When to perform percutaneous coronary interventions in TAVI patients? Recent advances

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ABSTRACT

Coronary artery disease (CAD) is prevalent in c. 50% of patients with severe aortic valve stenosis undergoing transcatheter aortic valve implantation (TAVI). The impact of CAD on TAVI outcomes and optimal management strategies remains unclear.

This article considers the latest evidence on assessing CAD in TAVI patients and determining the timing for treating it to optimize clinical outcomes and resource utilization.

We discuss the current methods for CAD diagnosis, including invasive coronary angiography (ICA), coronary computed tomography angiography, and the role of functional assessment indices such as fractional flow reserve and instantaneous wave-free ratio in guiding revascularization decisions. While ICA remains the standard for determining CAD severity in TAVI candidates, coronary computed tomography angiography has shown the potential to reduce unnecessary ICA procedures. When indicated, fractional flow reserve seems more reliable than the instantaneous wave-free ratio in aortic valve stenosis patients, particularly when evaluated post-TAVI. Recent data suggests that percutaneous coronary intervention post-TAVI may be associated with improved outcomes compared to pre-TAVI interventions.

In summary, the optimal management of CAD in TAVI patients is still under investigation. The current evidence supports a tailored approach, considering pre- and post-TAVI percutaneous coronary intervention strategies based on individual patient characteristics and procedural complexities. Further randomized trials are needed to establish definitive guidelines.

Key words: aortic valve stenosis, coronary artery disease, coronary revascularization, fractional flow reserve, instantaneous wave-free ratio, transcatheter aortic valve implantation

INTRODUCTION

The prevalence of coronary artery disease (CAD) in patients with severe aortic valve stenosis (AVS) undergoing transcatheter aortic valve implantation (TAVI) is approximately 50% [1–4], with variations ranging from 15% to 80% in major clinical trials based on patient age and risk profile [5–9]. Notably, CAD prevalence is lower in low-risk patients compared to those at intermediate and high risk. Among TAVI recipients with CAD, about half have multivessel disease, and there is often involvement of the left main (LM)/left anterior descending artery (LAD) [10, 11].

Early observational studies conducted shortly after the introduction of TAVI produced mixed results regarding the impact of coexisting CAD on patient outcomes. Some studies found no significant differences in survival between patients with and without significant coronary lesions [12, 13], or between those who underwent complete versus incomplete revascularization. On the other hand, other studies reported the opposite findings [14]. Additionally, higher rates of procedural complications have been observed when percutaneous coronary intervention (PCI) is performed concurrently with TAVI, potentially leading to adverse outcomes in this vulnerable patient population [15]. However, it is important to note that most studies have had a limited follow-up period, i.e., less

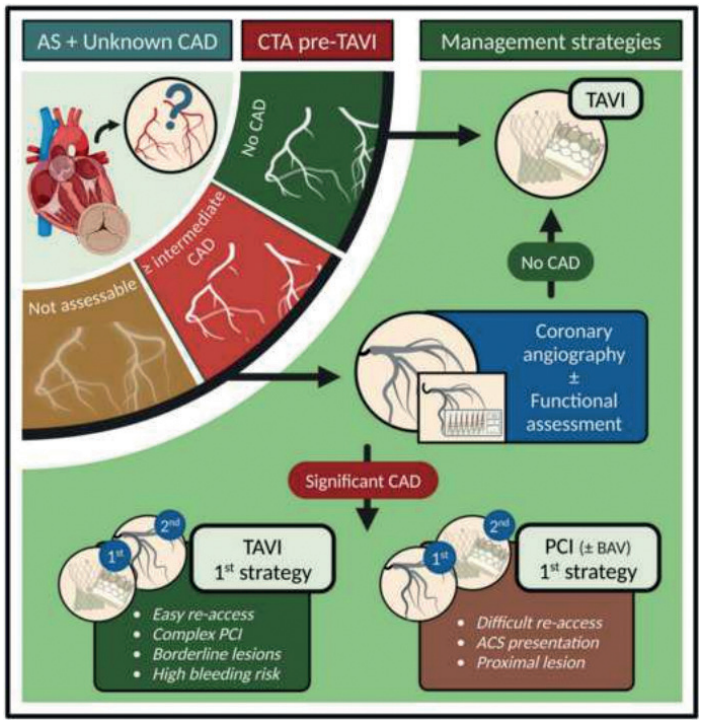

Figure 1. Proposed algorithm for CAD severity assessment and treatment in patients undergoing TAVI. CAD should be ruled out by CTA when available. If not, or if CCTA shows abnormal findings, coronary angiography is required before valve implantation. In the case of detecting intermediate stenosis, the TAVI-first strategy is recommended when feasible, according to clinical presentation and patient characteristics (expected easy coronary re-access, high bleeding risk, etc.). Once TAVI is performed, functional evaluation of intermediate stenosis should be performed with pressure wire or image-based functional assessment to guide eventual revascularization. If the PCI-first approach is desirable (large ischemic myocardium, acute settings, etc.), operators might consider performing aortic balloon valvuloplasty before PCI as a bridge to TAVI

Abbreviations: ACS, acute coronary syndrome; AS, aortic stenosis; BAV, balloon aortic valvuloplasty, CAD, coronary artery disease; CCTA, cardiac computed tomography angiography; CTA, coronary tomography angiography; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve replacement

than 2 years, and a longer duration may be necessary to accurately assess the impact of CAD on clinical outcomes post-TAVI.

Moreover, there is no consensus regarding how to evaluate the clinical relevance of identified stenoses in AVS patients with CAD or on the timing of revascularization, with many operators relying solely on angiographic severity to guide PCI decisions.

Currently, these specific issues have not been definitively addressed by the scientific community, and the management of CAD is often left to the experience of individual operators or centers. This article aims to consider the latest evidence on the potential timing strategies for the treatment of CAD in patients undergoing TAVI to optimize patient outcomes and healthcare resource utilization (Figure 1).

CAD SEVERITY ASSESSMENT IN PATIENTS WITH SEVERE AORTIC STENOSIS: INDICATIONS FOR PCI

Given the fragility of this population, the primary goal is to achieve diagnosis while conserving resources, saving time, and minimizing the risk of complications. This approach will enhance patient comfort and optimize the use of medical resources. There are several methods to investigate the presence and significance of CAD: invasive coronary angiography (ICA), coronary computed tomography angiography (CCTA), and non-invasive ischemia tests. However, TAVI candidates are often not ideal for non-invasive ischemia tests due to their fragility, which prevents them from performing physical stress tests, and the frequent presence of left ventricular (LV) hypertrophy, which can confound results.

Given that TAVI patients necessarily require ECG-gated computed tomography (CT) before TAVI, some authors have suggested using this imaging technique to select patients for ICA based on CT results. A dedicated study showed that this hybrid strategy is feasible and potentially clinically relevant, with CA performed in only a quarter of patients due to the detection of obstructive stenosis on CT, without affecting clinical outcomes when ICA was deferred [16]. As expected from experiences with non-AVS patients, compared to ICA, CCTA has an excellent negative predictive value and sensitivity, but low specificity, which decreases further in the presence of previous stented segments or heavy calcifications [17]. Despite these limitations, a recent large meta-analysis also demonstrated that using CT as a gatekeeper for ICA in the TAVI workup could reduce the number of coronary angiographies by 37%. With an increasing number of low-risk TAVI patients, this reduction is likely to grow, given the lower probability of CAD and calcified lesions in younger patients [18].

However, to date, ICA remains the standard examination for determining the presence and severity of CAD in TAVI candidates. The current European Society of Cardiology guidelines [19] state that myocardial revascularization using PCI should be considered in patients with a primary indication for TAVI and who are presenting, based on angiography alone, with coronary artery diameter stenosis >70% in proximal segments although this recommendation has a low level of evidence (C). In contrast, no recommendations are provided for non-proximal or less severe stenosis. Notably, the equivalent American Guidelines indicate that investigation of intermediate CAD through

invasive physiological assessment is safe, even in the presence of AVS [20].

Although angiographic stenosis of >70% seems a reliable threshold for detecting critical stenosis in patients with aortic stenosis [21, 22], coronary physiology studies suggest that 20% of these cases have a normal fractional flow reserve (FFR), a percentage that increases dramatically (up to 65%) with 50%–70% stenosis [23]. While this is well-documented for non-AVS patients, similar conclusions cannot be drawn for AVS patients, where morphological and hemodynamic changes induced by the valve disease may affect functional indices [24].

Theoretically, LV hypertrophy with interstitial fibrosis, commonly found in AVS, increases LV end-diastolic pressure and induces microvascular dysfunction, with both potentially leading to blunted vasodilatory capacity and increased "back pressure" (Pd), which results in altered FFR values. Although the instantaneous wave-free ratio (iFR) does not require pharmacological vasodilation, it may also be affected by LV end-diastolic pressure. High left ventricular filling pressures impact coronary resting flow by increasing myocardial metabolic demand. It has been reported that increasing resting flow reduces the pressure drop along the target vessel, resulting in falsely higher iFR values [25].

Additionally, LV obstruction reduces systemic pressure, and consequently the pressure upstream of the stenosis, causing a concomitant decrease in aortic pressure. Based on this hypothesis, when using FFR or iFR we might expect an increased Pd due to impaired vasodilatory response to adenosine or higher resting flow, which combined with lower aortic pressure could result in falsely higher values.

However, comparing FFR and iFR to myocardial perfusion imaging (stress single photon emission computed tomography [SPECT]) in AVS patients has shown that these functional indices perform relatively well. FFR, in particular, had the best agreement with SPECT (85%), with an area under the curve of 0.91 and a negative predictive value of 95% for detecting ischemia. On the other hand, iFR produced a significant proportion of false positives (39% of negative SPECT) using the standard cut-off of ≤0.89 while using a pre-specified 0.82 cut-off improved iFR's agreement with SPECT to 73% [26].

This finding was further confirmed in another study which showed that the conventional iFR cut-off had a lower diagnostic agreement with FFR classification of coronary lesions in the presence of AVS, compared to non-AVS, patients. According to this data, the best iFR cut-off for predicting FFR ≤0.8 was lower (0.83) than the standard one (0.89) [27, 28].

Further studies have investigated the variability of FFR and iFR after TAVI, once LV obstruction was removed, which reflected a more physiological condition. Regarding FFR, only minor variations were observed after TAVI compared to baseline. Notably, the direction of these variations (improvement or worsening) depended on pre-TAVI FFR results: positive FFR values tended to worsen post-TAVI, while negative FFR values tended to improve post-TAVI [24]. TAVI, by inducing an immediate decrease in hyperemic microvascular resistance and an increase in hyperemic flow velocity, is associated with an immediate improvement in coronary microcirculation's vasodilator capacity. This pathophysiological assumption may be one of the factors underlying FFR variations post-TAVI although dedicated studies are needed [29].

Similar patterns were not observed for iFR, which showed wide individual variations after TAVI, with a higher delta (iFR after TAVI — iFR before TAVI) associated with a greater drop in transaortic gradient after valve intervention [22].

Considering that TAVI patients will live without AVS, it is intuitive that the functional significance of intermediate coronary lesions should be evaluated in the absence of this condition, hence after valve implantation. The available literature supports FFR as a more reliable parameter than iFR and even suggests measuring it post-TAVI for a more accurate assessment of the need for myocardial revascularization, especially for borderline FFR values that may decrease after AVS removal [24].

Moreover, the recent advent of image-based functional assessment techniques (e.g., quantitative flow ratio) is timely, given that TAVI candidates represent an ideal population for their application. The ability to examine the functional significance of coronary stenosis without wiring the vessel is appealing, particularly when post-TAVI measurement is desirable. Mejía-Rentería et al. [30] analyzed the diagnostic performance of the quantitative flow ratio in AVS patients against FFR, reporting per-vessel sensitivity, specificity, area under the ROC curve, and accuracy of 84% (95% CI, 71%–92%), 80% (95% CI, 69%–88%), 0.88 (95% CI, 0.82–0.93), and 81%, respectively [30, 31].

Beyond these peculiarities, clinical outcomes after physio-guided revascularization of intermediate stenosis in TAVI patients support the validity of this strategy. An observational study including 216 patients compared FFR guidance to angio-guidance for myocardial revascularizations in the TAVI context. It showed that patients evaluated with FFR had significantly better outcomes at 2 years compared to those guided by angiography alone (major adverse cardiac and cerebrovascular events-free survival 92.6% vs. 82.0%; $P = 0.035$), mainly due to a higher rate of periprocedural myocardial infarction in the angio-group. Most (72%) lesions assessed by FFR were negative, and these patients, treated medically, performed better than those treated by angio-guided PCI [32]. In line with this, investigating the residual functional SYNTAX score (rFSS) after TAVI showed that functional incomplete revascularization (rFSS >0) was associated with worse event-free survival at follow-up [33].

Despite the observational nature of these studies, the data is reassuring about the safety of PCI deferral based on negative FFR, while cautioning against the

Table 1. Main studies on CAD severity assessment in patients with severe aortic stenosis

Study	Objective	Design	Sample size	Publication year	Key findings
Chieffo A	CCTA to rule out CAD	Observational retrospective	491	2015	Only 25% of patients underwent CA
van den Boogert TPW	Diagnostic accuracy of CCTA for CAD diagnosis	Meta-analysis	1275	2018	High NPV and sensitivity, but low specificity. CA spared in 37%
Scarsini R	Correlation between SPECT and FFR/iFR	Observational prospective	28	2019	FFR <0.80 — SPECT agreement 85%, iFR <0.82 — SPECT 73%
Scarsini R	Comparison FFR vs. iFR in AS	Observational retrospective	179	2017	Best iFR cut-off to predict FFR <0.80: 0.83
Pesarini G	FFR variations before vs. after TAVR	Observational prospective	133	2016	No significant variations after TAVR. 6% only changed indication to treat
Scarsini R	iFR variations before vs. after TAVR	Observational prospective	145	2018	Erratic individual variations. 15% changed indication to treat
Mejía-Rentería H	QFR diagnostic performance in AVS	Observational retrospective	138	2020	Accuracy in predicting FFR <0.80: 81%
Lunardi M	Angio- vs. functional-guidance for PCI	Observational retrospective	216	2021	Higher 2y MACCE-free survival in functional arm
FAITAVI trial	Angio- vs. functional-guidance for PCI	Randomized clinical trial	320	–	–
NOTION-3 trial	FFR-guided PCI or medical treatment	Randomized clinical trial	452	–	–
TAVI-PET trial	Correlation of FFR and iFR with cardiac PET perfusion	Observational prospective	20	–	–

Abbreviations: AS, aortic stenosis; AVS, aortic valve stenosis; CA, coronary angiography; CCTA, coronary computed tomography angiography; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; MACCE, major adverse cardiac and cerebrovascular events; NPV, negative predictive value; PET, positron emission tomography; QFR, quantitative flow ratio; SPECT, single photon emission computed tomography; TAVR, transcatheter aortic valve replacement; other — see Figure 1

risks of angio-driven PCI. The upcoming results of randomized clinical trials (FAITAVI — NCT03360591, NOTION-3 — NCT03058627, TAVI-PET — NCT04882488) that are focused on this specific topic will further elucidate the role of invasive functional assessment in determining when to perform PCI in TAVI patients (Table 1).

PCI TIMING IN PATIENTS UNDERGOING TAVI

Once the indication for PCI is established, it is common practice to perform it upstream of TAVI, still in the presence of severe AVS, through a staged procedure or during TAVI before valve deployment, with initial studies supporting such a strategy [15, 19, 34–37]. This is also the recommendation provided in the current American Guidelines [20], while European guidelines do not specify timing for coronary revascularization, suggesting that it should be based on clinical presentation and coronary anatomy complexity [19]. These guidelines have generally been interpreted as confirmation of the feasibility of the PCI pre-TAVI approach, rather than a comparison of different timings for PCI (pre- and post-TAVI).

However, operators choosing this strategy must contend with several drawbacks. These include an increased risk of acute kidney injury, increased bleeding and vascular complications during TAVI due to dual antiplatelet therapy before TAVI [38], and systemic hypoperfusion derived from aortic valve obstruction, which might complicate some complex PCI procedures. On the other hand, performing PCI before TAVI is desirable in the presence of ongoing ischemia (i.e., acute coronary syndromes) because it allows easier coronary access, and might be preferred in the case of ostial/proximal lesions to prevent large myocardial ischemia during LV pacing (Table 2).

Table 2. Examples of preferred PCI timing based on clinical scenarios

PCI timing	Clinical scenario
Pre-TAVI	• Acute coronary syndromes (i.e., when ischemia is acute issue) • Ostial/proximal right coronary artery or left main stenosis (possibly leading to large myocardial ischemia during left ventricular pacing implanting valve) • Specific anatomies leading to unfavorable interactions between selected valve and coronary ostia, making coronary cannulation after TAVI more challenging (e.g., low coronary ostia, ectopic ostia, narrow sinuses, valve-in-valve procedures, etc.) • Following balloon aortic valvuloplasty (bridge to TAVI) when tight severe aortic stenosis is present (particularly high aortic-ventricular gradients)
Post-TAVI	• Expected complex and lengthy PCI procedures (e.g., requiring debulking techniques, etc), when presence of aortic valve obstruction, thus systemic hypoperfusion, might place PCI at higher risk of procedural complications • Presence of severe chronic kidney disease and high risk of contrast-induced acute kidney injury (normalization of systemic perfusion after TAVI promotes better kidneys perfusion and reduces risk of acute injury during additional contrast medium administration) • Patients presenting with high bleeding risk or on anticoagulation should not be qualified for TAVI on double antithrombotic therapy • Borderline coronary stenosis severity at coronary angiogram/physiology before TAVI requires functional re-evaluation after aortic valve stenosis treatment

Abbreviations: see Figure 1

An appealing alternative consists of alleviating LV overload by performing a balloon aortic valvuloplasty followed by PCI during the same procedure [39, 40]. This approach, when tolerated, reduces systemic hypoperfusion and potential secondary ischemic PCI complications,

Table 3. Main studies on PCI timing in patients undergoing TAVR

Study	Objective	Design	Sample size	Publication year	Key findings
Venturi G	Concomitant vs. staged CA	Observational retrospective	339	2021	Staged CA increased risk of CI-AKI
Ochiai T	Comparison of different timings for PCI	Observational retrospective	258	2020	No differences at 2 years in outcomes between pre-, concomitant, and post-TAVR PCI
Lunardi M	Comparison of pre-TAVR vs. post-TAVR PCI	Observational retrospective	144	2022	Higher in-hospital stroke rate, and 2-year MACCE in pre-TAVR arm
TAVI PCI trial	Comparison of pre-TAVR vs. post-TAVR PCI (iFR guided)	Randomized clinical trial	986	–	–
Lunardi M	Feasibility and 2-year outcomes of RA after TAVR	Observational retro/prospective	19	2020	15% inotropic support, 100% success, 100% 30-day survival, 84% 2-year survival
Naganuma T.	Feasibility and 30 days outcomes of RA before TAVR	Observational retrospective	25	2017	40% inotropic support, 100% success, 100% 30-day survival
Lippmann M.	Feasibility and immediate outcomes of RA before TAVR	Observational retrospective	29	2017	30% inotropic support, 100% success, 100% immediate survival
REVASC-TAVI registry	Comparison of pre-TAVR vs. concomitant vs. post-TAVR PCI	Observational retrospective	1603	2023	PCI performed before, after or concomitantly with TAVR in 65.6% (n = 1052), 9.8% (n = 157) or 24.6% (n = 394). 2-year all-cause death in post-TAVR, pre-TAVR, and concomitant: 6.8% vs. 20.1% vs. 20.6%; *P* <0.001

Abbreviations: CI-AKI, contrast-induced acute kidney injury; RA, rotational atherectomy; TAVR, transcatheter aortic valve replacement; other — see Figure 1 and Table 1

serving as a bridge to TAVI in patients with temporary TAVI contraindications.

Conversely, few studies have investigated the potential advantages of performing PCI after TAVI in the absence of AVS, hampered by the risk of ischemic and hemodynamic complications potentially inducible during the TAVI procedure due to the presence of a large ischemic territory [41–44].

Ochiai et al. [45], using balloon-expandable valves only, reported similar clinical outcomes between pre-TAVI (n = 143), concomitant (n = 77), or post-TAVI (n = 38) PCI groups at 2 years. However, the use of balloon-expandable valves only limits the generalization of such results to the real-world population, where self-expandable valves notably hinder coronary access.

Another study examined the feasibility, periprocedural complications, and 2-year outcomes of PCI pre- vs. post-TAVI in 144 patients, 73% (n = 105) of whom underwent PCI of LM, proximal LAD, or proximal dominant right coronary artery (RCA). Both self- and balloon-expandable valves were included [44]. While procedural success was achieved in all cases, and overall periprocedural complications were similar, a higher incidence of in-hospital stroke was reported in the PCI pre-TAVI group. Additionally, at 2 years, major adverse cardiac and cerebrovascular events-free survival was lower in patients who underwent PCI before TAVI.

These results have recently been corroborated by the REVASC-TAVI registry, a large multicenter international study. Based on data from 1603 patients, the study concluded that performing PCI after TAVI seems to be associated with improved 2-year clinical outcomes compared to other revascularization timing strategies, significantly reducing all-cause deaths, as well as a composite of all-cause death, stroke, MI, or unplanned rehospitalization for heart failure [46] (Table 3).

These findings offer interesting insights: firstly, PCI after TAVI appears safe and feasible, at least as a PCI-first approach. The similar rate of periprocedural complications suggests that even the presence of high-risk lesions (i.e., LM or proximal LAD stenosis), with a large ischemic burden, does not compromise the TAVI procedure when coronary lesions are treated after TAVI, regardless of the valve type.

Available data on the feasibility of coronary access after TAVI suggests greater difficulties with high-frame, supra-annular prostheses compared to low-frame, intra-annular valves [47, 48]. However, even considering only supra-annular high frame prostheses (e.g., Medtronic Evolut device), an inability to cannulate the coronary arteries ranges between 0 and 15%, with most studies reporting almost 100% success [43, 49–53].

While the type of prosthesis plays a key role in this setting, other risk factors for difficult coronary cannulation include patients' anatomical characteristics and procedural techniques.

Procedural factors are particularly relevant today, as increasing attention paid by prosthesis manufacturers and operators to developing enhanced devices to achieve commissural alignment and the ideal implant height during valve implantation. It has been demonstrated that orienting the Medtronic Evolut device with the flush port placed at 3 o'clock, and keeping the Evolut hat marker at the outer curve of the thoracic aorta, reduces the misalignment rate between device commissures and coronary ostia from 38% to 24% [54]. Similarly, the COMALIGN study showed that orienting the specific fluoroscopic markers of any prosthesis according to the cusp overlap angiographic view (left and right cusps) can achieve correct commissural alignment in up to 90% of patients [55].

Such rates of successful coronary engagement after TAVI also referred to earlier TAVI periods when operators

paid less attention to commissural alignment. Considering the current improved implantation techniques and devices, today we may expect a lower failure rate of coronary access after TAVI. These findings can help operators either guide the decision to perform PCI before or after TAVI based on the prosthesis selected for a given patient or choose a specific valve type (e.g., low frame, intra-annular) to facilitate post-TAVI PCI.

Additional advantages of a TAVI-first approach are worth mentioning, as they might be relevant in selected settings. These include complex PCI procedures, chronic kidney disease, high bleeding risk, and borderline stenosis severity (Table 2). The opportunity to remove LV obstruction and improve systemic perfusion before PCI is particularly relevant in cases of potential ischemic or mechanical complications related to complex PCI. These complications could further impair cardiac output, even if only transiently, and affect organs with low ischemic thresholds, such as the kidneys and the brain, which are already hypoperfused in patients with severe AVS. The immediately favorable hemodynamic effect of TAVI might explain the better kidney tolerance and the lower stroke rate observed [56].

In this regard, it has been demonstrated that TAVI has a protective effect on contrast-induced acute kidney injury incidence (odds ratio, 0.334; 95% CI, 0.193–0.579; P <0.001) [57] when compared to any other coronary procedure (either diagnostic angiograms or PCI).

This observation suggests that the impact of contrast administration on kidney function in patients who have undergone TAVI may be better tolerated because of the hemodynamic changes following aortic valve replacement. This supports the PCI post-TAVI strategy in patients at higher risk of contrast induced-acute kidney injury.

On the other hand, explaining the lower incidence of strokes is less straightforward, considering that such events might derive from either prolonged brain hypoperfusion in the context of diffuse cerebral vascular disease or thromboembolism. The latter deserves particular attention, as there exist numerous cerebral protection devices [58], potentially helpful in preventing that event. However, considering the still limited — and not conclusive — evidence about their use during TAVI [19], a decision to use such devices should be taken on a case-by-case basis. In the setting of PCI and TAVI, the higher risk of strokes observed when PCI is performed first (hence while not intervening on the calcified aortic valve) suggests that the former physiopathology is the most likely. Hence, the potential use of cerebral protection devices should be limited to patients considered with a higher risk of strokes, on the sole basis of the aortic valve disease anatomy and expected TAVI complexity, regardless of the subsequent PCI.

Considering CAD in AVS patients is often associated with a high burden of coronary calcification. Complex procedures are sometimes needed, including debulking techniques (e.g., intravascular lithotripsy and rotational atherectomy [RA]), which could be better tolerated thanks to improved myocardial contractile reserve and global hemodynamics. When implemented before TAVI, RA has required the use of balloon pumps and/or inotropic support in a considerable number of patients, testifying to the higher ischemic burden in the presence of AVS [59, 60]. Conversely, other observational data has reported the feasibility and safety of RA after TAVI, either through self-expandable or a balloon-expandable valves [61–63], without periprocedural major cardiovascular or cerebral adverse events.

Importantly, with regard to bleeding, performing TAVI after PCI in most cases implies the use of dual anti-platelet therapy, or even triple antithrombotic therapy in the case of patients requiring anticoagulation. Although TAVI can be deferred until triple therapy is shifted to anticoagulant plus clopidogrel, this association has been demonstrated to incrementally raise the risk of bleeding and vascular complications (a 1.6-fold risk compared to anticoagulation alone) according to the recent POPULAR TAVI study [38]. This evidence strongly supports operators performing TAVI first in patients under anticoagulant medications (or at high bleeding risk) to secure vascular access healing before starting any additional antithrombotic agent.

Furthermore, the absence of AVS permits a more accurate diagnosis of the ischemic potential of a given angiographic intermediate stenosis by physiological assessment, as previously reported [22, 24, 64].

Lastly, one may suppose that some conduction disturbances after TAVI might present an ischemic component (e.g., right coronary severe disease), prompting the need for revascularization before TAVI. It is worth noting that the incidence of new-onset conduction disorders requiring permanent pacemaker implantation remains relatively high, and represents a cause for concern [65, 66]. Currently, definitive evidence is lacking on the effect of functional assessment and/or PCI before or after TAVI and its association with post-TAVI conduction disturbances.

However, there are no available randomized clinical trials clearly defining the best timing approach for myocardial revascularization in AVS patients. An ongoing trial (Optimal Timing of Transcatheter Aortic Valve Implantation and Percutaneous Coronary Intervention — the TAVI PCI Trial, NCT04310046) comparing PCI pre- vs. post-TAVI (according to iFR ≤0.89 or angiographic stenosis >90%) will offer more solid evidence on this topic.

For the time being, the available literature suggests both approaches are feasible [67]. Regarding safety, they are mostly comparable, and as to clinical benefits, differences may be subtle and could emerge only after analyzing a larger number of cases not yet available. Until definitive evidence becomes available, choosing a TAVI-first approach addresses the primary clinical problem, while concomitant stable CAD remains an occasional finding, and, as such the need for treatment is uncertain and can always be considered after a thorough clinical or instrumental evaluation.

CONCLUSIONS AND TAKE-HOME MESSAGES (FIGURE 1)

The best management of CAD in TAVI candidates is still under investigation, and most of the available evidence is based on observational studies from high-volume centers (Tables 1 and 2). Therefore, definitive indications cannot yet be formulated. The following messages are reasonable advice arising from the abovementioned studies:

Streamline CAD Detection: Operators should streamline CAD detection by utilizing CCTA to select patients with abnormal findings for ICA.

Functional Evaluation for Intermediate Stenosis: Once CAD is detected, functional evaluation is desirable in cases of intermediate stenosis (at least >50%) to guide revascularization and avoid pointless and potentially harmful interventions.

Timing of Functional Evaluation: Functional evaluation should be carried out after valve deployment to avoid the hemodynamic influence generated by LV obstruction. Among functional indices, FFR has shown the best correlation with myocardial nuclear imaging in detecting ischemia, providing more reliability when measured before and after TAVI.

Timing of PCI: Ischemia-driven interventions are feasible and safe either pre- or post-TAVI. Potential advantages may arise from performing PCI after valve replacement; however, as there is no one-size-fits-all approach, the best strategy should be to tailor treatment on a case-by-case basis.

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