Cite this article as: Grubitzsch H, Zobel S, Christ T, Holinski S, Stangl K, Treskatsch S *et al.* Redo procedures for degenerated stentless aortic xenografts and the role of valve-in-valve transcatheter techniques. Eur J Cardiothorac Surg 2017;51:653-9.

# Redo procedures for degenerated stentless aortic xenografts and the role of valve-in-valve transcatheter techniques<sup>+</sup>

Herko Grubitzsch<sup>a,\*</sup>, Sebastian Zobel<sup>a</sup>, Torsten Christ<sup>a</sup>, Sebastian Holinski<sup>a</sup>, Karl Stangl<sup>b</sup>, Sascha Treskatsch<sup>c</sup>, Volkmar Falk<sup>a</sup> and Michael Laule<sup>b</sup>

<sup>a</sup> Department of Cardiovascular Surgery, Campus Charité Mitte, Charité – Universitätsmedizin Berlin, Berlin, Germany

<sup>b</sup> Department of Cardiology, Campus Charité Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany

<sup>c</sup> Department of Anesthesiology and Intensive Care Medicine, Campus Charité Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany

\* Corresponding author. Klinik für Kardiovaskuläre Chirurgie, Charité – Universitätsmedizin Berlin, Charité-Platz 1, 10117 Berlin, Germany. Tel: +49-30-450522092; fax: +49-30-450522921; e-mail: herko.grubitzsch@charite.de (H. Grubitzsch).

Received 2 September 2016; received in revised form 28 October 2016; accepted 10 November 2016

# Abstract

**OBJECTIVES:** This study evaluates reinterventions for degenerated stentless aortic xenografts.

**METHODS:** Between 2010 and 2015, 52 consecutive patients (age 72.3 ± 9.7 years, EuroSCORE II 11.1 ± 8.9%) underwent reintervention for failed stentless aortic valves (60% porcine, 40% pericardial, 87% sub-coronary, 81% isolated/combined regurgitation).

**RESULTS:** Based on age, EuroSCORE II, the presence of pulmonary hypertension, renal failure, a patent internal mammary artery graft and required concomitant procedures, the heart team assigned 25 patients to reoperation and 27 to valve-in-valve transcatheter aortic valve implantation (ViV-TAVI). Valve implantation was successful in all surgical (24% root replacement) and in 24 transcatheter cases (93% transfemoral, 56% balloon-expandable). Procedural complications were aortic dissection (n = 1) during reoperation and coronary obstruction (n = 4), device malpositioning (n = 3), deployment of >1 valve (n = 2) and vascular access site complications (n = 2) during ViV-TAVI. Thirty-day mortality (10%, three ViV-TAVI patients, two surgical patients, P = 1.0) was associated with preoperative renal failure, >1 concomitant procedure, life-threatening bleeding, coronary obstruction and necessity for prolonged circulatory support. ViV-TAVI was beneficial regarding ventilation time, transfusion requirements and the incidence of sepsis. Overall, functional (94% New York Heart Association Class I/II) and echocardiographic results (indexed effective orifice area  $0.95 \pm 0.27 \text{ cm}^2/\text{m}^2$ , mean transvalvular gradient  $14 \pm 6.8 \text{ mmHg}$ ) were favourable. After ViV-TAVI, aortic regurgitation was mild and moderate in two and three patients. One-year survival was  $82.3 \pm 5.4\%$  and similar after surgery ( $83.1 \pm 7.7\%$ ) and ViV-TAVI ( $81.5 \pm 7.5\%$ , P = 0.76).

**CONCLUSIONS:** Reinterventions for degenerated stentless aortic valves are challenging. Although ViV-TAVI is appropriate in high-risk patients, limitations and potential complications must be considered. Redo surgery has its place in low-risk patients and if concomitant procedures are required.

Keywords: Stentless aortic xenograft • Reoperation • Valve-in-valve transcatheter aortic valve implantation

# INTRODUCTION

In recent years, stentless xenografts have been increasingly used for aortic valve replacement (AVR) due to their favourable haemodynamic profile [1–3]. Compared with conventional stented bioprostheses, less structural deterioration was initially expected, but could not be confirmed. Thus, an increase in the number of reoperations after stentless aortic valve implantation can be anticipated, as these valves will soon reach the limits of their durability. Reoperations after stentless AVR have been reported as

<sup>†</sup>Presented at the 30th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Barcelona, Spain, 1–5 October 2016.

challenging and are associated with an increased risk of death [4]. After the introduction of catheter-based AVR, valve-in-valve transcatheter aortic valve implantation (ViV-TAVI) has evolved as an additional treatment option. Today, a huge body of literature exists demonstrating the feasibility and success of treating degenerated conventional stented bioprostheses with transcatheter heart valves (THV) [5–11]. In contrast, less experience is published regarding ViV-TAVI in degenerated stentless aortic valves and these reports frequently deal with degenerated homografts used for aortic root replacement [10, 12–14]. This study analyses results with redo surgery and ViV-TAVI for treatment of degenerated porcine and pericardial stentless aortic bioprostheses, aiming to define the potential role of ViV-TAVI in this particular setting.

# **MATERIALS AND METHODS**

#### Patients

We reviewed 52 consecutive patients (77% male, mean age 72.3 ± 9.7 years, 21% ≥80 years) who underwent reintervention for a degenerated stentless aortic valve from January 2010 to December 2015 (Ethics Committee approval EA4/095/16). Other causes for reintervention, e.g. prosthetic valve endocarditis, were excluded. Mean time from the index operation was 10 ± 4.8 years and seven patients (14%) had more than one previous cardiac surgery. The heart team, consisting of an interventional cardiologist, a cardiac surgeon, an echocardiographer and an anaesthetist specialized in cardiothoracic procedures discussed all cases and recommended either reoperation or ViV-TAVI based on clinical presentation, coexisting conditions, anatomical details of the aortic root and the predicted risk. All patients gave written informed consent. Clinical data were assessed before the procedure, at 30 days, at 12 months and yearly thereafter. End-points were defined according to the Valve Academic Research Consortium-2 criteria [15]. At baseline, at Days 5-10, and at follow-up, echocardiographic parameters were assessed using standard techniques.

# Surgery

All reoperations were performed via median sternotomy, using an oscillating saw. Cardiopulmonary bypass, installed by cannulation of the ascending aorta, the aortic arch or femoral artery and the right atrium or femoral vein, was used with systemic normothermia or mild hypothermia (32 °C) if a patent mammary artery bypass was present. Myocardial protection was achieved with intermittent antegrade blood cardioplegia. Previously implanted stentless valves were either debrided or completely removed. The choice of prosthesis or root replacement was at the discretion of the surgeon. Concomitant procedures were performed according to the standard techniques.

# Valve-in-valve transcatheter aortic valve implantation

A standard trans-femoral or transapical TAVI procedure was performed for implantation of balloon-expandable (Edwards Lifesciences Sapien<sup>TM</sup>, Sapien XT<sup>TM</sup>) or self-expanding valves (Medtronic CoreValve<sup>TM</sup> and CoreValve Evolute<sup>TM</sup>, Boston Scientific Lotus<sup>TM</sup>). The choice for the prosthesis was based on aortic root dimensions determined by multislice computed tomography, angiography and/or echocardiography, the type, size and implantation technique of the existing valve, and the experience of the team performing the implantation. To aid delineation of the target landing zone, either fluoroscopic images coaxial to valvular calcifications or root angiography with the pigtail catheter in the non-coronary sinus in the absence of calcifications was used. In critical cases, balloon inflation and aortic root angiography were performed to exclude potential coronary obstruction before THV implantation. Usually, rapid ventricular pacing (140-180 beats per minute) plus angiography was applied for cardiac output reduction and exact device alignment during deployment. ViV-TAVI cases requiring surgical treatment were analysed as that of the ViV-TAVI group.

# Data analysis

Data reporting and statistical analysis followed published definitions and guidelines [15-17]. Categorical variables are presented as absolute and relative frequencies. For continuous data, means and standard deviations or medians with lower (LQ) and upper quartiles (UQ) were calculated, respectively. Continuous variables were compared between two groups using the Mann-Whitney U-test and categorical data by Fisher's exact test. Survival was analysed using the Kaplan-Meier estimator and sub-groups were compared by the Log-Rank test. Univariate binary regression analysis was used to determine factors of operative mortality. Results are presented as odds ratio with 95% confidence interval. Due to the limited cohort size and the small number of events, no multivariate analysis was performed. A P-value <0.05 was considered to be statistically significant. All the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

# RESULTS

# **Baseline status**

Preprocedural characteristics are given in Table 1. The majority of patients (90.4%) presented with heart failure [New York Heart Association (NYHA) class  $\geq$ III]. Isolated or combined aortic regurgitation (AR) was the leading indication for reintervention (81%). Previously implanted stentless valves were of porcine origin in 60% (15 Edwards Lifesciences Prima Plus<sup>TM</sup>, 8 St. Jude Medical Toronto SPV<sup>TM</sup>, 7 Vascutek Elan<sup>TM</sup> and 1 Shelhigh superstentless<sup>TM</sup>) and pericardial valves in 40% (9 Sorin Pericarbon Freedom<sup>TM</sup>, 8 Medtronic 3F<sup>TM</sup> and 4 Sorin Freedom SOLO<sup>TM</sup>). In 87%, they were implanted in sub-coronary technique. Overall, 40% of patients were at high risk (EuroSCORE II >10%). Except for age, EuroSCORE II, the incidence of pulmonary hypertension and renal failure (Table 2), baseline characteristics were similar between ViV-TAVI and surgical patients.

# **Procedural results**

Table 2 lists the most important criteria of the heart team decision for redo surgery or ViV-TAVI. During the study period, the relative frequency of ViV-TAVI performed ranged from 20% to 71% per year (Fig. 1). Detailed procedural data are given in Table 3. For ViV-TAVI, procedure time and fluoroscopy time was 92 ± 28.6 and 15 ± 8.9 min, respectively. For redo surgery, operation, cardiopulmonary bypass and aortic cross clamp times were 212 ± 59.3, 125 ± 36.3 and 101 ± 25.3 min for isolated procedures and 351 ± 133.0, 229 ± 127.0 and 162 ± 78.0 min for combined procedures, respectively. Valve implantation was successful in all surgical and in 24 (89%) ViV-TAVI cases. Root replacement was performed for an urysm correction (n = 1), a ortic root enlargement (n = 1) and tissue defects caused by excision of the previous prosthesis (n = 4). With ViV-TAVI, the following complications occurred in nine patients (33%): THV malpositioning (n = 3), coronary obstruction (n = 4, Supplementary Table S1), intraprocedural resuscitation (n = 4) and implantation of covered stents for vascular access site complications (n = 2). In 11%, conversion to open surgery was required due to coronary obstruction (n=2) and failed THV implantation (n=1). Deployment of

#### Table 1: Baseline characteristics

Variable	n (%)	Mean ± SD
Age		72.3 ± 9.7 years
Male gender	40 (77)	7210 = 717 youro
Weight		80 3 + 15 4 kg
Height		$1725 \pm 86 \text{ cm}$
Pody surface area		$10 \pm 0.0$ cm <sup>2</sup>
Douy surface area		$1.9 \pm 0.2$ m
Body mass index	17 (00)	26.9 ± 4.6 kg/m
Heart failure NYHA>III	47 (90)	
Aortic valve stenosis	10 (19)	
Aortic valve regurgitation	31 (60)	
Combined lesion	11 (21)	
Mitral valve regurgitation 2+	28 (54)	
Tricuspid regurgitation 2+	21 (40)	
Coronary artery disease	26 (50)	
Prior myocardial infarction	3 (6)	
Prior stents	9 (17)	
Prior CABG	13 (25)	
Left ventricular end-diastolic diameter		53.7 ± 7.89 mm
LVEF		52.0 ± 11.4%
LVEF <40%	6 (12)	
Pulmonary hypertension	33 (64)	
Systolic PAP >55 mmHg	17 (33)	
Sinus rhythm	38 (73)	
AV block	1 (2)	
Bundla branch block	12 (22)	
Atrial fibrillation	20 (20)	
	20 (39)	
Dersistent	7 (14) 12 (25)	
Persistent De several en //CD	15 (25)	
Pacemaker/ICD	6(12)	
COPD	12 (23)	
Renal failure	20 (39)	
Stage I	10 (19)	
Stage II	5 (10)	
Stage III	5 (10)	
Extracardiac arteriopathy	9 (17)	
Previous cerebrovascular accident	12 (23)	
Stroke	6 (12)	
Transient ischaemic attack	8 (15)	
Time from previous AVR		10.0 ± 4.8 years
>1 previous cardiac operation	7 (14)	
Size of previous stentless aortic valve		26.2 ± 2.3 mm
21	2 (4)	
23	7 (14)	
25	13 (25)	
27	16 (31)	
29	14 (27)	
Root replacement/inclusion cylinder	7 (14)	
Pericardial valve	21 (40)	
Previous isolated AVR	31 (60)	
Previous combined procedures	21 (40)	
CABG	13 (25)	
Mitral valvo ropair/roplacomont	8 (15)	
	1 (2)	
Aortoplasty	1 (2)	
Atrial fibrillation chlation	1 (Z) 2 (C)	
	5 (D)	111 + 0.00/
	21 (40)	11.1 ± 0.9%
EULOSCOKE II > 10%	21 (40)	

AV: atrioventricular; AVR: aortic valve replacement; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PAP: pulmonary artery pressure.

more than one THV and postimplant balloon-dilatation was necessary in two and five patients, respectively. There was no instance of annular rupture. One case of aortic dissection occurred during surgery. Analysis of valve sizes and types of reintervention

#### Table 2: Most important criteria for heart team decision

	ViV-TAVI (n = 27)	Redo surge (n = 25)	eryP-value
Age, Mean ± SD	75.3 ± 9.9 vears	69.0 ± 8.6 vears	0.060
EuroSCORE II, Mean ± SD Pulmonary	13.0 ± 10.4 21 (78)	4 8.9 ± 6.5 12 (48)	0.054 0.043
hypertension, n (%)	2.(/0)	(10)	0.010
Renal failure, n (%)	16 (59)	4 (16)	0.006
Patent IMA graft, n (%)	9 (33)	2 (8)	0.040
Concomitant intervention required, n (%	) 3 (11)	15 (60)	< 0.001

IMA: internal mammary artery; ViV-TAVI: valve-in-valve transcatheter aortic valve implantation.



**Figure 1:** Frequency of reinterventions over time. Columns depict absolute frequency of reoperations and ViV-TAVI during the study period. The dots of the line graph reflect relative frequency of ViV-TAVI in the respective year. ViV-TAVI: valve-in-valve transcatheter aortic valve implantation.

is given in Fig. 2. No technique was preferentially used for smaller valve sizes (<21 mm).

#### Early outcome

Table 4 summarizes outcome regarding mortality and morbidity. Overall, there were four procedural deaths, two after surgery (one intractable bleeding and one refractory vasoplegia) and two after ViV-TAVI (one coronary obstruction and one heart failure). Within 30 days, another ViV-TAVI patient died due to coronary obstruction requiring emergency surgery. At 30 days, overall mortality was 10%, similar after surgery and ViV-TAVI (8% vs 11%, P = 1.0). Univariate predictors of early mortality are listed in Table 5. Between surgical and TAVI patients, there was no significant difference in 30-day morbidity except for the incidence of sepsis (P = 0.02). Median mechanical ventilation time was 5.5 (LQ 3.0, UQ 19.5) h overall and significantly longer after redo surgery [11.0 (LQ 4.5, UQ 42.0) vs 4.0 (LQ 2.0, UQ 12.0) h, P = 0.005]. Although seven surgical patients (28%) required pharmacological circulatory support (inotropes/vasopressors) for >48 h compared with three patients (11%) after ViV-TAVI, this difference was not significant (P = 0.17). Overall, 31 patients (60%) received any transfusion (red blood cells, platelets and/or

	ViV-TAVI	Redo surgery
	(n = 27) n (%)	(n = 25) n (%)
Size of new aortic valve prosthesis		
21		3 (12)
23	7 (26)	5 (20)
25	( )	9 (36)
26	13 (48)	( )
27	1 (4)	6 (24)
29	5 (19)	2 (8)
31	1 (4)	
Transcatheter valves		
Self-expanding	12 (44)	NA
Balloon-expandable	15 (56)	NA
Trans-femoral access	25 (93)	NA
Transapical access	2 (7)	NA
Surgical valves		
Mechanical	NA	2 (8)
Conventional stented bioprostheses	NA	7 (28)
Stentless bioprostheses	NA	16 (64)
Root replacement/inclusion cylinder	NA	6 (24)
Concomitant procedures		
Percutaneous coronary intervention	1 (4)	
CABG	NA	5 (20)
Mitral valve plasty		5 (20)
Mitral valve replacement	1 (4)	5 (20)
Tricuspid valve plasty		1 (4)
Replacement of ascending aorta	NA	1 (4)
>1 concomitant procedure	- ()	4 (16)
Mechanical circulatory support	3 (11)	4 (16)
Extracorporeal life support	3 (11)	4 (16)
Intra-aortic balloon pump		1 (4)

Table 3: Procedural characteristics

CABG: coronary artery bypass grafting; NA: not applicable; ViV-TAVI: valve-in-valve transcatheter aortic valve implantation.

fresh frozen plasma), 20 (80%) after surgery and 11 (41%) after ViV-TAVI (P = 0.005). Median ICU and hospital stay were 4.0 (LQ 2.3, UQ 8.8) and 12.0 (LQ 8.0, UQ 18.5) days overall. There were no significant differences after surgery and ViV-TAVI regarding ICU stay [6.0 (LQ 2.5, UQ 11.5) vs 3.0 (LQ 2.0, UQ 6.0) days, P = 0.27] and hospital stay [13.0 (LQ 7.5, UQ 21.5) vs 11.0 (LQ 9.0, UQ 17.0) days, P = 0.74].

#### Late outcome

Median follow-up was 21 months (LQ 6.1 months, UQ 40.8 months). It was 96% complete (two patients were lost). Within the first year another four patients died, two after surgery (one ischaemic colitis and one heart failure) and two after ViV-TAVI (one mitral valve endocarditis and one pneumonia). At one year, overall survival was 82.3 ± 5.4%, similar after surgery (83.1 ± 7.7%) and ViV-TAVI (81.5  $\pm$  7.5%, P = 0.76). Within the first year, 13 patients (25%) required rehospitalization. Causes were cardiovascular in six patients (mitral valve endocarditis, pacemaker implantation, implantable cardioverter defibrillator exchange for resynchronization therapy, stroke, transient ischaemic attack and tachyarrhythmia) and non-cardiovascular in seven patients. Although rehospitalization was more frequent after ViV-TAVI (Table 4), the difference was not significant (P = 0.37). No aortic valve reintervention was necessary. The majority of patients



Identical and larger size of new aortic valve

Figure 2: Type of reintervention and aortic valve size. (A) Absolute frequency of reoperations and ViV-TAVI performed in different sizes of previous stentless aortic valves (P = 0.30). (B) The label-size of the new aortic valve (y-axis) in relation to the label-size of the existing stentless valve (x-axis) in individual patients (bullet points). Unchanged valve size is given as reference (dotted lines). The new valve was of identical or larger size in 18 (67%) ViV-TAVI patients compared with nine (36%) surgical patients (P=0.051). (C) Percentages of identical or larger-sized new aortic valve prostheses (related to the size of the previous stentless valve) in different types of transcatheter and surgical substitutes. More frequently, but not significantly, the new valve was of identical or larger size in self-expanding compared with balloon-expandable THVs (P = 0.22) as well as in stentless compared with non-stentless surgical valves (P=0.40). ViV-TAVI: valve-in-valve transcatheter aortic valve implantation; THV: transcatheter heart valves

(94%) was in NYHA Class I or II, similar after surgery and ViV-TAVI.

# **Echocardiographic results**

Based on mean indexed effective orifice area (EOAI) of  $0.95 \pm 0.27 \text{ cm}^2/\text{m}^2$  and mean transvalvular gradient ( $p_{\text{mean}}$ ) of 14.2 ± 6.8 mmHg, reintervention resulted in good systolic aortic valve function. Figure 3 shows the haemodynamic results in subgroups. Transvalvular gradients were significantly lower with identical or larger size of the new aortic valve, in particular after surgery (right panels of Fig. 3A and C). Furthermore, lower transvalvular gradients were observed after ViV-TAVI compared with reoperation and with self-expanding compared with balloon-expandable

#### Table 4: Outcome regarding mortality and morbidity

	All patients (n = 52) n (%)	ViV-TAVI (n = 27) n (%)	Redo surgery (n = 25) n (%)
Early outcome ( $\leq$ 30 days)		- (-)	- (-)
Procedural deaths (0-3 days)	4 (8)	2 (7)	2 (8)
30-day mortality	5 (10)	3 (11)	2 (8)
Myocardial infarction	1 (2)	1 (4)	
Neurological events	3 (6)	2 (7)	1 (4)
Stroke	1 (2)	- / ->	1 (4)
Transient ischaemic attack	1 (2)	1 (4)	
Intracerebral haemorrhage	1 (2)	1 (4)	
Delirium	10 (19)	3 (11)	7 (28)
New bundle branch	5 (10)	3 (11)	2 (8)
and/or AV block	- ( -)		- (-)
New permanent pacemaker	3 (6)	1 (4)	2 (8)
New atrial fibrillation	11 (21)	4 (15)	7 (28)
Ventricular tachycardia	3 (6)	1 (4)	2 (8)
Resuscitation	3 (6)	1 (4)	2 (8)
Vascular complications	2 (4)	2 (7)	
Major	1 (2)	1 (4)	
Minor	1 (2)	1 (4)	
Bleeding (any)	15 (29)	9 (33)	6 (24)
Life-threatening	6 (12)	3 (11)	3 (12)
Major	4 (8)	2 (7)	2 (8)
Minor	5 (10)	4 (15)	1 (4)
Acute kidney injury (any)	12 (23)	4 (15)	8 (32)
Stage I			
Stage II	3 (6)		3 (12)
Stage III	9 (17)	4 (15)	5 (20)
Pneumonia	8 (15)	4 (15)	4 (16)
Reintubation	2 (4)	1 (4)	1 (4)
Tracheostomy	4 (8)	1 (4)	3 (12)
Sepsis	5 (10)		5 (20)
Access site infection			
Late outcome			
All-cause mortality	9 (17)	5 (19)	4 (16)
(cumulative at 1 year)			
Cardiovascular mortality	7 (14)	4 (15)	3 (12)
Non-cardiovascular mortality	2 (4)	1 (4)	1 (4)
Re-hospitalization	13 (25)	9 (33)	4 (16)
Re-intervention			
Aortic valve endocarditis			
Heart failure NYHA>III	3 (6)	2 (7)	1 (4)

AV: atrioventricular; NYHA: New York Heart Association; ViV-TAVI: valve-in-valve transcatheter aortic valve implantation.

 Table 5:
 Univariate predictors of 30-day mortality

	30-day mortality (%)	OR	95% CI	P-value
Preoperative renal failure ≥ stage II	60	7.3	1.1-51.1	0.045
>1 concomitant procedure	40	15.0	1.5-146.9	0.020
Coronary obstruction	67	22.0	1.3-362.9	0.031
Life-threatening bleeding	60	22.0	2.6-186.5	0.005
Mechanical circulatory support	80	58.7	4.9-703.3	0.001
Inotropes and/or vasopressors >48 h	60	12.6	1.7-94.5	0.014

95% CI: 95% confidence interval; OR: odds ratio.



**Figure 3:** Mean transvalvular gradients in sub-groups. Sub-group analysis of mean aortic valve gradients ( $p_{mean}$ ) after reintervention in all patients (**A**) as well as after ViV-TAVI (**B**) and reoperation (**C**). Figures in parentheses indicate numbers of measurements per sub-group.

THVs (left panels of Fig. 3A and B). Six patients presented with  $p_{\text{mean}} \ge 20 \text{ mmHg}$ , one after ViV-TAVI using a balloon-expandable valve and five after reoperation (P = 0.20). In these five cases, the new valve was smaller than the previous stentless valve. According to the accepted threshold of an EOAI <0.65 cm<sup>2</sup>/m<sup>2</sup>, patient-prosthesis mismatch occurred in three patients, in two after ViV-TAVI with balloon-expandable valves and in one after reoperation with a conventional stented xenograft (P = 0.58). Overall, no more than trace AR was demonstrated in 39 patients (93%), not different after surgery and ViV-TAVI (100% vs 81%, P = 0.39). Mild and moderate AR was present in two (8%) and three (12%) patients after ViV-TAVI, respectively. There were no cases of severe AR. After ViV-TAVI, no case of device migration was observed.

# DISCUSSION

# **Principal findings**

The heart team assigned roughly half of the patients requiring reintervention for degenerated stentless aortic valves each to ViV-TAVI and reoperation. ViV-TAVI patients were older and at higher operative risk than patients undergoing redo surgery. They also presented more frequently with pulmonary hypertension, renal failure and a patent internal mammary artery graft. By comparison, redo surgery was more frequently performed in younger patients and in those requiring concomitant procedures. Despite the significantly higher predicted risk of death, mortality after ViV-TAVI was not significantly different from that after redo surgery. Early mortality (<30 days) was associated with preoperative renal failure, life-threatening bleeding and necessity for prolonged medical or mechanical circulatory support. After ViV-TAVI, early mortality was in particular associated with intraprocedural coronary obstruction whereas after redo surgery it was associated with more than one concomitant procedure. After surgery, patients required longer respiratory support and more transfusions and developed more frequently sepsis. At follow-up, the majority of patients reported symptomatic improvement regardless of surgical or transcatheter reintervention. Echocardiography demonstrated excellent valve function in most instances, but patient-prosthesis mismatch and paravalvular AR after ViV-TAVI remain a concern.

#### **Risks of reintervention**

Reoperations after stentless AVR are considered to be challenging and risky, but the increased risk is primarily associated with prosthetic valve endocarditis, concomitant procedures and reoperation within 1 year [4, 18]. The 30-day mortality rate after redo surgery of 8% reported herein is identical with results of stentless aortic valve reoperation in 40 patients (excluding prosthetic valve endocarditis) from the Toronto group [4]. It is obvious that ViV-TAVI for treatment of degenerated stentless aortic valves is also associated with relevant risk even though no early death was reported in two series [12, 14]. After ViV-TAVI, 30-day mortality was 11% in this study and 7.6% in 459 patients (20.3% stentless xenografts) from the Valve-in-Valve International Registry [10]. Attention to the technique of reintervention, myocardial preservation and haemostasis may prevent complications, in particular bleeding (redo surgery) and coronary obstruction (ViV-TAVI), being most important to reduce the risk of mortality.

#### Haemodynamic considerations

Surgical as well as transcatheter reintervention re-established aortic valve function. Excellent haemodynamics were achieved with ViV-TAVI, in particular with self-expanding valves, and with reoperation, if the new prosthesis was identical or larger than the previous stentless xenograft (Fig. 3). Mild and moderate AR was an issue only after ViV-TAVI. Compared with ViV-TAVI, redo surgery resulted more frequently in a valve diameter reduction compared with the size of the existing stentless valve (Fig. 2B). In fact, with the use of conventional stented biological or mechanical prostheses for failing stentless xenografts a reduction by approximately two sizes has been reported [19]. It is noteworthy that with implantation of stentless valves as a new substitute size reduction was still an issue in more than 50% of patients (Fig. 2C). This may explain, why haemodynamic results were not superior with stentless xenografts (Fig. 3C). Although aortic root replacement could be an alternative avoiding down scaling, its operative risk is not negligible [4, 19]. There was a non-significant trend to use a larger size of self-expanding compared with balloon-expandable THVs for ViV-TAVI in this series, which is in line with recent findings [12, 14]. Duncan et al. [12] implanted self-expanding prostheses (CoreValve<sup>™</sup>) in 22 degenerated stentless aortic valves (77% homografts) and used up to 24% oversized devices in 91% of patients, whereas Bapat *et al.* implanted balloon-expandable THVs (Sapien<sup>TM</sup>, Sapien XT<sup>TM</sup> and Sapien  $3^{TM}$ ) in 10 degenerated stentless valves (60% homografts) using larger sizes in only 20% [14]. For haemodynamic results and in contrast to redo surgery, there is no reason to choose an oversized THV (Fig. 3B).

#### Recommendations for degenerated stentless valves

With ViV-TAVI after stentless AVR. one of the most critical issues is the definition of the type and size of the THV. Several difficulties and potential complications have to be considered: types and implantation techniques (sub-coronary, inclusion cylinder and root replacement) of the existing stentless valve, usually lack of annular calcification, occasionally bulky calcified leaflets, definition of the target landing zone, device malpositioning, migration and embolization, coronary obstruction, and the risk of annular or sinus rupture [8, 9, 14]. As a stent or sufficient calcifications supporting anchoring are usually lacking, an oversized THV is frequently recommended to prevent migration and embolization [12, 20]. For the same reason, some authors prefer selfexpanding valves [12]. An oversized valve implant may cause coronary obstruction. It is important to realize that the geometry of the aortic root is the key factor for this life-threating complication, as (i) the annulus will often be closer to the coronary ostia, in particular after sub-coronary implantation where the proximal suture line more or less presents the annulus and (ii) without a stent, there will be a significant smaller or no gap between the THV and the coronary ostia, especially in case of a cylindrical configuration of the aortic root with a sinus diameter not wider than the diameter of the annulus. In addition, leaflet height, which is typically larger in stentless pericardial valves, and occasional bulky calcifications of the leaflets have to be regarded. All of the four cases of coronary obstruction, which occurred within the first years of our series, involved stentless xenografts implanted with the sub-coronary technique. Three were pericardial valves, but only one THV was oversized. Self-expanding and balloon-expandable THVs were used in two cases each. As stated by others, meticulous planning by preprocedural imaging is essential to control the diametrical risks of coronary obstruction and valve migration [12, 14]. Multislice computed tomography is the most appropriate tool to assess the individual anatomy of the aortic root. Its results have to be included in the heart team discussion enabling a decision for ViV-TAVI-and the most suitable THV-or surgery. Reoperation should still be regarded as standard treatment and certainly preferred if aortic root configuration may complicate TAVI. How the appropriate procedure could be determined by specific criteria has to be assessed in prospective studies. The VIV aortic app, a reference guide in form of a freely downloadable 'app' (www.ubgo.com/viv) should be used very cautiously, as its recommendation is only based on structural features of the implanted bioprosthesis [20]. It is helpful for conventional stented bioprostheses, but rather unsuitable for stentless valves for the aforementioned reasons. Thus, our choice of THV and the recommendation of the 'app' matched in only 39%. As final analysis, aortic root angiography during balloon inflation should be used to visualize potential coronary obstruction before device implantation as the inflated balloon simulates the displacement of the leaflets of the stentless valve by the THV [8, 14].

# CONCLUSION

Reinterventions—redo surgery as well as ViV-TAVI—for degenerated stentless aortic valves are technically challenging and accompanied by a significant periprocedural risk. Early mortality is associated with preoperative renal failure, more than one concomitant procedure, occurrence of complications such as life-threatening bleeding or coronary obstruction, and the necessity for prolonged circulatory support. ViV-TAVI is a reasonable option, especially in elderly patients with high surgical risk due to comorbidity and/or previous coronary artery bypass grafting, but limited success and potential complications have to be considered. Therefore, assessing the individual anatomy of the aortic root is of paramount importance. Redo surgery has its place in younger patients with lower risk, in particular in those requiring concomitant surgical procedures.

# SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

**Conflict of interest:** Herko Grubitzsch received lecture fees (Sorin Biomedica). Karl Stangl received speaker honoraria (Edwards Lifesciences) and proctors THV implantation (Edwards Lifesciences, Medtronic). Sascha Treskatsch received lecture fees (Edwards Lifesciences). Volkmar Falk is principal investigator of the studies EchoNav, Biovalve (Biotronik) and Respond (Boston Scientific) and received industry funding (Medtronic: Engager Feasibility and Pivotal Trial) and lecture fees (Medtronic, Edwards Lifesciences, St. Jude Medical). Michael Laule received research funding (Edwards Lifesciences) and speaker honoraria (Edwards Lifesciences) and proctors THV implantation (Edwards Lifesciences, Medtronic, St. Jude Medical). Sebastian Zobel, Torsten Christ and Sebastian Holinski have no conflicts of interest to declare.

# REFERENCES

- Walther T, Falk V, Langebartels G, Krüger M, Bernhardt U, Diegeler A et al. Prospectively randomized evaluation of stentless versus conventional biological aortic valves: impact on early left ventricular hypertrophy. Circulation 1999;100:116–10.
- [2] Borger MA, Carson SM, Ivanov J, Rao V, Scully HE, Feindel CM et al. Stentless aortic valves are hemodynamically superior to stented valves during mid-term follow-up: a large retrospective study. Ann Thorac Surg 2005;80:2180–5.
- [3] Grubitzsch H, Wang S, Matschke K, Glauber M, Heimansohn D, Tan E et al. Clinical and haemodynamic outcomes in 804 patients receiving the Freedom SOLO stentless aortic valve: results from an international prospective multicentre study. Eur J Cardiothorac Surg 2015;47:e97–104.
- [4] Borger MA, Prasongsukarn K, Armstrong S, Feindel CM, David TE. Stentless aortic valve reoperations: a surgical challenge. Ann Thorac Surg 2007;84:737-44.

- [5] Gurvitch R, Cheung A, Ye J, Wood DA, Willson AB, Toggweiler S et al. Transcatheter valve-in-valve implantation for failed surgical bioprosthetic valves. J Am Coll Cardiol 2011;58:2196-209.
- [6] Piazza N, Bleiziffer S, Brockmann G, Hendrick R, Deutsch MA, Opitz A et al. Transcatheter aortic valve implantation for failing surgical aortic bioprosthetic valve: from concept to clinical application and evaluation (part 1). JACC Cardiovasc Interv 2011;4:721–32.
- [7] Piazza N, Bleiziffer S, Brockmann G, Hendrick R, Deutsch MA, Opitz A et al. Transcatheter aortic valve implantation for failing surgical aortic bioprosthetic valve: from concept to clinical application and evaluation (part 2). JACC Cardiovasc Interv 2011;4:733-42.
- [8] Webb JG, Dvir D. Transcatheter aortic valve replacement for bioprosthetic aortic valve failure: the valve-in-valve procedure. Circulation 2013;127:2542-550.
- [9] Lange R, Piazza N. Transcatheter aortic valve-in-surgical aortic valve implantation: current status and future perspectives. Eur J Cardiothorac Surg 2013;44:403–6.
- [10] Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S et al. Valvein-valve international data registry investigators. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. JAMA 2014;312:162–70.
- [11] Ye J, Cheung A, Yamashita M, Wood D, Peng D, Gao M et al. Transcatheter aortic and mitral valve-in-valve implantation for failed surgical bioprosthetic valves. An 8-year single-center experience. J Am Coll Cardiol Intv 2015;8:1735-44.
- [12] Duncan A, Davies S, Di Mario C, Moat N. Valve-in-valve transcatheter aortic valve implantation for failing surgical aortic stentless bioprosthetic valves: a single-center experience. J Thorac Cardiovasc Surg 2015;150:91–8.
- [13] Chan PH, Di Mario C, Davies SW, Kelleher A, Trimlett R, Moat N. Transcatheter aortic valve implantation in degenerate failing aortic homograft root replacements. J Am Coll Cardiol 2011;58:1729-30.
- [14] Bapat V, Davies W, Attia R, Hancock J, Bolter K, Young C et al. Use of balloon expandable transcatheter valves for valve-in-valve implantation in patients with degenerative stentless aortic bioprosthesis: technical considerations and results. J Thorac Cardiovasc Surg 2014;148:917-24.
- [15] Kappetein AP, Head SJ, Genereux 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 (VARC-2). Eur Heart J 2012;33:2403–18.
- [16] Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL *et al.* Councils of the American Association for thoracic surgery, Society of thoracic surgeons, European Association for cardiothoracic surgery, Ad Hoc Liason Committee for standardizing definitions of prosthetic heart valve morbidity. Guidelines for reporting mortality and morbidity and cardiac valve interventions. Eur J Cardiothorac Surg 2008;33:523–8.
- [17] Hickey GL, Dunning J, Seifert B, Sodeck G, Carr MJ, Burger HU, et al. Statistical and data reporting guidelines for the European Journal of Cardio-Thoracic Surgery and the Interactive CardioVascular and Thoracic Surgery. Eur J Cardiothorac Surg 2015;48:180-93.
- [18] Böning A, Niemann B, Ennker I, Richter M, Roth P, Ennker J. Are aortic valve reoperations after primary replacement with stentless heart valve prostheses more demanding than after stented biological prostheses? Thorac Cardiovac Surg 2014;62:475–81.
- [19] Finch J, Roussin I, Pepper J. Failing stentless aortic valves: redo aortic root replacement or valve in a valve? Eur J Cardiothorac Surg 2013;43:495–504.
- [20] Bapat V. Valve-in-valve apps: why and how they were developed and how to use them. EuroIntervention 2014;10:U44-51.