102574

JSCAI

The official journal of the Society for Cardiovascular Angiography & Interventions

Comprehensive Review

Coronary Artery Disease and Transcatheter Aortic Valve Replacement

Richard Tanner, MB, BCh [a,b], Sean Gilhooley, MD [a], David Power, MB, BCh [a], Gilbert H.L. Tang, MD, MSc, MBA [c], Annapoorna S. Kini, MD [a], Samin K. Sharma, MD [a,*]

[a] *Mount Sinai Fuster Heart Hospital, Icahn School of Medicine at Mount Sinai, New York, New York;* [b] *Department of Cardiology, Mater Private Network, Cork, Ireland;* [c] *Department of Cardiovascular Surgery, Mount Sinai Health System, New York, New York*

ABSTRACT

Concomitant coronary artery disease (CAD) and severe aortic stenosis (AS) are frequently encountered in patients evaluated for transcatheter aortic valve replacement (TAVR). Invasive coronary angiography remains the mainstay for anatomical assessment of CAD, whereas coronary computed tomography angiography may be used in patients with a low pretest probability of CAD. Adjunctive functional evaluation of coronary lesions has proven safe in the presence of AS, but uncertainty remains over the impact of AS on the results of functional testing. For patients with CAD, revascularization of significant lesions (≥90% stenosis, fractional flow reserve ≤0.80) is associated with improved clinical outcomes compared to medical therapy. However, the optimal timing of percutaneous coronary intervention (PCI) remains unclear with no clear benefit to revascularization in advance of TAVR. When planning post-TAVR PCI, careful consideration should be given to the type of valve implanted, with short-frame valves having more favorable coronary access after TAVR. Planning for future coronary access is particularly relevant for patients who have either unrevascularized obstructive coronary lesions or unknown coronary anatomy in advance of TAVR. Moreover, post-TAVR PCI will likely increase, given the younger age profile of patients being treated and the trend to defer revascularization until after valve replacement.

Introduction

Symptomatic severe aortic stenosis (AS) and coronary artery disease (CAD) frequently coexist. Delineating the relative contribution of each disease to a patient's symptom burden is difficult, given the overlap in symptoms between AS and obstructive CAD. Furthermore, the clinical challenge facing physicians is underlined by the expanding number of transcatheter aortic valve replacements (TAVR) being performed and the uncertainty over the timing and ultimate clinical benefit of coronary revascularization.[1–3] Importantly, patients with complex CAD (unprotected left main, multivessel disease, and Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery [SYNTAX] score >22) were excluded from the pivotal TAVR randomized control trials, making decision-making on coronary revascularization controversial. New evidence has emerged in recent years that can enhance clinical decision-making regarding CAD in patients undergoing TAVR built on limited clinical practice guidelines.[3,4] This contemporary review aims to provide a comprehensive and up-to-date review of the diagnosis, management, and special considerations in the management of CAD among patients undergoing TAVR and redo-TAVR.

Epidemiology

Up to 80% of patients undergoing TAVR have documented CAD, with the incidence varying based on the patient's surgical risk profile (extreme, high, intermediate, low risk) and the criteria used to define CAD.[5–8] In the Placement of Aortic Transcatheter Valves (PARTNER) 1B trial (extreme surgical risk), the frequency of any CAD, prior coronary artery bypass grafting (CABG), and percutaneous coronary intervention (PCI) were 67.6%, 37.5%, and 30.5% respectively.[5] More recently, the PARTNER 3 trial (low surgical risk) reported CAD in 27.6% of TAVR recipients; just 2.5% and 14.2% had a history of CABG and PCI, respectively, in the Evolut Low-Risk trial.[7–9] Thus the trend toward a lower incidence of CAD is occurring in parallel to a progressively younger and less comorbid patient population undergoing TAVR.

Although the frequency of CAD in patients undergoing TAVR is well documented in the literature, the rates of revascularization in patients who have undergone TAVR are not as well-established. In 2 recent studies, the rates of unplanned PCI after TAVR were low, ranging from 0.9% to 2.2% after 10 years of follow-up.[10,11]

Abbreviations: ACS, acute coronary syndrome; AS, aortic stenosis; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CT, computed tomography; FFR, fractional flow reserve; ICA, invasive coronary angiogram; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

Keywords: aortic stenosis; coronary artery disease; revascularization; transcatheter aortic valve replacement.

* Corresponding author: samin.sharma@mountsinai.org (S.K. Sharma).

https://doi.org/10.1016/j.jscai.2025.102574
Received 16 October 2024; Received in revised form 27 October 2024; Accepted 10 January 2025; Available online 11 March 2025

The majority of patients in these studies underwent PCI due to acute coronary syndrome (ACS). Notably, ACS after TAVR, particularly with ST-segment elevation myocardial infarction, has been associated with an increased risk for both in-hospital and 30-day mortality, especially if a noninvasive treatment approach is taken.[12,13] Known predictors of ACS after TAVR include a history of CAD, prior revascularization, male sex, diabetes, and valve-in-valve TAVR.[11,12] More recently, medical management of obstructive CAD (≥90% stenosis or fractional flow reserve [FFR] ≤0.8) in patients subsequently treated with TAVR was found to be associated with an increased risk of myocardial infarction (MI) and the need for urgent revascularization after TAVR.[14] Thus, patients with CAD represent an important subset of patients undergoing TAVR who require individualized assessment and management.

CAD assessment in patients undergoing TAVR

Assessment of CAD is recommended in patients undergoing TAVR in all cases.[3,4] Invasive coronary angiography (ICA) and coronary computed tomography angiography (CCTA) are the modalities of choice for anatomical evaluation of CAD with functional testing frequently being performed when intermediate coronary lesions are found (Table 1).

Table 1. Imaging modalities for CAD assessment in patients with severe AS.

Modality	Advantages	Disadvantages
ICA alone	• Clear anatomical assessment • No blooming artifact as seen with CCTA • Can be done at the time of TAVR (↓ patient visits)	• Invasive procedure • No functional assessment of lesions • Interpretation subject to interobserver variability
ICA + FFR	• Functional assessment of coronary stenosis • Validated in several nonaortic stenosis studies to guide management of intermediate stenosis	• Requires adenosine to induce hyperemia • FFR result may be modified by the presence of aortic stenosis • Requires pressure wire and therapeutic anticoagulation
ICA + iFR	• Functional assessment of coronary stenosis • No vasodilator requirement • iFR less affected by aortic stenosis compared to FFR	• May overestimate coronary stenosis severity • Higher rate of all-cause mortality and major adverse cardiac events at 5-year follow-up compared to FFR
ICA + QFR	• Functional assessment without the need for a wire • No requirement for drug-induced hyperemia • Less patient discomfort and risk of heart block vs FFR	• Diagnostic efficiency ↓ in critical AS (AVA ≤0.6 cm^2) • Up to 20% unsuitable for QFR secondary to poor image quality • Limited supporting evidence in patients with severe AS
CCTA	• Noninvasive • Lower cost compared to ICA • Excellent negative predictive value	• Coronary calcifications limit interpretation • Moderate positive predictive value
CT-FFR	• Functional assessment of coronary stenosis without the need for a pressure wire	• Limited experience with LM stenosis, post CABG or PCI • Reduced accuracy in patients with high calcium burden
Stress echo	• Noninvasive • Concomitant assessment of flow reserve possible	• High dose dobutamine contraindicated in severe AS

AS, aortic stenosis; AVA, aortic valve area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; FFR, fractional flow reserve; ICA, invasive coronary angiogram; iFR, instantaneous wave-free ratio; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio.

ICA

Invasive coronary angiography remains the gold standard for both CAD diagnosis and risk stratification. Given the age profile of patients undergoing TAVR, the frequency of known CAD, and the high incidence of coronary artery calcification, ICA will frequently be superior to CCTA. Furthermore, adjunctive ICA physiology testing can easily be performed and enrich decision-making on coronary revascularization.[2,4] The American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend ICA for patients with an intermediate or high pretest probability of CAD. CCTA may be considered for patients with a low pretest probability of CAD.

Although coronary assessment is recommended before TAVR, the timing of this assessment is not specified in ACC/AHA and European Society of Cardiology (ESC) valvular guidelines.[3,4] In practice, the time interval between ICA and TAVR is highly variable. An increasing number of TAVR centers are performing ICA plus TAVR concomitantly in selected cases, given the associated reduced costs, increased patient convenience, and potential for fewer vascular injuries.[15] This approach is most likely suited to cases with a low pretest probability of significant CAD, preserved left ventricular systolic function, normal renal function, and nonsurgical candidates.

Invasive physiological assessment of CAD

Fractional flow reserve and instantaneous wave-free ratio (iFR) play a critical role in assessing intermediate CAD lesions, and their use has been validated in several non-AS studies.[16–18] Furthermore, iFR and FFR have been found helpful in guiding intervention for patients with severe AS, and the 2020 ACC/AHA valvular heart disease (VHD) guidelines endorse the standard iFR (0.89), FFR (0.80) thresholds for defining significant CAD.[3,19] Meanwhile, the 2021 ESC VHD guidelines cite that FFR of 0.80 has not been validated in patients with AS.[4]

The evidence base for FFR and iFR use in patients with AS is drawn largely from observational studies and 1 recent randomized control trial. Initial concerns regarding the use of wire-guided hemodynamic measurements with vasodilator administration (adenosine) have been addressed by several studies demonstrating the safety of FFR use in the presence of severe AS.[20–24] A reduction in major adverse cardiac events after TAVR when pre-TAVR FFR-guided PCI has been reported in 1 retrospective study.[25] More recently, the Nordic Aortic Valve Intervention (NOTION-3) trial concluded that patients with hemodynamically significant CAD (≥90% stenosis or FFR ≤0.80 in a vessel ≥2.5 mm) treated with PCI (74% pre-TAVR) had a lower rate of death from any cause, MI, or urgent revascularization at a median follow-up of 2 years compared to conservative treatment (26% vs 36%; hazard ratio [HR], 0.71; 95% CI, 0.51-0.99).[14] This composite end point was driven by a lower frequency of urgent revascularization (2% vs 11%; HR, 0.20; 95% CI, 0.08-0.51) and MI (periprocedural and spontaneous) (7% vs 14%; HR, 0.54; 95% CI, 0.30-0.97), with no significant difference in all-cause death (23% vs 27%; HR, 0.85; 95% CI, 0.59-1.23).[14]

One concern with performing FFR in the presence of severe AS is the interaction between AS and coronary artery stenosis, which may influence the hyperemic FFR result.[22,26] AS is associated with increased left ventricle afterload, left ventricle hypertrophy, reduced mean arterial pressure, and reduced coronary flow reserve.[2,22] These changes result in reduced coronary perfusion pressure, microvascular dysfunction, and a blunted response to adenosine as the microvascular bed is already dilated to meet the increase in oxygen demand. One study (n = 54 patients, 133 lesions) demonstrated that patients with a baseline positive FFR had a further reduction immediately after TAVR (0.71 ± 0.11 vs 0.66 ± 0.14). In contrast, patients with a normal pre-TAVR FFR saw an increase in FFR after valve replacement (negative FFR values improved after TAVR [0.92 ± 0.06 vs 0.93 ± 0.07]).[23] Conversely, a more recent study

(n = 40 patients, 50 lesions) compared FFR pre-TAVR with FFR results 6 months after TAVR and found that FFR had not significantly changed at follow-up (0.84 [0.81-0.89] vs 0.86 [0.78-0.90]; $P = .72$).[27] Thus, the impact of AS on FFR results remains unclear, and studies on invasive physiology testing have been limited to small cohorts of patients.

Instantaneous wave-free ratio offers an alternative to FFR with potentially less variability and obviates the need for pharmacologic hyperemia with vasodilators. A number of studies have demonstrated that unloading the ventricle with TAVR does not significantly change the iFR result.[22,28,29] One of these studies examined the impact of severe AS on microcirculation and assessed if concomitant CAD influenced this. In the group with severe AS (n = 55), TAVR significantly increased microvascular resistance (independent of coronary stenosis severity). Microvascular resistance also improved in the group with no AS undergoing PCI (n = 85), with the improvement in microvascular resistance post-TAVR being equivalent to that produced by stenting coronary lesions with an iFR of 0.74. Thus, the authors suggest that PCI may be reserved for those undergoing TAVR with an intermediate coronary stenosis that has an iFR of <0.74, as this stenosis is likely the predominant lesion affecting microvascular resistance.[30] However, the iFR threshold to guide PCI has been derived from 1 study, with significant differences in baseline characteristics between groups. Thus, further validation is required.

Discordance between FFR and iFR readings in patients with severe AS is more common than in patients without AS (29% vs 14%-20%).[31–33] Furthermore, 1 study that compared iFR and FFR in severe AS with concomitant CAD found that negative discordance was the predominant subgroup (iFR ≤0.89 and FFR >0.80) (45 out of 48 discordant cases), which differs from the more equal distribution between positive and negative discordance in patients without AS. In addition, LAD lesions and very severe AS (peak velocity ≥5 m/s), were independently associated with negative discordance.[32] A recent retrospective study compared iFR and FFR in patients with (n = 293) and without (n = 1882) severe AS. The incidence of a significant FFR (≤0.80) was similar in patients with and without severe AS (45.3% vs 43.9%, $P = .6$), whereas a significant iFR was more common in patients with severe AS compared to those without AS (66.6% vs 31.8%, $P < .001$). Moreover, among those with severe AS, 36.2% had an iFR ≤0.89, but an FFR >0.80. Importantly, for patients in this discordant group, an iFR ≤0.89 did not carry a risk of deferred lesion failure. This is in contrast to untreated lesions with an FFR ≤0.80, where there was a significant risk of deferred lesion failure (adjusted HR, 2.71; 95% CI, 1.08-6.80; $P = .034$).[34]

In summary, several questions remain unanswered despite the significant investigations into using FFR and iFR in patients with severe AS. NOTION-3 is the first randomized control trial to indicate a potential benefit to FFR-guided PCI over conservative treatment, with the primary end point just reaching the threshold for statistical significance ($P = .04$). Ongoing trials include Functional Assessment In TAVI (FAITAVI; NCT03360591) (FFR-guided vs angiographic-guided PCI, and FFR compared with iFR), and the TransCatheter Valve and Vessels Trial (TCW; NCT03424941) (FFR-guided PCI + TAVR vs CABG + surgical aortic valve replacement [SAVR] for multivessel disease) will help clarify the role of FFR-guided PCI among patients treated with TAVR.

CCTA

In patients with AS, CCTA is recommended for coronary assessment when there is a low pretest probability of CAD.[3,4] Advantages to CCTA include forgoing the risks associated with ICA, reduced cost, and potentially improved workflow as CCTA can be combined with standard multislice computed tomography (CT) for TAVR evaluation, in select patients. Furthermore, no difference in clinical outcomes was observed at 30 days and 1 year compared to when ICA was used.[29] However, AS is frequently associated with coronary artery calcification, which often limits the interpretation of lumen stenosis due to blooming artifacts.[35] Furthermore, artifacts can also result from prosthetic material in the heart and chest. A recent meta-analysis (n = 7000, 27 studies) reported a pooled sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of 95%, 73%, 97%, and 64%, respectively, when using CCTA in diagnosing obstructive CAD.[36] Thus, the strength of CCTA is the NPV, which is why it is best reserved for patients with a low pretest probability of CAD. Notably, this study only included patients with a coronary calcium score <400 and excluded those with prior CABG or PCI.[37] More recently, a study (N = 2217) examined the efficacy of using a patient's pre-TAVR multislice CT (noncoronary dedicated CT scanning) to screen for significant left main or proximal CAD stenosis in patients with no prior PCI.[38] Using a ≥70% stenosis cutoff, the analysis found a sensitivity of 91%, specificity of 97%, PPV of 83%, and NPV of 99% for proximal stenosis. In addition, this approach for assessing bypass graft patency revealed a sensitivity of 86%, specificity of 97%, PPV of 84%, and NPV of 98%. Reassuringly, only 3 patients required revascularization within 1 year of TAVR. Finally, ultrahigh-resolution CT promises to improve spatial resolution, mitigate artifacts from calcium, and improve visualization of stented and small vessels.[39–41] In 1 of these studies, a high degree of accuracy was seen in patients with severe CAD (mean calcium score of 1205) when compared to ICA: ultrahigh-resolution CT had a specificity of 88%.[40]

Coronary computed tomography angiography may serve as a superior predictor of obstructive CAD when compared to traditional functional testing modalities.[42,43] There have been multiple randomized control trials demonstrating the prognostic value of CCTA, and its ability to predict future cardiovascular events.[44,45] In a study examining the 5-year follow-up of the Scottish Computed Tomography of the Heart trial, CCTA was found to significantly reduce the incidence of MI and death due to ischemic heart disease without increasing the use of invasive testing, when compared to standard of care.[46,47] The Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial further demonstrated the prognostic superiority of CCTA compared to traditional functional testing modalities, especially in patients with type 2 diabetes mellitus.[44,48]

Noninvasive functional measurements

Coronary computed tomography angiography with adjunctive FFR (CT-FFR) offers a noninvasive modality for assessing the functional significance of coronary stenosis and further informs discussion on the need for revascularization. The CAST-FFR study (N = 42) found CT-FFR to be safe and feasible, and CT-FFR results strongly correlated with measured FFR in patients with severe AS ($r = 0.64$; $P < .0001$).[49] Importantly, this study excluded patients with prior CABG, PCI in the vessel of interest, left ventricular ejection fraction (LVEF) <30%, left main stenosis, and MI in the prior 3 months. Furthermore, the correlation between FFR and CT-FFR was strongest ($r = 0.85$) in patients with lower coronary calcium scores. A second study (N = 338) found that CT-FFR increased the diagnostic accuracy of standard CCTA and increased the number of patients in whom ICA could be safely avoided (43.6% vs 57.1%).[50] In this retrospective study, CCTA and CT-FFR had a sensitivity of 76.9% and 84.6%, specificity of 64.5% and 88.3%, NPV of 92.1% and 96.0%, and PPV of 34.0% and 63.2%, respectively. Notably, the incidence of CAD in this study was low (23%) relative to typical TAVR studies, which may have increased the NPV and reduced the PPV.

Quantitative flow ratio (QFR) represents an alternative noninvasive modality for functional assessment of coronary stenosis using data from the ICA. Compared with invasive FFR, this technique detected CAD lesions causing myocardial ischemia at similar rates (46% vs 40% for < 0.80, respectively, $P = .315$).[51] Furthermore, the use of a QFR-guided PCI strategy has been associated with improved clinical outcomes compared with standard angiographic guidance.[52] Notably, a recent retrospective study (N = 318) found that patients with medically

managed CAD who subsequently underwent TAVR had a significantly higher mortality risk at 3-year follow-up if they had a QFR significant stenosis compared to a QFR negative stenosis (51.1% vs 12.1%; $P < .001$).[53] However, QFR is not as extensively studied as FFR/iFR in the assessment of intermediate coronary lesions, and limited evidence suggests that the accuracy of QFR is reduced in critical AS (aortic valve area ≤ 0.6 cm^2).[54] Finally, up to 20% of ICA may not be suitable for QFR analysis due to image quality and overlapping anatomy.[55]

Management of CAD in patients undergoing TAVR

Since TAVR was introduced, there has been uncertainty over the management of concomitant CAD. For patients treated with SAVR, revascularization of lesions with $\geq$70% stenosis is routinely performed at the time of aortic valve replacement.[3,56] This is supported by evidence showing that patients with untreated, significant CAD had a higher risk of adverse perioperative and long-term outcomes after valvular heart surgery.[56,57] Notably, both of these studies are retrospective, and adjustment for comparisons between groups can never be perfect. Meanwhile, the impact of performing PCI in addition to TAVR is unclear and may be impacted by CAD complexity. We present a practical algorithm (Figure 1) for managing CAD in patients undergoing TAVR.

Argument for medical management alone for CAD

The overlap in symptoms between severe AS and CAD makes drawing a definite conclusion on the contribution of CAD to the overall symptom burden near impossible. Furthermore, in the presence of AS, angina from CAD may be exacerbated by reduced coronary perfusion pressure owing to an elevated left ventricular diastolic pressure. In clinical trials, PCI has never demonstrated a reduction in all-cause mortality compared to optimal medical therapy (OMT) among patients with chronic coronary syndrome (CCS), including those with moderate or severe ischemia and/or severe left ventricular systolic dysfunction.[58–60] Furthermore, despite some studies finding CAD to be associated with an increased risk of mortality post-TAVR, revascularization by PCI has failed to mitigate this risk.[61,62] Hence, in keeping with PCI for stable CAD in patients without VHD, the primary role of PCI should be to alleviate ischemic symptoms refractory to medical therapy and/or valve replacement. Finally, deferring PCI until after TAVR removes the need for dual antiplatelet therapy, which may increase the risk of bleeding complications during and after the procedure.

An argument in favor of revascularization

The addition of CABG to SAVR for patients with $\geq$50% CAD stenosis has been found to offer a mortality benefit beyond 1 year of the procedure.[56] For patients undergoing TAVR with concomitant CAD, the role of PCI is often extrapolated from studies that examined PCI vs OMT for patients with isolated CCS. However, this approach is limited as many such patients were excluded from these pivotal trials. In the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial, patients with significant left main stenosis were excluded, and the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial excluded patients with an LVEF <30%, markedly positive stress test, and those with coronary anatomy "not suitable" for PCI.[58,59] Meanwhile, the Surgical Treatment for Ischemic Heart Failure (STICH) trial found that revascularization (with CABG) reduced the risk of all-cause death and hospitalization in patients with ischemic cardiomyopathy (3-vessel disease) and LVEF of <35% at the 10-year follow-up.[63] The randomized NOTION-3 trial (n = 455) provides the most compelling evidence for revascularization of significant stenosis (FFR $\leq$0.80 or $\geq$90% stenosis, low complexity lesions) rather than conservative treatment. PCI was associated with a significant reduction in the frequency of urgent revascularization and MI in the 2 years after TAVR.[14]

Mode of revascularization

Although revascularization can only be achieved through PCI or CABG, there are many nuances in the decision-making process. Important considerations for the Heart Team include coronary disease complexity, comorbidities, diabetic status, conduit availability, frailty, left ventricular systolic function, ability to achieve complete revascularization, and patient wishes. Current ACC/AHA guidelines for the management of VHD recommend (2a, C-LD) choosing SAVR + CABG over TAVR + PCI in patients with significant CAD consisting of bifurcation left main and/or multivessel CAD with a SYNTAX score >33.[3] Revascularization with PCI is considered reasonable for patients with isolated significant left main or proximal vessel CAD (2a, C-LD). Studies in patients without AS support these recommendations, showing the superiority of CABG to PCI in patients with multivessel disease, especially if diabetes is present.[64,65] However, in clinical practice, many patients with complex coronary disease are not surgical candidates or decline the Heart Team recommendation for SAVR + CABG. A propensity-matched analysis with 156 matched pairs from 2021 attempted to address this issue by comparing clinical outcomes between TAVR + PCI (within 3 months preceding TAVR and concomitantly) and SAVR + CABG among patients with complex CAD (unprotected left main or SYNTAX score >22). A similar proportion of patients had left main lesions in both groups (57.1% vs 55.8%), and complete revascularization was more common in the SAVR + CABG group (96%) compared to the TAVR + PCI group (50%). At a median follow-up of 3 years, there were no significant differences in all-cause mortality, MI, and stroke.[66] A caveat to these findings was the observation that reintervention was higher in those who received PCI at 2 years (24.4% vs 4.1; $P = .002$), and a landmark analysis at 30 days showed SAVR + CABG to be associated with a lower rate of major adverse cardiovascular and cerebrovascular events (MACCE) and all-cause mortality.[66] Furthermore, a recent meta-analysis (N = 104,220) found that TAVR + PCI was associated with a higher risk of all-cause mortality and a need for additional coronary revascularization at the weighted follow-up of 30.2 months (HR, 1.35; 95% CI, 1.11-1.65; $P = .003$ and HR, 4.14; 95% CI, 1.74-9.86; $P = .001$, respectively). However, it should be noted that a heterogeneous cohort of patients was included; 6 of the 8 studies were observational, and the time interval between PCI and TAVR was variable (up to 12 months before concomitant).[67]

For now, SAVR + CABG appears to be the optimal treatment strategy for patients with a high SYNTAX score (>33) who are at low or intermediate surgical risk (STS <8) (Central Illustration). In comparison, when the surgical risk is high (STS >8), TAVR + PCI is usually the preferred option, accepting that complete revascularization becomes less likely as the SYNTAX score increases. The Heart Team should guide the decision between the surgical and percutaneous approach for intermediate and low-risk surgical patients with a SYNTAX score <33.[1] Patients with severe AS, multivessel disease, and impaired left ventricular systolic function may also benefit from revascularization with CABG rather than PCI. This is supported by the STICH trial and a large Canadian cohort study (N = 12,113), which found that patients treated with PCI had a higher rate of major adverse cardiac events (HR, 2.0; 95% CI, 1.9-2.2) and all-cause mortality (HR, 1.6; 95% CI, 1.3-1.7) compared to CABG.[63,68] Furthermore, PCI was not superior to medical therapy in the REVIVED trial, suggesting that CABG may be the only beneficial revascularization strategy in cases of reduced LVEF.[60]

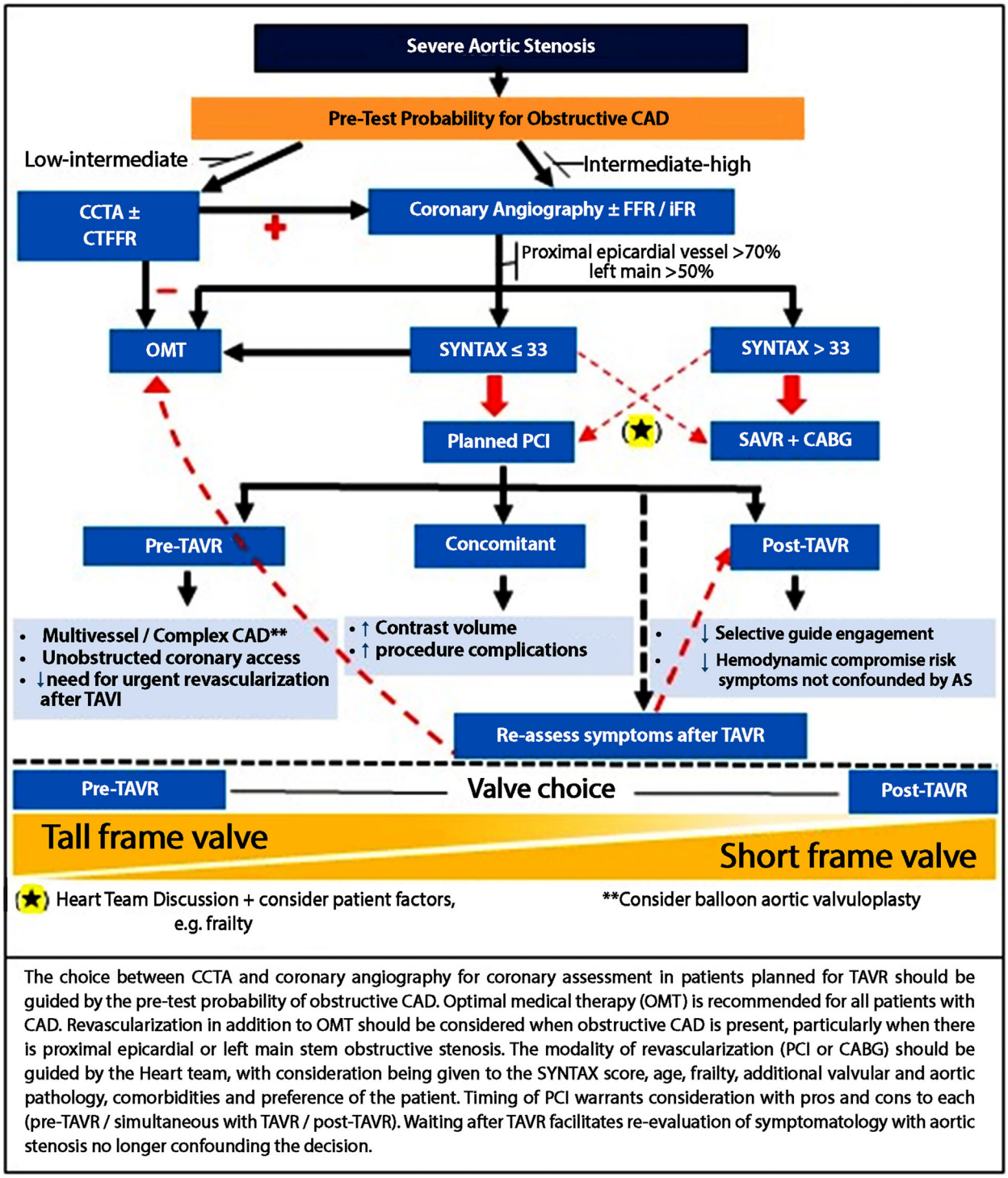
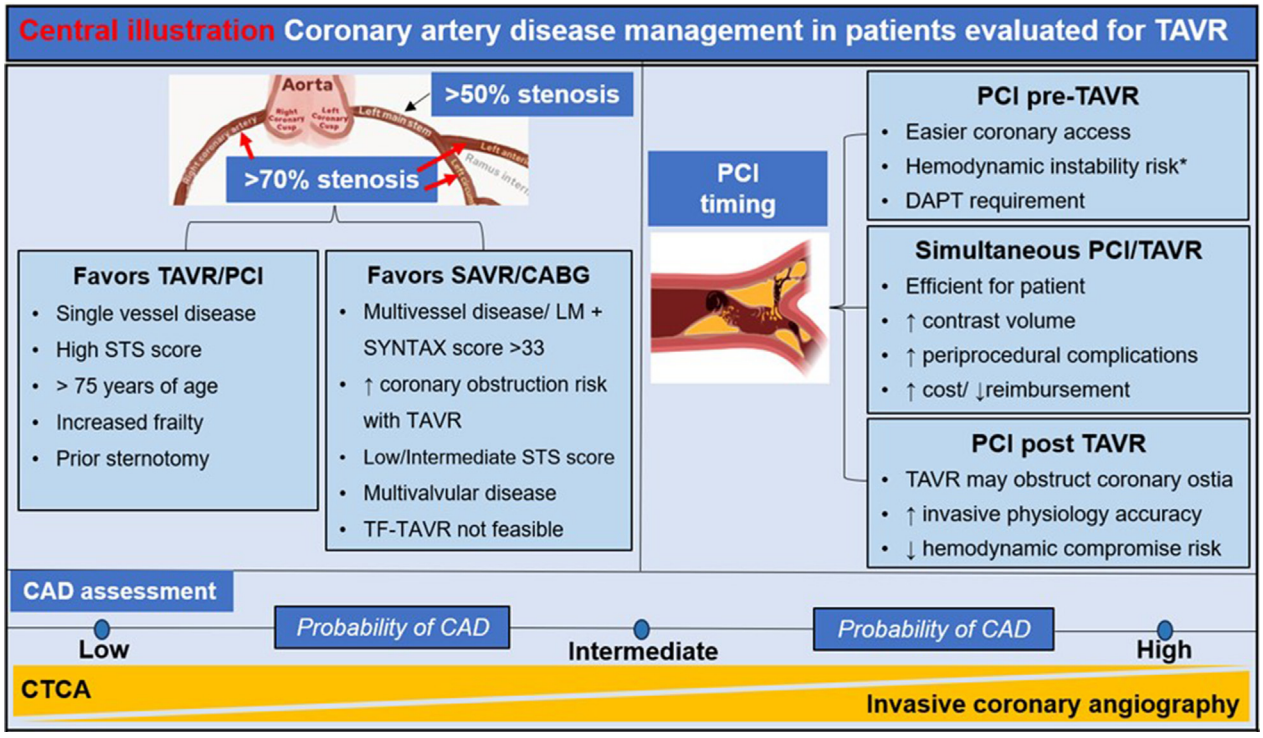


Figure 1.
Proposed algorithm for the management of coronary artery disease (CAD) in transcatheter aortic valve replacement (TAVR). CABG, coronary artery bypass grafting; CCTA, coronary computed tomography angiography; CT-FFR, computed tomography–derived fraction flow reserve; FFR, fraction flow reserve; iFR, instantaneous wave-free ratio; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; SYNTAX score, Synergy between PCI with Taxus and Cardiac Surgery Trial score.

PCI timing in TAVR patients

Approximately 25% of patients treated with TAVR also undergo PCI before, during, or after TAVR.[69] However, the timing of PCI in relation to TAVR is not specified in these current clinical guidelines, and each approach has advantages and disadvantages (Central Illustration). Notably, in a meta-analysis of 5580 patients, no difference in 30-day outcomes (all-cause mortality, stroke, acute kidney injury [AKI]) was seen between patients undergoing TAVR + PCI (pre or concomitantly) and those treated with TAVR alone.[70] Contemporary registry data indicate that pre-TAVR PCI remains the preferred strategy (65% of cases in the Management of myocardial REVASCularization in patients undergoing TAVR with coronary artery disease [REVASC-TAVI] registry).[71]



Central Illustration.

Coronary artery disease (CAD) management in patients evaluated for transcatheter aortic valve replacement (TAVR). *During complex PCI/with PCI complications. CABG, coronary artery bypass grafting; CCTA, coronary computed tomography angiography; DAPT, dual antiplatelet therapy; LM, left main; LVEF, left ventricle ejection fraction; PCI, percutaneous coronary intervention; TF, transfemoral; SAVR, surgical aortic valve replacement; STS, society of thoracic surgeons; SYNTAX Score, Synergy between PCI with Taxus and Cardiac Surgery Trial Score.

PCI before TAVR

Patients presenting with ACS and AS carry the same indication for ICA ± revascularization as patients without AS.[3] When patients present with CCS or asymptomatic obstructive CAD on pre-TAVR ICA or CCTA, the appropriate management is less clear. Traditionally, clinicians have favored revascularization before TAVR, given concerns for ischemic complications during rapid ventricular pacing and potentially challenging coronary reaccess after TAVR placement.[72,73] However, several studies have failed to show a clinical benefit to performing PCI over OMT in patients ultimately treated with TAVR.[10,66,74,75] A limitation to some of these studies is that patients who became asymptomatic after PCI despite having severe or critical AS may have been excluded as clinical practice guidelines only recommend aortic valve replacement for symptomatic AS.

The randomized PercutAneous Coronary inTervention prIor to transcatheter aortic VAlve implantaTION (ACTIVATION) trial failed to show a benefit of PCI of significant CAD (>70% major epicardial vessel or >50% if protected left main or vein graft) over OMT (7.5% noninferiority margin) in advance of TAVR. Notably, this trial was terminated early, with lower than anticipated enrollment (n = 234) and the majority of patients had no angina at baseline (>68%).[62] Conversely, the recent NOTION-3 trial found that revascularization was associated with lower rates of urgent revascularization and MI after TAVR compared to conservative treatment. Although 74% of PCI procedures were done before TAVR in this trial, an analysis of PCI timing on clinical outcomes was not an objective of this study.

A caveat to forgoing PCI until after TAVR is the challenge that the new valve prosthesis can present to catheter engagement of the coronary ostia. This is particularly relevant when a tall frame TAVR is planned, and the coronary disease is complex.

Concomitant PCI and TAVR

Performing PCI at the same time as TAVR has the inherent advantage of a single procedure, hospital admission, and better use of hospital resources. However, PCI extends the duration of the TAVR procedure, and managing antiplatelet therapy can be challenging if the TAVR is complicated by vascular injury. Among 22,334 TAVR performed between 2011 and 2013 and entered into the Nationwide Inpatient Sample, 2.7% (n = 608) underwent PCI + TAVR during the same hospitalization. Patients in the matched analysis treated with TAVR + PCI experienced higher in-hospital mortality (10.7% vs 4.6%, $P = .008$), and vascular injury requiring surgery was more common (8.5% vs 4.2%, $P < .001$).[76] Notably, this study did not differentiate between PCI performed concomitantly with TAVR and staged in-hospital PCI. Contrast-associated nephropathy remains a concern given the higher volume of contrast required and studies have produced conflicting results on this risk.[71,77,78] An analysis from the National Readmissions Database (2016 to 2019) found that concomitant PCI and TAVR were associated with lower rates of AKI and 90-day readmission compared with PCI shortly after TAVR (<30 days).[77] Moreover, a separate analysis from the National Readmissions Database found lower rates of AKI in patients undergoing concomitant PCI compared to PCI at a later date. However, those treated with concomitant TAVR and PCI were more likely to have single-vessel disease and better baseline renal function.[78]

PCI after TAVR

Coronary revascularization after TAVR has the advantage of less risk of hemodynamic compromise during PCI, and AS no longer confounds the diagnosis of angina due to CAD. In addition, invasive physiologic

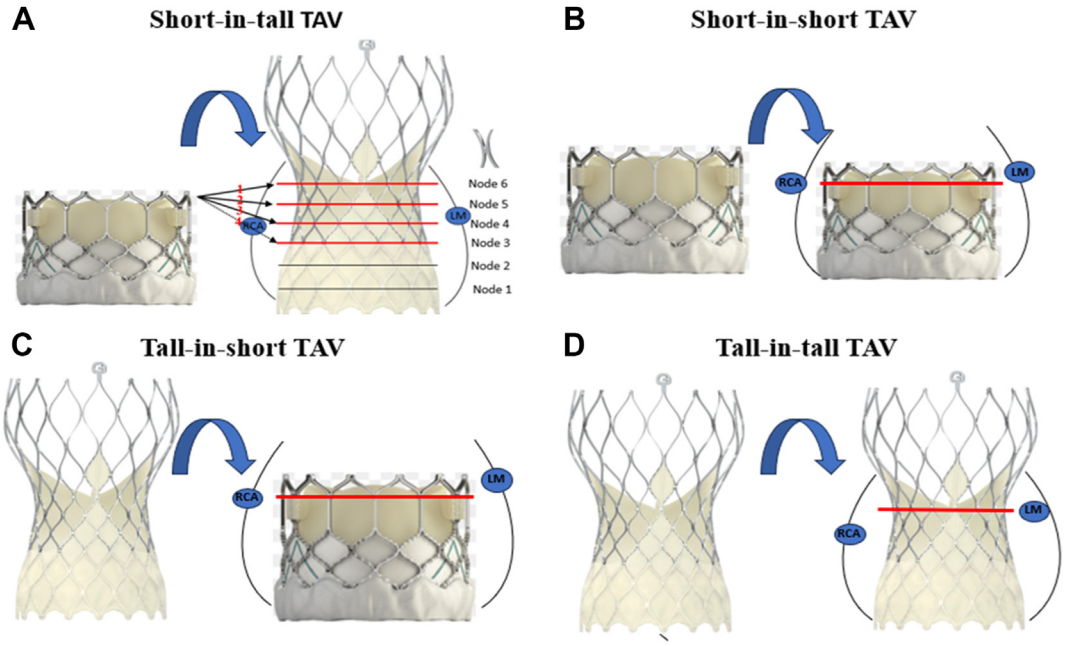


Figure 2.
Neoskirt concept in redo-TAVR. Neoskirt = covered tube formed when the index TAV leaflets are pinned open by the second transcatheter aortic valve (TAV). Neoskirt height depends on the redo-TAV combination (A-D) and the implant depth of the index and second valve (A, Nodes 3-6). Coronary access is not possible through the valve frame below the top of the neoskirt (red line on A-D). TAVR, transcatheter aortic valve replacement.

testing may be more reliable. On the other hand, engaging the coronary ostia can be challenging and occasionally not feasible, particularly when tall frame valves are used.[79,80] An analysis from the international, multicenter REVASC-TAVI registry compared clinical outcomes between patients treated with PCI pre (n = 1052), during (n = 157) and post (n = 1052) TAVR.[71] CAD complexity was similar between groups, except bifurcation lesions were more common in those treated with PCI after TAVR. At the 2-year follow-up, the composite outcome of all-cause death, stroke, MI, and heart failure rehospitalization was significantly lower in patients undergoing PCI after TAVR compared with PCI before or concomitantly (17.4% vs 30.4% vs 30.0%, $P < .01$). The lower incidence of the composite outcome was driven by lower all-cause death (6.8% vs 20.6% vs 20.1%, $P < .01$) between groups. These findings align with another recent observational study (n = 144) in which PCI pre-TAVR was associated with a higher rate of stroke and lower major adverse cardiac and cerebral events-free survival at 24 months compared to post-TAVR PCI.[81] The TAVI-PCI trial (NCT04310046) is currently randomizing patients planned for an SAPIEN transcatheter heart valve (Edwards Lifesciences) to angiographic-guided PCI before (1-45 days) or after TAVR (1-45 days) and will help clarify the optimal timing of PCI in the per-TAVR period. Finally, The Staged Complete Revascularization for Coronary Artery Disease versus Medical Management Alone in Patients with AS Undergoing Transcatheter Aortic Valve Replacement (COMPLETE TAVR; NCT04634240) is randomizing patients after TAVR with significant CAD to PCI (1-45 days) or medical therapy alone. This trial aims to enroll 4000 patients and should significantly enhance the understanding of CAD in patients with severe AS.

In summary, although there are no guidelines as to when PCI should be performed in patients undergoing TAVR, the currently available evidence suggests no improvement in clinical outcomes when PCI is performed before TAVR compared to post-TAVR.

Coronary access after TAVR

Coronary access after TAVR is a crucial consideration, given the high prevalence of CAD in patients undergoing TAVR. Within the first year after TAVR, approximately 2% of patients will undergo ICA, increasing to 16% at 5 years.[80,82] The Swedish Transcatheter Cardiac Intervention Registry recently reported that 5.8% of patients required an ICA at a median follow-up of 841 days (IQR, 346-1457 days) with non-ST elevation ACS (45.8%), CCS (30.3%) and ST-segment elevation MI (6.9%) being the most frequent indications. Furthermore, as the indications for TAVR extend to a younger cohort of patients, there will be a more significant number of years at risk for the progression of CAD and ACS.[6] Special consideration needs to be given to patients treated with a valve-in-valve procedure (TAVR-in-TAVR and TAVR in surgical bioprostheses) given that the additional bioprosthetic material will likely further hinder coronary access.[83]

Valve type and position

The type of TAV implanted impacts coronary access. The short-frame SAPIEN 3 valves (Edwards Lifesciences) have an expanded frame height of 15.5 mm to 22.5 mm compared to the 45 mm height of the Evolut family (Medtronic) of valves and 47 to 48 mm height of Navitor (Abbott). In addition, the Evolut valves have supraannular leaflets, and the commissural posts stand at 26 mm. The intraannular Navitor valve has commissural post heights ranging from 21 to 25 mm, with larger cell sizes than the Evolut FX valve. Hence, coronary access in patients with tall frame valves will almost be exclusively through the cell struts. In contrast, the coronary ostia can often be accessed above rather than through the short-frame valves.

Many clinicians intentionally implant TAV high relative to the aortic annulus in an effort to reduce interaction with the membranous septum which may lead to conduction disturbances and the need for permanent pacemaker insertion. However, high TAV replacement may impede coronary access, particularly when tall frame valves are used.[79,84] This issue can be exacerbated in cases where commissural alignment is not achieved during valve deployment.[84–87] In the Reobtain Coronary Ostia Cannulation Beyond Transcatheter Aortic Valve Stent (RE-ACCESS) study, unsuccessful coronary ostia cannulation occurred in 23 cases (7.7%) and almost exclusively in Evolut R/PRO valves (22 of the 23

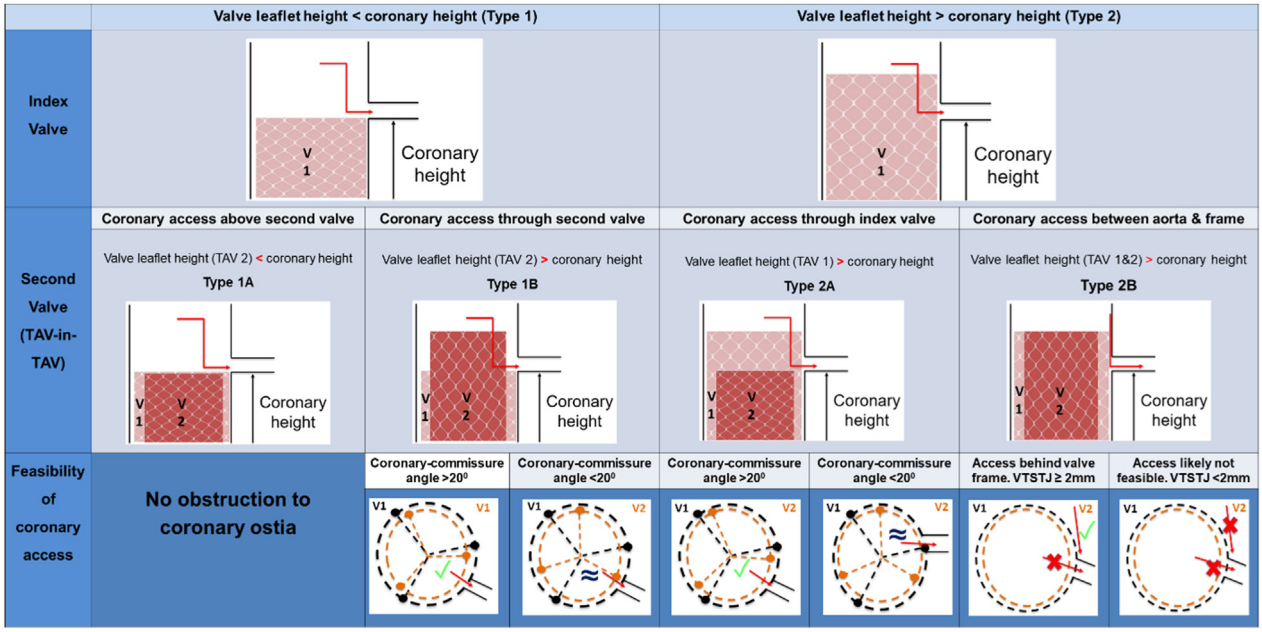


Figure 3.
Classification of transcatheter aortic valve (TAV) position in relation to coronary height and the related feasibility of coronary access after redo-TAVR. Coronary height, measured height from the aortic annulus to the inferior border of the coronary ostium; V1, first valve; V2, second valve. Symbols: Green tick, straightforward coronary access; Blue equals sign, coronary access with immediate difficulty; Red X, coronary access not feasible; Red arrow, catheter enlargement pathway.

cases).[79] Independent predictors of inability to cannulate the coronaries were the use of an Evolut R/PRO TAV (odds ratio [OR], 29.6; 95% CI, 2.6-335; $P < .01$), mean TAVR depth (OR, 1.7 per 1 mm decrease; 95% CI, 1.3-2.3; $P < .01$) and sinus of Valsalva oversizing (OR, 1.1 per 1 mm increase; 95% 1.0-1.2, $P < .01$).[79] A model combining these factors was able to predict with high accuracy the risk of unsuccessful coronary ostia cannulation (area under the curve, 0.94; $P < .01$). In the RE-ACCESS 2 study, the rate of unsuccessful coronary cannulation in patients treated with self-expanding (Evolut R/PRO/PRO+, ACURATE neo2 [Boston Scientific]) valves using a commissural alignment technique reduced to 5.5% and the rate of selective coronary ostia cannulation increased significantly.[88] Conversely, in the retrospective Acute Myocardial Infarction After Transcatheter Aortic Valve Implantation (AMITAVI) registry, PCI of native coronary arteries (N = 258) was successful in 91.4% of cases, independent of TAV type.[89] Importantly, in the 6 cases that guide engagement was unsuccessful, 3 required CABG, and 3 patients died.

To help overcome these challenges clinicians have described catheter engagement techniques specific for each valve with the aim of mitigating the frequency of guide engagement failure.[90] Operator experience, and the use of adjunct equipment such as guide catheter extension increase the rate of success in challenging cases. Moreover, as TAV commissural alignment and subsequent coronary artery engagement are inherently linked, all manufacturers are now focusing on improving their delivery systems and refining implantation techniques to reduce the frequency of commissural misalignment.[85,86,91]

Special considerations: valve-in-valve

Unique to redo-TAVR is the formation of a neoskirt that extends from the inflow of the index valve to the top of the commissural posts as the old leaflets are pinned open, forming a tube graft (Figure 2).[80,92,93] The

Table 2. Upcoming trials on CAD assessment and treatment in patients undergoing TAVR.

Study	Trial design (sample size)	Description	Patient population	Primary outcome	Completion date
FAITAVI (NCT03360591)	RCT (N = 320)	Angiography-guided vs physiology (FFR/iFR) guided PCI	CAD and severe AS undergoing TAVR, >50% stenosis (FFR: 0.8)	1-year composite of all-cause mortality, MI, stroke, major bleeding events, and TVR	2024
TCW trial (NCT03424941)	RCT (N = 328)	FFR-guided PCI + TAVR vs CABG + SAVR	Multivessel CAD (≥2 lesions), severe AS, >50% diameter stenosis	1-year composite of all-cause mortality, MI, disabling CVA, unscheduled TVR, valve reintervention, and life-threatening or disabling bleeding	2024
COMPLETE TAVR (NCT04634240)	RCT (N = 4000)	Staged complete revascularization after TAVR (with BEV) vs medical management	CAD undergoing TAVR, > 70% diameter stenosis (in a native vessel with ≥2.5 mm diameter)	Composite of CV death, new MI, ischemia-driven revascularization, or hospitalization for unstable angina/HF after 3.5 years	2026
TAVI-PCI (NCT04310046)	RCT (N = 986)	iFR-guided complete revascularization pre-TAVR (1-45 days) vs post-TAVR (days 1-45)	> 90% diameter stenosis or iFR ≤0.89	1-year composite of all-cause mortality, nonfatal MI, ischemia-driven revascularization, rehospitalization, and life-threatening/disabling bleed	2028

AS, aortic stenosis; BEV, balloon-expandable valve; CABG, coronary artery bypass graft; CAD, coronary artery disease; CV, cardiovascular; CVA, cerebrovascular accident; FFR, fractional flow reserve; HF, heart failure; iFR, instantaneous wave-free ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCT, randomized control trial; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; TVR, target vascular revascularization.

clinical importance of the neoskirt plane is highlighted in 1 study that found the neoskirt extending above the coronary ostia in 90% of CoreValve/Evolut TAV cases and 67% of SAPIEN 3 cases.[94] Hence, when the neoskirt extends above the coronary risk plane (level of lowest coronary ostia), engaging the coronary may be challenging if the sinotubular junction (STJ) is large (valve to STJ/aorta >2 mm) or near impossible if STJ is small (valve to STJ/aorta <2 mm) (Figure 3).[2] In patients with a prior SAV, the height of the surgical bioprosthetic leaflet determines the neoskirt height, and the leaflets can be displaced more toward the coronary ostia. Unlike in a TAV, a valve frame does not restrict the displacement of SAV leaflets, particularly in valves with externally mounted leaflets.[2] Having an SAV as the index valve should, however, have the advantage of resected native leaflets and commissural alignment.

Future perspectives

In light of the increasing number of patients treated with TAVR worldwide, delineating the most efficient assessment and optimal management of concomitant CAD remains a priority. Although ICA remains the mainstay of the evaluation for CAD, CCTA has proven to have an excellent NPV in patients with a low pretest probability of CAD. Furthermore, recent evidence has suggested that a patient's pre-TAVR CCTA can rule out proximal obstructive CAD with high sensitivity, specificity, and NPV. Moreover, in the future, ultrahigh-resolution CCTA will mitigate the effect of blooming calcium artifacts and increase the proportion of patients who can be assessed with CCTA rather than ICA. Several questions remain regarding the role and interpretation of invasive physiology testing in patients with intermediate stenosis on ICA. The FAITAVI and the TCW trials will help clarify if invasive physiology-guided PCI is superior to angiographic-guided PCI in patients with severe AS (Table 2). A degree of equipoise remains over timing and the need for revascularization of obstructive coronary disease in patients planned for TAVR.

Conclusion

Physicians will continue to face challenges in managing obstructive CAD in patients undergoing TAVR. However, recent evidence has helped clarify the safety of functional testing in the presence of severe AS. Furthermore, there is now evidence that PCI, compared to conservative treatment, reduces the rate of adverse clinical outcomes after TAVR. Finally, clinical judgment is needed when deciding on the timing of PCI, with coronary disease severity, complexity, and the planned prosthesis type being key considerations.

Declaration of competing interest

Gilbert H.L. Tang has received speaker's honoraria and served as a physician proctor, consultant, advisory board member, TAVR publications committee member, APOLLO trial screening committee member, and IMPACT MR steering committee member for Medtronic, has received speaker's honoraria and served as a physician proctor, consultant, advisory board member and TRILUMINATE trial anatomic eligibility and publications committee member for Abbott Structural Heart, has served as an advisory board member for Boston Scientific and JenaValve, a consultant for NeoChord, Shockwave Medical, Peija Medical and Shenqi Medical Technology, and has received speaker's honoraria from Siemens Healthineers. Richard Tanner, Sean Gilhooley, David Power, Annapoorna S. Kini, and Samin K. Sharma reported no financial interests.

Funding sources

This work was not supported by funding agencies in the public, commercial, or not-for-profit sectors.

Ethics statement and patient consent

The authors retrieved and synthesized data from previously published studies; therefore, no ethical approval was required or obtained.

References

1. Del Portillo JH, Farjat-Pasos J, Galhardo A, et al. Aortic stenosis with coronary artery disease: SAVR or TAVR-when and how? *Can J Cardiol*. 2024;40(2):218–234. https://doi.org/10.1016/j.cjca.2023.09.023
2. Tarantini G, Tang G, Nai Fovino L, 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
3. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143(5):e35–e71. https://doi.org/10.1161/CIR.0000000000000932
4. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Article in Italian. *G Ital Cardiol (Rome)*. 2022;23(5 Suppl 1):e1–e75. https://doi.org/10.1714/3787.37722
5. 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
6. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374(17):1609–1620. https://doi.org/10.1056/NEJMoa1514616
7. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med*. 2019;380(18):1695–1705. https://doi.org/10.1056/NEJMoa1814052
8. Arnold SV, Petrossian G, Reardon MJ, et al. Five-year clinical and quality of life outcomes from the CoreValve US Pivotal Extreme Risk Trial. *Circ Cardiovasc Interv*. 2021;14(6):e010258. https://doi.org/10.1161/CIRCINTERVENTIONS.120.010258
9. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med*. 2019;380(18):1706–1715. https://doi.org/10.1056/NEJMoa1816885
10. Stefanini GG, Cerrato E, Pivato CA, et al. Unplanned percutaneous coronary revascularization after TAVR: a multicenter international registry. *JACC Cardiovasc Interv*. 2021;14(2):198–207. https://doi.org/10.1016/j.jcin.2020.10.031
11. Okuno T, Demirel C, Tomii D, et al. Long-term risk of unplanned percutaneous coronary intervention after transcatheter aortic valve replacement. *EuroIntervention*. 2022;18(10):797–803. https://doi.org/10.4244/EIJ-D-22-00342
12. Faroux L, Munoz-Garcia E, Serra V, et al. Acute coronary syndrome following transcatheter aortic valve replacement. *Circ Cardiovasc Interv*. 2020;13(2):e008620. https://doi.org/10.1161/CIRCINTERVENTIONS.119.008620
13. Mentias A, Desai MY, Saad M, et al. Incidence and outcomes of acute coronary syndrome after transcatheter aortic valve replacement. *JACC Cardiovasc Interv*. 2020;13(8):938–950. https://doi.org/10.1016/j.jcin.2019.11.027
14. 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
15. Rodés-Cabau J. Combining transcatheter aortic valve replacement and coronary angiography/percutaneous coronary intervention procedures: ready for prime time? *Circ Cardiovasc Interv*. 2017;10(8):e005664. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005664
16. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. *N Engl J Med*. 2017;376(19):1813–1823. https://doi.org/10.1056/NEJMoa1616540
17. De Bruyne B, Pijls NHJ, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367(11):991–1001. https://doi.org/10.1056/NEJMoa1205361
18. Tonino PAL, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360(3):213–224. https://doi.org/10.1056/NEJMoa0807611
19. Di Gioia G, Pellicano M, Toth GG, et al. Fractional flow reserve-guided revascularization in patients with aortic stenosis. *Am J Cardiol*. 2016;117(9):1511–1515. https://doi.org/10.1016/j.amjcard.2016.02.023
20. Ahmad Y, Götberg M, Cook C, et al. Coronary hemodynamics in patients with severe aortic stenosis and coronary artery disease undergoing transcatheter aortic valve replacement: implications for clinical indices of coronary stenosis severity. *JACC Cardiovasc Interv*. 2018;11(20):2019–2031. https://doi.org/10.1016/j.jcin.2018.07.019

21. Mylotte D, Wijns W. Anatomical or functional assessment of coronary artery disease in aortic stenosis: haven't we been down this road before? *J Am Heart Assoc*. 2019; 8(22):e014367. https://doi.org/10.1161/JAHA.119.014367
22. Patel KP, Michail M, Treibel TA, et al. Coronary revascularization in patients undergoing aortic valve replacement for severe aortic stenosis. *JACC Cardiovasc Interv*. 2021;14(19):2083–2096. https://doi.org/10.1016/j.jcin.2021.07.058
23. Pesarini G, Scarsini R, Zivelonghi C, et al. Functional assessment of coronary artery disease in patients undergoing transcatheter aortic valve implantation: influence of pressure overload on the evaluation of lesions severity. *Circ Cardiovasc Interv*. 2016; 9(11):e004088. https://doi.org/10.1161/CIRCINTERVENTIONS.116.004088
24. Yamanaka F, Shishido K, Ochiai T, et al. Instantaneous wave-free ratio for the assessment of intermediate coronary artery stenosis in patients with severe aortic valve stenosis: comparison with myocardial perfusion scintigraphy. *JACC Cardiovasc Interv*. 2018;11(20):2032–2040. https://doi.org/10.1016/j.jcin.2018.07.027
25. Lunardi M, Scarsini R, Venturi G, et al. Physiological versus angiographic guidance for myocardial revascularization in patients undergoing transcatheter aortic valve implantation. *J Am Heart Assoc*. 2019;8(22):e012618. https://doi.org/10.1161/JAHA.119.012618
26. Michail M, Davies JE, Cameron JD, Parker KH, Brown AJ. Pathophysiological coronary and microcirculatory flow alterations in aortic stenosis. *Nat Rev Cardiol*. 2018;15(7):420–431. https://doi.org/10.1038/s41569-018-0011-2
27. Sabbah M, Joshi FR, Minkkinen M, et al. Long-term changes in invasive physiological pressure indices of stenosis severity following transcatheter aortic valve implantation. *Circ Cardiovasc Interv*. 2022;15(1):e011331. https://doi.org/10.1161/CIRCINTERVENTIONS.121.011331
28. Scarsini R, Pesarini G, Lunardi M, et al. Observations from a real-time, iFR-FFR "hybrid approach" in patients with severe aortic stenosis and coronary artery disease undergoing TAVI. *Cardiovasc Revasc Med*. 2018;19(3 Pt B):355–359. https://doi.org/10.1016/j.carrev.2017.09.019
29. Kotronias RA, Scarsini R, Rajasundaram S, et al. Transcatheter aortic valve replacement influence on coronary hemodynamics: a quantitative meta-analysis and proposed decision-making algorithm. *J Invasive Cardiol*. 2020;32(1):37–40. https://doi.org/10.25270/jic/19.00284
30. Ahmad Y, Vendrik J, Eftekhari A, et al. Determining the predominant lesion in patients with severe aortic stenosis and coronary stenoses: a multicenter study using intracoronary pressure and flow. *Circ Cardiovasc Interv*. 2019;12(12): e008263. https://doi.org/10.1161/CIRCINTERVENTIONS.119.008263
31. Cook CM, Jeremias A, Petraco R, et al. Fractional flow reserve/instantaneous wave-free ratio discordance in angiographically intermediate coronary stenoses: an analysis using Doppler-derived coronary flow measurements. *JACC Cardiovasc Interv*. 2017;10(24):2514–2524. https://doi.org/10.1016/j.jcin.2017.09.021
32. Yamanaka F, Shishido K, Yokota S, et al. Discordance between fractional flow reserve and instantaneous wave-free ratio in patients with severe aortic stenosis: a retrospective cohort study. *J Cardiol*. 2023;81(2):138–143. https://doi.org/10.1016/j.jjcc.2022.08.005
33. Kovarnik T, Hitoshi M, Kral A, et al. Fractional flow reserve versus instantaneous wave-free ratio in assessment of lesion hemodynamic significance and explanation of their discrepancies. International, multicenter and prospective trial: the FiGARO study. *J Am Heart Assoc*. 2022;11(9):e021490. https://doi.org/10.1161/JAHA.121.021490
34. Jo HH, Kang DY, Lee JM, et al. Evaluation of instantaneous wave-free ratio and fractional flow reserve in severe aortic valve stenosis. *Circ Cardiovasc Interv*. 2024;17(5):e013237. https://doi.org/10.1161/CIRCINTERVENTIONS.123.013237
35. Chieffo A, Giustino G, Spagnolo P, et al. Routine screening of coronary artery disease with computed tomographic coronary angiography in place of invasive coronary angiography in patients undergoing transcatheter aortic valve replacement. *Circ Cardiovasc Interv*. 2015;8(7):e002025. https://doi.org/10.1161/CIRCINTERVENTIONS.114.002025
36. Diller GP, Gerwing M, Boroni Grazioli S, et al. Utility of coronary computed tomography angiography in patients undergoing transcatheter aortic valve implantation: a meta-analysis and meta-regression based on published data from 7458 patients. *J Clin Med*. 2024;13(2):631. https://doi.org/10.3390/jcm13020631
37. Rossi A, De Cecco CN, Kennon SRO, et al. CT angiography to evaluate coronary artery disease and revascularization requirement before trans-catheter aortic valve replacement. *J Cardiovasc Comput Tomogr*. 2017;11(5):338–346. https://doi.org/10.1016/j.jcct.2017.06.001
38. Kondoleon NP, Layoun H, Spilias N, et al. Effectiveness of pre-TAVR CTA as a screening tool for significant CAD before TAVR. *JACC Cardiovasc Interv*. 2023; 16(16):1990–2000. https://doi.org/10.1016/j.jcin.2023.05.030
39. Serruys PW, Kotoku N, Nørgaard BL, et al. Computed tomographic angiography in coronary artery disease. *EuroIntervention*. 2023;18(16):e1307–e1327. https://doi.org/10.4244/EIJ-D-22-00776
40. Latina J, Shabani M, Kapoor K, et al. Ultra-high-resolution coronary CT angiography for assessment of patients with severe coronary artery calcification: initial experience. *Radiol Cardiothorac Imaging*. 2021;3(4):e210053. https://doi.org/10.1148/ryct.2021210053
41. Schuijf JD, Lima JAC, Boedeker KL, et al. CT imaging with ultra-high-resolution: opportunities for cardiovascular imaging in clinical practice. *J Cardiovasc Comput Tomogr*. 2022;16(5):388–396. https://doi.org/10.1016/j.jcct.2022.02.003
42. Patel MR, Dai D, Hernandez AF, et al. Prevalence and predictors of nonobstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. *Am Heart J*. 2014;167(6):846–852.e2. https://doi.org/10.1016/j.ahj.2014.03.001
43. Abdelrahman KM, Chen MY, Dey AK, et al. Coronary computed tomography angiography from clinical uses to emerging technologies: JACC state-of-the-art review. *J Am Coll Cardiol*. 2020;76(10):1226–1243. https://doi.org/10.1016/j.jacc.2020.06.076
44. Hoffmann U, Ferencik M, Udelson JE, et al. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). *Circulation*. 2017;135(24):2320–2332. https://doi.org/10.1161/CIRCULATIONAHA.116.024360
45. SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet*. 2015;385(9985):2383–2391. https://doi.org/10.1016/S0140-6736(15)60291-4
46. SCOT-HEART Investigators, Newby DE, Adamson PD, et al. Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med*. 2018; 379(10):924–933. https://doi.org/10.1056/NEJMoa1805971
47. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med*. 2015;372(14):1291–1300. https://doi.org/10.1056/NEJMoa1415516
48. Sharma A, Coles A, Sekaran NK, et al. Stress testing versus CT angiography in patients with diabetes and suspected coronary artery disease. *J Am Coll Cardiol*. 2019;73(8):893–902. https://doi.org/10.1016/j.jacc.2018.11.056
49. Michail M, Ihdayhid AR, Comella A, et al. Feasibility and validity of computed tomography-derived fractional flow reserve in patients with severe aortic stenosis: the CAST-FFR study. *Circ Cardiovasc Interv*. 2021;14(1):e009586. https://doi.org/10.1161/CIRCINTERVENTIONS.120.009586
50. Peper J, Becker LM, van den Berg H, 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
51. Cerrato E, Mejía-Rentería H, Franzè A, et al. Quantitative flow ratio as a new tool for angiography-based physiological evaluation of coronary artery disease: a review. *Future Cardiol*. 2021;17(8):1435–1452. https://doi.org/10.2217/fca-2020-0199
52. Xu B, Tu S, Song L, et al. Angiographic quantitative flow ratio-guided coronary intervention (FAVOR III China): a multicentre, randomised, sham-controlled trial. *Lancet*. 2021;398(10317):2149–2159. https://doi.org/10.1016/S0140-6736(21)02248-0
53. Colaiori I, Paolucci L, Mangiacapra F, et al. Natural history of coronary atherosclerosis in patients with aortic stenosis undergoing transcatheter aortic valve replacement: the role of quantitative flow ratio. *Circ Cardiovasc Interv*. 2024;17(8):e013705. https://doi.org/10.1161/CIRCINTERVENTIONS.123.013705
54. Mejía-Rentería H, Nombela-Franco L, Paradis J-M, et al. Angiography-based quantitative flow ratio versus fractional flow reserve in patients with coronary artery disease and severe aortic stenosis. *EuroIntervention*. 2020;16(4):e285–e292. https://doi.org/10.4244/EIJ-D-19-01001
55. Byrne RA, McGovern L. Angiography-derived quantitative flow ratio guidance of coronary intervention: measure twice, cut once. *Lancet*. 2021;398(10317): 2130–2131. https://doi.org/10.1016/S0140-6736(21)02397-7
56. Thalji NM, Suri RM, Daly RC, et al. The prognostic impact of concomitant coronary artery bypass grafting during aortic valve surgery: implications for revascularization in the transcatheter era. *J Thorac Cardiovasc Surg*. 2015;149(2):451–460. https://doi.org/10.1016/j.jtcvs.2014.08.073
57. Lund O, Nielsen TT, Pilegaard HK, Magnussen K, Knudsen MA. The influence of coronary artery disease and bypass grafting on early and late survival after valve replacement for aortic stenosis. *J Thorac Cardiovasc Surg*. 1990;100(3):327–337. https://doi.org/10.1016/S0022-5223(19)35524-2
58. Sedlis SP, Hartigan PM, Teo KK, et al. Effect of PCI on long-term survival in patients with stable ischemic heart disease. *N Engl J Med*. 2015;373(20):1937–1946. https://doi.org/10.1056/NEJMoa1505532
59. Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med*. 2020;382(15):1395–1407. https://doi.org/10.1056/NEJMoa1915922
60. Perera D, Clayton T, O'Kane PD, et al. Percutaneous revascularization for ischemic left ventricular dysfunction. *N Engl J Med*. 2022;387(15):1351–1360. https://doi.org/10.1056/NEJMoa2206606
61. Minten L, Wissels P, McCutcheon K, et al. The effect of coronary lesion complexity and preprocedural revascularization on 5-year outcomes after TAVR. *JACC Cardiovasc Interv*. 2022;15(16):1611–1620. https://doi.org/10.1016/j.jcin.2022.06.019
62. Patterson T, Clayton T, Dodd M, et al. ACTIVATION (PercutAneous Coronary inTervention prIor to transcatheter aortic VAlve implantaTION): a randomized clinical trial. *JACC Cardiovasc Interv*. 2021;14(18):1965–1974. https://doi.org/10.1016/j.jcin.2021.06.041
63. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med*. 2016;374(16):1511–1520. https://doi.org/10.1056/NEJMoa1602001
64. Thuijs DJFM, Kappetein AP, Serruys PW, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *Lancet*. 2019;394(10206):1325–1334. https://doi.org/10.1016/S0140-6736(19)31997-X
65. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med*. 2012;367(25): 2375–2384. https://doi.org/10.1056/NEJMoa1211585
66. Alperi A, Mohammadi S, Campelo-Parada F, et al. Transcatheter versus surgical aortic valve replacement in patients with complex coronary artery disease. *JACC Cardiovasc Interv*. 2021;14(22):2490–2499. https://doi.org/10.1016/j.jcin.2021.08.073

67. Sakurai Y, Yokoyama Y, Fukuhara S, Takagi H, Kuno T. Complete transcatheter versus surgical approach to aortic stenosis with coronary artery disease: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg*. 2024;167(4):1305–1313.e9. https://doi.org/10.1016/j.jtcvs.2022.08.006
68. Sun LY, Gaudino M, Chen RJ, Bader Eddeen A, Ruel M. Long-term outcomes in patients with severely reduced left ventricular ejection fraction undergoing percutaneous coronary intervention vs coronary artery bypass grafting. *JAMA Cardiol*. 2020;5(6):631–641. https://doi.org/10.1001/jamacardio.2020.0239
69. 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
70. Lateef N, Khan MS, Deo SV, et al. Meta-analysis comparing outcomes in patients undergoing transcatheter aortic valve implantation with versus without percutaneous coronary intervention. *Am J Cardiol*. 2019;124(11):1757–1764. https://doi.org/10.1016/j.amjcard.2019.08.024
71. Rheude T, Costa G, Ribichini FL, et al. Comparison of different percutaneous revascularisation timing strategies in patients undergoing transcatheter aortic valve implantation. *EuroIntervention*. 2023;19(7):589–599. https://doi.org/10.4244/EIJ-D-23-00186
72. Fefer P, Bogdan A, Grossman Y, et al. Impact of rapid ventricular pacing on outcome after transcatheter aortic valve replacement. *J Am Heart Assoc*. 2018;7(14):e009038. https://doi.org/10.1161/JAHA.118.009038
73. Selle A, Figulla HR, Ferrari M, et al. Impact of rapid ventricular pacing during TAVI on microvascular tissue perfusion. *Clin Res Cardiol*. 2014;103(11):902–911. https://doi.org/10.1007/s00392-014-0728-9
74. López Otero D, Ávila-Carrillo A, González Ferreiro R, et al. Impact of coronary revascularization in patients who underwent transcatheter aortic valve implantation. *Am J Cardiol*. 2019;123(6):948–955. https://doi.org/10.1016/j.amjcard.2018.12.007
75. D'Ascenzo F, Conrotto F, Giordana F, et al. Mid-term prognostic value of coronary artery disease in patients undergoing transcatheter aortic valve implantation: a meta-analysis of adjusted observational results. *Int J Cardiol*. 2013;168(3):2528–2532. https://doi.org/10.1016/j.ijcard.2013.03.062
76. Singh V, Rodriguez AP, Thakkar B, et al. Comparison of outcomes of transcatheter aortic valve replacement plus percutaneous coronary intervention versus transcatheter aortic valve replacement alone in the United States. *Am J Cardiol*. 2016;118(11):1698–1704. https://doi.org/10.1016/j.amjcard.2016.08.048
77. Park DY, Simonato M, Ahmad Y, Banks AZ, Lowenstern A, Nanna MG. Insight into the optimal timing of percutaneous coronary intervention and transcatheter aortic valve replacement. *Curr Probl Cardiol*. 2024;49(1 Pt A):102050. https://doi.org/10.1016/j.cpcardiol.2023.102050
78. Tran Z, Hadaya J, Downey P, et al. Staged versus concomitant transcatheter aortic valve replacement and percutaneous coronary intervention: a national analysis. *JTCVS Open*. 2022;10:148–161. https://doi.org/10.1016/j.xjon.2022.02.019
79. Barbanti M, Costa G, Picci A, et al. Coronary cannulation after transcatheter aortic valve replacement: the RE-ACCESS study. *JACC Cardiovasc Interv*. 2020;13(21):2542–2555. https://doi.org/10.1016/j.jcin.2020.07.006
80. Nai Fovino L, Scotti A, Massussi M, et al. Incidence and feasibility of coronary access after transcatheter aortic valve replacement. *Catheter Cardiovasc Interv*. 2020;96(5):E535–E541. https://doi.org/10.1002/ccd.28720
81. Lunardi M, Venturi G, Del Sole PA, et al. Optimal timing for percutaneous coronary intervention in patients undergoing transcatheter aortic valve implantation. *Int J Cardiol*. 2022;365:114–122. https://doi.org/10.1016/j.ijcard.2022.07.030
82. Millan-Iturbe O, Sawaya FJ, Lønborg J, et al. Coronary artery disease, revascularization, and clinical outcomes in transcatheter aortic valve replacement: real-world results from the East Denmark Heart Registry. *Catheter Cardiovasc Interv*. 2018;92(4):818–826. https://doi.org/10.1002/ccd.27440
83. Carroll JD, Mack MJ, Vemulapalli S, et al. STS-ACC TVT registry of transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2020;76(21):2492–2516. https://doi.org/10.1016/j.jacc.2020.09.595
84. Ochiai T, Yamanaka F, Shishido K, et al. Impact of high implantation of transcatheter aortic valve on subsequent conduction disturbances and coronary access. *JACC Cardiovasc Interv*. 2023;16(10):1192–1204. https://doi.org/10.1016/j.jcin.2023.03.021
85. Tarantini G, Nai Fovino L, Scotti A, et al. Coronary access after transcatheter aortic valve replacement with commissural alignment: the ALIGN-ACCESS study. *Circ Cardiovasc Interv*. 2022;15(2):e011045. https://doi.org/10.1161/CIRCINTERVENTIONS.121.011045
86. Tang GHL, Zaid S, Fuchs A, et al. Alignment of Transcatheter Aortic-Valve Neo-Commissures (ALIGN TAVR): impact on final valve orientation and coronary artery overlap. *JACC Cardiovasc Interv*. 2020;13(9):1030–1042. https://doi.org/10.1016/j.jcin.2020.02.005
87. Vinayak M, Tang GHL, Li K, et al. Commissural vs coronary alignment to avoid coronary overlap with THV-commissure in TAVR: a CT-simulation study. *JACC Cardiovasc Interv*. 2024;17(6):715–726. https://doi.org/10.1016/j.jcin.2024.01.073
88. Costa G, Sammartino S, Strazzieri O, et al. Coronary cannulation following TAVR using self-expanding devices with commissural alignment: the RE-ACCESS 2 study. *JACC Cardiovasc Interv*. 2024;17(6):727–737. https://doi.org/10.1016/j.jcin.2023.12.015
89. Kim WK, Pellegrini C, Ludwig S, et al. Feasibility of coronary access in patients with acute coronary syndrome and previous TAVR. *JACC Cardiovasc Interv*. 2021;14(14):1578–1590. https://doi.org/10.1016/j.jcin.2021.05.007
90. Yudi MB, Sharma SK, Tang GHL, Kini A. Coronary angiography and percutaneous coronary intervention after transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2018;71(12):1360–1378. https://doi.org/10.1016/j.jacc.2018.01.057
91. Attizzani GF, Gabasha S, Ukaigwe A, et al. Coronary cannulation, commissure, and coronary alignment post-TAVR with Evolut FX system: CANNULATE TAVR study. *JACC Cardiovasc Interv*. 2024;17(6):825–827. https://doi.org/10.1016/j.jcin.2023.10.033
92. Kawamura A, Maeda K, Shimamura K, et al. Coronary access after repeat transcatheter aortic valve replacement in patients of small body size: a simulation study. *J Thorac Cardiovasc Surg*. 2024;168(1):76–85.e8. https://doi.org/10.1016/j.jtcvs.2022.11.023
93. Vinayak M, Leone PP, Tanner R, et al. Transcatheter aortic valve replacement: current status and future indications. *J Clin Med*. 2024;13(2):373. https://doi.org/10.3390/jcm13020373
94. De Backer O, Landes U, Fuchs A, et al. Coronary access after TAVR-in-TAVR as evaluated by multidetector computed tomography. *JACC Cardiovasc Interv*. 2020;13(21):2528–2538. https://doi.org/10.1016/j.jcin.2020.06.016