Coronary Revascularisation in Transcatheter Aortic Valve Implantation Candidates: Why, Who, When?

Davide Cao, Mauro Chiarito, Paolo Pagnotta, Bernhard Reimers and Giulio G Stefanini

Department of Biomedical Sciences, Humanitas University, Pieve Emanuele-Milan, Italy; Cardio Center, Humanitas Research Hospital, Rozzano-Milan, Italy

Abstract

Coronary artery disease (CAD) and aortic stenosis (AS) frequently coexist. The presence of CAD has been consistently associated with an impaired prognosis in patients undergoing surgical aortic valve replacement during short- and long-term follow-up. Accordingly, current guidelines recommend coronary revascularisation of all significant stenoses in patients undergoing surgical aortic valve replacement. Conversely, the management of concomitant CAD in patients with severe AS undergoing transcatheter aortic valve implantation (TAVI) is still a matter of debate. The aim of this review article is to provide an overview on the role of coronary revascularisation in TAVI patients.

Keywords

Concomitant PCI, coronary artery disease, percutaneous coronary intervention, severe aortic stenosis, staged PCI, Syntax Score, transcatheter aortic valve implantation

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Correspondence: Giulio G Stefanini, Department of Biomedical Sciences, Humanitas University, Pieve Emanuele-Milan, Italy. E: giulio.stefanini@hunimed.eu

The prevalence of concomitant coronary artery disease (CAD) in patients with severe aortic stenosis (AS) varies widely among different reports. This depends primarily on the definition used to assess CAD as well as study design and patient selection, therefore making a uniform estimate difficult. Major trials investigating transcatheter aortic valve implantation (TAVI) highlighted a substantial majority of high- and intermediate-risk patients (63–75 %) with concomitant CAD.^{1–4} Contemporary multicentre TAVI registries of real-world patients reported a slightly lower but still considerable incidence of CAD (*Table 1*).^{5–13} The large Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) registry revealed that only 37 % of patients undergoing TAVI in the USA are free from significant CAD.¹⁴ However, it should be noted that CAD prevalence is often reported according to either angiographic evidence of epicardial coronary stenosis, or based on history of previous myocardial infarction or revascularisation, thereby entailing a risk of overestimation in those previously fully revascularised.

Elderly patients with severe AS complaining of angina frequently exhibit concomitant CAD.^{15,16} Whether myocardial ischaemia is determined by insufficient oxygen supply due to the underlying valvular disease or due to the presence of CAD is a matter of debate.¹⁷ Interestingly, recent studies showed that coronary blood flow and vasodilator reserve are immediately improved after TAVI, with consequent symptom relief.^{18–21} Of note, due to the mutual worsening of myocardial ischaemia by concomitant CAD and severe AS, clinical manifestations of the two conditions may overlap, rendering the ischaemic relevance of each condition difficult to interpret. Therefore, combined percutaneous coronary intervention (PCI) and TAVI require careful evaluation of the prognostic impact of both CAD and AS.

According to most recent European guidelines, PCI should be considered in patients with significant stenosis of major epicardial

vessels undergoing TAVI.²² The objective of the present review is to provide an overview of available evidence on the role of PCI in TAVI patients, focusing on rationale for treatment, patient selection and optimal timing of intervention.

Why Treat: Impact of Coronary Artery Disease on Clinical Outcomes after TAVI

Initial studies exploring the influence of concomitant CAD in patients with severe AS undergoing TAVI reported conflicting results.^{23–26} This lack of consensus was likely to be a result of several issues such as limited experience with first-generation bioprosthesis, heterogeneity of the study population, small sample size and the absence of a standardised definition of CAD. More recently, different contemporary large-scale registries investigating outcomes in a broad TAVI population found the presence of concomitant CAD to be related to adverse clinical outcomes and impaired survival (*Table 1*). In an analysis from the German TAVI registry, patients with CAD presented higher crude rate of in-hospital mortality and lower unadjusted 30-day survival compared with those without CAD. However, this difference was no longer significant after adjusting for confounders, suggesting that outcomes could be largely explained by comorbidities.²⁷ Similar findings were reported within the SOURCE XT registry. Although not quite statistically significant on multivariate analysis (HR 1.22; 95 % CI [1.00–1.49], $p=0.0552$), the presence of CAD at baseline was associated with a higher risk of 1-year mortality.⁹ Along this line, data from the Bern University Hospital PCI and TAVI registries were extrapolated to analyse three age- and gender-matched cohorts of 248 subjects each. A significantly increased rate of major adverse cardiovascular and cerebrovascular events (MACCE) at 1 year was observed in patients undergoing TAVI with concomitant CAD (16.8 %) compared with TAVI without CAD (9.8 %), and stable CAD undergoing PCI without AS (9.5 %), primarily due to a higher risk of cardiovascular death. Moreover, the first cohort presented more

Table 1: Large Multicentre Studies on Prevalence and Impact of CAD in TAVI

Study	Year	Pts (n)	CAD (%)	History (%)			Findings
				Prior MI	Prior CABG	Prior PCI	
Randomised clinical trials							
PARTNER 1A¹	2011	348	74.9 [†]	26.8	42.6	34.0	
COREVALVE²	2014	390	75.4	25.4	29.5	34.1	
PARTNER 2A³	2016	1011	69.2	18.3	23.6	27.1	
SURTAVI⁴	2017	864	62.6	14.5	16.0	21.3	
Major real-world multicentre registries							
SOURCE⁵	2011	1,038	51.7		22.7	25.0	CAD associated to 1-year mortality on univariable (HR 1.45; p=0.02) but not on multivariate analysis
FRANCE 2⁶	2012	3,195	47.9	16.4	18.2		CAD associated to higher rate of transapical TAVI
German TAVI²⁷	2012	1,382	62.2	15.8	18.4	35.1	CAD associated to higher crude rate of in-hospital mortality (OR 1.90; p<0.01) and lower survival at 30 days (91.6 % vs. 94.7 %, p=0.04). No longer significant after adjusting for confounders (OR 1.41; p=0.18)
Italian CoreValve²⁶	2013	659	38*	21.7	15.8	28.5	CAD not associated with procedural outcomes, MACCE (HR 0.76; p=0.353) or survival (HR 0.74; p=0.331) at 1 year
ADVANCE⁷	2014	1,015	57.8	16.4	21.5	31.5	CAD, history of MI, PCI or CABG did not predict mortality at 1 year
GARY⁸	2014	3,875	54.5	16.6	21.2	29.1	
SOURCE XT⁹	2015	2,688	44.2	15.1	16.0	30.5	1-year mortality associated to CAD (HR 1.39; p=0.0002) and prior MI (HR 1.40; p=0.0026) CAD not an independent predictor of mortality on multivariate analysis (HR 1.22; p=0.0552) Previous PCI and CABG not associated with mortality at 1 year
UK TAVI, Ludman¹⁰	2015	3,980	45.2	22.5		21.2	CAD independent predictor of mortality at 2 years on univariate (HR 1.23; p=0.003) and multivariate (HR 1.08; p=0.036) analysis CAD did not predict 30-day mortality
UK TAVI, Snow¹¹	2015	2,588	45.2	22.7			CAD not associated with early (30-days, p=0.36) or late (4 years, p=0.10) survival on multivariate analysis
STS/ACC TVT¹⁴	2016	26,414	63	25.3	31.4	35.6	
Singh¹²	2016	22,344	66.9	13.0			Higher rates of mortality (10.7 % vs 4.6 %), vascular (8.2 % vs 4.2 %), cardiac (25.4 % vs 18.6 %), respiratory (24.6 % vs 16.1 %), and infectious (10.7 % vs 3.3 %) complications (p<0.001 % for all) in TAVI + PCI group vs TAVI alone
SOURCE 3¹³	2017	1,947	51.5	11.7	11.4	33.8	

CABG = coronary artery bypass grafting; CAD = coronary artery disease; MACCE = major adverse cardiovascular and cerebrovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; pts = patients; TAVI = transcatheter aortic valve implantation. [†]Patients requiring revascularisation were excluded; *CAD defined as history of prior PCI or CABG.

frequently with diabetes mellitus, peripheral artery disease, chronic renal failure and a greater extent and complexity of coronary lesions compared with patients with stable CAD without AS.²⁸

Conversely, results from the UK TAVI registry outlined that CAD, albeit associated with greater comorbid conditions, predicted neither short- nor long-term survival.¹¹ Similarly, in the ADVANCE study, neither CAD, nor history of MI or prior revascularisation were found to be predictors of mortality at 12 months.⁷

Several small studies showed the feasibility of PCI in TAVI patients (Table 2). A recent meta-analysis by Kotronias and colleagues included 3,858 patients who did or did not undergo PCI prior to or concomitant with TAVI.²⁹ Interestingly, coronary revascularisation was associated with an increased risk of major vascular complications and higher 30-day mortality. However, this association was no longer present at 1 year, suggesting that early adverse outcomes could be ascribed to a worse preoperative risk profile of the PCI group. Indeed, PCI negative impact vanished when outcomes were compared only among studies with 100 % prevalence of CAD in both revascularised and non-revascularised groups. Furthermore, no difference between the two

cohorts was observed with respect to 30-day cardiovascular mortality, myocardial infarction and acute kidney injury.

Of note, CAD is a complex and heterogeneous disease, not only due to its frequent association with various comorbidities, but also in terms of extent of myocardium at risk, which may explain the discrepancy between different reports. For this purpose, stratifying patients according to disease severity – i.e. by means of Syntax score – may allow assessment of the prognostic implications of CAD on clinical outcomes after TAVI with greater accuracy (Table 3). In a retrospective analysis of 445 patients from the Bern TAVI registry, severity of CAD was associated with impaired clinical outcomes at 1 year after TAVI. Specifically, this study showed that patients with a Syntax score >22 received less complete revascularisation and had a higher risk of cardiovascular death, stroke or MI than patients without CAD or with a lower Syntax score.³⁰ These findings were confirmed by a recent multicentre study of 1,270 TAVI patients that identified the same threshold of Syntax score >22 as an independent predictor of all-cause mortality (HR 2.09; p=0.017).³¹ In another observational study, Khawaja and colleagues found a residual Syntax score of 9 to be independently associated with mortality (HR 1.95;

Table 2: Studies on Safety and Feasibility of PCI in TAVI Patients

Study	Year	Pts (n)	CAD (%)	% PCI (in CAD pts)	Timing of PCI	Stent type (%)	Follow-up	Outcomes	Additional findings
Abdel-Wahab⁴⁴	2012	125	44	44 (100)	Before or combined with TAVI (median of 10 days before)	DES: 71 BMS: 24 DES + BMS: 5	Up to 3 years	No difference in 30-day mortality (2 % vs 6 %, p=0.27) and long-term survival (p=0.36) between PCI + TAVI and isolated TAVI	No difference in 30-day VARC combined (11 % vs 13 %, p=0.74) and individual endpoints
Gasparetto⁴³	2013	191	59.2	20.4 (34.5)	Median of 27 days before TAVI	BMS: 56.4	12.9 ± 9.5 months	No adverse events with PCI	No difference between CAD and no CAD in 30-day and 1-year in all-cause mortality and other adverse events
Codner⁴⁸	2013	153	23.5	23.5 (100)	Before or during TAVI		Up to 2 years (mean: 454 days)	No difference in 2-year mortality between PCI + TAVI and TAVI alone (p=0.67)	Increased baseline creatinine (HR 1.55; p=0.049) predicted all-cause mortality
Ussia²⁶	2013	275	100	66.5 (66.5)	Mean of 32 ± 10 days before TAVI		Up to 1 year	Similar 1-year MACCE (p=0.594) and mortality (p=0.807) between complete, incomplete and no revascularization	Higher incidence of MI in pts without any revascularization (p=0.050)
Abramowitz⁴⁹	2014	249	57.8	24.5 (42.4)	Mean of 56.6 ± 29.4 days before TAVI	DES: 86.9 BMS: 11.5 DES + BMS: 1.6	Up to 3 years (mean: 17 months)	No difference in 30-day mortality and VARC endpoints between CAD and no CAD pts, and between PCI and no PCI group among CAD pts	No difference between groups in long-term survival (p=0.68)
Penkalla⁴⁰	2015	593	51.9	12.8 (24.7)	100 % combined after transapical TAVI		Up to 5 years	No difference in 30-day mortality (p=0.609) and 3-year survival between transapical TAVI without CAD, with CAD and no PCI, and with PCI	Trend towards increased 3-year mortality in pts with CAD due to higher pre-operative risk and comorbidities PCI + TAVI associated to higher amount of contrast but not to renal injury
Chakravarty⁴¹	2016	204 TAVI + LM PCI 1188 TAVI alone	128 pts with 1:1 case-control matching		Before (81.9 %), during (12.7 %) or after (5.4 %) TAVI	BMS: 14.2 DES: 73.0 DES + BMS: 1.0	Up to 1 year	Similar 30-day (p=0.67) and 1-year mortality (p=0.83) between the TAVI + LM PCI pts and matched controls undergoing TAVI alone	Similar outcomes in unprotected vs protected, ostial vs nonostial, and with LM PCI less vs more than 3 months before TAVI Higher mortality in unplanned vs planned LM PCI

BMS = bare metal stent; CAD = coronary artery disease; DES = drug eluting stent; LM = left main; MACCE = major adverse cardiovascular and cerebrovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; pts = patients;
TAVI = transcatheter aortic valve implantation; VARC = Valve Academic Research Consortium.

Table 3: Studies on TAVI Outcomes According to CAD Severity and Revascularisation Extent

Study	Year	Pts (n)	Assessment of relevant CAD	Prevalence of CAD (%)	% PCI (in CAD pts)	Completeness of revascularization among CAD pts	Follow-up	Outcomes	Conclusions
Van Mieghem³⁴	2013	263	Coronary stenosis >50 % SYNTAX Score in pts without prior CABG	47	14.8 (31.5)	20.2 % bSS 9, rSS 5	Median of 16 months	Complete revascularization (p=0.85) and rSS threshold of 8 (p=0.71) did not impact on 1-year survival	Revascularization status not associated to outcomes
Stefanini³⁰	2014	445	SYNTAX Score: low SS 0-22, high SS >22	65.5 SS 0-22: 46.5 SS >22: 18	31.2 (48.4)	Low SS: bSS 10.1, rSS 4.0 High SS: bSS 33.2, rSS 21.2	Up to 1 year	bSS >22 associated with 2-fold increased risk of 1-year cardiovascular mortality (p=0.029) Higher rSS associated with increased ischemic outcomes	Severity of CAD and less complete revascularization associated with impaired 1-year outcomes Higher bSS received less complete revascularization
Khawaja³²	2015	271	QCA: coronary stenosis ≥70 % (or ≥50 % if left main or vein graft) SYNTAX Score	34.3	9.2 (26.9)		Median of 683 days	SS threshold of 9 independently predicted mortality (HR 1.95, p=0.006) High SS (>33) associated with mortality (p= 0.007), conversely CAD per se was not (p=0.805)	No effect of CAD (p=0.805) and PCI among CAD pts (p=0.918) on mortality at 30 days and 1 year
Witberg³¹	2017	1270	SYNTAX Score: moderate CAD (SS 0-22), severe CAD (SS >22)	35.7 SS 0-22: 26.1 SS >22: 9.6	32.3 (90.2) SS 0-22: 88.6 SS >22: 94.3		Median of 1.9 years	SS >22 (HR 2.09; p=0.017) and rSS >8 (HR 1.72; p=0.031) independently predicted mortality	More complete revascularization may lower the impact of severe CAD on mortality Survival with moderate CAD and reasonable incomplete (rSS <8) revascularization was comparable to prognosis without CAD
Shamekhi³⁹	2017	666	SYNTAX Score: low SS 0-24, high SS >24 SYNTAX Score II	65.6	24.3 (37.1)	Low SS: bSS 7.0, rSS 2 High SS: bSS 38.5, rSS 11	Median of 593 days	Higher bSS (p=0.001), rSS (p=0.01), and SS-II (p<0.001) associated with increased 3-year mortality bSS, rSS and SS-II did not independently predict mortality	Severity of CAD at baseline and after PCI associated with survival after TAVI
Paradis³⁷	2017	377	QCA-derived SYNTAX Score: low SS 1-22, intermediate SS 23-32, high SS ≥33	78.2	42.2 (53.6)	Low SS: bSS 11.5, rSS 6.4 Intermediate SS: bSS 27.7, rSS 16.4 High SS: bSS 45.9, rSS 33.8	Median of 452 days	CAD presence, bSS, rSS threshold of 8, and CABG-SS did not impact on 30-day and 1-year outcomes	Neither severity of CAD, nor completeness of revascularization after PCI or CABG were associated with worse clinical outcomes

bSS = baseline SYNTAX Score; CAD = coronary artery disease; CABG = coronary artery bypass grafting; MACCE = major adverse cardiovascular and cerebrovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; pts = patients; QCA = quantitative coronary angiography; rSS = residual SYNTAX Score; SS = SYNTAX Score; TAVI = transcatheter aortic valve implantation.

Table 4: Studies on Timing of PCI in TAVI Patients

Study	Year	Pts (n)	% PCI (in CAD pts)	Timing of PCI	Stent type (%)	Follow-up	Outcomes	Conclusions	Additional findings
Before and concomitant									
Wenaweser⁴⁵	2011	256	23.0 (35.3)	34 ± 26 days before TAVI (39 %) Concomitant with TAVI (61 %)	DES: staged 52.5, concomitant 88.4	Up to 2 years	No difference in 30-day mortality (5.6 % vs 10.2 %, p=0.24) and VARC endpoints between isolated TAVI and PCI + TAVI	Staged and concomitant PCI safe and feasible	Completeness of revascularization did not impact on long-term survival (p=0.16)
Conradi⁴⁶	2011	28	100 (100)	14.3 ± 9.6 days before TAVI (75 %) Concomitant prior to TAVI (25 %)	BMS: 69.5 DES: 34.1	30 days	In-hospital and 30-day mortality rate of 7.1 % (2/28 deaths all in the PCI concomitant to TAVI group)	Staged and concomitant PCI safe and feasible	No periprocedural MI or stroke Higher risk of renal failure with concomitant strategy
Griese⁵¹	2014	411	15.8	Before (74 %) or concomitant (26 %) with TAVI	BMS: 71	Median of 16 months	PCI + TAVI associated to increased rate of 30-day MI (6 % vs 1 %; p=0.01) and mortality (15 % vs 5 %; p=0.01), and worse 2-year survival (p=0.03)	Similar 2-year survival between staged and concomitant PCI (p=0.65)	PCI associated to an elevated risk of MI and death regardless of synchronous or staged strategy
Before									
Van Rosendal⁵⁰	2015	96	100	<30 days (50 %) ≥30 days (50 %)	DES: 44 <30 days: 40 ≥30 days: 48	Up to 3 years	3-year mortality not associated to timing of staged PCI (p=0.363)	Shortly or remotely staged PCI before TAVI yields comparable results	Higher rates of minor bleeding (p=0.011) and vascular injury (p=0.016) with PCI <30 days
After									
Pasic⁴⁷	2012	419	11.0	Same session after transapical TAVI		Up to 3 year	4.3 % mortality rate at 30 day 87.1 % survival rate at 1 year, 69.7 % at 2 and 3 years	PCI immediately after transapical TAVI safe and feasible	100 % technical procedural success
Blumenstein⁵⁴	2015	35	100	Any time after TAVI (232.8 ± 158.4 days)		Procedural success of PCI	Coronary cannulation failed in 9/15 cases with valve covering coronary ostia	Supracoronary devices and high valve implantation may impair PCI success after TAVI	Coronary cannulation was feasible with all devices in subcoronary position
Allali⁵⁵	2016	17	100	Any time after TAVI (median of 17.7 months)	DES: 86.2	In-hospital	Successful coronary cannulation in 95.8 % of procedures	PCI safe and feasible after self-expandable TAVI	1 procedural failure and consequent death in emergency setting

BMS = bare metal stent; CAD = coronary artery disease; DES = drug eluting stent; MI = myocardial infarction; PCI = percutaneous coronary intervention; pts = patients; TAVI = transcatheter aortic valve implantation.

p=0.006).³² Consistently, a meta-analysis of 979 patients showed that a low extent of CAD, estimated as baseline or residual Syntax Score ≤10, did not negatively affect outcomes at 30 days and 1 year.³³ Moreover, Van Mieghem and colleagues observed no impact on TAVI outcomes according to revascularisation status (complete or incomplete), nor by a residual Syntax score threshold of 8.³⁴ Based on these observations, the authors concluded that only a carefully selective PCI of major proximal epicardial vessels subtending large areas of myocardium at risk is likely to confer a clinical benefit.

Taken together, these findings suggest that severe CAD, often encountered in association with a wide range of comorbid conditions, may negatively affect survival of patients with AS undergoing

TAVI. Therefore, reducing myocardial ischaemic burden through PCI appears a legitimate option to improve clinical outcomes after TAVI.

Who to Treat: Assessment of Relevant Coronary Artery Disease

Non-invasive Assessment

Assessment of myocardial ischaemia due to concomitant CAD in the presence of severe AS can be challenging because of the overt difficulties in interpreting symptoms when both diseases coexist. In patients with suspected CAD, exercise or pharmacological stress examination is essential in determining inducible ischaemia, which may benefit from coronary revascularisation. However, these tests are usually contraindicated in patients with severe AS. Nonetheless,

dobutamine echocardiography is accepted in cases of low-gradient AS to assess disease severity and guide treatment. Moreover, stress echocardiography is a prognostic tool for risk stratification by appraising contractile reserve in patients with severe AS and impaired left ventricular function.

Studies investigating safety and diagnostic accuracy of non-invasive testing with vasodilator stressor in severe AS demonstrated an overall feasibility due to absence of major adverse cardiac events related to the test, although specificity of results might be lower than in the absence of AS.³⁵ In fact, dipyridamole echocardiography on patients with severe AS and normal coronary artery may elicit an ischaemic susceptibility arising only from the aortic valve disease, which is possibly reversible after treatment of AS.³⁶

Coronary Angiography

Angiographic screening of coronary anatomy is recommended prior to any aortic valve intervention. Indication and survival benefit attributed to coronary artery bypass grafting (CABG) of $\geq 50\%$ coronary stenosis in subjects who are candidates for surgical aortic valve replacement has been established for decades.^{37,38}

Given the importance of assessing CAD severity to properly evaluate its clinical significance, coronary angiography allows quantification of the disease extent and complexity. For this purpose, the Syntax score represents an attractive tool for decision making also in patients with AS. Available evidence indicates that CAD in patients without a high ischaemic burden may bear a neutral effect on outcomes after TAVI. Indeed, as summarised above, several studies showed that survival of patients with moderate CAD and reasonably incomplete revascularisation was comparable with the prognosis of patients without CAD (*Table 3*).^{30,31,39}

Owing to its high negative predictive value in the detection of CAD, computed tomography angiography, regularly performed preoperatively to evaluate vascular access, annular and aortic root measurements, might also be useful for CAD assessment in TAVI patients. Indeed, Chieffo and colleagues reported that only 22 % of patients required additional coronary angiography after first-line CAD screening with coronary computed tomography angiography in a single centre registry.⁴⁰

Invasive Functional Assessment

Functional assessment of coronary lesions by means of fractional flow reserve (FFR) has been shown to accurately guide coronary revascularisation, determining clinical, rather than anatomical, relevance of flow-limiting stenosis. FFR evaluation is based on pressure-flow measurements during adenosine-induced maximal hyperaemia. As well as safety concerns related to vasodilator administration in AS, diagnostic accuracy of FFR has been arguable due to potential underestimation of functionally relevant intermediate stenosis secondary to haemodynamic changes derived from aortic valve disease.³⁵ Although apparently clinically feasible, a series of minor coronary flow variations were observed with FFR after TAVI, suggesting that borderline coronary lesions could become significant following the procedure.⁴¹

Alternatively, avoiding induced hyperaemia through instantaneous wave-free ratio (iFR) may be advantageous, increasing safety and reliability of functional evaluation of critical CAD in TAVI patients. Some authors also advocated a hybrid approach, opting for adenosine-

independent iFR as screening tool, while sparing the assessment of borderline lesions by means of FFR only after TAVI.⁴²

When to Treat: Timing of Percutaneous Coronary Intervention

Available data seem to suggest that PCI both before and along with TAVI are feasible and do not impact on early survival, but there are a few caveats.⁴³⁻⁴⁷ However, there is very limited evidence in support of staging PCI after TAVI (*Table 4*).

Before Transcatheter Aortic Valve Implantation

PCI can be safely performed in patients with severe AS, although low ejection fraction and high STS score determine a higher risk of short-term mortality.⁴⁸

Patients with stable CAD at high bleeding risk undergoing coronary stent implantation require dual antiplatelet therapy for a minimum of 3 months, yet a 1 month duration may also be considered.⁴⁹ Performing early staged TAVI after PCI may result in an additional periprocedural haemorrhagic risk due to the ongoing antithrombotic therapy. Conversely, postponing TAVI until antithrombotic therapy cessation raises concerns about the delay of definitive treatment for severe symptomatic AS. Moreover, a delayed approach would further prolong patient exposure to dual antiplatelet therapy for 3–6 months immediately after TAVI, as suggested by current guidelines.²²

A study investigating optimal timing of PCI prior to TAVI stratified 96 patients in one group undergoing PCI ≥ 30 days before TAVI and another group undergoing PCI within 30 days before TAVI. Interestingly, the shortly staged PCI (<30 days) cohort was at higher risk of minor bleeding events and vascular injury after TAVI, although the lower haemoglobin level and higher incidence of atrial fibrillation at baseline in this group might have contributed to these findings.⁵⁰ Along the same lines, it appears reasonable to postpone TAVI until vascular access healing has occurred and enough time has passed since antiplatelet loading dose administration.

Finally, hypotension from rapid ventricular pacing has often been considered to potentially worsen myocardial ischaemia, therefore revascularisation before TAVI would allow mitigation of a patient's procedural risk.

Concomitant with Transcatheter Aortic Valve Implantation

Beyond reducing costs of intervention and rehospitalisation, another potential advantage of single-staged PCI and TAVI is the use of the same transarterial access for both procedures, with a lower consequent risk of vascular and bleeding complications. Although higher rates of periprocedural mortality, vascular complications and myocardial infarction have been reported in patients undergoing combined TAVI and PCI, no significant difference between staged and concomitant procedures was observed.^{29,51} However, a trend towards a reduced incidence of bleeding and vascular complications was noted in patients undergoing PCI and TAVI in the same session.^{45,51} Nevertheless, it must be acknowledged that studies are heterogeneous and no uniform information regarding ongoing therapy and time interval between the two procedures was provided.²⁹

There is also legitimate apprehension of concomitant PCI because of nephrotoxicity due to a prolonged intervention. Indeed, patients

Figure 1: Flow Chart of Suggested Strategies for Coronary Artery Disease Management in Transcatheter Aortic Valve Implantation Candidates

CAD = coronary artery disease; CTO = chronic total occlusion; LM = left main; PCI = percutaneous coronary intervention; TAVI = transcatheter aortic valve implantation.

undergoing simultaneous PCI and TAVI may receive a higher amount of contrast agent, therefore being more exposed to renal injury.^{46,52} However, correlation between contrast volume and acute kidney injury is weak in TAVI patients and many studies failed to show its predictive value.⁵³

After Transcatheter Aortic Valve Implantation

Since TAVI has been shown to improve coronary perfusion and anginal symptom relief, evaluation of CAD after valve intervention may allow a more physiological and accurate assessment of myocardium at risk of ischaemia, especially in the presence of borderline coronary lesions. However, this strategy entails a series of technical challenges. Coronary cannulation and catheter manipulation may be hampered later after valve deployment, especially with self-expandable prosthesis due to the bulky stented frame placed over coronary ostia. Malpositioning of the valve, mainly in the case of high implantation and consequent aortic root distortion, are essential factors raising this risk.⁵⁴ More importantly, compromised cannulation of coronaries could be ominous in an emergency situation.⁵⁵ Notwithstanding, a recent study reported technical success in all 46 cases of PCI performed right after balloon-expandable TAVI within the same operative session, without additional procedural complexity.⁴⁷ This suggests that in the presence of extensive CAD and the possibility of future need for PCI, valve selection – i.e., favouring bioprosthesis with subcoronary implantation – may be crucial to allow coronary accessibility after TAVI.

Conclusion

CAD is frequent among TAVI patients and PCI is commonly performed in this setting. However, assessment of relevant CAD in the presence

of severe AS can be difficult and symptoms potentially misleading. Available evidence in support of different revascularisation strategies is mostly based on retrospective, single-centre studies reporting unadjusted and discordant outcomes. The ongoing percutaneous coronary intervention prior to transcatheter aortic valve implantation (ACTIVATION) study is the first randomised controlled trial designed to evaluate non-inferiority of PCI compared with not treating such coronary lesions before TAVI.⁵⁶

While awaiting further data to provide solid recommendations, the decision to pursue coronary revascularisation in TAVI patients should be tailored case-by-case and based on clinical and anatomical variables, appraised by multi-disciplinary consensus within the local Heart Team. For this purpose, Syntax score may help stratify CAD severity to guide selection of patients who will benefit the most from concomitant PCI. At this point, it is reasonable to foster selective revascularisation strategies of proximal epicardial coronary arteries in subjects with signs of high ischaemic burden (Figure 1). Finally, staging PCI either before or concomitant with TAVI appears feasible. Optimal timing should be decided on an individual basis, taking into consideration patients and procedural characteristics.

Overall, current management of CAD in TAVI patients is largely based on observational evidence. Given the broad expansion of TAVI indication in lower risk patients, large and well-designed randomised trials investigating strategies for the optimal management of CAD in TAVI patients are needed. ■

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