European Heart Journal (2017) **0**, 1–10
doi:10.1093/eurheartj/ehx455

CLINICAL RESEARCH
Valvular heart disease

Incidence, predictors, and clinical outcomes of coronary obstruction following transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: insights from the VIVID registry

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Received 2 January 2017; revised 8 May 2017; editorial decision 30 June 2017; accepted 19 July 2017

Aims There are limited data on coronary obstruction following transcatheter valve-in-valve (ViV) implantation inside failed aortic bioprostheses. The objectives of this study were to determine the incidence, predictors, and clinical outcomes of coronary obstruction in transcatheter ViV procedures.

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Methods and results A total of 1612 aortic procedures from the Valve-in-Valve International Data (VIVID) Registry were evaluated. Data were subject to centralized blinded corelab computed tomography (CT) analysis in a subset of patients. The virtual transcatheter valve to coronary ostium distance (VTC) was determined. A total of 37 patients (2.3%) had clinically evident coronary obstruction. Baseline clinical characteristics in the coronary obstruction patients were similar to controls. Coronary obstruction was more common in stented bioprostheses with externally mounted leaflets or stentless bioprostheses than in stented with internally mounted leaflets bioprostheses (6.1% vs. 3.7% vs. 0.8%, respectively; $P < 0.001$). CT measurements were obtained in 20 (54%) and 90 (5.4%) of patients with and without coronary obstruction, respectively. VTC distance was shorter in coronary obstruction patients in relation to controls (3.24 ± 2.22 vs. 6.30 ± 2.34, respectively; $P < 0.001$). Using multivariable analysis, the use of a stentless or stented bioprosthesis with externally mounted leaflets [odds ratio (OR): 7.67; 95% confidence interval (CI): 3.14–18.7; $P < 0.001$] associated with coronary obstruction for the global population. In a second model with CT data, a shorter VTC distance predicted this complication (OR: 0.22 per 1 mm increase; 95% CI: 0.09–0.51; $P < 0.001$), with an optimal cut-off level of 4 mm (area under the curve: 0.943; $P < 0.001$). Coronary obstruction was associated with a high 30-day mortality (52.9% vs. 3.9% in the controls, respectively; $P < 0.001$).

Conclusion Coronary obstruction following aortic ViV procedures is a life-threatening complication that occurred more frequently in patients with prior stentless or stented bioprostheses with externally mounted leaflets and in those with a short VTC.

Keywords Transcatheter aortic valve replacement • Prior surgical bioprosthesis • Coronary obstruction • Coronary occlusion • Valve-in-valve

Introduction

Coronary obstruction is a life-threatening complication of transcatheter aortic valve replacement (TAVR), and it is commonly secondary to displacement of a valve leaflet towards the coronary ostia.[1,2] We have recently conducted a multicentre registry on coronary obstruction showing that this is a rare (incidence < 1%) but life-threatening complication following TAVR. Specific anatomic factors such as low-lying coronary ostium and shallow sinus of Valsalva (SOV) were associated with this complication.[1,2] Also, coronary obstruction was much more frequent during TAVR for degenerative bioprosthetic valves ('valve-in-valve'—ViV).[2] However, the number of ViV cases was limited, precluding a thorough evaluation of this complication in such patients.

Transcatheter heart valve (THV) implantation inside failed aortic surgically implanted bioprosthetic valves represents an appealing less invasive alternative to reoperation, with growing indication worldwide. Of note, the Valve-in-Valve International Data (VIVID) Registry, which is the largest evaluation of ViV to date, has also revealed a much higher rate of coronary obstruction as compared with native aortic valves (~four-fold greater), in accordance to the aforementioned reports.[3–5] Nonetheless, prior studies presented limited number of ViV cases suffering this complication without any comparison against a control group, preventing the determination of its exact incidence, in function of the different surgically implanted bioprosthetic valves, associated factors and outcomes. The objectives of the present study were therefore to evaluate the baseline characteristics, predictive factors, and clinical outcomes of coronary obstruction as a complication of TAVR in patients with prior surgically implanted aortic bioprosthesis.

Methods

Registry design

The VIVID Registry is a global data collection of ViV procedures, including different THV devices and valve positions.[4] Since 2010, the registry prospectively collects data from centres in Europe, North America, South America, Africa, Oceania, and the Middle East. Data collection is performed using dedicated case report forms. In the following analysis, all of the cases from April 2007 until May 2016 were included, though patients undergoing ViV in non-aortic positions were excluded. No restriction to the THV or aortic bioprosthesis type and size were considered. The patients presenting coronary obstruction were compared with those without coronary obstruction and served as controls. Inconsistencies were resolved directly with local investigators and on-site data monitoring. All patients gave written informed consent to the transcatheter aortic ViV procedures.

Definitions

All information on clinical presentation, diagnosis, and treatment of the coronary obstruction complication, as well as 30-day and late clinical outcomes were entered. The clinical events were defined according to the VARC-2 criteria.[6] The mechanism of bioprosthetic valve degeneration (i.e. regurgitation, stenosis, or combined) was evaluated using criteria set by previous guidelines.[7,8] Patients with at least a moderate degree of both stenosis and regurgitation were included in the combined group. Other patients were categorized according to the primary mechanism of degeneration, either stenosis or regurgitation.

Computed tomography

Centralized core laboratory assessment of the computed tomography (CT) from 20 patients with coronary obstruction and 90 consecutive controls from 2 centres were performed by two experienced operators blinded to all clinical results (St. Paul's Hospital, Vancouver, Canada). The main baseline bioprosthetic valve characteristics of the patients in the control group with and without CT data are shown in Supplementary material online, *Table S1*. In addition, the main baseline characteristics between patients with CT data pre-TAVR with and without coronary obstruction are shown in Supplementary material online, *Table S2*. The CT measurements included the surgical frame mean diameter and area, coronaries height in relation to aortic annulus, aortic annulus diameter and area, SOV width, and the diameter of the sinotubular junction. The coronary artery heights were measured relative to basal ring of the prosthetic valve. Likewise, we sought to validate the previously described Vancouver

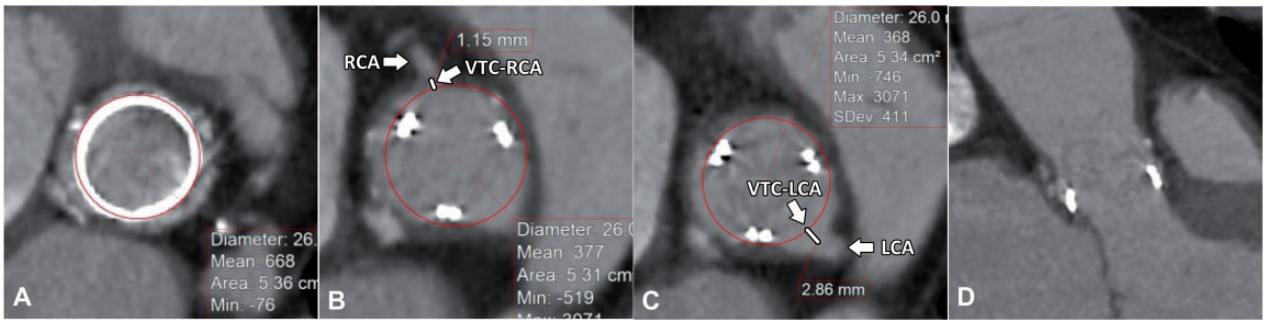

Figure 1 Multidetector computed tomography evaluation pre-TAVR showing the measurement of the distance between a virtual transcatheter ring at a size of the implanted device at the level of each coronary ostium (VTC) with a case example of short VTC for both coronary arteries. (*A*) Virtual ring; (*B*) VTC to the right coronary artery ostium (RCA); (*C*) VTC to the left coronary artery ostium (LCA); (*D*) Effaced sinus of Valsalva.

method[5,9] for predicting the risk of coronary occlusion as determined by the distance between a virtual transcatheter valve, at a size of the implanted device, towards each coronary ostium in both groups (VTC; *Figure 1*). Essentially, the VTC is obtained by identifying the basal ring plane and the geometric centre of the surgical valve. Then, a virtual cylinder with the estimated nominal size of the THV (i.e. a 26 mm THV leads to a cylinder with the same height of the THV and a 26 mm diameter) is placed in the middle of the basal ring. The centres of the basal ring and of the cylinder are aligned. Finally, the horizontal distance between the edge of the cylinder and the ostia of the coronary arteries is measured with a caliper measurement tool of the CT imaging software. The anticipated area of the THV was estimated by the circle area formula: πR^2, where the radius (R) is obtained dividing the diameter of the device by 2. Therefore, in the case of self-expanding devices such as the CoreValve the worst-case scenario was used.[9] Thus, for both the Sapien XT and CoreValve the following areas were used: 20 mm (314 mm^2), 23 mm (415 mm^2), 26 mm (531 mm^2), 29 mm (661 mm^2), and 31 mm (754 mm^2). For the Sapien 3 device, the following values were used: 20 mm (309 mm^2), 23 mm (409 mm^2), 26 mm (519 mm^2), 29 mm (649 mm^2).[9]

Statistical analysis

Categorical variables are reported as *n* (%) and continuous variables are expressed as mean (standard deviation) or median [interquartile range (IQR)] depending on variable distribution. Group comparisons were analysed using the Student *t*-test or Wilcoxon rank sum test. The χ^2 test and the Fisher exact test were performed for categorical variables, and *post hoc* analysis used the Bonferroni correction. Time-to-event curve was calculated using the Kaplan–Meier method. To further determine the independent predictors of coronary obstruction after VIV procedures a multivariable analysis was performed, using logistic regression. Variables with $P < 0.10$ in the univariable analysis were further examined in a stepwise model. The initial selection of variables included the whole cohort of 1612 patients and the following variables were included in the multivariable model: type of bioprosthetic valve, STS-PROM, balloon post-dilatation, and prior coronary artery bypass grafting (CABG). A second model including only the subgroup of patients with CT data was performed and the following variables were included in the model: type of bioprosthetic valve, VTC distance, and SOV mean diameter. The results of the multivariable analysis are presented as odds ratio (OR) with 95% confidence interval (CI). Correlations between CT parameters were assessed by Pearson's coefficient. All analyses were conducted using the statistical package SPSS 22 (IBM Inc., Armonk, NY, USA).

Results

Of 1612 patients who underwent a ViV procedure in 135 centres worldwide, a total of 37 cases (2.3%) of symptomatic coronary obstruction occurred following THV implantation. The incidence of coronary obstruction according to the type of surgically implanted bioprostheses is shown in *Figure 2*, while its distribution with respect to the type of transcatheter valve, approach, and mechanism of bioprosthetic surgical valve failure is shown in Supplementary material online, *Figure S1*. A higher incidence of this complication was only seen with regards to the type of bioprosthesis. The main baseline characteristics of the study population, according to the occurrence of coronary obstruction, are shown in *Table 1*. Patients who suffered symptomatic coronary obstruction presented similar baseline clinical characteristics with respect to controls, apart from the differences in the type of surgically implanted bioprostheses. In addition, CABG was less frequent in those with coronary obstruction in relation to controls ($P = 0.05$). The main procedural and 30-day outcomes are shown in *Table 2*. The procedural variables were similar between both groups, except for a trend towards a higher rate of post-dilatation in the coronary obstruction group (22.2% vs. 12.7%, respectively; $P = 0.07$). At 30 days, death rate was much higher in this group vs. controls (48.6% vs. 3.7%; $P < 0.001$).

Computed tomography data

Pre-TAVR CT data were available in 20 of the 37 patients with coronary obstruction (54%). CT data of the patients with coronary obstruction in relation to the control group are shown in *Table 3*. Patients with coronary obstruction exhibited a smaller SOV diameter (27.44 ± 4.05 vs. 32.55 ± 3.98; $P < 0.001$). In addition, although the coronary artery heights with respect to the annulus were similar between both groups, the VTC distance to the left and right coronary arteries [left coronary artery (LCA) and right coronary artery (RCA), respectively] were much shorter in the coronary obstruction group in relation to controls ($P < 0.001$ for both).

Predictors of coronary obstruction

The main predictors of coronary obstruction are shown in *Table 4*. Using multivariable analysis, the use of a stentless or stented

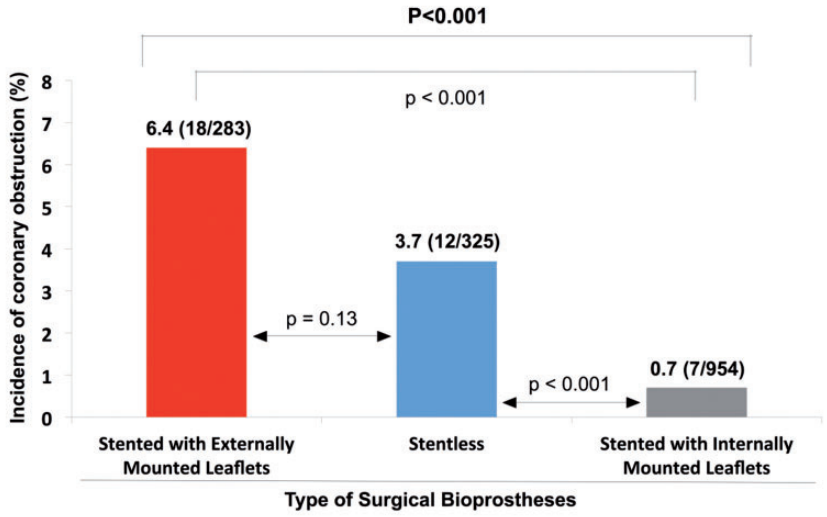

Figure 2 Incidence of coronary obstruction following valve-in-valve procedures according to surgical bioprosthesis type.

bioprosthesis with externally mounted leaflets (OR: 7.67; 95% CI: 3.14–18.7; $P < 0.001$) was an independent predictor of coronary obstruction in the overall population. Likewise, when including only the patients with a CT pre-TAVR, the multivariable analysis showed that the VTC was the only predictor of coronary obstruction (OR: 0.22 per 1 mm increase; 95% CI 0.09–0.51; $P < 0.001$), even after adjusting for SOV width. In addition, the SOV width presented significant collinearity with the VTC ($R^2 = 0.688$, $P < 0.001$; Supplementary material online, *Figure S2*). A VTC cut-off value of 4 mm best identified those patients at higher risk for coronary obstruction (area under the curve: 0.943 [0.893–0.991]; sensitivity = 85%, specificity = 89%; $P < 0.001$). The distribution of the VTC relative to the LCA and RCA ostia is shown in *Figure 3* for both groups.

Clinical presentation and management

Data on clinical presentation and management of coronary obstruction were available for 36 patients (97% of the population), as shown in *Table 5*. Coronary obstruction occurred at the ostium of the LCA in most cases (91.7%) either alone or in association with RCA occlusion, and the diagnosis was made by coronary angiography in all but one patient. Coronary obstruction was related to the displacement of bioprosthetic valve leaflet towards the coronary ostium in all patients, and occurred most frequently immediately after valve implantation (58.3%). Still, it occurred within days following the procedure in 36.1% of the patients (76.9% of the time with self-expandable devices). Most cases (58.3%) presented with severe persistent hypotension or electrocardiographic (ECG) changes (52.8%), mainly driven by ST-segment deviation and ventricular arrhythmias.

Coronary revascularization with percutaneous coronary intervention (PCI) was not attempted in eight patients (22.2%). One patient died within the few minutes following a complete left coronary obstruction with insufficient time for any coronary revascularization attempt; in four patients the occlusion occurred within the hours following the procedure with no time for PCI; one patient went directly to urgent CABG; in one patient the obstruction occurred after pre-dilatation, with temporary occlusion of the LMS and subsequent abandoning of the procedure; and in one patient a repositionable valve allowed the relief of the obstruction by retrieving the device (Lotus valve). PCI was attempted in 28 patients (77.8%), and it was successful (residual stenosis < 20% and TIMI flow 3) in 64.3% of attempted procedures. Revascularization failures by PCI were mainly due to wire crossing failure (50%) or cannulation failure (30%). A total of three patients underwent urgent coronary artery bypass graft, and in two patients occurring after PCI failure. A total of 13 patients (36.1%) required haemodynamic support.

Procedural death occurred in 8 patients (22.2%), and among those patients who survived the procedure 10 additional patients died within 30 days, all of them related to the periprocedural complications, leading to a 30-day mortality rate of 48.6% (18 patients). Among the patients with PCI failures, 80% died within 30 days. In patients with coronary obstruction, the echocardiographic data showed a mean residual gradient of 11.1 ± 5.2 mmHg, aortic valve area of 1.46 ± 0.47 cm^2, with no patients presenting with more than mild aortic regurgitation. These results were similar as compared with the controls. As shown in the Kaplan–Meier curve the 1-year survival rate was 47.8% in the coronary obstruction group (*Figure 4*). At a median follow-up of 460 days (IQR 361–1014.25) among the survivors of the coronary obstruction group, the mean left ventricular ejection fraction was 55.9% ± 7.5 and 78.6% of the patients were in New York Heart Association class ≤ 2.

Discussion

The main findings of the present study evaluating coronary obstruction as a complication of TAVR, in patients with prior surgically implanted aortic bioprosthesis, were as follows: (i) coronary

Table 1 Baseline characteristics of patients undergoing aortic valve-in-valve

	Controls ($n = 1575$)	Coronary obstruction ($n = 37$)	*P*-value
Clinical variables			
Age (years)	77.8 ± 9.3	76.7 ± 12.2	0.50
Patient height (cm)	167.5 ± 10	164.6 ± 9.4	0.10
Patient weight (kg)	75.3 ± 16.5	75.4 ± 14.5	0.97
Body mass index (kg/m^2)	27 ± 11.7	27.8 ± 4.8	0.68
Female sex	662/1573 (42.1)	20/37 (54.1)	0.15
NYHA class			0.91
I–II	157/1534 (10.2)	4/37 (10.8)	
III–IV	1377/1534 (89.8)	33/37 (89.2)	
Diabetes mellitus	402/1572 (25.6)	10/37 (27.0)	0.84
Number of previous cardiac surgeries			0.66
1	1259/1483 (84.9)	34/37 (91.9)	
2	198/1483 (13.4)	3/37 (8.1)	
3	22/1483 (1.5)	0 (0)	
4	4/1483 (0.3)	0 (0)	
Prior CABG	387/1541 (25.1)	4/37 (10.8)	0.05
Cerebrovascular disease	216/1571 (13.7)	4/37 (10.8)	0.61
Peripheral vascular disease	335/1570 (21.3)	5/36 (13.9)	0.28
Renal failure (eGFR <60 mL/min)	774/1547 (50.0)	17/36 (47.2)	0.74
LVEF (%)	52.1 ± 13.1	51.8 ± 13.3	0.88
LogEuroSCORE (%)	29.1 ± 16.9	36.1 ± 23.1	0.08
EuroSCORE 2 (%)	14.5 ± 8.6	16.1 ± 11	0.37
STS-PROM score (%)	9.5 ± 8.4	12.1 ± 10.9	0.07
Bioprosthetic valve			
Time since last SAVR (years)	9 (6–13)	8 (5–12)	0.39
Type			<0.001
Stented with internally mounted leaflets[a]	954/1532 (62.3)	7/37 (18.9)	
Stented with externally mounted leaflets[b]	313/1532 (20.4)	12/37 (32.4)	
Stentless[c]	265/1532 (17.3)	18/37 (48.6)	
Mean label size (mm)	23.3 ± 2.2	23 ± 1.8	0.40
Distribution of label sizes			0.45
≤21 mm	427/1506 (28.4)	13/35 (37.1)	
>21 and <25 mm	559/1506 (37.1)	10/35 (28.6)	
≥25 mm	520/1506 (34.5)	12/35 (34.3)	
Mean true ID (mm)	20.1 ± 2.4	20.8 ± 2.9	0.20
Mechanism of failure			0.17
Regurgitation	415/1490 (27.9)	14/36 (38.9)	
Stenosis	589/1490 (39.5)	9/36 (25.0)	
Both	486/1490 (32.6)	13/36 (36.1)	
Mean aortic gradient (mmHg)	35.5 ± 17.6	35.1 ± 23.1	0.93
Aortic valve area (cm^2)	0.98 ± 0.65	1.13 ± 0.89	0.24

Values are expressed as *n* (%) or mean (±SD).
NYHA, New York Heart Association; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration ratio; LVEF, left ventricular ejection fraction; logEuroSCORE, logistic EuroSCORE predicted risk of mortality; STS-PROM, Society of Thoracic Surgeons predicted risk of mortality; SAVR, surgical aortic valve replacement; ID: internal diameter; SD, standard deviation.
[a]Aspire, Biocor, Carpentier Edwards, Epic, Hancock, Labcor, Magna, Mosaic, Soprano.
[b]Mitroflow, Trifecta.
[c]Cryolife O'Brien, Freedom, Freestyle, Toronto SPV.

Table 2 Main procedural characteristics and short-term results

	Controls ($n = 1575$)	Coronary obstruction ($n = 37$)	*P*-value
Procedural variables			
Approach			0.77
Transfemoral	1164/1574 (74)	30/37 (81.1)	
Transapical	339/1574 (21.5)	5/37 (13.5)	
Transaortic	24/1574 (1.5)	1/37 (2.7)	
Trans-subclavian	40/1574 (2.5)	1/37 (2.7)	
Other	7/1574 (0.4)	0 (0)	
Mean THV size (mm)	24.7 ± 2.1	24.6 ± 2.1	0.80
Distribution of THV sizes			0.79
20 mm	16/1546 (1)	1/36 (2.8)	
23 mm	793/1546 (51.3)	18/36 (50)	
25/26 mm	586/1546 (37.9)	13/36 (36.1)	
27/29 mm	133/1546 (8.6)	4/36 (11.1)	
31/34 mm	18/1546 (1.2)	0/36 (0)	
Ratio of true ID to THV size	0.82 ± 0.08	0.84 ± 0.09	0.14
Prosthesis type			0.85
Balloon-expandable valve (Sapien/Sapien XT)	544/1574 (34.6)	12/37 (32.4)	
Self-expandable valve (CoreValve)	780/1574 (49.6)	20/37 (54.1)	
Others[a]	250/1574 (15.9)	5/37 (13.5)	
Balloon pre-dilatation	357/1555 (23)	8/36 (22.2)	0.92
Balloon post-dilatation	182/1485 (12.3)	8/36 (22.2)	0.07
Need 2nd valve	67/1570 (4.3)	2/37 (5.4)	0.74
30-day results			
Death	56/1508 (3.7)	18/37 (48.6)	<0.001
Major stroke	22/1566 (1.4)	0 (0)	0.48
Major or life-threatening bleeding	91/1528 (6)	4/36 (11.1)	0.20
Vascular complication			0.18
Major	45/1571 (2.9)	3/37 (8.1)	
Minor	98/1571 (6.2)	2/37 (5.4)	
Echocardiographic results			
Maximal gradient (mmHg)	29.2 ± 14.7	21.6 ± 9.8	0.03
Mean gradient (mmHg)	16.3 ± 8.9	11.1 ± 5.2	<0.001
Aortic valve area (cm^2)	1.47 ± 0.49	1.46 ± 0.47	0.94
Aortic regurgitation > mild	91/1463 (6.2)	0 (0)	0.19
LVEF (%)	51.6 ± 11.9	48.2 ± 14.5	0.17

Values are expressed as *n* (%) or mean (±SD).
THV, transcatheter heart valve. Other abbreviations as in *Table 1*.
[a]Other valves included: SAPIEN 3, Evolut, Lotus, JenaValve and Portico.

obstruction following aortic ViV procedures is a life-threatening complication with high procedural and short-term mortality; (ii) coronary obstruction occurred more frequently in patients with prior stentless or stented with externally mounted leaflets bioprostheses; (iii) short VTC as evaluated by CT (<4 mm) predicted this complication; and (iv) clinical presentation included most likely persistent severe hypotension and ST-segment changes, and although PCI may be attempted in the majority of the patients, haemodynamic support and conversion to open heart surgery were still required in a significant proportion of them, with more than half dying within 30 days following TAVR.

Coronary obstruction and valve-in-valve: incidence and associated factors

The risks of coronary obstruction following TAVR have been stressed since the first experimental and clinical experiences,[10–12] and it was first reported in the context of ViV procedures in 2011.[13] Since then, the reported incidence of coronary obstruction has been higher during ViV procedures, reaching up to 3.5% of the patients,[3] as opposed to systematically <1% in native aortic valves.[1,2] In the present study, including a large series of ViV-TAVR, we have shown an incidence of 2.3%, supporting the

Table 3 Computed tomography data, according to the occurrence of coronary obstruction following transcatheter aortic valve replacement

	Controls (*n* = 90)	Coronary obstruction (*n* = 20)	*P*-value
Surgical frame mean diameter (mm)	20.6 ± 2.6	21.1 ± 3.3	0.39
Surgical frame area (cm^2)	3.37 ± 0.85	3.59 ± 1.25	0.35
SOV width (mm)	32.55 ± 3.98	27.44 ± 4.05	<0.001
STJ height (mm)	19.25 ± 3.97	20.01 ± 7.58	0.52
LCA height to annulus distance (mm)	9.69 ± 4.12	9.48 ± 2.67	0.82
RCA height to annulus distance (mm)	11.17 ± 4.33	11.97 ± 2.52	0.43
LCA originates above the posts	5/86 (5.8)	0 (0)	0.27
RCA originate above the posts	14/86 (16.3)	0 (0)	0.05
VTC to LCA (mm)	6.30 ± 2.34	3.24 ± 2.22	<0.001
VTC to RCA (mm)	6.08 ± 2.43	3.90 ± 3.49	0.002

Values are expressed as mean ±SD.
SOV, sinus of Valsalva; STJ, sinotubular junction; LCA, left coronary artery; RCA, right coronary artery; VTC, distance between a virtual transcatheter ring at a size of the implanted device at the level of each coronary ostium; SD, standard deviation.

Table 4 Predictors of coronary obstruction following valve-in-valve procedures

	Univariable OR (95% CI)	*P*-value	Multivariable model OR (95% CI)	*P*-value
Model for the overall population (*n* = 1612)				
CABG to the left system	0.36 (0.13–1.03)	0.056	0.38 (0.13–1.09)	0.07
STS-PROM	1.03 (0.99–1.06)	0.068	1.02 (0.99–1.05)	0.21
Post-dilatation	2.05 (0.92–4.56)	0.080	1.82 (0.8–4.14)	0.15
Stented with external mounted leaflet or stentless bioprosthesis	7.07 (3.09–16.2)	<0.001	7.67 (3.14–18.7)	<0.001
Model for the computed tomography cohort (*n* = 110)				
VTC[a]	0.18 (0.08–0.39)	<0.001	0.22 (0.09–0.51)	<0.001
Sinus of Valsalva mean diameter	0.70 (0.58–0.83)	<0.001	0.95 (0.72–1.25)	0.71
Stented with external mounted leaflet or stentless bioprosthesis	4.90 (1.51–15.9)	0.008	4.30 (0.85–21.7)	0.08

Abbreviations as in Tables 1 and 3.
[a]Per unit increase.

presence of certain surgically implanted valves (stentless or stented bioprostheses with externally mounted leaflets) as potential risk factors for this complication.[1,2,5]

The mechanisms underlying coronary obstruction following ViV appear to be displacement of the bioprosthetic leaflet towards the coronary ostium in all patients, and no cases of coronary obstruction related to the struts of the transcatheter valve frame or to the cuff/leaflets of the transcatheter valve itself were noted in the present study.[1,2] Also, according to prior smaller ViV studies,[4] this complication was more frequent with stented bioprostheses with externally mounted leaflets, and also with stentless bioprostheses, representing up to ~80% of the obstructions. In externally mounted bioprostheses, the relatively long leaflets outside the stent, in comparison with internally mounted leaflets, may be the causative factor for a higher rate of coronary obstruction.[13] Furthermore, the stentless bioprostheses are usually implanted in a supra-annular position, resulting in a shorter distance of the coronary ostia take-off in relation to the valve leaflets, which in association with lack of stent posts, may facilitate the interaction of the prosthetic leaflet and the coronary ostia.

Unlike prior studies in native aortic valves, no association of the transcatheter valve type with this complication was detected.[1,2] Also, we have noticed a higher rate of post-dilatation in the coronary obstruction group, even though this factor was not retained in the multivariable analysis. Of note, in a recent *in vitro* study with the SAPIEN XT THV implanted inside a Trifecta bioprosthesis (stented with externally mounted leaflet), the use of an undersized THV implantation successfully avoided coronary flow obstruction.[14] Future studies also may consider post-dilatation and relative THV sizing as predictors of coronary occlusion.

In addition, our study is the first to confirm the Vancouver method of the VTC distance by CT as an important factor related to this complication.[5,9] Also, we were able to define a cut-off associated with an increased risk of this severe complication (<4 mm; area under the curve: 0.943). Importantly, in the present study up to 90% (18/

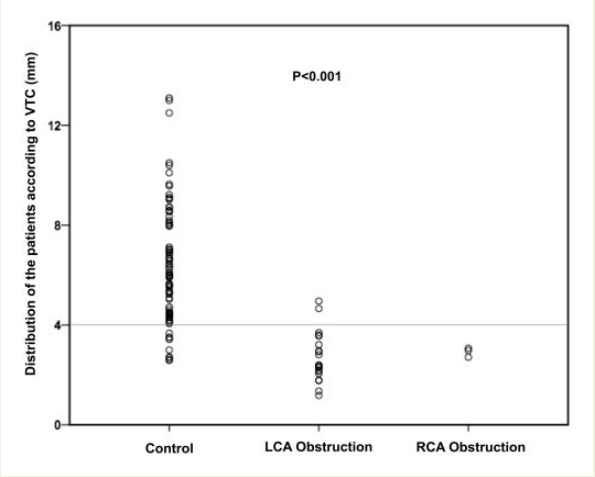

Figure 3 Distribution of distance between a virtual transcatheter ring at a size of the implanted device at the level of the coronary artery (VTC) in controls and in patients suffering coronary obstruction of the left coronary artery (LCA) and right coronary artery (RCA). The optimal cut-off level of 4 mm best predicts this complication for left coronary obstruction (area under the curve: 0.943; $P < 0.001$). All cases of RCA obstruction also occurred with concomitant LCA occlusion.

20) of the patients with CT data pre-TAVR and coronary obstruction had a VTC distance < 4 mm, supporting its inclusion in the workup prior to aortic ViV procedures. The SOV width was an important factor related to this complication in native valves. However, in the present study after adjusting for the VTC, this factor was not retained in the multivariable analysis. Most likely, the SOV presented a significant collinearity with respect to the VTC, and also it does not account for the occasional canted position of a slightly tilted and non-coaxial surgically implanted prosthesis.[5]

Collectively, in those patients considered at high risk for coronary obstruction, it is reasonable to suggest the implementation of additional security measures during ViV procedures, such as coronary protection with a guidewire and an undeployed stent in the coronary artery.[1,2,15,16] Finally, the use of a transcatheter valve that can be repositioned or retrieved in case of coronary obstruction following valve implantation should probably be recommended in such cases, although the occurrence of late coronary obstruction in up to one-third of the patients may mitigate such benefits.

Clinical presentation and management of coronary obstruction following valve-in-valve

The majority of the patients presented with persistent severe hypotension and ST-segment changes immediately after valve implantation. This clinical presentation is explained by the fact that the LCA was obstructed in the majority of the patients either alone or in association with RCA occlusion, and this is in accordance with prior studies in the context of native aortic valves.[1,2] Of note, the presence of persistent severe hypotension following valve implantation, and especially in conjunction with ECG changes, should prompt aortography and/or echocardiography to evaluate coronary flow abnormalities or new segmental abnormalities. In those cases where a pre-emptive coronary wire protection with or without stent placement were performed, prompt selective coronary injection may confirm the diagnosis and further expedite treatment with PCI.[16]

In the present study, PCI was attempted in the majority of the patients, and was successful in most of them. Still, in up to one-third of patients, urgent CABG or mechanical support was required. Overall, the 30-day mortality rate was close to half of the patients, and it reached 80% of those patients with unsuccessful PCI. This even higher mortality rates as compared with native aortic valves (41%)[2,3] underscores that these procedures should be performed in highly experienced centres with surgical capabilities, in order to potentially restore coronary flow by CABG in case of PCI failure. Also, as this complication may have delayed onset in a significant proportion of patients, especially with self-expandable devices (77% among late

Table 5 Clinical presentation and management of coronary obstruction following valve-in-valve ($n = 36$)

Obstructed coronary artery	
Left coronary artery	26/36 (72.2)
Right coronary artery	3/36 (8.3)
Both	7/36 (19.4)
Timing	
After balloon valvuloplasty	1/36 (2.8)
After valve implantation	21/36 (58.3)
After balloon post-dilatation	1/36 (2.8)
Within 24 h following TAVR	8/36 (22.2)
More than 24 h following TAVR	5/36 (13.9)
Clinical presentation	
Severe persistent hypotension	21/36 (58.3)
ECG changes	19/36 (52.8)
ST-segment elevation	13/19 (68.4)
Ventricular fibrillation	4/19 (21.1)
Atrial fibrillation	2/19 (10.5)
Stenosis severity	
Partial occlusion	20/35 (57.1)
Complete occlusion	15/35 (42.9)
Treatment	
PCI attempted	28/36 (77.8)
Successful	18/28 (64.3)
Unsuccessful	10/28 (35.7)
Coronary cannulation failure	3/10 (30.0)
Wire crossing failure	5/10 (50.0)
Stent could not be advanced	1/10 (10.0)
Stent implanted but no flow	1/10 (10.0)
Type of stent	
Bare-metal stent	6/18 (33.3)
Drug-eluting stent	10/18 (55.6)
Both stents	2/18 (11.1)
Urgent CABG	3/31 (9.7)
Need for haemodynamic support	13/36 (36.1)

Values are expressed as n (%) or mean (±SD).
TAVR, transcatheter aortic valve replacement; ECG, electrocardiographic; PCI, percutaneous coronary intervention. Other abbreviations as in *Table 1*.

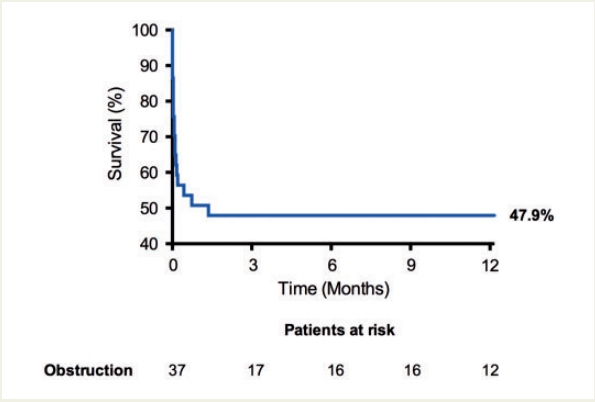

Figure 4 Kaplan–Meier survival curve at 1-year follow-up of patients undergoing transcatheter aortic valve implantation for degenerated bioprosthetic valve (valve-in-valve) with coronary obstruction.

obstructions) that tend to further expand following TAVR, such patients should probably be monitored longer in the intensive care unit.

Study limitations

Coronary angiograms leading to the diagnosis of coronary obstruction were analysed by the investigators of each centre. Pre-TAVR CT data were available in only part of the coronary obstruction patients and in a control group of 90 patients. While this represents only part of the entire cohort of the study, this is to date the largest pre-TAVR CT analysis in the context of aortic ViV procedures that was also entirely subject to centralized core laboratory analysis.[1,17–21] The number of patients undergoing TAVR with the new retrievable and repositionable delivery systems was small, and precluded the performance a separate analysis of such THVs in the context of ViV procedures. Finally, future studies with a larger number of patients will have to confirm the VTC as significant factor related to coronary obstruction in ViV, and also further evaluate the cut-offs proposed herein.

In conclusion, the present study evaluating coronary obstruction as a complication of ViV procedures has shown that this is a rare but life-threatening complication that occurs more frequently in patients with stentless and stented bioprostheses with externally mounted leaflets, and in those with a short VTC. Despite successful treatment (mainly PCI) in most cases, haemodynamic support and conversion to open heart surgery were still required in a large proportion of patients, highlighting that such high-risk TAVR procedures should probably be performed in very experienced centres.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

Dr. Rodés-Cabau holds the Canadian Chair 'Fondation Famille Jacques Larivière' for the Development of Structural Heart Disease Interventions.

Funding

H.B.R. was supported by a research PhD grant [246860/2012-0] from Conselho Nacional de Desenvolvimento Científico e Tecnológico. No other funding sources were utilized.

Conflict of interest: H.B.R. is a proctor and consultant for Edwards Lifesciences and Medtronic. J.R.C. has received research grants from Edwards Lifesciences, Medtronic, and St. Jude Medical. M.A.W. has received research grants from St. Jude and Biotronik, and is a proctor for Boston Scientific. M.G. has received research grant support and has served as proctor for Edwards Lifesciences. S.B. is a proctor and consultant for Medtronic, proctor for Boston Scientific and JenaValve. S.W. reports research grants to his institution from Abbott, Biotronik, Boston Scientific, Edwards Lifesciences, Medtronic and St. Jude Medical. A.L. is a consultant for Medtronic and DirectFlow Medical. D.H.S is a proctor for Boston Scientific, St. Jude Medical, Medtronic and Edwards Lifesciences. F.N. is a consultant for Edwards Lifesciences, Medtronic, St. Jude Medical and 4Tech. V.B is a consultant for Edwards Lifesciences, Boston Scientific, Medtronic and Sorin, has received research grants from Boston Scientific. D.D. is a consultant for Edwards Lifesciences, Medtronic and St. Jude Medical. No other disclosures were reported.

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