Clinical results of the Medtronic Mosaic porcine bioprosthesis up to 13 years

Friedrich-Christian Riess a,*, Eva Cramer a, Lorenz Hansen a, Sandra Schifflers b, Gunther Wahl a, Jürgen Wallrath b, Stephan Winkel a, Peter Kremer a

aAlbertinen Heart Center, Hamburg, Germany
bMedtronic Bakken Research Center, Cardiac Surgery Clinical Research Department, Maastricht, The Netherlands

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Abstract

Background: The Mosaic bioprosthesis is a third-generation stented porcine bioprosthesis combining physiologic fixation and alpha-aminoleic acid (AOA) antimineralisation treatment to improve haemodynamic performance and durability. This single-centre study reports the clinical results, including haemodynamic performance, of the Mosaic bioprosthesis after implant in aortic or mitral position. Methods: Between February 1994 and October 1999, 255 patients with aortic valve replacement (AVR; mean age: 67 years, range: 23–82 years) and 47 patients with mitral valve replacement (MVR; mean age: 67 years, range: 41–84 years) were enrolled in this prospective non-randomised clinical trial. Follow-up visits were performed 30 days and 6 months after implant and annually thereafter. The cumulative follow-up was 1976.2 patient-years (pt-yrs) after AVR (median: 8.3 years, maximum: 14.0 years) and 336.9 pt-yrs after mitral valve replacement (MVR) (median: 8.2 years, maximum: 13.3 years). Results: After AVR, mean systolic gradient and effective orifice area at 4, 8 and 13 years follow-up were 13.3 ± 5.6, 15.5 ± 7.7 and 16.0 ± 7.2 mmHg and 1.8 ± 0.5, 1.8 ± 0.5 and 1.7 ± 0.4 cm². After MVR, respective data were 4.7 ± 2.1, 4.3 ± 1.2 and 5.0 mmHg (only one recording) and 2.2 ± 0.7, 2.3 ± 0.6 and 1.8 cm². Transvalvular regurgitation at 13-year follow-up was mild or less in both the AVR and MVR patients. Thirteen-year survival was 63.1 ± 4.5% in the AVR group and 51.2 ± 13.6% in the MVR group. Early mortality after AVR and MVR was 1.2% and 0.0%, respectively; late mortality was 3.2% pt-yr⁻¹ and 3.3% pt-yr⁻¹, including a valve-related/unexplained mortality of 1.1% pt-yr⁻¹ and 0.9% pt-yr⁻¹. Freedom from adverse events in the AVR and MVR group was permanent neurological event: 97.4% and 93.8%; valvular thrombosis: 97.8 ± 1.1% and 100%; structural valve deterioration: 84.8 ± 7.8% and 93.8 ± 6.1%; explant: 73.3 ± 7.3% and 89.3 ± 6.5%. Conclusions: The Mosaic bioprosthesis demonstrates excellent clinical performance and safety after 13 years of follow-up. Continued follow-up will determine whether this new design will provide increased durability.

Keywords: Valve replacement; Mortality; Survival

1. Introduction

The Medtronic Mosaic bioprosthesis is a supra-annular third-generation stented porcine bioprosthesis introduced in 1994. Its design is based upon the historical durability of the Medtronic Hancock II valve [1] and technical innovations are incorporated to improve durability and haemodynamic performance [2]. Tissue fixation using the Physiologic Fixation™ process is performed with glutaraldehyde to minimise the consequences of antigenicity after porcine valve implantation [3]. Furthermore, valve preparation includes predilation of the porcine aortic root followed by zero pressure fixation across the leaflets to preserve natural leaflet morphology [4]. The tissue is mounted on a low-profile flexible polymer stent suitable for supra-annular implant. In addition, the low-profile stent minimises haemodynamic disturbance, which makes it suitable for implant in patients with small aortic root diameters. The Mosaic bioprosthesis is treated with the alpha-aminoleic acid (AOA), which binds to the aldehyde fractions of the glutaraldehyde-preserved porcine tissue by forming Schiff base covalent linkages. The AOA process has been shown to reduce porcine valve mineralisation of both leaflets and aortic wall and to improve valve gradients in several animal studies [5].

This single-centre study reports the clinical performance, including haemodynamic data, and safety of the Mosaic bioprosthesis in aortic or mitral position up to 13 years after implant. Patients were enrolled as part of a US Food and Drug Administration (FDA) multi-centre prospective non-randomised clinical evaluation study completed late 2000. Patient

Abbreviations: AOA, alpha-aminoleic acid; AT III, antithrombin III; AVR, aortic valve replacement; EOA, effective orifice area; FDA, Food and Drug Administration; HIT, heparin-induced thrombocytopenia; LVEF, left ventricular ejection fraction; MVR, mitral valve replacement; Pt-yr, patient-years; SVD, structural valve disease; SVG, systolic valve gradient.

* Corresponding author. Address: Albertinen Heart Center, Department of Cardiac Surgery, Suentelstrasse 11 a, 22457 Hamburg, Germany.
Tel.: +49 40 558 82445/52223; fax: +49 40 558 82421.
E-mail address: Friedrich-Christian.Riess@albertinen.de (F.-C. Riess).

follow-up was continued as part of an ongoing long-term post-FDA approval study.

2. Patients and methods

2.1. Patient population

Between February 1994 and October 1999, a total of 302 patients were enrolled in this prospective, non-randomised study: 255 patients (mean age: 67 ± 8.5 years, range: 23–82 years) required aortic valve replacement (AVR) and 47 patients (mean age: 67 ± 8.2 years, range: 41–84 years) required mitral valve replacement (MVR). Concomitant coronary artery bypass surgery was required in 95 patients (37%) in the AVR group and in eight patients (17%) in the MVR group. Further demographic data are summarised in Table 1. Patients requiring replacement of more than one valve or who had a pre-existing prosthetic heart valve in another position were excluded from the study.

The study was approved by the institutional ethics committee and all patients provided informed consent prior to participation.

2.2. Surgical technique and anticoagulation management

During surgery, standard cardioplegia, cardiac arrest and crystalloid or modified blood cardioplegia was applied. Mosaic bioprostheses were implanted in supra-annular position with felt-armed single stitches. In case of mitral valve implantation, posterior chordae were preserved, if possible.

All patients received unfractionated heparin through intravenous (IV) infusion during the first 24 h after implant, followed by subcutaneous injections until complete mobilisation. For 3 months postoperatively, 95 AVR patients (37%) and 38 MVR patients (81%) received phenprocoumon with a target international normalised ratio (INR) range of 2.5–3.0 for the AVR group and of 3.0–4.0 for the MVR group. Further indications for phenprocoumon treatment were permanent atrial fibrillation (AF) or severely impaired left ventricular ejection fraction (LVEF <30%).

2.3. Follow-up

Clinical performance and safety of the Mosaic bioprosthesis was assessed at the early follow-up interval (prior to discharge or within 30 days after implantation), late interval (3–6 months post implant), at one year follow-up (11–14 months post implant) and annually thereafter. The examination included a patient interview, 12-lead ECG and a laboratory check for haemolysis. Furthermore, a transthoracic echocardiography (TTE) was made to assess the structure and haemodynamics of the Mosaic bioprosthesis. The mean systolic valve gradient (SVG) for the aortic bioprosthesis was calculated using the long form of the Bernoulli equation, and the effective orifice area (EOA) was calculated using the continuity equation. Valve-related complications, composites of complications and deaths were classified and reported according to the guidelines of the Society of Thoracic Surgeons, the American Association of Thoracic Surgery and the European Association of Cardio-Thoracic Surgery.

Data are current through 27 June 2008. At that point in time, 94 AVR patients and 19 MVR patients (37% vs 40% of enrolled patients) are still being followed actively. Collected data provide a cumulative follow-up of 1976.2 patient-years (pt-yrs) in the AVR group (median: 8.3, maximum: 14.0 years) and 336.9 pt-yrs in the MVR group (median: 8.2, maximum: 13.3 years). A total of 67 patients from the AVR group and 14 patients from the MVR group are lost to follow-up. The reasons for lost to follow-up were patient refuses further participation (n = 22 vs n = 4), unknown location of patient (n = 38 vs n = 6), patient moved (n = 5 vs n = 2) and unknown reasons (n = 2 vs n = 2).

2.4. Statistical analysis

Statistical analysis was performed using SAS® statistical software, (SAS Institute Inc., Cary, NC, USA), version 9.1. Descriptive statistics are used to characterise patient population, operative and follow-up data. For continuous variables, the number of patients, mean or median, standard deviation (SD) and minimum and maximum is provided. For categorical variables, the number and percentage of patients are provided.

Early morbidity is defined as morbidity occurring within the first 30 days after implant. Early mortality is defined as mortality occurring within the first 30 days after implant or
occurring more than 30 days after implant, but before hospital discharge. Early adverse event rates are calculated as the number of patients having the event divided by the total number of patients, expressed as a percentage. Late adverse events are summarised using linearised rates, and calculated by dividing the number of late events by the sum of the late pt-yr, expressed as a percentage (% pt-yr⁻¹). Survival analysis using the actuarial Kaplan—Meier method is used to estimate survival and freedom from valve-related adverse events. Peto et al.’s formula [6] is used to calculate standard errors (SEs) of these estimates. Adverse events that occurred during the early and late postoperative periods are included in the analysis.

3. Results

3.1. Clinical status

Six years after implantation of the first Mosaic bioprosthesis in the aortic position, 145 patients had a documented follow-up. As many as 96% of patients were in New York Heart Association (NYHA) class I or II. With regard to cardiac rhythm, 86% of patients were in sinus rhythm (SR), 8% in AF/atrial flutter (AFL) and 7% were paced. In addition, 57% received aspirin, 9% were on phenprocoumon and 34% were not using any anticoagulant medication. Thirteen years after the first AVR, 10 patients had a documented follow-up. Nine patients were in NYHA class I or II. In addition, four patients were in SR, four patients in AF/AFL and two patients were paced. Anticoagulant therapy consisted of aspirin treatment in six patients, phenprocoumon treatment in three patients and no anticoagulant treatment in one patient.

Six years after implantation of the first Mosaic bioprosthesis in the mitral position, 24 patients had a documented follow-up. A total of 79% of patients were in NYHA class I or II. The 12-lead ECG revealed that 63% of patients were in SR, 29% in AF/AFL and 8% were paced. At the same time, 38% received aspirin, 50% phenprocoumon and 12% no anticoagulant therapy. Thirteen years after the first MVR, two patients had a documented follow-up. Both patients were in NYHA class II and received phenprocoumon. One patient was in SR and the other in AF/AFL.

3.2. Echocardiography

A TTE of the Mosaic bioprosthesis revealed a mean SVG of 16.0 ± 7.2 mmHg in the aortic position and 5.0 mmHg (only one recording) in the mitral position 13 years after implant. Respective EOA values were 1.7 ± 0.4 cm² and 1.8 cm². Transvalvular regurgitation at 13-year follow-up was mild or less in all patients of both AVR and MVR groups.

Mean SVG over time for AVR and MVR groups is given in Fig. 1, whereas mean EOA over time for both groups is given in Fig. 2. Transvalvular regurgitation over time for AVR and MVR groups is given in Fig. 3.

3.3. Survival

In the AVR group, 13-year survival was 63.1 ± 4.5% (Fig. 4). Three AVR patients (1.2% of enrolled patients) died within 30 days after surgery or before discharge. The causes of death were pulmonary hypertonus due to hypertrophic obstructive cardiomyopathy with left ventricular outlet obstruction on postoperative day 3, acute pericardial tamponade due to aortic dissection and perforation on postoperative day 13 and biventricular heart failure, hepatorenal syndrome and liver cirrhosis on postoperative day 36.

The linearised rate for late mortality was 3.2% pt-yr⁻¹ in the AVR group. Out of 62 late deaths, 10 were cardiac (0.5% pt-yr⁻¹), 30 were non-cardiac (1.5% pt-yr⁻¹), three were valve-related (0.2% pt-yr⁻¹) and 19 were unexplained (1.0% pt-yr⁻¹). The first valve-related death was of a 66-year-old man suffering from a cerebral haemorrhage while on phenprocoumon (target INR of 2) for permanent AF who...
developed septicaemia after a relieving operation on post-operative day 2119. The second valve-related death was a 49-year-old man on postoperative day 3098 due to low output syndrome after surgical valve replacement for endocarditis. The third valve-related death was a 68-year-old man from heart failure on postoperative day 983 after developing a stroke. No autopsy was performed in any of these patients. Thirteen-year freedom from valve-related or unexplained death was $82.9\pm 4.5\%$ (Fig. 5).

In the MVR group, 13-year survival was $51.2\pm 13.6\%$ (Fig. 1). There was no early mortality. The linearised rate for late mortality was $3.3\%$ pt-yr$^{-1}$. Out of 11 late deaths, one was cardiac ($0.3\%$ pt-yr$^{-1}$), seven were non-cardiac ($2.1\%$ pt-yr$^{-1}$), none was valve-related ($0.0\%$ pt-yr$^{-1}$) and three were unexplained ($0.9\%$ pt-yr$^{-1}$). Thirteen-year freedom from valve-related or unexplained death was $79.0\pm 14.7\%$ (Fig. 2).

3.4. Valve-related adverse events

Linearised rates for late valve-related adverse events and actuarial freedom from valve-related adverse event percentages after 4, 8 and 13 years of follow-up are summarised in Table 2 for both AVR and MVR patients.

3.4.1. Structural valve deterioration

In the AVR group, no early and nine late cases of structural valve deterioration (SVD) were observed during the 13-year follow-up period (range: 8.4—12.4 years after implant) (Fig. 6). SVD was combined with aortic valve regurgitation and stenosis in three cases, isolated stenosis in three cases and isolated regurgitation in three cases.
No early and only one late case of SVD was observed in the MVR group during the 13-year follow-up. The affected patient suffered from isolated mitral valve prosthesis stenosis. In nine cases, radiological explant analysis showed moderate/extensive mineralisation with stiff leaflets due to thrombotic appearing material in two cases (one aortic valve and one mitral valve). The tenth explanted valve had stiff leaflets due to thrombotic appearing material, but showed only traces of mineralisation.

3.4.2. Non-structural valve dysfunction

In the AVR group, one early case (0.4% of enrolled patients) of non-structural valve dysfunction was diagnosed. This considered a patient with a paravalvular leak diagnosed on day 6. His valve was explanted on day 106. In addition, four late cases of non-structural valve dysfunction occurred. In the first patient, the valve was explanted for patient bioprosthesis mismatch on day 34. In the second patient, the mismatched Mosaic bioprosthesis, as diagnosed on day 135, was still in place at the time of his death 6.9 years after implant. In the third patient, mismatch was diagnosed on day 139, but the valve was explanted for valvular thrombosis 2.4 years after implant. In the last patient, non-structural valve dysfunction due to pannus formation was diagnosed and the valve explanted 11.3 years after implant.

No case of non-structural valve dysfunction was diagnosed in the MVR group.

3.4.3. Thrombo-embolism

Two early cases (0.8% of enrolled patients) of thrombo-embolism occurred in the AVR group. One case was a 76-year-old female with paroxysmal AF who developed a stroke under heparin treatment on postoperative day 7. The other case was a 72-year-old female with permanent AF who developed a transient ischaemic attack with nausea, vertigo and amnesia on postoperative day 13. In addition, 15 late thrombo-embolic events occurred during the 13-year follow-up of the AVR group (range: 0.2—9.1 years after implant). Four of these patients had a permanent neurological event, five patients a transient ischaemic event, one patient a myocardial infarction and one patient a peripheral thrombo-embolic event. In addition, four patients had a thrombosed valve. The first valvular thrombosis was diagnosed on postoperative day 87. Phenprocoumon was discontinued on day 24 due to recurrent haemorrhage. The thrombosed valve was replaced by a Hancock II bioprosthesis that thrombosed during the early postoperative course as well and was replaced by a mechanical valve. Analysis of both the explanted Mosaic and Hancock II bioprosthesis revealed bland thrombotic occlusion without infection or calcification. The second valvular thrombosis was diagnosed under aspirin treatment 2.4 years after implant. The thrombosed valve was replaced by a mechanical valve. Analysis of the explanted valve showed extensive thrombosis, but no signs for cuspal degeneration, calcification or infection. The third valvular thrombosis was diagnosed under aspirin treatment 5.0 years after implant. The thrombosed valve was replaced by a second Mosaic bioprosthesis. The last valvular thrombosis was diagnosed 9.0 years after implant. The valve was replaced by a Hancock II bioprosthesis. Analysis of the explanted valve revealed brown thrombotic appearing material on two cusps.

In the MVR group, no early and two late thrombo-embolic events occurred: a peripheral thrombo-embolic event 6.1 years after implant and a stroke 7.3 years after implant. No valvular thrombosis was observed in the MVR group.

3.4.4. Endocarditis

No early and 10 late cases of endocarditis were observed after AVR (range: 0.7—9.8 years after implant). In four cases, a *Streptococcus* was isolated, in one case an *Enterococcus* and in the other cases no bacterium was reported. All patients had their infected valves explanted.
Table 2
Frequency and actuarial freedom from valve-related adverse events at 4, 8, and 13 years after aortic valve replacement (AVR, N = 255, 1976.2 late pt-yr) and after mitral valve replacement (MVR, N = 47, 336.9 late pt-yr).

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>AVR Late events</th>
<th>Actuarial freedom from event (% ± SE)</th>
<th>MVR Late events</th>
<th>Actuarial freedom from event (% ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%/pt-yr</td>
<td>4 years</td>
<td>8 years</td>
</tr>
<tr>
<td>Structural valve deterioration</td>
<td>9</td>
<td>0.5</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Non-structural valve dysfunction</td>
<td>4</td>
<td>0.2</td>
<td>98.4 ± 0.8</td>
<td>98.4 ± 0.8</td>
</tr>
<tr>
<td>Major paravalvar leak</td>
<td>0</td>
<td>0.0</td>
<td>99.6 ± 0.4</td>
<td>99.6 ± 0.4</td>
</tr>
<tr>
<td>Mismatch</td>
<td>3</td>
<td>0.2</td>
<td>98.8 ± 0.7</td>
<td>98.8 ± 0.7</td>
</tr>
<tr>
<td>Pannus formation</td>
<td>1</td>
<td>0.1</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Thrombo-embolism</td>
<td>15</td>
<td>0.8</td>
<td>95.3 ± 1.4</td>
<td>93.7 ± 1.7</td>
</tr>
<tr>
<td>Permanent neurological event</td>
<td>4</td>
<td>0.2</td>
<td>98.3 ± 0.9</td>
<td>98.3 ± 0.9</td>
</tr>
<tr>
<td>Transient neurological event</td>
<td>5</td>
<td>0.3</td>
<td>98.2 ± 0.9</td>
<td>97.7 ± 1.0</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>1</td>
<td>0.1</td>
<td>100.0</td>
<td>99.4 ± 0.6</td>
</tr>
<tr>
<td>Valvular thrombosis</td>
<td>4</td>
<td>0.2</td>
<td>99.2 ± 0.6</td>
<td>98.7 ± 0.8</td>
</tr>
<tr>
<td>Peripheral embolic event</td>
<td>1</td>
<td>0.1</td>
<td>99.6 ± 0.4</td>
<td>99.6 ± 0.4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>10</td>
<td>0.5</td>
<td>98.3 ± 0.8</td>
<td>97.2 ± 1.1</td>
</tr>
<tr>
<td>Major haemorrhages</td>
<td>7</td>
<td>0.4</td>
<td>97.5 ± 1.0</td>
<td>96.4 ± 1.3</td>
</tr>
<tr>
<td>Haemolysis</td>
<td>0</td>
<td>0.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Valve-related re-operation</td>
<td>29</td>
<td>1.5</td>
<td>96.7 ± 1.2</td>
<td>93.9 ± 1.7</td>
</tr>
<tr>
<td>Expant</td>
<td>29</td>
<td>1.5</td>
<td>96.7 ± 1.2</td>
<td>93.9 ± 1.7</td>
</tr>
</tbody>
</table>

In the MVR group, no early and two late cases of endocarditis occurred. In one patient, a Streptococcus was isolated 133 days after implant, in the other patient an Enterococcus 3.5 years after implant. Both patients had their infected Mosaic bioprosthesis explanted.

3.4.5. Major haemorrhages

In the AVR group, two early major haemorrhages (0.8% of enrolled patients) occurred: a severe cardiac tamponade under phenprocoumon treatment 23 days after surgery and a severe epistaxis under phenprocoumon treatment 24 days after surgery. Furthermore, seven late major haemorrhages (range: 0.3–5.8 years after implant) were observed in six patients, including cerebral haematoma in two patients, gastrointestinal haemorrhage in three patients, non-acute thoracic haemorrhage in one patient and haemoptoma of the thigh after an accident in one patient.

In the MVR group, one patient (2.1% of enrolled patients) suffered from an early major haemorrhage under phenprocoumon treatment 8 days after surgery. Furthermore, two late major haemorrhages occurred, one massive intestinal haemorrhage 73 days after surgery and one subdural haematoma 127 days after surgery. Both events occurred under phenprocoumon treatment.

3.4.6. Haemolysis

No cases of haemolysis were reported for the AVR and the MVR groups.

3.4.7. Valve-related re-operation and explant

In the AVR group, no early and 29 late Mosaic bioprosthesis-related re-operations occurred (range: 0.1–12.4 years after implant), all resulting in explant. Reasons for explant were SVD in nine patients, non-structural valve dysfunction in three patients, endocarditis in 10 patients and valvular thrombosis in four patients. In addition, three valves were replaced incidentally due to ascending aorta aneurysm.

In the MVR group, no early and three late Mosaic bioprosthesis-related re-operations occurred (range: 0.6–9.4 years after implant) that led to explant. Reasons for explant were endocarditis in two patients and SVD in one patient.

4. Discussion

This single-centre study reports the clinical performance, including haemodynamic data and safety of the Mosaic bioprosthesis in aortic or mitral position up to 13 years after
implant. The data of annual prospective serial standardised echocardiographic follow-up presented here is unique to this study cohort. The intermediate 13-year results demonstrate haemodynamic and clinical performance of this third-generation porcine valve prosthesis in aortic and mitral position.

The present echocardiographic data demonstrate stable transvalvar SVG and EOA during the 13-year follow-up, with lower SVG and higher EOA for bigger valve sizes (Figs. 1 and 2). The significant increase and decrease in SVG in the 29 mm were caused by the fact that this group contained only two patients, of which one developed SVD and had his valve explanted after 9.4 years. Data are comparable with those obtained in earlier Mosaic series [2,7]. Relatively low gradients were found in small valve sizes. It is assumed that these low transvalvar gradients are a direct benefit of this new valve design and tissue processing, preserving the normal architecture of the collagen tissue [4,8,9].

In the AVR group, 13-year survival after Mosaic bioprosthesis implant was 63%, with a freedom from valve-related and unexplained death of 83% (Fig. 5). This is in line with earlier reported survival rates of 70% after 10 years [10] and 40–77% after 15 years of implant [1,11,12], and a freedom from valve-related and unexplained death of 71–92% after 15 years of Hancock II implant [1,11] in the MVR group, 13-year survival was 51%, with a freedom from valve-related and unexplained death of 79%. This is in line with an earlier reported survival rate of 53% after 11 years [13] and 30–48% after 15 years of implant [1,11,12], and earlier freedom from valve-related or unexplained death rates of 84% after 11 years [13] and 68–86% after 15 years of implant [1,11].

The Mosaic bioprosthesis fixation process includes dilation of the aortic root at the time of preservation, resulting in normal plane closure of the leaflets without restriction. Additional anti-mineralisation treatment with AOA [14] would provide longer durability, especially in a younger population [2]. In our AVR group, nine out of 255 implanted Mosaic valves developed SVD, resulting in a 13-year freedom from SVD of 85% (Fig. 6). Freedom from SVD for other bioprosthetic valves in the aortic position ranged from 59–87% after 10 years of implant [10,15–17] to 70–85% after 15 years of implant [1,11,18,19], suggesting that the Mosaic SVD rates are lying on the upper range of reported values. Most remarkably in our study, only one case of SVD was observed in a total of 47 AVR patients, resulting in a 13-year freedom from SVD of 94%. Freedom from SVD for other bioprosthetic valves in the mitral position was 65–72% after 10 years [15–17] and 66–71% (actual) after 15 years of implant [1,11]. In addition, Marchand et al. reported a freedom from explant due to structural failure of 85% 11 years after Carpentier—Edwards (CE) Perimount implant in the mitral position [13]. These results suggest that the Mosaic bioprosthesis has a similar to higher durability as compared to other valves in the aortic position and a superior durability in the mitral position as compared to other valves. Our higher freedom from rate in the MVR group versus the AVR group is in contrast with findings from other authors, who reported tissue valves to be more durable in the aortic than in the mitral position [1,15,20]. It is suggested by Jamieson et al. that the difference in durability may be caused by elevated closing pressures and thus increased haemodynamic stresses in the mitral position [17]. This suggests that the Mosaic valve seems to be especially withstand the high stress in the mitral position.

As shown in Fig. 6, the first case of SVD occurred after 8.4 years of implant in the AVR group and 9.4 years in the MVR group. This is in line with an earlier report of the Mosaic bioprosthesis [2]. In comparison, SVD was most commonly reported after ~5 years of implant for the Intact valve [15], the Hancock II valve [1,11,19], the Mosaic valve [21], the CE Pericardial bioprosthesis [10,12] and the CE Perimount [13].

Although the new fixation process of the Mosaic bioprosthesis intended to provide a longer durability in the younger patients, 13-year freedom from SVD was similar for AVR patients younger or equal to 65 years of age at implant compared to patients older than 65 years (85.6 ± 5.1% vs 86.2 ± 11.6%). Age at implant of the individual AVR patients was 31 years; two times 55, 58 years; two times 59, 63, 69 and 73 years. Other studies showed clear age effects for patients younger and older than 65 years of age. Reported 15-year freedom from SVD rates were 75% versus 100% [19] and 76% versus 100% (actual) [1] after Hancock II implant, whereas 15-year freedom from SVD for the CE-SAV was 54% versus 92% [19]. Other authors also reported a higher durability in the aortic position for older patients [15,22]. The Mosaic bioprosthesis thus showed a higher durability in younger patients, whereas this was lower in the older group when compared to literature. However, we have a relatively small group of mitral valve patients, with only one case of SVD in a 65-year-old patient. David et al. [1] showed a 15-year actual freedom from SVD after Hancock II implant of 76% for patient younger than 65 years and 100% for patients older than 65 years of age. Yamak et al. [23] reported a 44% freedom from SVD rate 12 years after CE high-profile bioprosthesis in young patients (age range: 15–58 years). In contrast, Barrett-Boyes et al. [15] found no age effect on the freedom from SVD in the MVR group.

In the AVR group, one early and four late cases of non-structural valve dysfunction were diagnosed resulting in a freedom from rate of 96%. In comparison, no cases were found in the MVR group (Table 2). Barratt-Boyes et al. reported a 10-year freedom from non-structural valve dysfunction of 95% for all valves combined, primarily due to perivalvular leaks [15]. Our series consisted of one paravalvular leak, three mismatched valves of which one had to be explanted for that reason and one valve with pannus formation.

A major benefit of a bioprosthesis in comparison to a mechanical valve is the low incidence of thrombo-embolic and major anti-thrombo-embolic-related haemorrhage. In the present study, freedom from thrombo-embolic events was 91% and 92% in the AVR and MVR groups. This is favourable to other bioprosthetic valves with reported rates of 80–91% after AVR [1,10–12,15] and 72–92% after MVR [1,10,11–13]. In this context, it seems to be important that all patients without a need for phenprocoumon (e.g., permanent AF) were treated with aspirin.

Four valvular thromboses occurred in the AVR group and none in the MVR group resulting in freedom from valvular thrombosis rates of 98% and 100%, respectively. The first case was a 73-year-old female who, after explant of the Mosaic bioprosthesis on postoperative day 87, was diagnosed with a
congenital antithrombin (AT) deficiency. The residual AT III activity of only 20% can be considered the primary cause of this thrombosis. This theory is supported by the recurrent thrombosis of the second bioprosthesis. The third case was a 67-year-old male who developed valvular thrombosis 5 years after implant. During the early postoperative course, this patient suffered from acute heparin-induced thrombocytopenia (HIT) type II as well as acquired AT III deficiency that had to be treated with recombinant hirudin as alternative anticoagulant. The overlapping treatment with phenprocoumon had to be stopped early due to a gastrointestinal haemorrhage. Intra-operative findings and histological investigation of the explanted Mosaic bioprosthesis supported the theory of HIT, as a thin layer of white clot formation was found in all three cusps of the valve. For the other two cases of valvular thrombosis, there were no obvious explanations. In the literature, the incidence of bioprosthesis thrombosis is comparable to ours, although freedom from valvular thrombosis rates is not frequently provided [1,10,11,15].

Ten AVR patients and two MVR patients developed endocarditis resulting in 13-year freedom from endocarditis of 94% and 95%, respectively. The rates for infective endocarditis after Mosaic bioprosthesis implant are similar to those reported for other stented porcine and pericardial valves, such as Hancock II [1,11], CE Perimount [13,24], Biocor [25], Medtronic Intact [15] and the CE standard prosthesis [12] ranging from 91% to 98%. David et al. [1] reported the highest risk for endocarditis during the first year after the operation. In contrast, our 10 cases of endocarditis in the AVR group occurred 0.7–9.8 years (median: 5.2 years) after implant, and the two mitral cases 133 days and 3.5 years after implant.

The number of major haemorrhages was comparably low for both groups. Freedom from major haemorrhage at 13 years was 96% in the AVR group and 94% in the MVR group. Freedom from major haemorrhages was comparable to other series (AVR vs MVR: 99% after 10 years vs 99% after 8 years of CE Pericardial bioprosthesis [10], and 95% vs 89% after 15 years of Hancock II implant [11]. The reason might be the relatively low percentage of patients in our study under continuous anticoagulant therapy at 6 months after surgery.

In the current study, all valve-related re-operations resulted in Mosaic bioprosthesis explant. Freedom from explant was 73% and 89% in the AVR and MVR group, respectively. The most common reasons for explant in both groups were SVD and endocarditis. In literature, freedom from explant rates ranged from 64–84% after 10 years [10,15] to 77–82% after 15 years [1,11], of implant in the aortic position, and 67% after 10 years [10], 83% after 11 years [13] and 69–71% after 15 years [1,11], of implant in the mitral valve position. The most commonly reported indication for bioprosthesis explant in literature was SVD [1,10,11,13,15], followed by endocarditis [10,11]. This suggests that compared with the literature, explant rates are comparable in the AVR group and lower in the MVR group.

In conclusion, the long-term performance of the Mosaic bioprosthesis is encouraging, as this third-generation porcine heart valve continues to provide excellent haemodynamic data, a small number of valve-related adverse events and a low incidence from SVD. Continued clinical follow-up and monitoring of this patient population should demonstrate if indeed this valve will provide patients with increased durability and low morbidity, when compared to bioprosthetic valves of an earlier design and generation.

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