European Journal of Cardio-Thoracic Surgery 56 (2019) 55–63
doi:10.1093/ejcts/ezy471 Advance Access publication 27 January 2019

ORIGINAL ARTICLE

Cite this article as: Ferrari E, Stortecky S, Heg D, Muller O, Nietlispach F, Tueller D *et al.* The hospital results and 1-year outcomes of transcatheter aortic valve-in-valve procedures and transcatheter aortic valve implantations in the native valves: the results from the Swiss-TAVI Registry. Eur J Cardiothorac Surg 2019;56:55–63.

The hospital results and 1-year outcomes of transcatheter aortic valve-in-valve procedures and transcatheter aortic valve implantations in the native valves: the results from the Swiss-TAVI Registry

Enrico Ferrari [a,*†], **Stefan Stortecky**[b†], **Dik Heg**[b], **Olivier Muller**[c], **Fabian Nietlispach**[d], **David Tueller**[e], **Stefan Toggweiler**[f], **Stéphane Noble**[g], **Francesco Maisano**[d], **Marco Roffi**[g], **Raban Jeger**[h], **Jürg Grünenfelder**[i], **Christoph Huber**[j], **Stephan Windecker**[b] and **Peter Wenaweser**[i]

[a] Department of Cardiac Surgery, Cardiocentro Ticino, Lugano, Switzerland
[b] Department of Cardiology, Swiss Cardiovascular Center, Bern University Hospital, Bern, Switzerland
[c] Department of Cardiology, Lausanne University Hospital, Lausanne, Switzerland
[d] Department of Cardiology and Cardiovascular Surgery, Zurich University Hospital, Zurich, Switzerland
[e] Department of Cardiology, Triemlispital, Zurich, Switzerland
[f] Department of Cardiology, Cantonal Hospital, Luzern, Switzerland
[g] Department of Cardiology, Geneva University Hospital, Geneva, Switzerland
[h] Department of Cardiology, Basel University Hospital, Basel, Switzerland
[i] Heart Clinic Hirslanden, Zurich, Switzerland
[j] Department of Cardiovascular Surgery, Geneva University Hospital, Geneva, Switzerland

* Corresponding author. Department of Cardiac Surgery, Cardiocentro Ticino, Via Tesserete 48, 6900 Lugano, Switzerland. Tel: +41-91-8053144; fax: +41-91-8053148; e-mail: enrico.ferrari@cardiocentro.org (E. Ferrari).

Received 10 October 2018; received in revised form 9 December 2018; accepted 13 December 2018

Key question

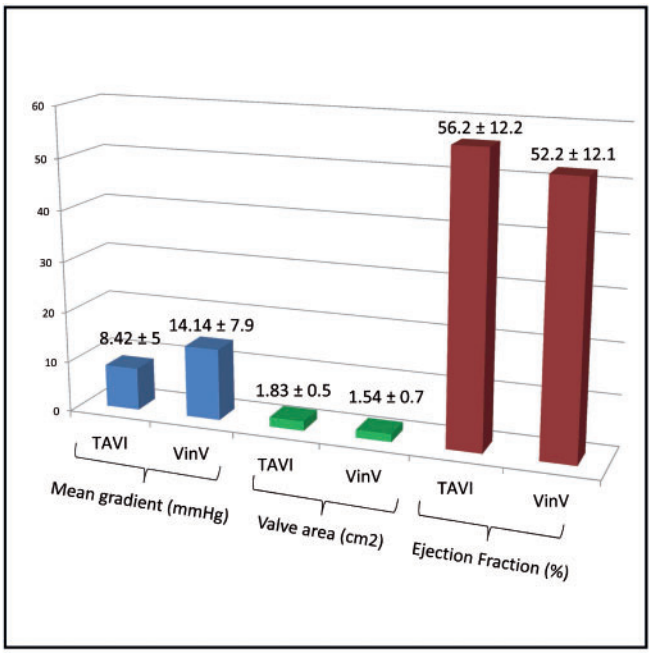
What are the 30-day and 1-year outcomes of patients undergoing valve-in-valve and TAVI procedures in Switzerland?

Key findings

Patients with valve-in-valve procedures have favourable 1-year clinical outcomes compared with TAVI for native valve disease.

Take-home message

Valve-in-valve procedures for a failed bioprosthesis can be safely performed with good 1-year outcomes.



†The first two authors contributed equally to this study.

Abstract

OBJECTIVES: The SwissTAVI Registry includes all consecutive patients undergoing transcatheter aortic valve implantation (TAVI) and valve-in-valve (VinV) procedures for a failed bioprosthesis in Switzerland. We report the real world, all-comers, 30-day and 1-year outcomes of patients undergoing VinV and standard TAVI procedures.

METHODS: Prospectively collected data from the 2 groups (VinV and standard TAVI patients) were retrospectively analysed. In an adjusted analysis, in-hospital and 1-year outcomes of VinV patients were compared with those of patients undergoing TAVI for native aortic valve disease in the same registry. A subanalysis of VinV procedures in stenotic or regurgitant bioprosthesis was also performed.

RESULTS: Between February 2011 and December 2016, 4599 and 157 consecutive patients underwent TAVI in native aortic valves and VinV procedures in degenerate bioprosthesis, respectively. VinV patients were younger (78 ± 9.1 years vs 82.2 ± 6.3 years; $P < 0.001$) but at a higher risk for surgery (the logistic EuroSCORE: 28.48 ± 15.3% vs 18.2 ± 13.6%; $P < 0.001$; the Society of Thoracic Surgery (STS) score: 6.4 ± 5% vs 5.5 ± 4.3%; $P = 0.008$). Valve predilatation was less frequently performed during VinV procedures (22.9% vs 69.1%; $P < 0.001$), and the hospital stay was shorter after VinV procedure (8.46 ± 4.2 days vs 9.83 ± 6 days; $P = 0.005$). VinV patients showed higher predischarge transvalvular mean gradients (14.14 ± 7.9 mmHg vs 8.42 ± 5.0 mmHg; $P < 0.001$), smaller mean valve surface area (1.54 ± 0.7 cm^2 vs 1.83 ± 0.5 cm^2; $P < 0.001$) and a lower risk of moderate/severe paravalvular leak (1.3% vs 5%). Post-procedural kidney injury (1.3% vs 4.8%; $P = 0.06$) and new pacemakers for conduction abnormalities (3.3% vs 18.5%; $P < 0.001$) were higher after TAVI. All-cause mortality and cardiovascular mortality at 30 days were similar between the 2 groups (1.9% vs 3.8%; $P = 0.242$ and 1.9% vs 3.4%; $P = 0.321$), whereas after 1 year, all-cause mortality was lower for VinV patients (6.8% vs 13%; $P = 0.035$). The bioprosthetic valve size correlated inversely with postoperative gradients after VinV procedures.

CONCLUSIONS: VinV aortic procedures showed favourable 30-day and 1-year clinical outcomes compared with TAVI procedures for the native aortic valve disease. Despite higher transvalvular mean gradients following VinV implants, this appears not to impact the early clinical outcomes.

Keywords: Transcatheter aortic valve implantation • Bioprosthetic aortic valve • Valve-in-valve procedure

INTRODUCTION

Surgical aortic valve (SAV) replacement is an established treatment for the management of symptomatic aortic valve disease, and because of the ageing population, the number of bioprostheses implanted is increasing. Transcatheter aortic valve implantation (TAVI) has gained popularity and has become the treatment of choice for high-risk patients with aortic stenosis [1–5]. In case of prosthetic valve degeneration, patients with previously implanted SAV can also be treated with TAVI procedure, the so-called valve-in-valve (VinV) technique. This approach is performed transfemorally, transapically, transaortically or through the carotid or the subclavian artery and can be performed regardless of the SAV failure mechanism. The main advantage is that patients, in particular elderly patients with comorbidities, do not need to undergo redo surgery and benefit from faster recovery and short hospital stay [6–10]. In this study, we investigated the 30-day and 1-year outcomes of VinV patients included in the SwissTAVI Registry compared with patients undergoing TAVI for native aortic valve disease. The SwissTAVI Registry includes all TAVI procedures performed in Switzerland and, therefore, represents an all-comers population requiring transcatheter aortic valve replacement.

METHODS

Design and data collection

The SwissTAVI Registry is based on prospective collection of clinical, procedural and follow-up data of consecutive patients undergoing TAVI in Switzerland (registered at clinicaltrials.gov NCT01368250). All centres performing TAVI in Switzerland (15 centres in total) obligatorily participate to the SwissTAVI Registry, include patients and provide the follow-up. A web-based database (www.swisstavi.ch) with standardized case report forms is used for data collection at baseline and during follow-up, which is performed according to a prespecified protocol. Clinical events are prospectively collected and adjudicated by a dedicated clinical event committee according to the standardized criteria of the Valve Academic Research Consortium (VARC-2) [11]. The Clinical Trials Unit of Bern is responsible for central data monitoring to verify the completeness of data, check plausibility and independently perform statistical analysis. The study protocol of the SwissTAVI Registry was approved by the local cantonal ethics committee and by the institutional review board of all participating sites. All patients signed informed consent for study participation and follow-up assessment.

Study population

Between February 2011 and December 2016, all patients with degenerated SAV undergoing TAVI procedures were extracted from the SwissTAVI Registry and represented the study population (the VinV group). All patients with native aortic valve disease undergoing TAVI procedures during the same period of time were considered as the control group (the TAVI group). The selection of patients, the indication for TAVI and VinV procedures and the choice of the transcatheter device, vascular access site and periprocedural management were left to the discretion of the operator and was not standardized among different Swiss centres.

Statistical analysis

The primary study end point is all-cause mortality at 1-year follow-up. Secondary end points include cardiovascular mortality, cerebrovascular events, myocardial infarction, stage 3 acute kidney injury, life-threatening or major bleeding and vascular access site complications according to the VARC-2 definitions at 30-day and 1-year follow-up.

Table 1: Baseline characteristics

	TAVI (*N* = 4599)	VinV (*N* = 157)	*P*-value	VinV in stenosis (*N* = 106)	VinV inregurgitation (*N* = 51)	*P*-value
Age (years)	82.21 ± 6.29	78.62 ± 9.11	<0.001	79.09 ± 8.05	77.64 ± 11.02	0.353
Female gender	2290 (49.8)	62 (39.5)	0.012	50 (47.2)	12 (23.5)	0.005
Body mass index (kg/m^2)	26.72 ± 5.11	26.63 ± 4.97	0.829	27.23 ± 5.50	25.39 ± 3.33	0.029
Cardiac risk factors						
Diabetes mellitus	1183 (25.7)	32 (20.4)	0.137	27 (25.5)	5 (9.8)	0.033
Dyslipidaemia	2408 (52.4)	86 (54.8)	0.570	60 (56.6)	26 (51.0)	0.608
Hypertension	3657 (79.6)	120 (76.4)	0.366	82 (77.4)	38 (74.5)	0.693
Past medical history						
Previous pacemaker implantation	461 (10.0)	24 (15.3)	0.043	17 (16.0)	7 (13.7)	0.815
Previous myocardial infarction	640 (13.9)	20 (12.7)	0.814	13 (12.3)	7 (13.7)	0.802
Previous cardiac surgery	541 (11.8)	157 (100.0)	<0.001	106 (100.0	51 (100.0)	
Previous stroke or TIA	534 (11.6)	23 (14.6)	0.255	14 (13.2)	9 (17.6)	0.477
Clinical features						
Peripheral vascular disease	770 (16.7)	26 (16.6)	1.000	17 (16.0)	9 (17.6)	0.821
COPD	575 (12.5)	20 (12.7)	0.902	15 (14.2)	5 (9.8)	0.610
Coronary artery disease	2671 (58.1)	85 (54.5)	0.410	56 (53.3)	29 (56.9)	0.733
LVEF (%)	54.99 ± 14.27	54.57 ± 13.07	0.749	54.76 ± 13.51	54.16 ± 12.18	0.815
Aortic valve area (cm^2)	0.70 ± 0.23	0.82 ± 0.36	<0.001	0.76 ± 0.21	1.05 ± 0.64	0.004
Transaortic mean gradient (mmHg)	43.54 ± 18.82	33.03 ± 17.06	<0.001	35.21 ± 14.89	26.48 ± 21.35	0.018
Moderate/severe aortic regurgitation	421 (10.0)	87 (58.4)	<0.001			
Symptoms on admission						
NYHA functional class			0.007			0.714
I or II	1619 (36.0)	38 (25.3)	0.007	27 (26.2)	11 (23.4)	0.840
III or IV	2875 (64.0)	112 (74.7)	0.007	76 (73.8)	36 (76.6)	0.840
CCS angina class			0.006			0.659
No angina	3577 (78.2)	139 (88.5)	0.001	95 (89.6)	44 (86.3)	0.596
CCS I or II	670 (14.6)	14 (8.9)	0.049	8 (7.5)	6 (11.8)	0.385
CCS III or IV	330 (7.2)	4 (2.5)	0.025	3 (2.8)	1 (2.0)	1.000
Risk assessment						
Logistic EuroSCORE (%)	18.18 ± 13.61	28.48 ± 15.30	<0.001	28.45 ± 15.43	28.51 ± 15.33	0.987
STS score (%)	5.49 ± 4.29	6.42 ± 5.03	0.008	6.70 ± 5.31	5.85 ± 4.41	0.326

The values are presented as means with standard deviations (*P*-value from *t*-tests) or counts (% of all patients; *P*-value from the Fisher's exact or the χ^2 tests).
CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; LVEF: left ventricle ejection fraction; NYHA: New York Heart Association; STS: Society of Thoracic Surgery; TAVI: transcatheter aortic valve implantation; TIA: transient ischaemic attack; VinV: valve-in-valve.

All patients undergoing VinV procedures were compared with patients undergoing TAVI procedures. VinV patients were further stratified according to the mode of SAV degeneration: stenotic or regurgitant. Post-procedural transvalvular mean gradients of VinV patients were also categorized according to the SAV size using linear regression.

Continuous variables are reported as means ± standard deviation, whereas categorical variables are reported as number of patients and percentage. Events are reported at 30-day follow-up and again up to 1-year follow-up (% from life-table estimates, censoring patients at death or last valid contact). Event rates per group were compared using the Cox regression analysis. Reported are crude hazard ratios [HRs with 95% confidence intervals (CIs)] with *P*-values from Wald χ^2 tests or continuity correct risk ratios with *P*-values from the Fisher's exact tests in case of zero events in 1 of the 2 patient groups.

Reports are adjusted HR (95% CI) comparing the groups after adjustment for age, gender, body mass index (BMI) ≤20 kg/m^2, diabetes, prior pacemaker, peripheral artery disease, chronic lung disease, coronary artery disease, Society of Thoracic Surgery (STS) PROM and post-TAVI regurgitation moderate/severe (univariable effect of $P < 0.1$ on all-cause death at 1 year). Overall, no adjusted analysis was performed for clinical outcomes with less than 10 events. The Kaplan–Meier curves are presented for all-cause and cardiovascular mortality at 30 days and 1 year. Two-sided *P*-values <0.05 were considered statistically significant. All analyses were performed with the Stata version 14.2 (StataCorp, College Station, TX, USA).

RESULTS

Between 15 February 2011 and 31 December 2016, 4756 consecutive patients underwent TAVI procedures in 15 centres across Switzerland. Among them, 4599 procedures were TAVI for native aortic valve disease (10% with moderate/severe aortic regurgitation) and 157 (3.4%) were VinV for failed bioprosthesis (both stenotic and regurgitant failed prostheses). Baseline characteristics are summarized in Table 1. Compared to TAVI patients, VinV patients were younger (78 ± 9.1 years vs 82.2 ± 6.3 years; $P < 0.001$), with a lower proportion of women (39.5% vs 49.8%; $P = 0.012$), with a higher risk profile (logistic EuroSCORE: 28.48 ± 15.3% vs 18.2 ± 13.6%; $P < 0.001$; STS score: 6.4 ± 5% vs 5.5 ± 4.3%; $P = 0.008$) and presented more often with dyspnoea New York Heart Association class III–IV (74.7% vs 64%; $P = 0.007$). Medical history and cardiovascular risk factors were balanced between the groups. The preoperative valve area was larger in the VinV group than in the TAVI group (0.82 ± 0.36 cm^2 vs 0.70 ± 0.23 cm^2; $P < 0.001$) with lower transvalvular gradients (33.0 ± 17.0 mmHg vs 43.5 ± 18.8 mmHg; $P < 0.001$).

Table 2: Procedural characteristics

	TAVI (*N* = 4599)	VinV (*N* = 157)	*P*-value	VinVinstenosis (*N* = 106)	VinVinregurgitation (*N* = 51)	*P*-value
Procedure time (min)	72.56 ± 38.32	70.68 ± 36.78	0.578	68.53 ± 31.48	75.67 ± 46.96	0.306
Contrast (ml)	173.67 ± 98.70	126.54 ± 91.60	<0.001	119.88 ± 79.03	142.84 ± 116.48	0.194
Access			0.136			0.035
Transfemoral	4083 (88.8)	142 (90.4)	0.606	98 (92.5)	44 (86.3)	0.251
Transapical	409 (8.9)	11 (7.0)	0.477	8 (7.5)	3 (5.9)	1.000
Trans-subclavian	41 (0.9)	1 (0.6)	1.000	0 (0.0)	1 (2.0)	0.325
Transaortic	41 (0.9)	0 (0.0)	0.646	0 (0.0)	0 (0.0)	
Other	25 (0.5)	3 (1.9)	0.063	0 (0.0)	3 (5.9)	0.033
Device features						
Prior balloon aortic valvuloplasty	3177 (69.1)	36 (22.9)	<0.001	27 (25.5)	9 (17.6)	0.316
Device implanted[a]			<0.001			0.009
Medtronic CoreValve	887 (19.3)	38 (24.2)	0.151	25 (23.6)	13 (25.5)	0.843
Edwards SAPIEN XT	584 (12.7)	21 (13.4)	0.808	20 (18.9)	1 (2.0)	0.002
Symetis Acurate	241 (5.3)	1 (0.6)	0.005	0 (0.0)	1 (2.0)	0.325
JenaValve	59 (1.3)	0 (0.0)	0.266	0 (0.0)	0 (0.0)	
SJM Portico	219 (4.8)	5 (3.2)	0.446	3 (2.8)	2 (3.9)	0.660
Medtronic Engager	2 (0.0)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	
Direct Flow Medical	39 (0.9)	3 (1.9)	0.161	0 (0.0)	3 (5.9)	0.033
Edwards SAPIEN 3	1654 (36.1)	29 (18.5)	<0.001	17 (16.0)	12 (23.5)	0.277
BSC Lotus	285 (6.2)	3 (1.9)	0.025	1 (0.9)	2 (3.9)	0.247
Medtronic Evolut R	612 (13.3)	57 (36.3)	<0.001	40 (37.7)	17 (33.3)	0.723
BSC Lotus Edge	5 (0.1)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	
Aortic regurgitation at discharge			<0.001			0.061
Grade 0	1942 (42.5)	96 (61.1)	<0.001	69 (65.1)	27 (52.9)	0.164
Grade 1	2398 (52.4)	59 (37.6)	<0.001	37 (34.9)	22 (43.1)	0.380
Grade 2	212 (4.6)	2 (1.3)	0.048	0 (0.0)	2 (3.9)	0.104
Grade 3	20 (0.4)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	
Paravalvular leak	2375 (51.6)	59 (37.6)	<0.001	36 (37.9)	23 (45.1)	0.480
In-hospital course (days)						
Overall in-hospital stay	9.83 ± 6.03	8.46 ± 4.26	0.005	8.49 ± 4.37	8.41 ± 4.07	0.915
Intensive care unit stay	1.21 ± 2.42	1.00 ± 1.89	0.273	0.77 ± 1.21	1.47 ± 2.77	0.029
Intermediate care stay	1.77 ± 2.43	1.48 ± 1.75	0.147	1.39 ± 1.66	1.67 ± 1.93	0.364
General ward stay	6.88 ± 5.29	6.01 ± 3.74	0.041	6.36 ± 3.84	5.27 ± 3.44	0.089

The values are presented as means with standard deviations (*P*-values from *t*-tests) or counts (% of all patients; *P*-values from the Fisher's exact tests or the χ^2 tests).

[a]In 12 patients, the TAVI procedure was aborted, no device implanted.

TAVI: transcatheter aortic valve implantation; VinV: valve-in-valve.

Procedural outcomes

Characteristics are displayed in Table 2. The procedure time was comparable, whereas the amount of contrast was smaller during VinV implantations (126.5 ± 91.6 ml vs 173.6 ± 98.7 ml; $P < 0.001$). Differences in the type of implanted transcatheter valves reflect both the availability of alternative catheter-based valve models in different centres and the decision-making process of operators facing native valves or failed SAV. The JenaValve, Medtronic Engager and the Boston Lotus were not used for VinV implants. Predilatation was performed less often during VinV (22.9% vs 69.1%; $P < 0.001$). Concerning the failed SAV, the mean valve size was 23.7 ± 2.3 mm and the mean time since surgical implant was 9.2 ± 4.6 years (Table 3).

Predischarge echocardiograms showed higher gradients (14.14 ± 7.9 mmHg vs 8.42 ± 5.0 mmHg; $P < 0.001$) and smaller areas (1.54 ± 0.7 cm^2 vs 1.83 ± 0.5 cm^2; $P < 0.001$) in VinV patients (Fig. 1A). Standard TAVI patients showed more paravalvular leak of any degree (51.6% vs 37.6%; $P < 0.001$).

30-Day outcomes. Mortality was similar between the groups (1.9% VinV and 3.8% TAVI; $P = 0.24$), but the need for a permanent pacemaker was significantly higher after standard TAVI (3.3% VinV and 18.5% TAVI) (HR 0.16, 95% CI 0.07–0.39; $P < 0.001$). There were no significant differences between the groups concerning cerebrovascular accidents, myocardial infarctions, vascular complications and bleedings. TAVI patients more often developed post-procedural acute renal failure (4.8% vs 1.3%; $P = 0.06$) (Table 4).

1-Year outcomes. All-cause mortality at 1 year was higher for TAVI patients (6.8% vs 13%) (adjusted HR 0.47, 95% CI 0.25–0.88; $P = 0.018$), and cardiovascular mortality showed a similar trend (4.8% vs 9.0%) (adjusted HR 0.51, 95% CI 0.24–1.08; $P = 0.078$) (Fig. 2A and B). In the multivariable analysis, age, female gender, BMI ≤20, diabetes, previous pacemaker, peripheral artery disease, chronic lung disease, coronary disease and high STS score were predictors of all-cause mortality (Tables 4 and 5).

Table 3: Surgical prosthesis

	N=157
Valves,[a] *n* (%)	*n* = 156
Aspire	1 (1)
Baxter	4 (3)
Carpentier-Edwards	20 (13)
Edwards Magna Ease	10 (6)
Edwards Perimount	5 (3)
Edwards Perimount Magna	17 (11)
Edwards Prima Plus	2 (1)
Hancock	1 (1)
Hancock-II	1 (1)
Homograft	2 (1)
Labcor	2 (1)
Livanova Mitroflow	35 (22)
Livanova Solo	6 (4)
Livanova Perceval	3 (2)
Medtronic	2 (1)
Medtronic Enable	1 (1)
Medtronic Freestyle	2 (1)
Medtronic Mosaic	7 (4)
Medtronic Mosaic-Ultra	2 (1)
SPV-Toronto Stentless	3 (2)
Shelhigh composite graft	8 (5)
St. Jude Biocor	4 (3)
St. Jude Epic	7 (4)
St. Jude Trifecta	8 (5)
Stentless 3F	1 (1)
Stentless valve conduit	2 (1)
Size[a]	*n* = 153
Average (mm), mean ± SD	23.7 ± 2.3
18, *n* (%)	1 (1)
19, *n* (%)	4 (3)
21, *n* (%)	33 (22)
23, *n* (%)	49 (32)
25, *n* (%)	41 (27)
27, *n* (%)	20 (13)
29, *n* (%)	4 (3)
31, *n* (%)	1 (1)
Years since valve implantation, mean ± SD	*n* = 157, 9.2 ± 4.6

[a]Device was unclear in *n* = 1 patient, and size was unclear in *n* = 3 patients.
SD: standard deviation.

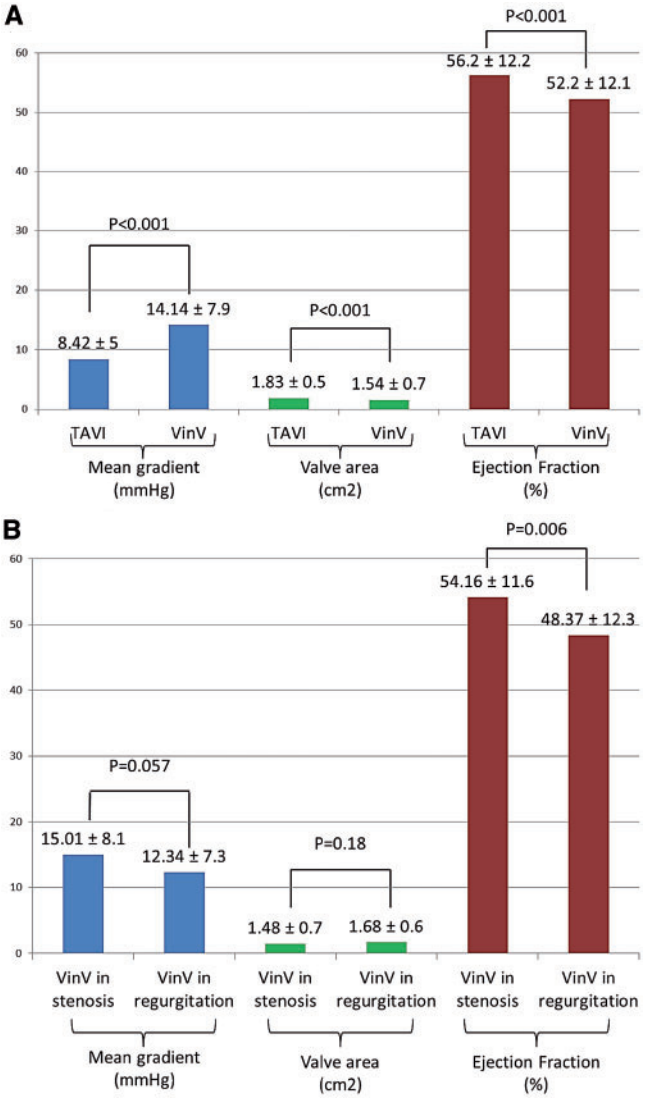


Figure 1: (**A**) Post-procedural echocardiographic data. (**B**) Post-procedural echocardiographic data of VinV in regurgitant and stenotic failed bioprostheses. TAVI: transcatheter aortic valve implantation; VinV: valve-in-valve.

Valve-in-valve subanalysis

The mode of SAV degeneration was more frequently stenotic in female patients (47.2% vs 23.5%; $P = 0.005$), diabetic patients (25.5% vs 9.8%; $P = 0.033$) and obese patients (BMI 27.23 vs 25.39; $P = 0.029$) (Table 1). Intensive care unit stay was longer for patients with regurgitant SAV (1.47 ± 2.77 days vs 0.77 ± 1.2 days; $P = 0.029$), but hospital stay was equivalent (8.49 ± 4.37 days vs 8.41 ± 4.07 days; $P = 0.91$) (Table 2). The postoperative echocardiogram showed higher gradients in the stenotic VinV subgroup (15.01 ± 8.1 mmHg vs 12.34 ± 7.3 mmHg; $P = 0.057$) (Fig. 1B). Compared to standard TAVI, VinV in the stenotic bioprosthesis showed lower all-cause mortality (adjusted HR 0.40, 95% CI 0.18–0.91; $P = 0.028$) but similar cardiovascular mortality (adjusted HR 0.42, 95% CI 0.16–1.13; $P = 0.085$) (Fig. 2C and D). Compared to balloon-expanding valves, self-expanding valves showed higher all-cause ($P = 0.03$) but similar cardiovascular mortality ($P = 0.10$) at 1 year (Fig. 2E and F). The VinV group was also divided into 3 subgroups according to the original SAV size: 18–21 mm, 23 mm and 25–31 mm. One-year mortality was not affected by the size of the failed bioprosthesis (Fig. 2G and H).

Effect of surgical aortic valve size on gradients

Gradients after VinV with balloon or self-expanding valves depending on SAV size showed, in both cases, a statistically significant, negative effect of small bioprostheses (Fig. 3).

DISCUSSION

The salient findings of this study investigating VinV procedures in Switzerland are as follows:

1. VinV procedure is a safe procedure with comparable 30-day outcomes to standard TAVI procedures for native aortic stenosis treatment and lower 1-year all-cause mortality.

Table 4: Clinical outcomes

	TAVI (*N* = 4599), *n* (%)	VinV (*N* = 157), *n* (%)	Crude Cox's regressions		Adjusted Cox's regressions	
			HR or RR (95% CI)	*P*-value	Adjusted HR or RR (95% CI)	Adjusted *P*-value
30-Day outcomes						
Mortality	174 (3.8)	3 (1.9)	0.51 (0.16–1.58)	0.242	0.52 (0.16–1.63)	0.260
Cardiovascular mortality	157 (3.4)	3 (1.9)	0.56 (0.18–1.76)	0.321	0.59 (0.19–1.86)	0.367
Cerebrovascular accident	162 (3.6)	1 (0.6)	0.18 (0.03–1.28)	0.086	0.20 (0.03–1.42)	0.107
Disabling stroke	86 (1.9)	0 (0.0)	0.17 (0.01–2.73)	0.118		
Non-disabling stroke	53 (1.2)	1 (0.6)	0.55 (0.08–3.98)	0.555	0.60 (0.08–4.35)	0.610
TIA	23 (0.5)	0 (0.0)	0.62 (0.04–10.16)	1.000		
Myocardial infarction	25 (0.5)	2 (1.3)	2.34 (0.55–9.89)	0.247	2.53 (0.58–10.97)	0.215
Periprocedural myocardial infarction	21 (0.5)	2 (1.3)	2.79 (0.65–11.89)	0.166	3.15 (0.71–13.87)	0.130
Spontaneous myocardial infarction	4 (0.1)	0 (0.0)	3.24 (0.18–59.92)	1.000		
Acute kidney injury	216 (4.8)	2 (1.3)	0.27 (0.07–1.07)	0.062	0.25 (0.06–1.02)	0.054
Stage 1	86 (1.9)	0 (0.0)	0.17 (0.01–2.73)	0.118		
Stage 2	40 (0.9)	0 (0.0)	0.36 (0.02–5.83)	0.642		
Stage 3	90 (2.0)	2 (1.3)	0.65 (0.16–2.63)	0.542	0.54 (0.13–2.22)	0.393
Bleeding	818 (17.9)	30 (19.2)	1.08 (0.75–1.55)	0.680	1.12 (0.78–1.62)	0.534
Life-threatening bleeding	265 (5.8)	5 (3.2)	0.55 (0.23–1.33)	0.185	0.52 (0.21–1.27)	0.152
Major bleeding	333 (7.3)	15 (9.6)	1.33 (0.79–2.23)	0.281	1.40 (0.83–2.37)	0.205
Minor bleeding	237 (5.2)	10 (6.4)	1.24 (0.66–2.33)	0.511	1.43 (0.75–2.72)	0.272
Vascular access-related complications	750 (16.3)	23 (14.7)	0.89 (0.59–1.35)	0.597	0.96 (0.63–1.45)	0.837
Major vascular complications	442 (9.6)	15 (9.6)	0.99 (0.59–1.66)	0.983	1.04 (0.62–1.75)	0.883
Minor vascular complications	308 (6.7)	8 (5.1)	0.76 (0.38–1.53)	0.437	0.84 (0.41–1.70)	0.629
Permanent pacemaker implantation	840 (18.5)	5 (3.3)	0.16 (0.07–0.39)	<0.001	0.17 (0.07–0.42)	0.000
1-Year outcomes						
Mortality	569 (13.0)	10 (6.8)	0.51 (0.27–0.95)	0.035	0.48 (0.26–0.90)	0.022
Cardiovascular mortality	392 (9.0)	7 (4.8)	0.52 (0.25–1.10)	0.085	0.53 (0.25–1.11)	0.094
Cerebrovascular accident	209 (4.8)	3 (2.2)	0.41 (0.13–1.29)	0.129	0.43 (0.14–1.37)	0.154
Disabling stroke	112 (2.6)	0 (0.0)	0.13 (0.01–2.08)	0.053		
Non-disabling stroke	67 (1.5)	2 (1.5)	0.87 (0.21–3.54)	0.844	0.93 (0.23–3.85)	0.923
TIA	31 (0.7)	1 (0.7)	0.94 (0.13–6.88)	0.950	1.00 (0.13–7.48)	0.997
Myocardial infarction	55 (1.3)	2 (1.3)	1.05 (0.26–4.31)	0.944	1.10 (0.26–4.56)	0.899
Spontaneous myocardial infarction	34 (0.9)	0 (0.0)	0.42 (0.03–6.82)	0.628		
Bleeding	916 (20.3)	34 (22.1)	1.09 (0.78–1.54)	0.605	1.12 (0.79–1.59)	0.516
Life-threatening bleeding	313 (7.0)	6 (3.9)	0.56 (0.25–1.25)	0.156	0.53 (0.23–1.19)	0.124
Major bleeding	372 (8.3)	17 (11.1)	1.35 (0.83–2.19)	0.227	1.41 (0.86–2.30)	0.175
Minor bleeding	275 (6.2)	11 (7.2)	1.17 (0.64–2.14)	0.608	1.28 (0.69–2.35)	0.433
Permanent pacemaker implantation	905 (20.2)	7 (4.7)	0.21 (0.10–0.44)	<0.001	0.22 (0.10–0.46)	<0.001

The values are indicated as number of first events with % of all patients censored at 30 days since procedure or 1 year since procedure, in both cases with % from Kaplan–Meier estimates. Cox's regression HR (with 95% CIs). Continuity-corrected RR (95% CI) with *P*-value from the Fisher's exact test in case of zero event. Adjusted HR or RR: comparing the groups in case of more than 10 events, after adjustment for age, sex, BMI ≤20, diabetes, prior pacemaker, peripheral arterial disease, COPD, coronary artery disease, STS PROM score and post-TAVI regurgitation moderate or severe.

BMI: body mass index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; RR: relative risk; STS: Society of Thoracic Surgery; TAVI: transcatheter aortic valve implantation; TIA: transient ischaemic attack; VinV: valve-in-valve.

2. The VinV group showed a lower rate of moderate/severe paravalvular leak than the TAVI group.
3. Small SAV size negatively affects VinV gradients but without clinical repercussions on 1-year all-cause mortality and cardiovascular mortality.

Our data are in line with 2 important VinV registries, the VIVID Registry and the PARTNER II Aortic VinV Registry, and suggest that VinV represents a safe treatment with the favourable results and a low complication rate at 1 year [7, 9, 12]. The all-cause mortality at 1 year of 6.8% is lower than the previously reported rates of 12.4% and 16.8% [7, 9]. With regard to the mode of SAV failure, our findings confirm that after 1 year patients with regurgitant bioprosthesis have a slightly lower mortality rate than patients with stenotic SAV, a finding also reported in VIVID and PARTNER II [7, 9].

After VinV, we observed a neurological complication rate of 0.6% at 30 days, which is in line with data from other registries (1.7% and 2.7% of major stroke) and lower than reported data for standard TAVI procedures [7, 12]. As a possible explanation, balloon valvuloplasty is less often performed during VinV (23% vs 69%) carrying a lower risk of debris embolization.

Post-procedural major vascular complications during VinV were the most frequently observed adverse events (9.6% in our series; 9.2% in the VIVID Registry; and 4.1% in the PARTNER II Registry) suggesting that alternative access sites should also be considered in case of diseased aorta or peripheral arteries. Although the transaortic approach can be a challenge in redo patients operated on for aortic valve replacement, transapical VinV can be performed with an acceptable low risk of apical damage and bleeding with new low-sized introducer sheaths [13, 14]. Moreover, the use of small introducer sheaths and apical plugs may further lower this risk [15, 16].

With regard to the paravalvular leak after VinV, stented SAV represents a valid grip for transcatheter valves, and our data confirm the low rate (1.3%) of moderate/severe leak among VinV patients at discharge echocardiogram. Similar registries report

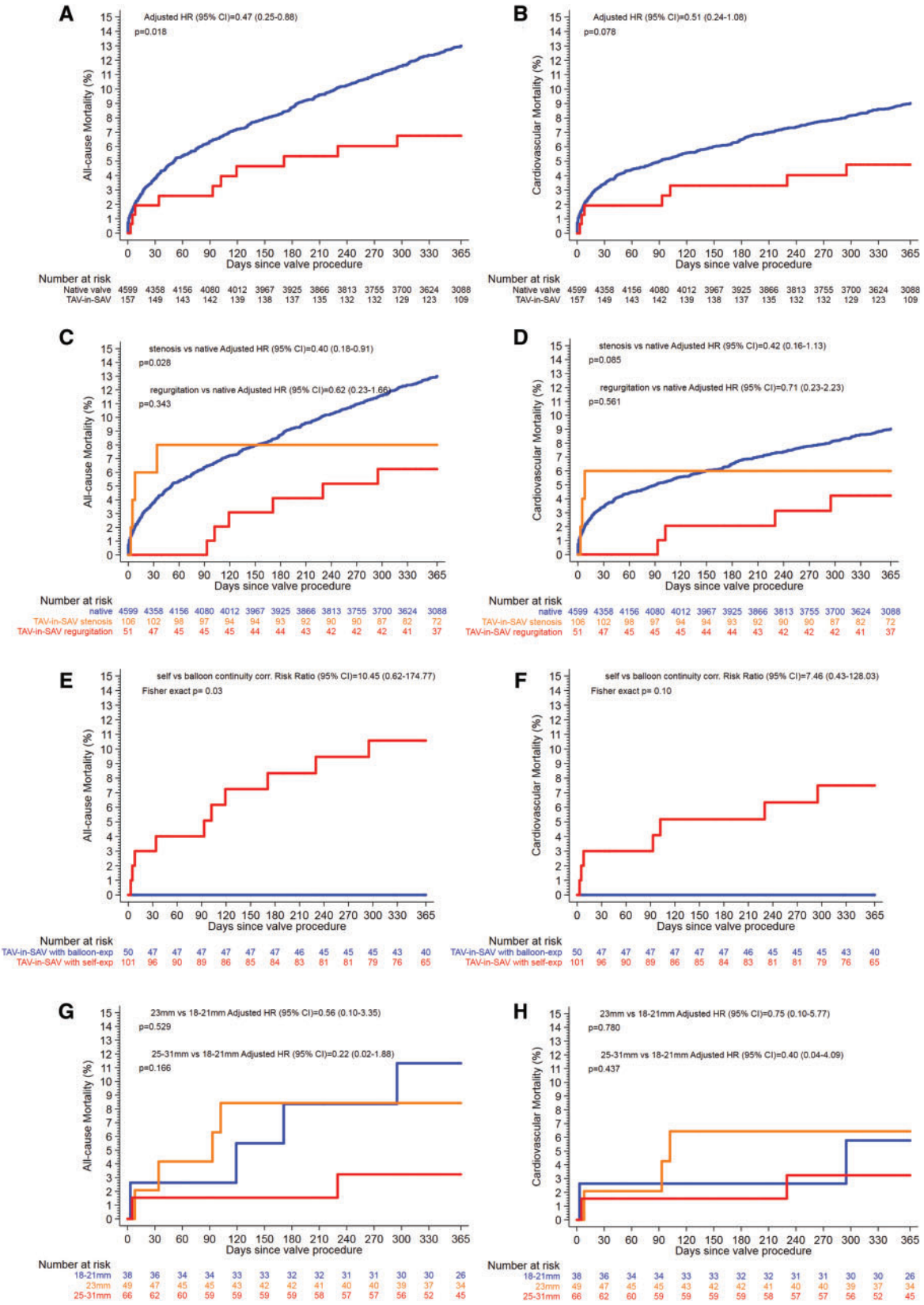


Figure 2: The Kaplan–Meier curves. All-cause mortality (**A**) and cardiovascular mortality (**B**) at 1-year follow-up for the VinV (red line) and TAVI groups (blue line); all-cause mortality (**C**) and cardiovascular mortality (**D**) at 1-year follow-up for TAVI (blue line), VinV in the stenotic bioprosthesis (orange line) and VinV in regurgitant bioprosthesis (red line); all-cause mortality (**E**) and cardiovascular mortality (**F**) at 1-year follow-up for VinV performed with balloon-expandable (blue line) or self-expanding valves (red line); all-cause mortality (**G**) and cardiovascular mortality (**H**) at 1-year follow-up for VinV patients with bioprosthesis of 18–21-mm (blue line), 23-mm (orange line) and 25–31-mm (red line) size. CI: confidence interval; HR: hazard ratio; SAV: surgical aortic valve; TAV: transcatheter aortic valve; VinV: valve-in-valve.

Table 5: Predictors of all-cause mortality at 1 year

	Univariable Cox's regressions		Multivariable Cox's regressions	
	HR (95% CI)	*P*-value	Adjusted HR or RR (95% CI)	Adjusted *P*-value
All-cause mortality at 1 year (579 in 4756 patients)				
Age (years)	1.02 (1.00–1.03)	0.021	1.01 (1.00–1.03)	0.063
Female gender	0.79 (0.67–0.93)	0.005	0.80 (0.68–0.96)	0.014
BMI ≤20	1.35 (1.02–1.80)	0.038	1.34 (1.00–1.79)	0.049
Diabetes mellitus	1.42 (1.19–1.69)	<0.001	1.28 (1.06–1.54)	0.009
Previous pacemaker implantation	1.40 (1.11–1.78)	0.005	1.32 (1.04–1.67)	0.024
Peripheral artery disease	1.50 (1.24–1.83)	<0.001	1.24 (1.01–1.51)	0.038
COPD	1.67 (1.36–2.06)	<0.001	1.47 (1.18–1.82)	0.001
Coronary artery disease	1.39 (1.17–1.65)	<0.001	1.22 (1.02–1.46)	0.029
STS score	1.07 (1.06–1.09)	<0.001	1.06 (1.05–1.08)	0.000
History of myocardial infarction	1.45 (1.18–1.79)	<0.001		*0.232*
History of cerebrovascular accident	1.15 (0.91–1.47)	0.243		*0.586*
History of cardiac surgery	1.16 (0.93–1.45)	0.179		*0.341*
Dyslipidaemia	1.12 (0.95–1.32)	0.174		*0.744*
Hypertension	0.98 (0.81–1.20)	0.882		*0.162*
Coronary revascularization	1.20 (0.88–1.63)	0.255		*0.518*
Surgical access	1.26 (1.03–1.54)	0.027		*0.479*
Femoral access	0.74 (0.59–0.94)	0.012		*0.389*

Cox's regression HR (with 95% CIs). A single imputation of missing data. Baseline variables with *P*-value <0.1 are included, and italicized values are *P*-values for those variables finally not included if added to the multivariable model.

BMI: body mass index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; RR: relative risk; STS: Society of Thoracic Surgery.

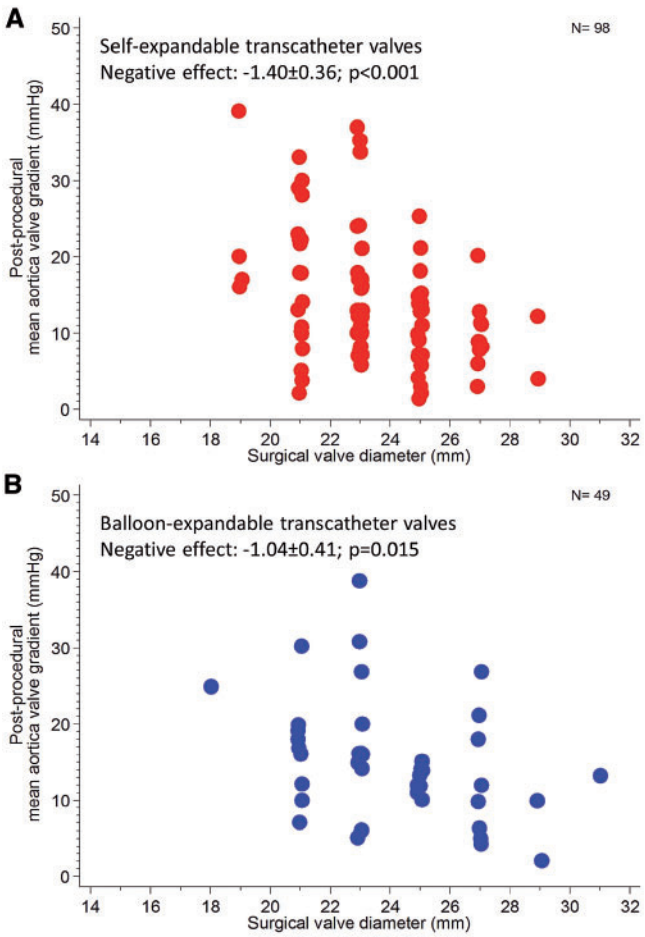


Figure 3: The mean gradients after valve-in-valve (VinV) procedures depending on the size of the previously implanted bioprosthesis. (**A**) VinV procedure with self-expanding valves and (**B**) VinV procedure with balloon-expandable valves.

1.9% (PARTNER II) and 5.4%, 6.9% (VIVID) of paravalvular regurgitation greater than mild [7, 9, 12].

Another important point is the size of the previously implanted SAV and its impact on VinV gradients. As expected, the SwissTAVI Registry showed that small SAVs had higher post-VinV gradients than TAVI, but this did not seem to affect the 1-year survival in this elderly population. Similarly, the subanalysis of VIVID patients with prosthesis–patient mismatch showed an incidence of moderate/severe mismatch of 85.6% and high gradients in 27.9% of patients, but without association with outcome at 1-year follow-up [12]. Nevertheless, younger lower-risk patients with small SAV should be carefully considered for VinV procedures.

The results of this study should be interpreted while taking into account the limitations. This was a retrospective study without randomization and the study population was relatively small. However, our analysis reflects routine clinical practice with VinV and standard TAVI procedures in Switzerland.

Funding

The SwissTAVI Registry is supported by a grant from the Swiss Heart Foundation and the Swiss Working Group of Interventional Cardiology, and by unrestricted funds from Medtronic, Edwards Lifesciences, Symetis, JenaValve and St. Jude Medical.

Conflict of interest: Enrico Ferrari is a consultant for Edwards Lifesciences and received institutional educational grants from Edwards Lifesciences. Christoph Huber is a proctor for Edwards Lifesciences and Boston Scientific/Symetis. Raban Jeger serves as a consultant for Abbott and received reimbursement for travel expenses from Boston Scientific, Medtronic and Edwards Lifesciences. Francesco Maisano is a consultant for Medtronic,

Abbott and Edwards Lifesciences and received research grants from Medtronic, Abbott, Edwards Lifesciences, Boston Scientific and Biotronik. Olivier Muller serves as a consultant for Abbott and received speaker fees from Edwards Lifesciences. Fabian Nietlispach serves as a consultant for Abbott. Stéphane Noble serves as a consultant for Medtronic. Marco Roffi has received institutional research grants from Abbott Vascular, Boston Scientific, Biotronik, Terumo and Medtronic. Stefan Stortecky has received research grants to the institution from Edwards Lifesciences, Biotronik, Medtronic and Boston Scientific. Stefan Toggweiler is a proctor and consultant for Boston Scientific and NVT and received research grants from Boston Scientific. David Tueller received speaker fees from Edwards Lifesciences, Boston Scientific and received reimbursement for travel expenses from Edwards Lifesciences, Boston Scientific and Medtronic. Peter Wenaweser is a proctor for Edwards Lifesciences, Medtronic and Boston Scientific. Stephan Windecker reports having received research contracts to the institution from Abbott, Amgen, Boston Scientific, Biotronik. All other authors have no conflict of interest to declare.

REFERENCES

[1] Hecker F, Arsalan M, Kim WK, Walther T. Transcatheter aortic valve implantation (TAVI) in 2018: recent advances and future development. Minerva Cardioangiol 2018;66:314–28.

[2] Mariathas M, Rawlins J, Curzen N. Transcatheter aortic valve implantation: where are we now? Future Cardiol 2017;13:551–66.

[3] Tarantini G, Purita PAM, D'Onofrio A, Fraccaro C, Frigo AC, D'Amico G *et al*. Long-term outcomes and prosthesis performance after transcatheter aortic valve replacement: results of self-expandable and balloon-expandable transcatheter heart valves. Ann Cardiothorac Surg 2017;6: 473–83.

[4] Wenaweser P, Stortecky S, Heg D, Tueller D, Nietlispach F, Falk F *et al*. Short-term clinical outcomes among patients undergoing transcatheter aortic valve implantation in Switzerland: the Swiss TAVI registry. EuroIntervention 2014;10:982–9.

[5] Binder RK, Stortecky S, Heg D, Tueller D, Jeger R, Toggweiler S *et al*. Procedural results and clinical outcomes of transcatheter aortic valve implantation in Switzerland: an observational cohort study of Sapien 3 versus Sapien XT transcatheter heart valves. Circ Cardiovasc Interv 2015; 8:e002653.

[6] Ferrari E. Transcatheter aortic "valve-in-valve" for degenerated bioprostheses: choosing the right TAVI valve. Ann Cardiothorac Surg 2012;1: 260–2.

[7] Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S *et al*. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. JAMA 2014;312:162–70.

[8] Gallo M, Dvir D, Demertzis S, Pedrazzini G, Berdajs D, Ferrari E. Transcatheter valve-in-valve implantation for degenerated bioprosthetic aortic and mitral valves. Expert Rev Med Devices 2016;13: 749–58.

[9] Webb JG, Mack MJ, White JM, Dvir D, Blanke P, Herrmann HC *et al*. Transcatheter aortic valve implantation within degenerated aortic surgical bioprostheses: PARTNER 2 valve-in-valve registry. J Am Coll Cardiol 2017;69:2253–62.

[10] Huber C, Praz F, O'Sullivan CJ, Langhammer B, Gloekler S, Stortecky S *et al*. Transcarotid aortic valve-in-valve implantation for degenerated stentless aortic root conduits with severe regurgitation: a case series. Interact CardioVasc Thorac Surg 2015;20: 694–700.

[11] Kappetein AP, Head SJ, Généreux P, Piazza N, Van Mieghem NM, Blackstone EH *et al*. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. Eur J Cardiothorac Surg 2012;42: S45–60.

[12] Bleiziffer S, Erlebach M, Simonato M, Pibarot P, Webb J, Capek L *et al*. Incidence, predictors and clinical outcomes of residual stenosis after aortic valve-in-valve. Heart 2018;104:828–34.

[13] Ferrari E, Muller O, Demertzis S, Moccetti M, Moccetti T, Pedrazzini G *et al*. Transaortic transcatheter aortic valve replacement through a right mini-thoracotomy with balloon-expandable Sapien™ 3 valve. Multimed Man Cardiothorac Surg 2016;2016: pii: mmw011. doi: 10.1093/mmcts/mmw011.

[14] Ferrari E, Eeckhout E, Keller S, Muller O, Tozzi P, Berdajs D *et al*. Hospital outcome and risk factor analysis of transapical versus transfemoral approach for transcatheter aortic valve replacement. J Cardiothorac Surg 2017;12:78.

[15] Ferrari E, Demertzis S, Angelella J, Berdajs D, Tozzi P, Moccetti T *et al*. Apical closure device for full-percutaneous transapical valve implantation: stress-test in an animal model. Interact CardioVasc Thorac Surg 2017;24:721–6.

[16] Ferrari E. Apical access and closure devices for transapical transcatheter heart valve procedures. Swiss Med Wkly 2016;146:w14237.