

Transcatheter aortic valve in transcatheter aortic valve: Clinical characteristics and outcomes

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Dear Editor,

Transcatheter aortic valve implantation (TAVI) is an efficacious treatment for aortic stenosis (AS).^{1,2} With more TAVI performed in younger patients, concerns about durability/treatment once index prostheses degenerate have arisen.³ We examined data to evaluate clinical characteristics of patients with TAVI bioprosthetic valve dysfunction (BVD) and treatment with transcatheter aortic valve (TAV)-in-TAV at a tertiary cardiac centre.

TAVI patients at the National Heart Centre, Singapore, were included in a registry (CIRB 2014-2165). We retrospectively searched the registry from 2009–2024 to identify BVD requiring TAV-in-TAV. Clinical outcomes and severe BVD were assessed according to Valve Academic Research Consortium (VARC)-3 definitions.⁴ We limited this study to severe BVD from structural deterioration requiring TAV-in-TAV in aortic position.

During the study period, 692 TAVI were performed: 654 for native aortic valves and 38 in failed surgical aortic valves (TAV-in-SAV). Index prostheses included supra-annular self-expanding valves (SEV) (44%), balloon-expandable valves (BEV) (47%), intra-annular SEV (7%) and others (2%). Ten patients required TAV-in-TAV for BVD. Nine patients had index and repeat valvular interventions in our centre. One patient (case 6) had index procedure in another hospital and underwent TAV-in-TAV in our centre. Complete follow-up records were available for 96% of study patients. No patients had BVD and refused reintervention or were found unsuitable for TAV-in-TAV based on multi-detector computer tomography (MDCT).

Table 1 shows data on index TAVI and TAVI-in-TAVI procedures. Index TAVI was performed for native AS in 8 patients, native aortic regurgitation (AR) in 1 patient, and SAV replacement (SAVR) AR in another patient. Index TAVI valves were SEV (60%) and BEV (40%) and accounted for 1.7% of the total SEVs and 1.3% of the total BEVs in the registry, respectively. Index procedures

were successful. None had moderate or severe patient prosthesis mismatch (PPM): index effective orifice area (iEOA) of $\leq 0.85 \text{ cm}^2/\text{m}^2$ and $\leq 0.65 \text{ cm}^2/\text{m}^2$. Post-index TAVI AR was predominantly trivial.

Mean time from index procedure to reintervention was 70.0 months (SEV: 67.0 months; BEV: 74.5 months). Modes of BVD were regurgitation (50%) and restenosis (50%). Modes of SEV BVD were restenosis (16.7%) and regurgitation (88.3%). Mode of BEV BVD was restenosis (100%). Four had BVD within 5 years of index procedure.

MDCT was performed for all TAV-in-TAV patients. No hypo-attenuated leaflet thromboses were found. TAV-in-TAV prostheses were sized using index TAVI internal diameters. Risks of coronary occlusion were assessed. All patients were found to have either adequate valve-to-coronary distance (VTC) $>4 \text{ mm}$ or patent coronary artery bypass grafts (CABG) with low risk of coronary occlusion. Similarly, all patients had sufficient valve-to-sinotubular junction (VTSTJ) $>4 \text{ mm}$, patent CABG conduits, or coronary risk plane below the sinotubular junction.

All BEV BVD were treated with SEV. Of 6 patients with SEV BVD, 2 received SEV and 4 received BEV. All reinterventions were successful with resolution of regurgitation and restenosis (mean aortic gradient of 12.0 mmHg post-reintervention). One patient with BEV BVD treated with SEV had moderate PPM with iEOA of $0.70 \text{ cm}^2/\text{m}^2$. No patient had severe PPM. None had mortality, coronary occlusion, pacemaker implantation or stroke during TAV-in-TAV hospitalisation. Four patients died at 6, 28, 54 and 70 months after TAV-in-TAV from non-cardiac-related mortality.

Long-term durability of TAVI is uncertain. Low-risk TAVI trials showed non-inferior durability compared to SAVR of up to 5 years.^{1,2} However, long-term results are not available.

NOTION trial compared SEV versus SAVR treatment of low-risk AS patients. Ten-year results were reassuring with BVD lower after SEV versus

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Table 1. Clinical, imaging, procedural and outcome data of index TAVI and TAVI-in-TAVI procedures.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Index TAVI procedural data										
Aortic valve morphology	Tricuspid	Tricuspid	Tricuspid	Tricuspid	Tricuspid	Tricuspid	Tricuspid	Bioprosthetic valve	Tricuspid	Tricuspid
TAVI indication	AS	AS	AS	AS	AS	AS	AS	AR	AS	AR
Access	TF	TF	TF	TF	TF	TF	TF	TF	TF	TF
Anaesthesia	GA	GA	GA	GA	GA	Unknown	GA	GA	LA	LA
TAVI platform	Sapien XT	Sapien XT	Sapien	Corevalve Evolut R	Sapien	Corevalve Evolut R	Corevalve	Corevalve Evolut R	Corevalve Evolut Pro	Corevalve Evolut R
TAVI Size (mm)	23	26	23	29	23	34	26	23	26	34
Pre-dilation balloon size (mm)	20	20	20	20	20	Unknown	18	Nil	18	23
Post-dilation balloon size (mm)	Nil	Nil	Nil	Nil	Nil	Unknown	Nil	Nil	20	Nil
In-hospital complications	No	No	No	No	No	No	No	No	No	No
Post-index TAVI echocardiogram										
Aortic valve area (cm ²)	1.8	2.1	1.5	2.4	1.8	Unknown	1.9	2.3	2.2	2.2
Indexed EOA (cm ² /m ²)	1.1	1.2	1.0	1.5	1.1	Unknown	1.2	1.3	1.3	1.2
Aortic MPG (mmHg)	18	13	12	8	16	Unknown	14	4	7	13
AV peak velocity (cm/s)	298	240	260	200	240	Unknown	270	128	183	259
LVEF (%)	61	62	66	46	67	Unknown	69	45	60	59
Aortic regurgitation	Trivial	Mild	Trivial	Trivial	Trivial	Unknown	Trivial	Trivial	Trivial	Trivial
Patient clinical characteristics during TAV-in-TAV										
Age, years	88	61	81	104	78	84	81	86	78	73
Sex	Female	Female	Female	Male	Female	Male	Male	Male	Male	Male
Symptoms	Dyspnoea	Dyspnoea/ chest pain	Nil	Dyspnoea	Dyspnoea	Dyspnoea	Nil	Nil	Dyspnoea	Nil

Table 1. Clinical, imaging, procedural and outcome data of index TAVI and TAVI-in-TAVI procedures. (Cont'd)

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
NYHA class	II	II	I	II	II	II	I	I	III	I
STS score	2.0	8.7	2.1	22.5	1.2	2.7	2.6	20.5	2.0	3.7
High risk features	Porcelain aorta	Patent LIMA	Porcelain aorta	NA	Porcelain aorta	Patent LIMA	Porcelain aorta	Patent LIMA	NA	Porcelain aorta
Smoking history	N	N	N	N	N	N	N	N	N	N
Hypertension	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Dyslipidaemia	Y	Y	N	N	Y	Y	Y	Y	Y	N
Diabetes mellitus	N	Y	N	N	Y	N	N	Y	N	N
Previous PCI	N	Y	N	Y	Y	Y	N	N	Y	Y
Previous CABG	N	Y	N	N	N	Y	N	Y	N	N
Previous SAVR	N	N	N	N	N	N	N	Y	N	N
Previous PPM	N	N	N	Y	N	N	N	N	N	Y
Dialysis	N	Y	N	N	N	N	N	N	N	Y
Time from index TAVI (months)	85	24	85	43	104	57	109	44	75	74
Pre-TAV-in-TAV echocardiogram										
Aortic valve area (cm ²)	0.9	0.7	0.7	1.4	0.6	2.1	0.9	1.8	2.5	1.7
AVA indexed (cm ² /m ²)	0.5	0.4	0.6	0.9	0.3	1.2	0.6	1.0	1.5	1.0
Aortic MPG(mmHg)	40	47	40	5	40	9	45	11	8	10
AV peak Velocity (cm/second)	410	460	416	157	410	230	406	214	193	214
LVEF (%)	70	62	62	64	60	60	61	60	62	43
Transvalvular AR	Mild	Mild	Trivial	Severe	Mild	Severe	Trivial	Severe	Severe	Severe
TAV-in-TAV indication	AS	AS	AS	AR	AS	AR	AS	AR	AR	AR

Table 1. Clinical, imaging, procedural and outcome data of index TAVI and TAVI-in-TAVI procedures. (Cont'd)

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Pre-procedural MSCT										
Aortic annulus area (mm ²)	252	384	316	405	282	471	325	275	358	405
Aortic annulus perimeter (mm ²)	57.0	69.8	64.5	74.0	60.4	77.2	64.0	59.0	66.0	72.0
Average annular diameter (mm ²)	17.8	22.1	20.6	23.8	19	24.3	20.5	18.6	20.6	26.0
LM height (mm)	9.7	13.4	18.5	12.4	12.3	10.0	14.0	9.9	12.2	13.3
RCA height (mm)	11.6	17.1	16.5	13.2	13.4	12.0	15.0	14.0	17.9	18.1
Average SOV width (mm)	28.8	33.1	27.1	33.0	28.0	42.0	30.0	29.0	30.0	37.0
STJ diameter (mm)	26.0	28.0	26.0	35.0	20.3	35.9	27.0	32.0	25.0	30.4
VTC (mm)	6	NA s/p CABG	LM and RCA above XT	9	5	NA s/p CABG	RCA 4, LM 6	9	5	9
VTSTJ (mm)	Index TAVI below STJ	NA s/p CABG	Index TAVI below STJ	6	Index TAVI below STJ	NA s/p CABG	3	NA s/p CABG	3	6
Procedural characteristics										
Access	TF	TF	TF	TF	TF	TF	TF	TF	TF	TF
Anaesthesia	GA	GA	LA	GA	GA	LA	LA	LA	LA	LA
Transcatheter heart valve	Corevalve evolut R	Corevalve evolut Pro	Corevalve evolut R	Corevalve evolut R	Corevalve evolut R	Sapient 3	Sapient 3	Corevalve evolut FX	Sapient 3	Sapient 3
Valve size (mm)	23	26	23	29	23	29	23	23	23	23
Pre-dilation	N	N	N	N	N	N	N	N	N	N
Post-dilation	N	N	N	N	N	N	N	N	N	N
Cerebral embolic protection	N	N	N	N	N	Y	N	N	N	N
In-hospital complications	N	N	N	N	Y-Vascular	N	N	N	N	N

Table 1. Clinical, imaging, procedural and outcome data of index TAVI and TAVI-in-TAVI procedures. (Cont'd)

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Post-TAV-in-TAV echocardiogram										
Aortic valve area (cm ²)	1.7	1.2	1.2	2.6	1.6	1.7	1.9	1.6	1.5	2.2
Indexed EOA (cm ² /m ²)	1.0	0.7	0.9	1.6	0.9	0.9	1.2	0.9	0.9	1.3
Aortic MPG (mmHg)	15	9	15	5	12	9	15	10	11	10
AV peak velocity (cm/s)	259	217	267	164	220	196	254	187	227	217
LVEF (%)	63	60	64	60	67	40	63	57	56	35
AR	Nil	Mild	Mild	Nil	Mild	Trivial	Trivial	No	No	Trivial
Follow-up data										
Duration of mortality from TAV-in-TAV (months)	70	54	NA	NA	28	NA	NA	6	NA	NA
Age at time of mortality (years)	94	66	NA	NA	81	NA	NA	86	NA	NA
Cause of mortality	Pneumonia	Limb gangrene	NA	NA	Intestinal bleed	NA	NA	Intracranial Bleed	NA	NA

AR: aortic regurgitation; AS: aortic stenosis; AV: aortic valve; CABG: coronary artery bypass surgery; EOA: effective orifice area; GA: general anaesthesia; LA: local anaesthesia; LCC: left coronary cusp; LIMA: left internal mammary artery; LM: left main; LVEF: left ventricular ejection fraction; MDCT: multi-detector computer tomography; MPG: mean pressure gradient; N: no; NA: not available; NYHA: New York Heart Association; NCC: non-coronary cusp; PCI: percutaneous coronary intervention; PPM: permanent pacemaker; RCA: right coronary artery; RCC: right coronary cusp; SAVR: surgical aortic valve replacement; SOV: sinus of Valsalva; s/p: status post; STJ: sinotubular junction; STS: Society of Thoracic Surgeons; TAV: transcatheter aortic valve implantation; TAVI: transcatheter aortic valve implantation; TF: transfemoral; VTC: valve-to-coronary; VTSTJ: valve-to-STJ; Y: yes.

SAVR. Nevertheless, no conclusion about long-term durability was made as only 36% of cohort was alive at 10 years.⁵

Our study found 10/692 patients (1.4%) required TAV-in-TAV for BVD. Four had early BVD within 5 years of index procedure. Causes of early BVD include young age at index TAVI procedure (case 2), post-dilatation of index TAVI (case 9), TAVI in degenerated surgical valve replacement (case 8) and end-stage renal failure (case 2 and case 10).

BVD was predominantly AR in SEV and exclusively restenosis for BEV. SEV has thinner porcine leaflets (0.28–0.35 mm) sutured in supra-annular position; BEV has thicker bovine leaflets (0.34–0.55 mm) in intra-annular position. In-vitro studies found lower leaflet stress for SEV compared to BEV.⁶ Differences in leaflet thickness and stress may explain susceptibility of SEV to tears and AR, while BVD in BEV was due to restenosis.

Treatment using TAVI for severe BVD includes TAVI explant or TAV-in-TAV. Higher 1-year mortality was found with explant compared to TAV-in-TAV (32.4% versus [vs] 15.4%; $P=0.001$).⁷ TAV-in-TAV will likely be the mainstay treatment for BVD.

MDCT is essential for TAV-in-TAV procedures to reduce periprocedural risks, optimise haemodynamics and maintain coronary access. Ease of coronary access is determined by index TAVI valve leaflets, which are pushed circumferentially by the new TAVI prosthesis to create a neoskirt covered stent. Particularly for tall-framed SEV with supra-annular leaflets, neoskirt will be high and hinder future coronary access. MDCT were reviewed to determine coronary occlusion risk by considering index TAVI (BEV vs SEV), index TAVI depth, coronary heights, sinus of Valsalva and sinotubular junction widths. MDCT allows projection of virtual valves to simulate TAV-in-TAV implantation and neoskirt heights at various implantation depths. Measurements of VTC and VTSTJ determine coronary obstruction risks and need for coronary wire protection or leaflet modification techniques, e.g. BASILICA/UNICORN.^{8,9} VTC/VTSTJ >4 mm suggests low-risk of coronary occlusion. When coronaries are located above neoskirt risk-plane, there is low risk of coronary occlusion whereas risk is high if coronaries are below risk-plane.

In our study, no patients had VTC < 4mm or had patent CABG grafts. None required coronary wire protection or leaflet modification.

SEV were implanted in all BEV BVD patients to optimise haemodynamics. Of the 6 SEV patients, 2 were treated with implantation of another SEV. One of these patients had patent CABG grafts, hence coronary access was not a consideration, and optimal

haemodynamic result was sought with SEV-in-SEV. Second patient was 104 years old with adequate VTC/VTSTJ. Decision was for SEV-in-SEV to optimise haemodynamics with little concern for coronary access because of patient's age.

Four patients with BVD of SEV were treated with BEV to maintain neoskirt risk-plane below coronary ostia. Upper edges of BEV were positioned in these patients below left-main to maintain coronary access, yet compromising optimal results by allowing leaflet overhang. Long-term outcome of this strategy is unknown.

No major complications occurred during TAV-in-TAV hospitalisation. There was good symptom relief. There were no patients with 30-day major adverse events, including death, myocardial infarction, stroke and major bleeding. Four patients died 6, 28, 54 and 70 months post-reintervention from non-cardiac mortality.

In conclusion, our retrospective study identified 10 TAVI patients (1.4%) with BVD occurring at a mean of 70 months post-index TAVI. TAV-in-TAV procedure was a safe/efficacious BVD treatment with careful pre-procedural planning.

Ethics statement

All patient consent were obtained for the study and approved by the SingHealth Centralised Institutional Review Board (2014-2165).

Declaration

Dr Ewe See Hooi has received speaker fees from Philips Healthcare and GE Healthcare. Dr Jonathan and Dr Kay Woon Ho are proctors for Medtronic and Edwards Lifesciences. The remaining authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: aortic stenosis, bioprosthetic valve dysfunction, cardiology, transcatheter valvular intervention, valvular heart disease

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