RESEARCH ARTICLE

Open Access

Aortic valve replacement in pediatric patients: 30 years single center experience



Johanna Schlein¹, Paul Simon¹, Gregor Wollenek¹, Eva Base², Günther Laufer¹ and Daniel Zimpfer^{1*}

Meeting presentation: Poster presentation at the 34th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Barcelona, Spain, 8–10 October 2020

Abstract

Background: The choice of aortic valve replacement needs to be decided in an interdisciplinary approach and together with the patients and their families regarding the need for re-operation and risks accompanying anticoagulation. We report long-term outcomes after different AVR options.

Methods: A chart review of patients aged < 18 years at time of surgery, who had undergone AVR from May 1985 until April 2020 was conducted. Contraindications for Ross procedure, which is performed since 1991 at the center were reviewed in the observed non-Ross AVR cohort. The study endpoints were compared between the mechanical AVR and the biological AVR cohort.

Results: From May 1985 to April 2020 fifty-five patients received sixty AVRs: 33 mechanical AVRs and 27 biological AVRs. In over half of the fifty-three AVRs performed after 1991 (58.5%; 31/53) a contraindication for Ross procedure was present. Early mortality was 5% (3/60). All early deaths occurred in patients aged < 1 year at time of surgery. Two late deaths occurred and survival was 94.5% \pm 3.1% at 10 years and 86.4% \pm 6.2% at 30 years. Freedom from aortic valve re-operation was higher (p < 0.001) in the mechanical AVR than in the biological AVR cohort with 95.2% \pm 4.6% and 33.6% \pm 13.4% freedom from re-operation at 10 years respectively.

Conclusions: Re-operation was less frequent in the mechanical AVR cohort than in the biological AVR cohort. For mechanical AVR, the risk for thromboembolic and bleeding events was considerable with a composite linearized event rate per valve-year of 3.2%.

Keywords: Congenital aortic valve disease, Pediatric aortic valve replacement, Pediatric mechanical aortic valve replacement, Pediatric homograft aortic valve replacement, Pediatric bioprosthetic aortic valve replacement

Background

Despite the encouraging results with aortic valve reconstruction, aortic valve replacement (AVR) might be required in pediatric patients with significant valve destruction after failed-repairs or interventions [1, 2]. Mechanical prostheses are available in small sizes (16

*Correspondence: daniel.zimpfer@meduniwien.ac.at

Waehringer Guertel 18-20, 1090 Vienna, Austria

infants or small children. Annular enlargement techniques (Nicks procedure [3], Manougian procedure [4], Konno procedure [5]) can enable implantation of a larger prosthesis [6, 7]. The need for life-long anticoagulation accompanying the choice of a mechanical prosthesis can be challenging in the pediatric cohort due to the lack of compliance with medication and activity restraints [7]. Anticoagulation regimen needs special consideration in female patients regarding a later pregnancy. The use of biological valve replacement is complicated by

and 18 mm) and suitable for older children, but not for



© The Author(s) 2021. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

¹ University Clinic of Cardiac Surgery, Medical University of Vienna,

Full list of author information is available at the end of the article

accelerated structural valve deterioration, which is faster than that seen in adults because of a greater immune competency and an increased calcium metabolism in young patients [8]. Aortic homografts offer an option for patients, who need more complex reconstruction of the aortic root and serves small children and infants. In recent years decellularized homografts were introduced showing promising results, also in pediatric patients [9, 10].

We reviewed the contraindications for Ross procedure in the observed non-Ross AVR cohort and report on outcomes after mechanical, bio-prosthetic and homograft AVR in pediatric patients.

Methods

Patients

This single-center study was conducted at a tertiary center with a pediatric heart center consisting of specialized pediatric cardiac surgeons, anesthetists and cardiologists. The study was approved by the local ethics committee board and requirement for individual patient consent was waived. A chart review of all AVR surgeries performed in patients aged < 18 years at time of surgery from May 1985 until April 2020 was conducted. The biological AVR group consisted of aortic homografts or prosthetic bioprostheses. The choice of implanted prosthesis in infant patients were homografts. Mechanical valves were used when patient age and expected compliance rendered hypocoagulation possible. All patients in the mechanical AVR cohort were treated with phenprocoumon (goal INR 2.0-3.0). Overall compliance was good, in two (6.1%; 2/33) teenaged patients temporary discontinuation of anticoagulation and permanently prescribed medication was reported. In the observed biological AVRs lifelong antiplatelet therapy was pursued with acetylsalicylic acid. Antithrombotic management differed over the study period. In the more recent years patients were additionally discharged with temporary anticoagulation therapy (phenprocoumon, goal INR 2.0-3.0), which was discontinued after the first three postoperative months.

Definitions

Parameters were obtained and measured as described in the Guidelines for Reporting Mortality and Morbidity after Cardiac Valve Interventions [11]. Primary outcome parameters were survival and incidence as well as timing of re-operations. Early mortality was defined as death occurring with 30 days of surgery or prior to hospital discharge. Mortality was cross-checked with the national health insurance database. Survival status on April 30th, 2020 is known for 92.7% (51/55) of patients. Four patients were transferred for surgery from foreign centers and could not be followed-up in the database. Survival time for these patients was calculated until the last confirmed living follow-up. Patients were included with all their aortic valve replacements performed when aged < 18 years at the center. Three patients were included with two AVRs and one patient with three AVRs during the study period. Valve numbers are used in the tables. Two patients underwent left ventricular assist device (LVAD) implantation in the setting of subacute myocarditis 5 days after AVR and cardiomyopathy 3.6 years after AVR respectively. These patients were censored from further valve-related analysis at time of LVAD implantation. As a high-volume Ross center, we reviewed the contraindications for Ross procedure in the observed non-Ross AVR cohort. The Ross procedure is offered to pediatric patients at our center since 1991. Until April 2020 onehundred-and-two pediatric patients underwent a Ross procedure. The frequency of AVR from 1985-2020 is seen in Fig. 1.

Statistical analysis

Normally distributed continuous data was expressed as mean \pm standard deviation, whilst skewed continuous data was expressed as median with interguartile range (IQR), and minimum and maximum. In order to identify significant differences between two subgroups, continuous variables were compared using the independentsamples Mann-Whitney U test and categorical variables with Fisher exact test. Time-related endpoints were analyzed and plotted using Kaplan-Meier actuarial survival curves accompanied by 95% confidence intervals. Freedom from re-intervention was compared in subgroups using the log-rank analysis. Patients, who did not experience outcome events were censored at the time of last follow-up. Univariable Cox-proportional hazard modelling was used to determine risk factors for mortality and re-operation. Linearized event rates per valve-year were calculated. Statistical significance was set at p < 0.05. Data was analyzed using the software package SPSS[®] 26 (IBM Corp., Chicago, Illinois, USA).

Results

Demographic and operative characteristics

From May 1985 until April 2020 60 AVRs were performed in 55 patients aged < 18 years at time of AVR. Patient and operative characteristics are given in Table 1. The patient cohort was predominantly male (70.9%; 39/55) and the median age at time of surgery was 12.1 years (IQR 7–15.4 years). Operative variables and the used valve types are given in Table 2 for the mechanical AVR (55%; 33/60: 22 mechanical AVR, 11 mechanical Bentall) and the biological AVR (45%; 27/60: 21 homograft AVRs, 6 bioprosthetic AVRs) cohorts respectively. The patients



receiving the mechanical AVRs were older (p=0.004) at time of surgery. In accordance the used valve sizes were smaller (p=0.003) in the biological cohort. Median valve sizes and performed annular enlargement strategies are seen in Table 2. In over half of the fifty-three AVRs performed after 1991 (58.5%; 31/53) a contraindication for Ross procedure was present as seen in the Table 3.

Early outcomes

Postoperative outcomes are listed in Table 4. There were three early deaths (11.1%, 3/27) due to multi organ failure in the biological AVR cohort and no early deaths (0/33) in the mechanical AVR cohort. The procedural early mortality rate for the AVR cohort is 5% (3/60). All early deaths occurred in patients aged < 1 year at time of surgery. Deaths are summarized in Table 5.

Follow-up

Patient-related follow-up

Two late deaths occurred and survival was $94.5\% \pm 3.1\%$ at 10 years, $86.4\% \pm 6.2\%$ at 20 years and at 30 years (Fig. 1). One patient died from myocardial infarction 16.5 years after AVR and one patient from unknown causes 18.8 years after AVR.

Valve-related follow-up

As shown in Fig. 2, freedom from aortic valve reoperation was $69.9\% \pm 8.3\%$ at 10 years, $46.6\% \pm 9.5\%$ at 20 years and $34.9\% \pm 12.4\%$ at 30 years. Freedom from aortic valve re-operation was significantly higher (p < 0.001) in the mechanical AVR compared to the biological AVR cohort with $95.2\% \pm 4.6\%$ and $33.6\% \pm 13.4\%$ freedom from reoperation at 10 years respectively (Fig. 3). At univariable Cox proportional hazard analysis smaller implanted valve size was a risk factor for reoperation (HR 0.8 for each increase in valve size mm; p=0.019). Five mechanical AVRs (15.2%; 5/33) and 12 biological AVRs (44.4%; 12/27: 11 homograft AVRs and one bioprosthetic valve) were re-operated at a median of 11.4 years (IQR 7.7–16.8 years) after mechanical AVR and at a median of 7.2 years (IQR 2.6–10.8 years) after biological AVR (p=0.082). The valve replacements requiring re-operation are detailed in Table 6.

There were three bleeding events in the mechanical AVR cohort (1.2% per valve-year). One 17-year-old female patient had to undergo laparoscopic surgery for corpus rubrum bleeding in the setting of over anticoagulation (initial international normalized ratio (INR) at admission: 9.9, subsequent INR controls at admission day were not measurable). The other two patients were in goal INR range at time of event. For mechanical AVR the linearized event rate per valve-year was 0.41% for valve thrombosis, and 1.6% for embolism (two transient ischemic attacks in one patient, two strokes in one patient). One patient with a Saint Jude Medical valve underwent emergency surgery for valve thrombosis with cardiogenic shock 41 days after initial AVR. In the setting of reduced left ventricular function and with valve opening being sufficient after intraoperative debridement of thrombotic material and rinsing with alteplase, the valve was not explanted. In the biological AVR cohort no bleeding or thromboembolic events occurred. The linearized event rate per valve-year for endocarditis was 6.5% in the biological AVR cohort. No endocarditis occurred

Table 1 Baseline characteristics

Characteristic	Patients
Patient cohort	
Number	55
Male	39 (70.9)
Native aortic valve anatomy	
Unicuspidal	1 (1.8)
Bicuspid	19 (34.5)
Tricuspid	15 (27.3)
Quadricuspid	1 (1.8)
Unknown	19 (34.5)
Underlying diagnosis	
Isolated aortic valve lesion	39 (70.9)
Complex congenital heart disease	13 (23.6)
Diagnoses	
Shunt (VSD, ASD, PFO, PDA)	8 (14.5)
Aortic isthmus stenosis	9 (16.4)
Hypoplastic aortic arch	2 (3.6)
Tetralogy of Fallot	1 (1.8)
Double outlet right ventricle	2 (3.6)
Dextro-transposition of the great arteries	5 (9.1)
Congenitally corrected transposition of the great arteries	2 (3.6)
Endocardial fibroelastosis	7 (12.7)
Operative	Valve implants
Valve implants of cohort	
Number	60
Age (ywars) at time of surgery	
Neonates	2 (3.3)
< 1 (including neonates)	4 (6.7)
1–5	8 (13.3)
6–13	26 (43.3)
14–18	22 (36.7)
Aortic valve at replacement	
Native	45 (75)
Tirone David	2 (3.3)
Mechanical Bentall AVR	1 (1.7)
Bioprosthetic AVR	1 (1.7)
Homograft AVR	4 (6.7)
Neoaortic valve (ASO, left-ventricle-neo-aortic-valve-tunnel)	7 (11.6)

Values are presented as n, n (%)

ASD, atrial septum defect; ASO, arterial switch operation; AVR, aortic valve replacement; PDA, persistent ductus arteriosus; PFO, patent foramen ovale; VSD, ventricular septum defect

in the mechanical AVR cohort, but pannus formation (0.8% per valve-year) and paravalvular leak (0.8% per valve year) occurred.

Discussion

The choice of AVR remains challenging in the pediatric cohort regarding hemodynamic profile and limitation of valve durability. Preoperative counseling for patients and their families is indispensable for taking each patient's individual social characteristics and needs into consideration.

A valve preserving strategy is aimed for to postpone AVR until older age and therefore somatic growth resulting in a likely decreased periprocedural risk and depending on deference of AVR the option of an adult size valve. In our cohort 55% (33/60) of patients had undergone at

Table 2 Operative characteristics

Actic value replacementIMechanical Refi22-Mechanical Refial11-Biopositiet: ARR-6Biopositiet: ARR-6Hornogal ARA-0Unaus InformationMechanical Refial120640Carbornedia120640St. Jude Medical110331On-X41(21)1Duromedia26610Biposibiley Monostrut163Biposibiley Monostrut163Biposibiley Monostrut163Biposibiley Monostrut163Biposibiley Monostrut163Bioposibiley Monostrut-12/2/4-Bioposibiley Monostrut163Bioposibiley Monostrut-12/3/1-Bioposibiley Monostrut-12/3/1-Hornogal Mark-15556)-Desellabark-12/3/112/3/10.064Voldei Hornogary Marsh12/69/157)89/24-14410.064Bishgin attrine of surgery (haj)14/12/45-43113/50.061Bishgin attrine of surgery (haj)12/69/17112/65/15310.061Bishgin attrine of surgery (haj)12/69/17112/65/15310.061Bishgin attrine of surgery (haj)12/69/17112/65/15310.061Bishgin attrine of surgery (haj) <td< th=""><th>Characteristic</th><th>Mechanical AVR</th><th>Homograft/bioprosthetic AVR</th><th><i>p</i> value</th></td<>	Characteristic	Mechanical AVR	Homograft/bioprosthetic AVR	<i>p</i> value
Mechanikal Benahl20	Aortic valve replacement			
Medianal line1-Biopraduet ARBiopraduet ARHomogiat ARValues implanted*Carbomedia1264/1St. Jack Medical103/3On-X4(2)Duromedia20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet Arg20/1Biopraduet ArgBiopraduet Arg <td>Mechanical AVR</td> <td>22</td> <td>-</td> <td></td>	Mechanical AVR	22	-	
BiopognitrAM-6HomognitrAMHomognitrAMMeximalleratSchowelka12040Schowelka12030Durancka12030Durancka2010AfS2010Bigh-Shleykonstrut0Bigh-ShleykonstrutBigh-ShleykonstrutSonifereitsens StemlesSonifereitsens StemlesSonifereitsens StemlesBiesheitsens StemlesSonifereitsens StemlesSonifereitsens StemlesBiesheitsens StemlesSonifereitsens StemlesSonifereitsen	Mechanical Bentall	11	_	
Homogent Wei-21Values inprometion16.43.0-Values inprometion16.43.0-Stude Medical16.43.0-On-A40.13.0-Durenedios20.10.0-Bytes Medical10.10.0-Tays10.10.0-Bytes Medical10.10.0-Bytes Medical10.10.0-Bytes MedicalBytes Medical <t< td=""><td>Bioprosthetic AVR</td><td>-</td><td>6</td><td></td></t<>	Bioprosthetic AVR	-	6	
NetwirdMachant20640-Carbonedis10330-Sub Medial10330-On-X4010-Durmedis2010-ATS2010-Bjø-Shly Monotnt10-Bjø-Shly MonotntMosicSub MedialMosic-10.0Son Pericabon StentesSon Pericabon Stentes-10.3Mosic-10.3Son Pericabon StentesSon Pericabon StentesMosicSon Pericabon StentesSon Pericabon StentesSon Pericabon StentesMosicSon Pericabon StentesMosicSon Pericabon StentesMosicMosicMosicSon Pericabon Stentes- <td< td=""><td>Homograft AVR</td><td>-</td><td>21</td><td></td></td<>	Homograft AVR	-	21	
Netarial/antialCarbondes1633-Chube Medial1033-On-A6103-Durandies3010-Binkonstant10-Binkonstant10-Binkonstant10-BinkonstantBinkonstantBinkonstantBinkonstantBinkonstantBinkonstantBinkonstantMasiaSain PreizzonstentesBinkonstentes-	Valves implanted ^a			
Carbonedics12(84)-St.Jok Medical1033-On-X1630-Dromedics8(3)-ATS26(3)-BighisShilly Monostrut10-BognetBognetBognet-27.4Bognet-27.4Spiris Resilia-20.4Sonin Pearly Resort-20.4Sonin Pearly Resort-20.4Homograft-13.7Decilulation Startles-13.7Homograft-13.7Decilulation Startles-13.6Cyclie Inongraft-13.6Option Startles-13.6Option Startles <td>Mechanical/Bentall</td> <td></td> <td></td> <td></td>	Mechanical/Bentall			
st.ude Medici1 (133)-On-X(12)-ATS26.01-ATS26.01-BinkBink Monstrut1.8-Boposther-27.4Inspirs Resilia-27.4Mosic-27.4Soin Peiraton Stentes-1.3.7Tissuened Freestyle Root-1.3.7Homogrif-1.5.56Perelulared Corlife-1.5.56Qerelulared Corlife Corlife-1.3.7Age at time of surgery (pars)1.609-15.78.32.4-14.4)0.004Weight attime of surgery (pars)1.609-15.78.32.4-14.4)0.004Weight attime of surgery (pars)1.609-15.78.32.4-14.4)0.004Weight attime of surgery (pars)1.609-17.71.11.0.5-1.5.3)0.018Roltared Forsurgery (pars)1.609-17.71.11.0.5-1.5.3)0.018Motaritime of surgery (pars)1.609-17.71.11.0.5-1.5.3)0.018Roltared For surgery (pars)1.609-17.71.11.0.5-1.5.3)0.018Motared For surgery (pars)1.609-17.71.11.0.5-1.5.3)0.018Roltared For surgery (pars)1.609-17.70.0141.014Mored For surgery (pars)1.609-17.70.0140.014Mored For surgery (pars)1.609-17.70.0140.014Mored For surgery (pars)1.609-17.70.0160.0140.014Mored For surgery (pars)1.609-17.70.0160.0140.014Mored For surgery (par	Carbomedics	12 (36.4)	-	
On-X4 (12)-Durenedes3(9)-ATs16)-Bipsit-Shiley Monstrut13)-Bipsit-Shiley MonstrutBipsit-Shiley MonstrutBipsit-Shiley Monstrut-7/4/	St. Jude Medical	11 (33.3)	-	
Duronedics3(3)-ATS2(6)-Bijht-Shig Monotrut10-BijotshigRosiac-2(74)Mosiac-2(74)Son Pericabon Stentless-10.7Tissend Freestyle Root-10.7Monograt-10.7Tomograt-10.7Tomograt-10.7Decellarized Corlife-10.5Cyclic Homograt-10.7Aget time of surgery (years)10.6 (0.7)10.9Melgin attime of surgery (years)10.0 (0.7)10.9Height attime of surgery (years)10.0 (0.9)10.0Melgin attime of surgery (years)10.0 (0.0)10.0Melgin attime of surgery (years)10.0 (0.0)10.0Melgin attime of surgery (years) <td>On-X</td> <td>4 (12.1)</td> <td>_</td> <td></td>	On-X	4 (12.1)	_	
AS26.01-BydNostrut10BydPorsbert-2.74.Inspirs Resilia-2.74.Mosic-3.74.Sorin Percarbon Stretless-3.74.Tssuened Freestyle Root-1.37.Homogaft-5.55.0.Evellularized Corlife-1.55.0.CypUic homograft-1.55.1.Apeating Surgery (years)3.6(9.7.5.7)0.41.4.Weight attime of surgery (years)1.6(9.7.5.7)0.41.4.Weight attime of surgery (years)1.6(9.7.7.7.0.41.4.Bodigating Surgery (years)1.6(9.7.7.7.0.41.4.Weight attime of surgery (years)1.6(9.7.7.7.0.41.4.Bodigating Surgery (years)1.6(9.7.7.0.41.4. <t< td=""><td>Duromedics</td><td>3 (9.1)</td><td>_</td><td></td></t<>	Duromedics	3 (9.1)	_	
Bjök-Shiley MonstrutIsl-Bigsix-Shiley MonstrutIslIslBigsix-Shiley MonstrutIslIslMosaicIslIslSoria Perciabon StentiesIslIslSoria Perciabon StentiesIslIslBiomagnitIslIslHomogratIslIslDeciliarized CorlifeIslIslCyclic IbanogratIslIslApartime of surgery (vers)IslIslMiley Apartime of surgery (vers)	ATS	2 (6.1)	_	
BioposthericInspin Sellia-C/04Moaic-C/04Soin Pericaton Stentless-18.7Tissued Freestyle Root-16.7HomografHomograf-16.7Age attime Storgery (war)16.016.7Age attime Storgery (war)16.09.0Height attime of surgery (war)16.09.0Hot Storgery (war)16.09.00.00Bedhaviore Surgery (war)16.09.00.00Height attime of surgery (war)14.010.00.00Bedhaviore Surgery (war)16.010.00.00Median Value Storgery14.00.000.00Morita Surgery (war)16.010.00.00Bother Surgery (war)16.010.00.00Median Value Storgery16.020.00.00Median Value Storgery16.020.00.00Morita Surgery16.020.00.00Median Value Storgery20.020.00.00Median Value Storgery16.020.00.00Median Value Storgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.020.00.00Morita Surgery20.	Björk-Shiley Monostrut	1 (3)	_	
Impiris Resilia-2(7.4)Mosic-2(7.4)Sorin Pericarbon Strutess-2(7.4)Sorin Pericarbon Strutess-1.8.7)Tissuened Freestyle Poot-1.8.7)Homograft-5(56.5)Decellularde Colifie-1.8.7)Chyclic Homograft-1.8.7)Age at time of surgery (yars)1.36 (9.7-15.7)8.9 (2.4-14.4)0.004Beight at time of surgery (yars)1.36 (9.7-15.7)8.9 (2.4-14.4)0.004BAshmook, at time of surgery (yars)1.30 (9.1-17.7)1.31 (9.5-15.3)0.016BAshmook, at time of surgery (yars)1.40 (1.29-17.7)1.31 (9.5-1.53)0.016BAshmook, at time of surgery (schild)1.31 (0.9-1.72.7)0.20 (angle 9-2.9)0.003Indication for surgery1.31 (0.9-1.72.7)0.20 (angle 9-2.9)0.003Indication for surgery1.60.7)1.11 (0.5-1.53)0.105Mixed serie (schild)2.60.7)1.76 (3.10)1.76Mixed and rive Jesories1.60.92.74 (3.10)0.01Indication for surgery2.60.7)1.76 (3.10)0.01Mixed and rive Jesories1.60.7)0.020.02Prior adia surgery2.60.7)0.610.010.01Prior adia surgery2.60.7)0.610.010.01Prior adia surgery2.60.7)0.610.010.01Prior adia surgery2.60.7)0.610.010.01Prior adia surgery2.66.7)0.610.01	Bioprosthetic			
Mosile-2 (7.4)SomPercarbon Stendes-(3.7)Tissuemed Freestyle Root-(3.7)Homograt-(5.5)Decellularized Confife-(5.5)Decellularized Confife-(3.7)Cyculic Homograt-(3.7)Age at time of surgery (years)(36 (9.7-15.7)89 (2.4-14.4)0.004Weight at time of surgery (kg)417 (24.5-6.3)(3.15 (1.5550.2)0.061Becklan Valve sizgery (many(3.10 (0.9317.7)1.11 (0.5615.3)0.0163Median Valve size (man)(3.10 (0.9317.7)1.11 (0.5615.3)0.0163Median Valve size (man)(3.10 (0.9317.7)1.11 (0.5615.3)0.0163Morit valve size (many)(3.10 (0.9317.7)1.11 (0.5615.3)0.0163Median Valve size (many)(3.10 (0.9317.7)1.11 (0.5615.3)0.0163Marci valve size (many)(3.10 (0.9217.7)1.01 (0.5615.1)0.016Marci valve size (many)(3.6)(7.4)2.020.023Andric valve regurgitation(3.0)(2.742.030.024Andric valve regurgitation(3.0)(3.7)0.0240.024Pior adiot valve lesson(3.0)(3.0)(3.0)0.01Pior adiot valve lesson(3.0)(3.0)0.010.01Pior adiot valve operation (years)(3.6)(3.0)0.010.01Pior adiot valve operation (years)(3.6)(3.7)0.0240.00Pior adiot valve operation (years)<	Inspiris Resilia	_	2 (7.4)	
Soin Pericabon Stends-10.7Tissued Freestyle Root-10.7Homograft-50.50.Decellularized Confife-50.50.Crychfe homograft-10.7Age att me of surgery (years)36.09.71.57.89.24.14.40.0.004.Weight att me of surgery (years)130.09.71.77.31.012.550.00.0010.001.Height att me of surgery (years)130.09.71.77.131.05.7.13.0.01.010.016.BeShigwock att time of surgery (years)130.09.71.77.131.05.7.13.0.01.010.016.Median Valve size (mm)20.69.71.0.0120.69.71.0.010.016.0.010.016.0.01Median Valve size (mm)20.69.71.0.0120.69.71.0.010.010.0.010.016.0.01Median Valve size (mm)20.69.71.0.0120.69.71.0.010.010.0.010.010.0.01Median Valve size (mm)20.69.71.0.0120.69.71.0.010.010.0.010.01Median Valve size (mm)20.69.71.0.0120.69.71.0.010.010.0.010.01Antic valve fersons20.69.71.0.0120.69.71.0.010.010.0.010.01Net and true valve disease30.01.0.0120.69.0.010.010.0.010.01Prior antic valve disease30.01.0.0120.69.0.010.010.01Oriental surgical antic valve operation (years)30.60.71.0.010.010.01Oriental surgical antic valve operation (years)30.60.71.0.010.010.01Oriental surgical antic valve operation (years)30.60.71.0.010.010.01Orie	Mosaic	_	2 (7.4)	
Tissuend Freestyle Root-137Homograft-1555.0Decellularzed Collife-16.55.0Cyolife homograft-16.7Aget time of surgery (vars)36.07-15.78.92.4-14.4)0.004Weight at time of surgery (kg)41.245-63.031.51.25-50.20.081Beshapscad, time of surgery (kg)31.092-17.131.052-15.30.064Shapscad, time of surgery (kg)31.092-17.731.052-15.30.064Median Valve size (km)31.092-17.730.076-15.30.076Motion of surgery31.092-17.70.076.90.076Andric valve size (km)31.092-17.70.076.90.076Andric valve size (km)31.092-17.70.076.90.076Andric valve size (km)31.092-17.70.076.90.076Andric valve size (km)31.092-17.70.076.90.076Andric valve size (km)31.092-17.70.076.90.076Miced and tirk size (km)31.092-17.70.0760.076Miced and tirk size (km)3	Sorin Pericarbon Stentless	_	1 (3.7)	
Homograft - 15 (55.6) Decelluarized Corific - 5 (18.5) Cryclife homograft - 13 (7) Age at time of surgery (years) 13.6 (9.7-15.7) 89 (2.4-14.4) 0.004 Weight at time of surgery (kg) 1.47 (245-63) 31.5 (12.5-50.2) 0.081 Height at time of surgery (cm) 1.91 (0.92-171) 1.91 (0.56-15.3) 0.064 Sh _{hipocck} at time of surgery (cm) 2.1 (ange 17-27) 2.0 (ange 9-25) 0.031 Indication for surgery 2.1 (ange 17-27) 2.0 (ange 9-25) 0.033 Indication for surgery 2.0 (ange 9-25) 0.031 Arrit cvalve stenois 1.30. 2.7 (4) .040 Arrit cvalve stenois 1.30. 2.7 (4) .040 Arrit cvalve stenois 1.3 (0.91 2.7 (4) .040 Mixed aoritic valve lesion 2.0 (6.1) 1.7 (6.3) .019 Reterial endocarditis 2.0 (6.1) 0.00 .245 Prior cardiac surgery 2.0 (6.1) 0.00 .245 Prior antic valve disease 3.0 (1)	Tissuemed Freestyle Root	_	1 (3.7)	
Horograft bank - 15 (55.6) Decellularized Corlife - 5 (18.5) CryoLife homograft - 16.37 Age at time of surgery (vars) 3.6 (97-15.7) 89 (24-14.4) 0.004 Weight at time of surgery (vgn) 1.7 (24.5-63) 15 (12.5-50.2) 0.011 BSA _{tapecek} at time of surgery (m) 1.9 (09.2-171) 13 (95-158) 0.064 BSA _{tapecek} at time of surgery (m) 1.3 (0.93-1.77) 1.11 (0.56-1.53) 0.105 Median Valve size (mm) 1.0 (0.91,2-123) 0.015 0.001 Indication for surgery 1.3 (0.93-1.77) 1.11 (0.56-1.53) 0.015 Antic valve size (mm) 1.0 (0.91,2-123) 0.015 0.016 Antic valve size (mm) 1.0 (3.0 2.7.4 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.024 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01	Homograft			
Decallularized Corlife - 5 (18.5) CryoLife homograft - 1 (3.7) Age at time of surgery (kgars) 136 (97-15.7) 89 (24-14.4) 0.004 Weight at time of surgery (kgars) 136 (97-15.7) 89 (24-14.4) 0.004 Weight at time of surgery (kg) 149 (129-17) 139 (95-158) 0.064 BSA _{hayood} at time of surgery (cm) 19 (109-17) 111 (0.56-15.3) 0.105 Median Valve size (mm) 131 (0.93-1.77) 1.11 (0.56-15.3) 0.003 Indication for surgery 21 (range 17-27) 20 (range 9-25) 0.003 Antic valve stenosis 13.0 2.74 0.003 Antic valve regurgitation 23 (69.7) 7 (63) 0.99 Rheumatic valve lesion 9 (29.1) 0.00 0.245 Prior cardiac surgery 23 (69.7) 17 (63) 0.917 Prior adlocarditis 2.9 (9.7) 16 (3.9) 0.906 Prior adlocardit valve lesion 3 (9.1) 16 (9.9) 0.907 Time from last surgical aprite valve operation (years) 5 (16.7-9) 0.600	Homograft bank	_	15 (55.6)	
Cyclife homograft - 1.0.7 Age at time of surgery (years) 136 (9.7-15.7) 89 (2.4-14.4) 0.004 Weight at time of surgery (kg) 41.7 (24.5-63) 13.5 (12.5-50.2) 0.081 Height at time of surgery (kg) 140 (129-171) 139 (95-158) 0.004 SA _{hipococ} , at time of surgery (cm) 131 (093-177) 111 (056-153) 0.105 BA(singer, at time of surgery) 131 (093-177) 20 (range 9-25) 0.003 Indication for surgery 21 (range 17-27) 20 (range 9-25) 0.003 Andric valve stenosis 16.0 2.7.4 . . Andric valve resurgitation 3 (9.7) 17 (63) . . Mixed andric valve lesion 9 (27.3) 8 (29.6) .	Decellularized Corlife	_	5 (18.5)	
Age at time of surgery (years) 136 (9.7–15.7) 8 (9.2–14.4) 0.004 Weight at time of surgery (kg) 41.7 (24.5–63) 31.5 (12.5–50.2) 0.081 Height at time of surgery (cm) 149 (129–171) 139 (95–158) 0.064 BSA _{hapcocc} at time of surgery 1.31 (0.93–1.77) 1.11 (0.55–1.53) 0.105 Media Nalve size (mm) 21 (range 17–27) 20 (range 9–25) 0.003 Indication for surgery 7.40 7.40 7.40 Aortic valve stenosis 1 (3.0) 2 (7.4) 7.63 Mixed aortic valve lesion 9 (27.3) 8 (29.6) 2.74 Prior adre surgery 23 (69.7) 17 (63) 0.297 Prior adre surgery 3 (9.1) 7 (25.9) 0.097 Prior balloon aortic valve lesione 5 (16.5–75) 0.6 (CrvoLife homograft	_	1 (3.7)	
Weight at time of surgery (kg) 417 (245-63) 15 (125-50.2) 0.081 Height at time of surgery (kg) 149 (129-171) 139 (95-158) 0.064 BSA _{bispcock} at time of surgery 131 (0.93-1.77) 1.11 (0.56-1.53) 0.105 Median Valve size (mm) 21 (range 17-27) 20 (range 9-25) 0.003 Indication for surgery . 0.740 Aortic valve stenosis 13.0) 2 (7.4) Aortic valve regurgitation 23 (69.7) 17 (63) Mixed aortic valve lesion 9 (27.3) 8 (29.6) Bacterial endocarditis 2 (6.1) 2 (7.4) Nixed aortic valve lesion 3 (9.1) 0 (0) 0.245 Prior acric surgery 12 (36.4) 14 (5.19) 0.297 Prior ballcon aortic valve loperation (years) 5 (16-7.9) 0.6004-3.3) 0.006 Prior ballcon aortic valve loperation (years) 5 (16-7.9) 0.6004-3.3) 0.066 Operative variable Ortic valve surgery 13 (103-233) 154 (90-235) .686 Operative	Age at time of surgery (vears)	13.6 (9.7–15.7)	8.9 (2.4–14.4)	0.004
Height at time of surgery (cm) 149 (129–171) 139 (95–158) 0.064 BSA _{Heighcol} at time of surgery 1.31 (0.93–1.77) 1.11 (0.56–1.53) 0.105 Median Valve size (mm) 21 (range 17–27) 20 (range 9–25) 0.003 Indication for surgery 21 (ange 17–27) 20 (range 9–25) 0.003 Antic valve stenosis 1 (3.0) 2 (7.4) 740 Aortic valve stenosis 1 (3.0) 2 (7.4) 740 Aortic valve stenosis 9 (27.3) 8 (29.6) 8 Bacterial endocarditis 2 (6.1) 2 (7.4) >0.99 Rheumatic valve lesion 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valve loperation (years) 3 (9.1) 7 (25.9) 0.007 Time form last surgical aortic valve operation (years) 3 (6.5-151) 9 (70–129) 0.999 CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 CPB (min) 16 (48.5)	Weight at time of surgery (kg)	41.7 (24.5–63)	31.5 (12.5–50.2)	0.081
Reference (Reference) Reference (Refere) Reference (Reference) <t< td=""><td>Height at time of surgery (cm)</td><td>149 (129–171)</td><td>139 (95–158)</td><td>0.064</td></t<>	Height at time of surgery (cm)	149 (129–171)	139 (95–158)	0.064
Inspire Inspire <t< td=""><td>BSA_{uloused} at time of surgery</td><td>1.31 (0.93–1.77)</td><td>1.11 (0.56–1.53)</td><td>0.105</td></t<>	BSA _{uloused} at time of surgery	1.31 (0.93–1.77)	1.11 (0.56–1.53)	0.105
Indication for surgery 0,740 Aortic valve stenosis 1 (3.0) 2 (7.4) Aortic valve regurgitation 23 (69.7) 17 (63) Mixed aortic valve lesion 9 (27.3) 8 (29.6) Bacterial endocarditis 2 (6.1) 2 (7.4) > 0.99 Rheumatic valve disease 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 12 (36.4) 14 (51.9) 0.297 Prior abloon aortic valvuloplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (16-7.9) 0.60 (0.4-3.3) 0.006 Operative variable CCT (min) 95 (66.5-151) 95 (70-129) 0.699 CPB (min) 158 (103-233) 154 (90-235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Aortic annulus enlargement	Median Valve size (mm)	21 (range 17–27)	20 (range 9–25)	0.003
Aortic valve step of 13.00 2(7.4) Aortic valve regurgitation 23 (69.7) 17 (63) Mixed aortic valve lesion 9 (27.3) 8 (29.6) Bacterial endocarditis 2 (6.1) 2 (7.4) > 0.99 Rheumatic valve disease 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve disease 3 (9.1) 0 (0) 0.245 Prior aortic valve surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valvolplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (16.7-59) 0.600 0.006 Operative variable 103 1510 95 (70-129) 0.662 CPR (min) 158 (103-233) 164 (90-235) 0.6682 Cinculatory ar	Indication for surgery			0.740
Anticative degregitation 23 (67) 7 (63) Mixed aortic valve lesion 9 (27.3) 8 (29.6) Bacterial endocarditis 2 (6.1) 2 (7.4) > 0.99 Rheumatic valve disease 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 23 (69.7) 17 (63) 0.596 Prior acridic valve surgery 23 (69.7) 14 (51.9) 0.297 Prior balloon aortic valve surgery 2 (3.4) 14 (51.9) 0.097 Prior balloon aortic valve operation (years) 5 (16.7.9) 0.097 0.097 Operative variable 5 (16.5.7.151) 0.097 0.969 CPB (min) 158 (103-233) 154 (90-235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 1 (3.7) 0.209 0.745 Nicks 1 (3) 0 (0) 7.44 7.59 Manougian 2 (6.1) 0 (0) 7.49 7.59	Aortic valve stenosis	1 (3.0)	2 (7.4)	
Native fails of the second s	Aortic valve regurgitation	23 (69 7)	17 (63)	
Bacterial endocarditis 2 (6.1) 2 (7.4) > 0.99 Rheumatic valve disease 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 23 (60.7) 17 (63) 0.596 Prior aortic valve surgery 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valve operation (years) 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (16.7 P.9) 0.6 (0.04-3.3) 0.006 Operative variable 2 5 (16.7 P.9) 0.6 (0.04-3.3) 0.006 Corecritive variable 5 (16.7 P.9) 0.6 (0.04-3.3) 0.006 CPF (min) 95 (66.5 - 151) 95 (70-129) 0.662 Circulatory arrest 5 (15.2) 13 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.00 0.00 0.00 Nicks 1 (3) 0.00 0.00 Manougian 2 (6.1) 0.00 0.00	Mixed aortic valve lesion	9 (27.3)	8 (29.6)	
Rheumatic valve disease 3 (9.1) 0 (0) 0.245 Prior cardiac surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valvuloplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (1.6–7.9) 0.6 (0.04–3.3) 0.006 Operative variable	Bacterial endocarditis	2 (6.1)	2 (7.4)	> 0.99
International conduction S (A) S (A) S (A) Prior cardiac surgery 23 (69.7) 17 (63) 0.596 Prior aortic valve surgery 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valvuloplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (1.6–7.9) 0.6 (0.04–3.3) 0.006 Operative variable 4 51.9 95 (70–129) 0.969 CPB (min) 158 (103–233) 154 (90–235) 0.682 0.209 Concomitant procedure 16 (48.5) 13.7 0.209 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 0.795 Nicks 1 (3) 0 (0) 0.745 0.745 0.745 Nicks 1 (3) 0 (0) 1.757 0.745 0.745	Bheumatic valve disease	3 (9 1)	0 (0)	0.245
Prior addressing 12 (36.4) 14 (51.9) 0.297 Prior balloon aortic valvuloplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valve operation (years) 5 (1.6–7.9) 0.6 (0.04–3.3) 0.006 Operative variable 7 7 7 7 7 ACCT (min) 95 (66.5–151) 95 (70–129) 0.669 CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 0.745 Nicks 1 (3) 0 (0) 14 (51.9)	Prior cardiac surgery	23 (69 7)	17 (63)	0.596
Prior balloon aortic valvuloplasty 3 (9.1) 7 (25.9) 0.097 Time from last surgical aortic valvuloplasty 5 (1.6–7.9) 0.6 (0.04–3.3) 0.006 Operative variable 4000 95 (66.5–151) 95 (70–129) 0.969 CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.00 0.745 Nicks 1 (3) 0 (0) 143	Prior aortic valve surgery	12 (36 4)	14 (51 9)	0.297
Time from last surgical aortic value operation (years) 5 (1.6–7.9) 0.6 (0.04–3.3) 0.006 Operative variable 4007 95 (66.5–151) 95 (70–129) 0.969 CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 Nicks 1 (3) 0 (0) Manougian 2 (6.1) 0 (0)	Prior balloon aortic valvuloplasty	3 (91)	7 (25 9)	0.097
Ministribution of the operation (each) F(10 Hz) Recent (each) Recent (each) <threcent (each)<="" th=""> Recent (each)</threcent>	Time from last surgical aortic valve operation (years)	5 (16-79)	0.6 (0.04–3.3)	0.006
ACCT (min) 95 (66.5–151) 95 (70–129) 0.969 CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 0.745 Nicks 1 (3) 0 (0) 14.50 Manougian 2 (6.1) 0 (0) 1 (3.7)	Operative variable	5 (1.5 7.5)		0.000
CPB (min) 158 (103–233) 154 (90–235) 0.682 Circulatory arrest 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 0.745 Nicks 1 (3) 0 (0) 1 Manougian 2 (6.1) 0 (0) 1	ACCT (min)	95 (66 5–151)	95 (70–129)	0.969
Circulatory arrest 5 (165 25) 15 (165 25) 0.002 Concomitant procedure 5 (15.2) 1 (3.7) 0.209 Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 0.745 Nicks 1 (3) 0 (0) 1 Manougian 2 (6.1) 0 (0) 1	CPB (min)	158 (103-233)	154 (90-235)	0.682
Concomitant procedure 16 (48.5) 12 (44.4) 0.799 Aortic annulus enlargement 0.745 0.745 Nicks 1 (3) 0 (0) Manougian 2 (6.1) 0 (0) Konno 1 (3) 1 (3.7)	Circulatory arrest	5 (15 2)	1 (37)	0.209
Aortic annulus enlargement 1 (3) 0 (0) Manougian 2 (6.1) 0 (0) Konno 1 (3) 1 (3.7)	Concomitant procedure	16 (48.5)	12 (44.4)	0.209
Nicks 1 (3) 0 (0) Manougian 2 (6.1) 0 (0) Konno 1 (3) 1 (37)	Aortic annulus enlargement			0.745
Manougian 2 (6.1) 0 (0) Konno 1 (3) 1 (37)	Nicks	1 (3)	0 (0)	0.7 15
Konno 1(3) 1(37)	Manougian	2 (61)	0 (0)	
	Konno	1 (3)	1 (3,7)	

Values are presented as n, n (%), median (interquartile range) or median (range minimum-maximum) in case of valve size (mm). Continuous variables were compared using the independent-samples Mann-Whitney U test and categorical variables with Fisher exact test

ACCT, Aortic cross clamp time; AVR, aortic valve replacement; BSA, body surface area; ccTGA, congenitally corrected transposition of the great arteries; CPB, cardiopulmonary bypass; VSD, ventricular septum defect

^a Carbomedics; Sorin Spa, Milan, Italy; St. Jude Medical; St. Jude Medical Inc, St. Paul, Minn; On-X; On-X Life Technologies Inc, Austin, Tex; Duromedics; Edwards Lifesciences, Irvine Ca; ATS; ATS Medical Inc, Minneapolis, Minn; Björk-Shiley Monostrut; Pfizer Inc, New York, NY; Inspiris Resilia; Edwards Lifesciences, Irvine Ca; Mosaic; Medtronic plc, Dublin, Ireland; Sorin Pericarbon Stentless; Sorin Spa, Milan, Italy; Tissuemed Freestyle Root; Tissuemed, Leeds, England; Decellularized Corlife; Corlife, Hannover, Germany; CryoLife; CryoLife; Kennesaw, GA

Table 3 Contraindications for Ross procedure

Contraindication	n (%)
	31 (100)
Patient's parents were against a Ross procedure	3 (9.7)
Bicuspid pulmonary valve	6 (19.4)
Tricuspid, but dysplastic or insufficient pulmonary valve	3 (9.7)
Size discrepancy between the aortic and the pulmonary valve at time of surgery	2 (6.5)
Massive adhesions between the aortic and the pulmonary root	1 (3.2)
Coronary anatomy	2 (6.5)
Connective tissue disease	3 (9.7)
Marfanoid habitus with hyperextensibility of the joints and a dilated pulmonary artery	1 (3.2)
Suitable pulmonary homograft not available at time of surgery (1999)	1 (3.2)
Due to hematoma of the aorta ascendens at the cannulation site a mechanical Bentall was performed	1 (3.2)

Values are presented as n, n (%)

Table 4 Postoperative outcomes

Characteristic	Mechanical AVR	Homograft/bioprosthetic AVR	p value
Permanent pacemaker insertion	2 (6.1)	0 (0)	0.497
Reoperation for bleeding	1 (3)	0 (0)	> 0.99
Reoperation for mitral regurgitation	1 (3)	1 (3.7)	> 0.99
Coronary ischemia	1 (3)	0 (0)	> 0.99
Ventilation (days) ^a	1 (0–2.5)	1 (0–1)	0.398
ICU stay (days) ^a	3.5 (1.3–5)	2 (1.5–3)	0.080
Hospital stay (days) ^a	18 (12.5–21.5)	11 (8–14)	0.001
Peritoneal dialysis	0 (0)	2 (7.4) ^b	0.198
ECMO	0 (0)	3 (11.1) ^c	0.085
Early mortality	0 (0)	3 (11.1)	0.085

Values are presented as n, n (%), median (interquartile range). Continuous variables were compared using the independent-samples Mann–Whitney U test and categorical variables with Fisher exact test

AVR, aortic valve replacement; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit

^a Times of the three patients, who died and one LVAD-receiving patient are excluded

^b In one case peritoneal dialysis had already been instated prior AVR

^c In one case ECMO had already been implanted prior AVR

least one aortic valve intervention (surgical or percutaneous) prior to AVR and the median time from the last surgical aortic valve intervention was shorter (p=0.006) in the biological AVR cohort than in the mechanical AVR cohort with 0.6 years (IQR 0.04–3.3 years) and 5 years (IQR 1.6–7.9 years) respectively, as patients in the mechanical AVR cohort were older (p=0.004) at time of surgery and therefore suitable for mechanical AVR with greater implanted valve sizes (p=0.003) than the patients in the biological cohort.

Two patients (3.3%; 2/60) underwent surgery during neonatal period and 4 patients (6.6%; 4/60; including the two neonates) were younger than <1 year at time of surgery. AVR in neonates and infants might become necessary as salvage surgery, when more conservative surgical

approaches or percutaneous interventions have been unsuccessful in establishing an acceptable hemodynamic situation. These patients represent a high-risk group with increased periprocedural complications and mortality rates. Woods et al., reported an in-hospital mortality after aortic valve replacement (Ross-Konno, Ross, homograft AVR) in neonates and infants of 18% (29/160) with 28% (12/43) for neonates and 14% (17/117) for infants. Of the three AVR groups, those who underwent homograft AVR had the highest mortality rate (40%; 6/15; all infants) [12]. In a meta-analysis Etnel et al. reported a pooled early mortality of 7.3% for mechanical AVR and 12.8% for homograft AVR [13].

Freedom from aortic valve re-operation was significantly higher (p < 0.001) in the mechanical AVR than in

Table 5 Early i	and late deaths						
Valve No. (sex)	Surgery (year)	Age	Diagnosis	Previous interventions	Concomitant procedure	Death (postoperative days/ years)	Cause of death
Early deaths							
No. 29 (m)	Homograft (2002)	19 days	Critical aortic stenosis with endocardial fibroelastosis, MV stenosis, admitted to the center in moribund state on the 8th day of life after home birth	Surgical valvulotomy	LVOT enlargement Konno, MV-reconstruction, ECMO	First postoperative day	Cardiorespiratory failure in MOV
No. 12 (m)	Homograft (1995)	17 days	Crittical aortic stenosis with endocardial fibroelastosis, MV regurgitation	Surgical valvulotomy	MV-reconstruction, ECMO	7 days	Cardiorespiratory failure in MOV
Na. 25 (f)	Freestyle Pulmo- nary Root (2000)	3 months	Critical aortic stenosis with endocardial fibroelastosis, subvalvular aortic stenosis, MV stenosis, Shones with borderline left ventricle structures	Surgical valvulotomy	LVOT enlargement Konno	28 days Mitral valve replacement 27 days after initial AVR	Cardiorespiratory failure in MOV
Late deaths							
No. 18 (m)	Homograft (1998)	14.9 years	Aortic regurgitation (tricuspid) VSD	VSD closure Aortic valve repair		16.5 years AVR re-operation (6.8 years)	Myocardial infarction (posterior wall)
No. 24 (f)	Homograft (2000)	13.8 years	Combined aortic lesion (bicuspid), ascendens ectasia, coarctation, Turner syndrome Endocarditis (staphylococcus aureus) with valve dehiscence in pseudo aneurysm of the aortic root after mechanical Bentall not performed at center	Coarctation repair Mechanical Bentall		18.8 years	Unknown aetiology

AVR, aortic valve replacement; ECMO, extracorporeal membrane oxygenation; LVOT, left ventricular outflow tract; MOV, multi organ failure; MV, mitral valve; VSD, ventricular septal defect



the biological AVR cohort with 95.2% and 33.6% freedom from reoperation at 10 years respectively. Re-operation was seen in the mechanical cohort due to patient-prosthesis mismatch (20%; 1/5), pannus formation (40%; 2/5) and paravalvular leak (40%; 2/5). In the pediatric cohort younger patients will experience patients-prosthesis mismatch, when outgrowing the implanted prosthesis regardless of mechanical or biological AVR. Re-operation for paravalvular leak might become necessary also late after initial implantation. Khan et al. report a higher (p < 0.001) 5-year freedom from composite endpoint of re-intervention and death of 95% for mechanical AVR (n=36) than for homograft AVR (n=74) with 52% [14]. Etnel et al. calculated a pooled event rate for aortic valve re-operation of 1.1% per year for mechanical AVR compared to 5.4% per year for homograft AVR [13]. Consistent with other studies [7, 14, 15] biological AVR has a higher re-operation rate than mechanical AVR. However, the risk for bleeding or thromboembolic events is not to be neglected in the mechanical AVR cohort with an estimated pooled event rate of 0.76% per year for thromboembolism and valve thrombosis, and 0.39% per year for bleeding [13].

Decellularized aortic homografts might offer an additional AVR option for pediatric patients. Horke et al., who compared the pediatric data from the ARISE Registry for aortic decellularized homografts with the results of recent meta-analyses for pediatric AVR [13, 16], show that AVR with decellularized homografts has better results than with cryopreserved homografts and that results are even comparable to the Ross procedure and mechanical AVR [9]. Kaplan–Meier estimated overall survival was 97.8% and freedom form aortic valve re-operation was 85% at 5 years respectively [9]. Recellularization is more likely to occur, when there are a nearnormal anatomic position and blood flow, and avoidance of wrapping procedures and the use of foreign material or tissue glue are recommended to prevent recellularization obstruction [10]. The five decellularized homografts in our cohort, which have been implanted since 2017 had uneventful perioperative course and remain free from re-operation with a short mean follow-up time of 0.2 ± 0.4 years.

The typical limitations, which are imminent to a retrospective study design are present in this study. It is possible that some aspects of surgical as well as post-operative treatment evolvement are not fully accounted for in our comparison by AVR type, though the use of a mechanical or a biological AVR was equally distributed (p=0.337) over the years. Nonetheless, this study offers a long patient-related follow-up time (median follow-up time of 7 years with a maximum follow-up of 32.5 years; 385 patient-years) and on account of a near-complete mortality follow-up (92.7%; 51/55) a patient rather than valve-related outcome analysis, which is an essential aspect regarding reoperation burden over lifetime and late mortality.

Conclusions

Re-operation was less frequent in the mechanical AVR cohort than in the biological AVR cohort consisting of homografts and bioprosthetic valve replacements.



Fig. 3 Freedom from aortic valve re-operation. A Kaplan–Meier estimated freedom from aortic valve re-operation. Curve with 95% confidence interval (CI). B Freedom from aortic valve re-operation in patients with mechanical AVR and biological AVR. Kaplan–Meier estimated freedom from aortic valve re-operation in patients following mechanical AVR versus patients following biological (homograft, bioprosthetic) AVR. AVR, aortic valve replacement

Valve No. (sex)	Surgery (year)	Age at time of surgery (years)	Valve size (mm)	Reason for aortic valve replacement re-operation	Time from initial to aortic valve replacement re-operation (years)	Performed re-operation (Valve No. ^a)
Mechanical AVR						
No. 2 (m)	Saint Jude Medical (1986)	15.4	23	Paravalvular leak	5.1	Mechanical AVR
No. 3 (m)	Duromedics (1986)	15.5	19	Paravalvular leak	20.9	Mechanical AVR
No. 26 (f)	Carbomedics Bentall (2001)	7.8	23	Stenosis and regurgitation due to circular pannus formation in LVOT	11.4	Mechanical Bentall
No. 31 (m)	Carbomedics-TopHat (2003)	9.2	23	Pannus formation	10.3	Mechanical AVR
No. 32 (f)	Carbomedics-TopHat (2003)	6.1	19	Patient-prosthesis mismatch	12.6	Mechanical AVR
Biological AVR						
No. 6 (f)	Homograft (1989)	15.4	21	Regurgitation	0.3	Mechanical AVR (No. 7)
No. 8 (f)	Homograft (1992)	2.4	20	Regurgitation	7.6	Ross
No. 11 (m)	Homograft (1994)	10.7	19	Mixed aortic valve disease	3.7	Homograft (No. 15)
No. 13 (m)	Homograft (1995)	14.8	21	Endocarditis	11.1	Ross
No. 14 (f)	Homograft (1997)	17.9	22	Extensive structural valve degeneration due to calcification was noticed during aortic arch surgery	9.5	Mechanical AVR
No. 15 (m)	Homograft (1998)	14.4	22	Regurgitation	6.4	Mechanical AVR
No. 16 (m)	Homograft (1998)	9	21	Mixed aortic valve disease	9.8	Ross
No. 17 (m)	Homograft (1998)	0.2	10	Regurgitation	0.9	Homograft (No. 20)
No. 18 (m)	Homograft (1998)	14.9	21	Endocarditis	6.8	Homograft
No. 19 (m)	Sorin Pericarbon Stent- less (1999)	8.9	21	Stenosis	2.3	Mechanical AVR (No. 28)
No. 20 (m)	Homograft (1999)	1.1	16	Regurgitation	12.2	Mechanical Bentall (No. 44)
No. 30 (f)	Homograft (2003)	7.8	20	Endocarditis	11.6	Biological Bentall
AVR, aortic valve replacer avalva No. is concised if z	ment; LVOT, left ventricular or	utflow tract	hemrofred heed herd	when mations was steed < 18 wasts (Three nations rac.	aived two included valves. N	0 Prod No. 7 No. 11 and No. 15

Table 6 Valve replacements requiring re-operation

Vo. 7, No. 11 and No. 15, g υ υ ß < 18 years (Three patie) was aged wnen раце g ğ ^a Valve No. is specified if reoperation valve was included in the study as AVK surgery had been per No. 19 and No. 28; one patient received three included valves: No. 17, No. 20 and No. 44) Regarding re-operation rates mechanical valve replacement is favorable, but the risk for thromboembolic and bleeding events was considerable with a composite linearized event rate per valve-year of 3.2%. Longer follow up times of AVR with decellularized homografts must be awaited to compare outcomes.

Abbreviations

AVR: Aortic valve replacement; CI: Confidence interval; ECMO: Extracorporeal membrane oxygenation; HZ: Hazard ratio; INR: International normalized ratio; IQR: Interquartile range; LVAD: Left ventricular assist device.

Acknowledgements

Not applicable.

Authors' contributions

Conceptualization, J.S., G.L., D.Z.; methodology, J.S., P.S., G.W.; validation, P.S., G.W., E.B., G.L., D.Z.; formal analysis, J.S., D.Z.; investigation, J.S.; resources, G.L., D.Z.; data curation, J.S., P.S., G.W.; writing—original draft preparation, J.S.; writing—review and editing, P.S., G.W., E.B., G.L., D.Z.; visualization, J.S.; supervision, D.Z.; project administration, D.Z. All authors read and approved the final manuscript.

Funding

This research received no external funding.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Ethics Committee of the Medical University of Vienna Ethics committee protocol number: 1414/2019). Requirement for individual patient consent was waived.

Consent for publication

Not applicable.

Competing interests

Zimpfer has received grants from Edwards Lifesciences, Medtronic, Abbott and Berlin Heart. All authors have reported that they have no relationships relevant to the content. Edwards Lifesciences, Medtronic, Abbott and Berlin Heart have no role in the design of the study; the collection or analyses of the data; in the interpretation and the decision to publish the results.

Author details

¹University Clinic of Cardiac Surgery, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria. ²Department of Anaesthesia, Intensive Care Medicine and Pain Medicine, Division of Cardiac Thoracic Vascular Anaesthesia and Intensive Care Medicine, Medical University of Vienna, Vienna, Austria.

Received: 6 July 2021 Accepted: 29 August 2021 Published online: 08 September 2021

References

- Vergnat M, Asfour B, Arenz C, Suchowerskyj P, Bierbach B, Schindler E, et al. Contemporary results of aortic valve repair for congenital disease: lessons for management and staged strategy. Eur J Cardio-thoracic Surg. 2017;52(3):581–7.
- D'Udekem Y, Siddiqui J, Seaman CS, Konstantinov IE, Galati JC, Cheung MMH, et al. Long-term results of a strategy of aortic valve repair in the pediatric population. J Thorac Cardiovasc Surg. 2013;145(2):461–9.
- Nicks R, Cartmill T, Bernstein L. Hypoplasia of the aortic root 1. Thorax. 1970;25(3):339–46.
- Manouguian S, Kirchhoff PG. Patch enlargement of the aortic and the mitral valve rings with aortic-mitral double-valve replacement. Ann Thorac Surg. 1980;30(4):396–9.
- Konno S, Imai Y, Iida Y, Nakajima M, Tatsuno K. A new method for prosthetic valve replacement in congenital aortic stenosis associated with hypoplasia of the aortic valve ring. J Thorac Cardiovasc Surg. 1975;70(5):909–17.
- Myers PO, Mokashi SA, Horgan E, Borisuk M, Mayer JE, del Nido PJ, et al. Outcomes after mechanical aortic valve replacement in children and young adults with congenital heart disease. J Thorac Cardiovasc Surg. 2019;157(1):329–40.
- Alsoufi B. Aortic valve replacement in children: Options and outcomes. J Saudi Hear Assoc. 2014;26(1):33–41.
- Manji RA, Zhu LF, Nijjar NK, Rayner DC, Korbutt GS, Churchill TA, et al. Glutaraldehyde-fixed bioprosthetic heart valve conduits calcify and fail from xenograft rejection. Circulation. 2006;114(4):318–27.
- Horke A, Bobylev D, Avsar M, Meyns B, Rega F, Hazekamp M, et al. Paediatric aortic valve replacement using decellularized allografts. Eur J Cardio-Thoracic Surg. 2020;58(May):817–24.
- Horke A, Tudorache I, Laufer G, Andreas M, Pomar JL, Pereda D, et al. Early results from a prospective, single-arm European trial on decellularized allografts for aortic valve replacement: the ARISE study and ARISE Registry data. Eur J Cardio-Thoracic Surg. 2019;2020:1–9.
- Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, et al. Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions. Ann Thorac Surg. 2008;85(4):1490–5.
- Woods RK, Pasquali SK, Jacobs ML, Austin EH, Jacobs JP, Krolikowski M, et al. Aortic valve replacement in neonates and infants: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. J Thorac Cardiovasc Surg. 2012;144(5):1084–9.
- Etnel JRG, Elmont LC, Ertekin E, Mokhles MM, Heuvelman HJ, Roos-Hesselink JW, et al. Outcome after aortic valve replacement in children: A systematic review and meta-analysis. J Thorac Cardiovasc Surg. 2016;151(1):143-152.e3.
- Khan MS, Samayoa AX, Chen DW, Petit CJ, Fraser CDJ. Contemporary experience with surgical treatment of aortic valve disease in children. J Thorac Cardiovasc Surg. 2013;146(3):511–2.
- Brown JW, Ruzmetov M, Vijay P, Rodefeld MD, Turrentine MW. Surgery for aortic stenosis in children: a 40-year experience. Ann Thorac Surg. 2003;76(5):1398–411.
- Etnel JRG, Grashuis P, Huygens SA, Pekbay B, Papageorgiou G, Helbing WA, et al. The Ross procedure: a systematic review, meta-analysis, and microsimulation. Circ Cardiovasc Qual Outcomes. 2018;11(12):e004748.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.