



Simultaneous Aortic and Pulmonary Valve Replacement in Repaired Congenital Heart Disease

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Abstract

Objectives Patients with congenital heart disease frequently require surgical or percutaneous interventional valve replacement after initial congenital heart defect (CHD) repair. In some of these patients, simultaneous replacement of both semilunar valves is necessary, resulting in increased procedural complexity, morbidity, and mortality. In this study, we analyze the outcomes of simultaneous aortic and pulmonary valve replacements following multiple surgical interventions for CHD.

Methods This was a retrospective study of 24 patients who after initial repair of CHD underwent single-stage aortic and pulmonary valve replacement at our institution between 2003 and 2021.

Results The mean age of the patients was 28 ± 13 years; the mean time since the last surgery was 15 ± 11 years. Decellularized valved homografts (DVHs) were used in nine patients, and mechanical valves were implanted in seven others. In eight patients, DVHs, biological, and mechanical valves were implanted in various combinations. The mean cardiopulmonary bypass time was 303 ± 104 minutes, and aortic cross-clamp time was 152 ± 73 minutes. Two patients died at 12 and 16 days postoperatively. At a maximum follow-up time of 17 years (mean 7 ± 5 years), 95% of the surviving patients were categorized as New York Heart Association heart failure class I.

Conclusion Single-stage aortic and pulmonary valve replacement after initial repair of CHD remains challenging with substantial perioperative mortality (8.3%). Nevertheless, long-term survival and clinical status at the latest follow-up were excellent. The valve type had no relevant impact on the postoperative course. The selection of the valves for implantation should take into account operation-specific factors—in particular reoperability—as well as the patients' wishes.

Keywords

- ▶ congenital heart disease
- ▶ aortic valve replacement
- ▶ pulmonary valve replacement
- ▶ mechanical valve
- ▶ valve prosthesis
- ▶ decellularized homografts

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Introduction

Due to advances in the field of congenital heart disease, the number of adult patients living with congenital heart defects (adult congenital heart diseases [ACHDs]) is steadily increasing. While primary correction of congenital heart defects in adults is rare, valve-related reoperations are on the rise in this patient population and currently account for more than half of all surgeries in ACHD patients.^{1,2} The most typical valve reoperation is pulmonary valve replacement following the reconstruction of the right ventricular outflow tract (RVOT) for the correction of conotruncal defects, or Ross surgery. However, heart defect-dependent or operation-typical enlargement of the aortic root with progressive aortic regurgitation often occurs in these patients, necessitating reoperation of both outlet valves in adulthood.^{3–6} Since most of these patients have had multiple prior surgeries, combined aortic and pulmonary valve replacement is surgically challenging.⁷ In addition, the choice of the valve substrate has far-reaching consequences in terms of possible reoperations and interventions, for example, the pulmonary vessels. As only few published studies address these issues,^{7,8} this study focuses on the evaluation of our surgical experience and follow-up results after combined aortic and pulmonary valve replacement using different valve types.

Patients and Methods

Study Population

This retrospective study included all 24 patients after the initial repair of congenital heart defects, who subsequently underwent simultaneous aortic and pulmonary valve replacement at Hannover Medical School between 2003 and 2021. The study was approved by the Institutional Ethics Committee (IRB approval #10438). Patients or their legal caregivers provided written informed consent for inclusion in this study. The perioperative surgical findings and clinical follow-up data of all patients were collected in a database (FileMaker 18, FileMaker Intl., Santa Clara, CA, United States) at Hannover Medical School. Outcome data were retrieved from the latest report provided by the outpatient clinic for adults with congenital heart defects or by the referring cardiologist. The study focused on the following clinical outcomes: perioperative (days 0–30) or late death, intraoperative complications, valve-related reoperations, and complications such as endocarditis, thromboembolism or bleeding.

Clinical Management and Operative Technique

The indication for simultaneous prosthetic aortic and pulmonary valve replacement and the timing of operation were determined in an interdisciplinary team meeting between cardiologists and congenital heart surgeons. The indication for surgery was aortic valve regurgitation or stenosis, with or without progressive aortic root dilatation, combined with pulmonary insufficiency or pulmonary conduit dysfunction. In cases of borderline indications, the patient's overall prognosis was assessed on an individual basis and a decision was taken by the team.

A computed tomography of the thorax with 3D reconstruction was performed preoperatively to determine the surgical strategy. In addition, the femoral vessels were examined by ultrasound to ascertain the feasibility of peripheral cardiopulmonary bypass (CPB) cannulation. The operations were performed under general anesthesia via median re-sternotomy. Antegrade cold blood cardioplegia (Buckberg) was applied to protect the myocardium. In cases of decellularized aortic homografts (DAH) implantation, a free-standing root replacement technique with reimplantation of the coronaries as buttons was used. The RVOT was reconstructed with free implantation of the decellularized pulmonary homograft after the removal of the pulmonary valve or degenerated conduit. For both anastomoses, proximal ventricular and distal to the pulmonary trunk, a continuous suture technique was used.

In cases of double mechanical valve implantation, isolated aortic valve replacement was performed with a mechanical valve or root replacement with a valved conduit. Subsequently, a self-constructed mechanical valved conduit consisting of a mechanical valve fixed in a Dacron prosthesis was used for RVOT reconstruction. Following surgery, transesophageal echocardiography was routinely performed to evaluate valve function.

Postoperative Management

Clinical follow-up included transthoracic echocardiographic evaluation performed according to the current guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.

In addition to mandatory lifelong endocarditis prophylaxis for all patients, acetylsalicylic acid therapy of 2 to 3 mg/kg body weight per day for 6 to 12 months was initiated in pediatric patients who received double valve replacement using cell-free homografts. In adult patients, coumarin therapy was recommended for 2 months, followed by antiplatelet therapy with 100 mg/d acetylsalicylic acid lifelong.

Patients undergoing mechanical aortic and pulmonary valve replacement were anticoagulated with coumarin with a target international normalized ratio (INR) between 3 and 3.5.

Results

Preoperative Clinical and Demographic Characteristics

All patients had previously undergone surgery for congenital heart defects. Seven patients had Tetralogy of Fallot (TOF) and had undergone surgical repair with or without previous palliation. A further six patients had undergone corrective repair of truncus arteriosus communis. One patient with d-transposition of the great arteries had previously undergone arterial switch repair, and another had combined congenital aortic and pulmonary valvar stenosis. Eight patients (33%) initially had single-valve disease: seven patients with an initial diagnosis of congenital aortic stenosis underwent a Ross procedure; one patient with the history of congenital pulmonary stenosis had surgical commissurotomy of the pulmonary valve in the neonatal period. The

mean age of the patients was 28 ± 13 years (4–59 years, 5 were children/adolescents), and the mean time since the last cardiac surgery was 15 ± 11 years. The demographic data for all patients are summarized in ►Table 1.

Intra- and Postoperative Data

All re sternotomies were performed without complications. In three patients, re sternotomy was performed only after CPB was initiated via the femoral vessels. It was the second sternotomy for 4 (16.5%) patients, the third for 12 (50%), the fourth for 4 (16.5%), fifth for 3 (12.5%), and sixth for 1 (4%) patient. The mean CPB time was 303 ± 104 minutes, and the mean aortic cross-clamp time was 152 ± 73 minutes.

A combined aortic root and pulmonary valve replacement using decellularized valve homografts (DVH) was performed in nine patients, and two mechanical valves were implanted in seven others. In another eight patients, the heart valve substrates were used in various combinations. The choice of valve prosthesis was made by the surgeon in consultation with the patient or their parents. In 15 patients, (all nine DVH implantations and six patients with mechanical aortic valves) an aortic root replacement was performed using the full root technique with coronary reimplantation.

Eight patients had concomitant procedures, with most procedures addressing the subvalvular/supravalvular region. In patient number 3, an unplanned single venous coronary artery bypass graft was performed on the proximal right coronary artery due to reduced right ventricular contractility during CBP weaning. In this patient, a concomitant resection of the subpulmonary stenosis was also performed through the right ventricle. In patient number 23, the proximal suture of the cryopreserved pulmonary homograft was torn out at sternal closure, which necessitated an immediate reconnection to CPB. The homograft was repaired with an autologous pericardium patch. Postoperatively, three patients required re thoracotomy for bleeding or pericardial tamponade and one patient received hemofiltration for isolated renal failure.

The mean length of stay in the intensive care unit was 4 ± 4 days. Two patients died early postoperatively. One patient died of pulmonary failure with preexisting pulmonary hypertension on the 16th postoperative day. The second patient (the oldest patient in our cohort, 59 years, repaired TOF) required additional, scheduled, multicoronary artery bypass surgery for the current dual-valve operation. His postoperative course became complicated with cardio-respiratory failure and the need for veno-arterial extracorporeal membrane oxygenation support on the 2nd postoperative day. He died of multiorgan failure and sepsis on the 12th postoperative day. The intraoperative and postoperative data are presented in ►Table 2.

Follow-up Status of Survivors

The mean observation time was 7 ± 5 years (range 0.2–17 years). There was no late mortality and no need for secondary pacemaker implantation during follow-up, but two valve-related reoperations were required. One reoperation was related to structural valve degeneration of a DAH, 5.5 years after implantation (patient number 3). This

female patient, who in the meantime had two uneventful pregnancies, underwent uncomplicated mechanical aortic valve replacement as her sixth open heart procedure. In the second case, a hemodynamically relevant subpulmonary stenosis developed in a patient (patient number 12) following double mechanical valve replacement. The subpulmonary stenosis was resected, and the mechanical pulmonary valve was exchanged for a cell-free pulmonary homograft after 15 years as a fifth heart surgery.

Most of the 22 surviving patients were characterized as asymptomatic in the midterm follow-ups. Ninety five percent of patients were categorized as New York Heart Association (NYHA) functional class I, and one patient had NYHA class II (5%). One patient who had undergone combined mechanical valve replacement (patient number 11) experienced a single event of gastrointestinal bleeding, which was managed conservatively. The other patients did not experience any thromboembolic or bleeding events. No events of endocarditis were observed. ►Table 3 summarizes the data of the latest follow-up for all patients.

Discussion

Although valve-related reoperations are the most common surgical procedures conducted in patients after the correction of congenital heart defects, combined aortic valve and pulmonary valve replacement are comparatively rare. In Holst's evaluation of multivalve interventions in ACHD patients, this proportion was 12%.⁷ Conotruncal malformations, as well as Ross aortic valve replacement, affect both outlet valves and may ultimately lead to valve replacement of the aortic and pulmonary valves. More than 80% of our patients can be assigned to one of these two groups.

Histologically, conotruncal defects display significant changes in smooth muscle, elastin and collagen, and ground substance in the aortic media, in addition to RVOT/pulmonary valve pathology.⁸ In truncus arteriosus up to 50% of patients have at least moderate truncal valve insufficiency,⁹ which usually results in truncus (aortic) valve replacement during the course of the disease. In contrast, aortic valve replacement in TOF is rare. In particular, prolonged volume loading of the aortic root, such as in late correction after shunt or pulmonary atresia, is associated with aortic dilatation and correlates with aortic regurgitation.^{10,11} The literature reports an incidence of aortic regurgitation of 3.5 to 12% after Fallot correction.^{12,13} Ross surgery is undoubtedly ingenious, but the mortgage of a two-valve disease remains. The average reoperation rate is 1.1%/y for autografts and 0.91%/y for RVOT, with the timing of Ross surgery in childhood associated with significantly worse outcomes,¹⁴ leading to heterogenous results across studies.

The surgical risk for death in simultaneous aortic and pulmonary valve replacement in our study was 8.4% perioperatively with no mortality during follow-up (mean 7 ± 5 years). Each operation represented an extreme challenge for the clinical team and required individual planning according to the three-step strategy model.¹⁵ We simulate a “step-by-step” approach in all complex redo-surgical procedures. A

Table 1 Patient characteristics

Patients	Gender	Age at AVR + PVR	Primary diagnosis	Previous surgery Procedures 1st OP (Age)	2nd OP (Age)	3rd OP (Age)	4th OP (Age)	5th OP (Age)	Indication for combined aortic and pulmonary valve replacement
1	M	31	AS, BAV	Ross operation (17 ys)	Re-AVR (18 y)	Re-Re-AVR (24 y)			Aorta asc dilatation, PV degeneration
2	F	10	TAC	Truncus repair (2 mo)	AVR, Re-PVR (1 y)	Re-Re-PVR (1 y)	Re-Re-Re-PVR (2 y)	Re-AVR (2 y)	AS, Aorta asc dilatation
3	F	16	TAC	Truncus repair (3 mo)	AV repair (3 y)	AVR (4 y)	PVR (9 y)		AS, Aorta asc dilatation, PR
4	F	38	AS, BAV	Ross operation (21 y)					AR, Aorta asc dilatation, PS
5	M	4	TAC	PA banding (2 days)	TAC repair (6 mo)				AR, PV degeneration
6	M	19	AS	Ross operation (3 mo)	Re-PVR (14 y)				AR, Aorta asc dilatation, PV degeneration
7	M	17	TAC	Truncus repair (1 mo)	Re-PVR (5 y)				AS/AR, PV degeneration
8	M	16	AS	Ross operation (6 y)	David op (14 y)				AR, PS/PR
9	F	28	AS, PS, VSD, CoA	CoA resection, VSD closure, AV valvotomy (1 week)	AVR, PVR (13 y)				AV degeneration; PV degeneration
10	M	34	TAC	PA banding (2 mo)	TAC repair (5 y)	Re-PVR (11 y)	Re-Re-PVR (18 y)		AR, Aorta asc dilatation, PV degeneration
11	M	27	TOF	BT-shunt (3 mo)	TOF repair (10 y)	PVR (22 y)			AR, Aorta asc dilatation, PV degeneration
12	M	38	TOF	Waterson-Shunt (3 y)	TOF repair (7 y)	PVR (24 y)			AR, Aorta asc dilatation, PV degeneration
13	M	30	TOF	TOF repair (8 mo)	PVR (26 y)				AR, Aorta asc dilatation, PV degeneration
14	F	32	AS	Ross operation (12 y)					AR, PV degeneration
15	M	30	PS	PV valvotomy (6 y)					AI, PI
16	M	20	TAC	TAC repair (2 mo)	PVR (10 y)				AR, PV degeneration
17	F	37	AS, BAV CoA	CoA resection (26 y)	Ross op (27 y)				AR, Aorta asc dilatation, PS
18	M	29	AS	AV valvotomy (2 mo)	Ross op (1 y)	Re-PVR (2 y)	AV repair, Re-Re-PVR (14 y)		AR, Aorta asc dilatation, PS
19	F	41	TOF	PV valvotomy (3 mo)	TOF repair (5 y)				AR, PS/PR
20	F	24	TGA, VSD	Arterial Switch, VSD closure (2 mo)	Transannular patch RVOT (2 y)	Re-Transannular patch RVOT (16 y)			AS/AR, PS
21	M	59	TOF	BT-shunt (2 mo)	TOF repair (12 y)				AR, PR; CAD
22	M	27	TOF	BT-shunt (3 mo)	TOF repair (3 y)				AR, PR
23	F	52	TOF	BT-shunt (13 mos)	TOF repair (19 y)				AR, PR
24	M	19	AS, PS	PV valvotomy (1 mo)					AS/AR, PR
mean ± SD		28 ± 13							

Abbreviations: AR, aortic regurgitation; Asc, ascending; AS, aortic stenosis; AV, aortic valve; AVR, aortic valve replacement; BAV, bicuspid aortic valve; BT-shunt, Blalock Taussig shunt; CAD, coronary artery disease; CoA, coarctation of the aorta; PR, pulmonary regurgitation; PS, pulmonary stenosis; PV, pulmonary valve; PVR, pulmonary valve replacement; TAC, truncus arteriosus communis; TOF, Tetralogy of Fallot.

Table 2 Perioperative data

Patients	Aortic valve (diameter, mm)	Pulmonary valve (diameter, mm)	Ao root replacement	Concomitant procedures	Temperature	Bypass time (min)	X-Cl. Time (min)	ICU stay (days)	Postoperative complications
1	DAH, 24	DPH, 25	^a	Asc. aortic replacement	32	275	140	3	None
2	DAH, 21	DPH, 30	^a	Pulmonary artery plastic	25	477	307	3	None
3	DAH, 23	DPH, 25	^a	Subpulmonary SR, CABG	29	466	273	4	None
4	DAH, 23	DPH, 25	^a	None	32	275	176	2	None
5	DAH, 20	DPH, 15	^a	None	21	346	229	6	None
6	DAH, 30	DPH, 25	^a	None	28	365	236	5	None
7	DAH, 30	DPH, 32	^a	Asc. aortic replacement	28	395	237	3	None
8	DAH, 22	DPH, 25	^a	None	28	304	191	2	None
9	DAH, 20	DPH, 25	^a	None	28	284	177	1	None
10	ATS mech, 25	SJM mech, 21	^a	None	25	421	142	16	Hemothorax, re-sternotomy
11	SJM mech, 29	SJM mech, 23	^a	None	25	335	100	1	None
12	SJM mech, 25	SJM mech, 23	^a	None	21	270	54	9	Hemothorax, re-sternotomy
13	ATS mech, 23	SJM mech, 21	^a	None	20	374	143	3	Renal failure
14	SJM mech, 23	SJM mech, 23	None	None	30	189	45	1	None
15	SJM mech, 23	SJM mech, 21	None	None	30	131	47	1	None
16	SJM mech, 27	SJM mech, 21	None	None	27	146	46	1	None
17	ATS mech, 23	DPH, 27	^a	None	26	313	120	4	None
18	SJM mech, 25	DPH, 27	^a	prox aortic arch replacement	21	523	203	8	None
19	SJM mech, 23	DPH, 26	None	Residual VSD closure	31	182	104	2	None
20	SJM mech, 21	DPH, 26	None	Subaortic SR	28	238	150	2	None
21	SJM mech, 25	Hancock bio, 25	None	CABG	30	257	69	12	VA-ECMO support, cardio-respiratory failure, sepsis
22	CE bio, 25	Hancock bio, 25	None	None	30	242	178	4	None
23	Magna Ease bio, 25	Homograft, 30	None	None	31	300	148	2	Rupture of homograft, second CPB
24	Magna Ease bio, 25	Homograft, 27	None	None	32	181	127	4	Pericardial tamponade, re-sternotomy
mean ± SD					27 ± 3.7	303 ± 104	152 ± 73	4 ± 4	

Abbreviations: Asc. ascending; CABG, coronary artery bypass surgery; CPB, cardiopulmonary bypass; DPH, decellularized pulmonary homograft; RCA, right coronary artery; SR, stenosis resection; VSD, ventricle septal defect; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

^aFull aortic root replacement.

Table 3 Postoperative data and outcome

Patents	Outcome	Late complications	Reopertaion	NYHA class	Follow-up (years)
1	Alive	None	None	I	7
2	Alive	None	None	I	5.3
3	Alive	None	AVR (mech, 21 mm)	I	5.5
4	Alive	None	None	I	5.9
5	Alive	None	None	I	4
6	Alive	None	None	I	2
7	Alive	None	None	I	2
8	Alive	None	None	I	1.9
9	Alive	None	None	I	0.2
10	Dead	—	—	—	—
11	Alive	Gastrointestinal bleeding	None	I	15.6
12	Alive	None	PVR (DPH, 25 mm)	II	17
13	Alive	None	None	I	9
14	Alive	None	None	I	16
15	Alive	None	None	I	11
16	Alive	None	None	I	12
17	Alive	None	None	I	10.8
18	Alive	None	None	I	6
19	Alive	None	None	I	0.9
20	Alive	None	None	I	0.7
21	Dead	—	—	—	—
22	Alive	None	None	I	9.4
23	Alive	None	None	I	2.8
24	Alive	None	None	I	3.5
Mean \pm SD					6.8 \pm 5.2

Abbreviations: AVR, aortic valve replacement; DPH, decellularized pulmonary homograft; PVR, pulmonary valve replacement; NYHA, New York Heart Association.

three-step sequential planning strategy is performed, comprised of mediastinal re-entry, cannulation for CPB, and the main procedure. In comparable studies, perioperative mortality ranged from 4.7%⁷ to 14%,¹⁶ with follow-up mortality of 11%⁷ at 5 years and 16%¹⁶ to 23%⁷ at 10 years. Rather, accurate planning and execution of injury-free resection and exact situs preparation is key for a successful surgery. With an average bypass time of 5 hours and a mean aortic clamping time of 2.5 hours, the intraoperative stress on the patient's organism is enormous. Therefore, in our opinion, the surgical procedure should be clear and meticulously planned even before the start of extracorporeal circulation. To save time, a safe reconstruction, especially of the aortic valve or root, is preferable;¹⁷ otherwise, valve or root replacement is necessary.

This also needs a preoperative discussion of valve selection with patients, their parents, and colleagues providing further treatment postoperatively. Biological heart valves are favored by the majority of patients as they do not need permanent anticoagulation, which is needed for mechanical heart valves. The better durability of mechanical heart valves

comes with a reduced quality of life due to this permanent medication, which constitutes a small, but constant risk for thromboembolic events and hemorrhage.

In principle, the choice of the valve in the aortic position determines the choice for the pulmonary position. Biological aortic valve replacement was performed in half of our patients, 75% of these as root replacement in a full root technique with a cell-free homograft. This choice of the valve was preferred for children with a growth-related need for valve replacement, in cases where patients wished to become pregnant later on, in cases of contraindications for the administration of vitamin K antagonists, and also due to lifestyle considerations. In our view, the results we have published for cell-free homografts justify their use, especially in children and young adults, in both aortic and pulmonary positions where suitable homografts are available.^{18–20}

Half of the 12 patients with mechanical aortic valve replacement received this valve as a root replacement. Contrary to reports in other studies,²¹ the total number of prior cardiac surgeries was not a decision criterion for the

choice of valve, but any aortic root re-replacement with a surgical mortality of 14%²² should be considered in prosthesis selection.

While all patients with a biological aortic valve replacement also received a biological pulmonary valve prosthesis, only 7 of the 12 patients with aortic artificial valve replacement received an artificial prosthesis in the pulmonary position. In all cases, the goal was to avoid further reoperation in these adult patients via strict anticoagulation with an INR between 3 and 3.5, as mechanical valves in the pulmonary position have been associated with a higher risk for thromboembolism and valve malfunction.

Transcatheter pulmonary valve replacement would have been another option for biological pulmonary valve replacement, but discussion within the heart team in this selected cohort favored surgical valve replacement for multiple reasons, mostly with respect to the appropriate positioning of the stent-valve and the potential need for extensive prestenenting. The option for future transcatheter pulmonary valve replacement was and is an additional argument for our preference for biological valves in the pulmonary position.

During the follow-up period, the goal of no reoperation was achieved in 85.7% of patients. In particular, the meta-analysis by Dunne has shown, with limited data, that with strict anticoagulation with vitamin K antagonists, mechanical valves also show good function at least within the first 10 years after implantation.²³ Significantly more studies are available on bioprosthetic pulmonary valves during follow-up, with long-term outcomes differing primarily by the type and size of implant and age of recipient in addition to underlying disease.²⁴ In a multicenter study of 1,278 patients under 30 years, the median time to retreatment in patients older than 18 years was 17.7 years. These excellent long-term results, as well as the future treatment option of percutaneous pulmonary valve implantation and the catheter interventional accessibility of the pulmonary vessels (especially in patients with TOF/pulmonary atresia), certainly justify the combination of an artificial valve in the aortic position with a biological valve prosthesis in pulmonary position, as performed in five patients in our cohort.

In the comparison of the two implant groups with biological or mechanical aortic valve implantation, we observed only a slight advantage in the use of biological valves in younger patients with a shorter follow-up time. Consequently, no preference regarding mechanical or biological valve replacement can be derived from our results.

Limitations

The main limitation of this retrospective study is the small number of patients from an extremely heterogeneous patient population. This heterogeneity results from a long observation period with different treatment options as well as the range of underlying diseases and the enormous variation in age at the time of surgery. Due to the formation of small patient cohorts, valid statistical comparisons between subgroups are not feasible.

Conclusion

Simultaneous replacement of the aortic and pulmonary valves is rare but may be necessary, especially in patients with corrected conotruncal heart defects or after Ross surgery. The surgical risk for these procedures remains at approximately 8% postoperative 30-day mortality in our patient population. Important factors for success are accurate planning of the re sternotomy as well as the surgical approach to the affected heart valves. Valve selection should take into account operation-specific aspects, in particular reoperability, as well as patients' priorities regarding lifestyle or wish of pregnancy. During the follow-up period of 7 ± 5 years, there were no patient deaths and 95% of patients were in good clinical condition (NYHA functional class I) at their last follow-up. As we observed only one conservatively treated gastrointestinal bleeding secondary to anticoagulation with an artificial valve implant, no clear preference regarding mechanical or biological valve replacement can be derived from our results.

Authors' Contribution

D.B. was responsible for conceptualization; data curation; project administration; writing—original draft; and writing—review and editing.

K.H. was responsible for data curation; formal analysis; software; and writing—review and editing.

M.A. was responsible for data curation; formal analysis; and supervision.

T.C. was responsible for data curation; formal analysis; and resources.

E.P. was responsible for data curation; formal analysis; and supervision.

S.S. was responsible for data curation; formal analysis; supervision; writing—original draft; and writing—review and editing.

M.W.-B. was responsible for data curation; formal analysis; and supervision.

G.H. was responsible for data curation; formal analysis; supervision; and writing—original draft.

A.H. was responsible for conceptualization; formal analysis; and supervision.

A.H. was responsible for conceptualization; data curation; formal analysis; project administration; supervision; writing—original draft; and writing—review and editing.

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Conflict of Interest

A.H. holds shares in Corlife oHG, the company providing the patented service of processing decellularized allografts used in this study. All other authors declared no potential conflict of interest with respect to the study, authorship, and publication of this article.

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