

## Early Bioprosthesis Failure: Report of Three Cases and Literature Review

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### ABSTRACT

**Background:** We experienced three rare early bioprosthesis failure (EBF) cases. In this study, we analyze the causes and discuss the coping strategy of EBF.

**Methods:** We reviewed all cases of EBF in patients who received a bioprosthesis replacement in Changhai Hospital between January 2001 and January 2014, and reviewed related articles that were published between 1994 and 2014, searching for keywords in PubMed such as “bioprosthesis,” “heart valve prosthesis,” “early failure,” and “bioprosthesis failure.”

**Results:** Only three cases were found in Changhai Hospital during this time period. The reasons for EBF in these 3 cases were: native valve attachment, early calcification caused by metabolic syndrome, and early valve thrombosis. Literature review identified additional 14 cases. The reasons for EBF in these 14 cases were as follows: native valve attachment in 6 cases; metabolic abnormalities in 3 cases; early valve thrombosis in 2 cases; chronic inflammation in 2 cases; and improper operation in 1 case.

**Conclusion:** EBF is a rare but serious complication. The cause of EBF is complex. Appropriate preventive measures should be developed according to the condition of the patient.

### INTRODUCTION

Bioprosthetic valves are widely used for their excellent hemodynamic performance and because they do not need anticoagulation. Each year, approximately 85,000 substitute valves are implanted in the United States and 275,000 are implanted worldwide; about half of them are bioprosthetic valves (Schoen 2005). As technology advances, current-generation bioprostheses have superior durability compared with first-generation porcine valves. Ongoing studies suggest that third-generation bioprostheses may be even more durable, with  $92 \pm 8\%$  freedom from structural valve deterioration in some condition [El Oakley 2008].

Early bioprosthesis failure (EBF) is defined as reoperation after implantation within 5 years. In China there is no literature to be found regarding this rare but life-threatening complication. Here, we report the only 3 EBF cases from 2001 to 2014 and review the related literature.

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### CASE 1

A 57-year-old man with severe tricuspid regurgitation underwent off-pump tricuspid valve replacement (OP-TVR) with a bioprosthetic valve (31-mm Medtronic, Minneapolis, MN, USA) in 2010, and his native tricuspid valve was reserved during operation. He received a right ventricle pacemaker implantation in 1996 and pacemaker replacement plus tricuspid valve plastic (TVR) in 2005. After OP-TVR, he was anticoagulated with aspirin (100mg/d) until rehospitalization. Three years after the first operation, the patient was rehospitalized with a 6-month history of repeated progressive dyspnea and edema of the lower extremity. Physical examination revealed a 2/6 decrescendo systolic blowing murmur consistent with tricuspid regurgitation. Echocardiogram revealed that the bioprosthetic valve had an enhanced echo with marked fibrosis and limited opening. Doppler interrogation revealed a mean gradient of 24 mm Hg and severe regurgitation. Electrocardiograph (ECG) revealed the pacemaker was normal. The patient subsequently underwent re-TVR. Intraoperatively, the bioprosthetic tricuspid valve was well-adhered to the native valve and fibroplasia was found in the bioprosthesis. A hyperplastic pannus was found around the valve (Figure 1). A mechanical prosthesis (31-mm St. Jude, Minneapolis, MN, USA) was implanted.

### CASE 2

A 72-year-old man with severe aortic regurgitation and coronary atherosclerotic heart disease underwent aortic

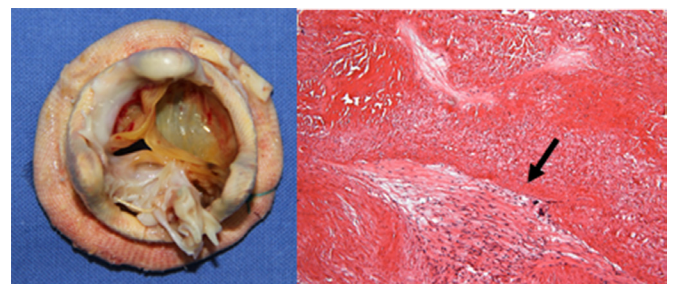


Figure 1. Gross (left) and pathology (right) images of the bioprosthesis after reoperation. Adhesion between the tricuspid valve and bioprosthesis, valve leaflet hyperplasia and pannus hyperplasia can be seen in the gross image. Fusion between the tricuspid valve and bioprosthesis and mesenchymal cells in the bioprosthesis can be seen in the pathology image (arrow)(HE  $\times$  100).

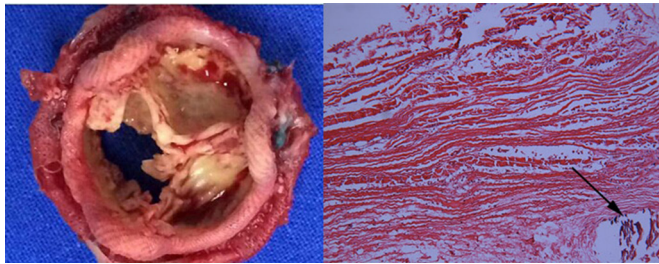


Figure 2. Gross (left) and pathology (right) images of the bioprosthesis after reoperation. Aortic valve calcification and failure, and right coronary cusp damage can be seen in the gross image. Small amounts of leukomonocytes and phlogocytes, extensive collagen hyperplasia and calcium deposits can be seen in the pathology image (arrow)(HE × 100).

valve replacement (AVR) and coronary artery bypass grafting (CABG) with a bioprosthetic valve (23-mm Carpentier Edwards, Irvine, CA, USA) in 2010. The patient was rehospitalized 3 years after the first operation with a 2-month progressive dyspnea after exercising. Physical examination revealed a 3/6 diastolic sighing murmur in the second aortic valve area and a 2/6 systolic blowing murmur in the auscultatory mitral area. Echocardiogram and Doppler interrogation revealed a severe aortic valve regurgitation and anterior leaflet prolapse with regurgitation of the mitral valve. Hyperlipidemia was laboratory confirmed. The patient subsequently underwent re-AVR and mitral valve repair (MVP). Aortic valve calcification and failure was seen during the operation (Figure 2). A bioprosthetic valve (23-mm St. Jude, Minneapolis, MN, USA) was implanted.

### CASE 3

A 67-year-old man with severe aortic valve regurgitation and right coronary cusp prolapse underwent AVR with a bioprosthetic valve (23-mm St. Jude, Minneapolis, MN, USA) in 2009. He was anticoagulated with warfarin for 6 months and then took aspirin until rehospitalization. The patient was rehospitalization 4 years after the first operation with a 1-year progressive dyspnea after exercising. Physical examination revealed a 3/6 systolic murmur in the second aortic valve area. Echocardiogram and Doppler interrogation revealed a severe aortic valve stenosis with a 128 mm Hg pressure gradient, and increased echo reflectance was found at the right coronary cusp. The patient subsequently underwent re-AVR with a mechanical valve (23-mm CarboMedics, Austin, TX, USA). A large number of fibers attached to the bioprosthetic valve leaflet was the cause of its difficulty in opening (Figure 3).

### MATERIALS AND METHODS

We reviewed the EBF-related literature from January 1994 to October 2014 by searching PubMed, Web of Knowledge, and Google Scholar using the following terms: bioprosthesis, heart valve prosthesis, early failure, bioprosthesis failure. All the references cited in the papers were also reviewed. Studies including case reports, case series, controlled clinical trials,

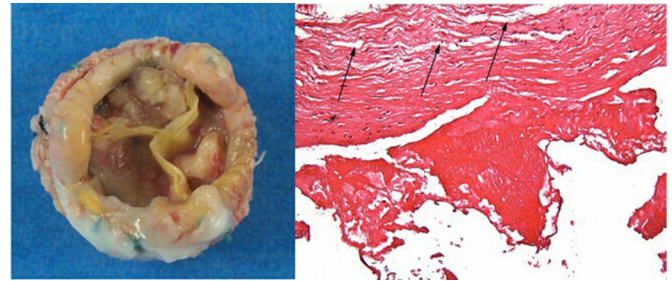


Figure 3. Gross (left) and pathology (right) images of the bioprosthesis after reoperation. Excrescence in effluent face, valve opening limitation and thrombogenesis can be seen in the gross image. Fiber breakage can be seen in the pathology image (arrows)(HE × 200).

and randomized controlled trials were considered, with no language restrictions. Animal studies were excluded.

### RESULTS

We reported on EBF cases caused by leaflet adhesion, metabolic syndrome (MS), and early thrombotic occlusion, respectively. The literature search identified 12 articles describing 14 cases of EBF for final analysis [Al Kindi 2012; Bajaj 2008; Bianchi 2013; Fasol 2000; Glaser 2013; Gualis 2009; Gutierrez 1996; Ito 2013; Izutani 2008; Robertson 2008; Takeda 2012; Wiedemann 2010]. Causes of EBF included leaflet adhesion in 6 cases [Bianchi 2013; Glaser 2013; Robertson 2008; Takeda 2012], MS in 3 cases [Ito 2013; Izutani 2008; Wiedemann 2010], early thrombotic occlusion in 2 cases [Fasol 2000; Gutierrez 1996], immuno-inflammatory responses in 2 cases [Al Kindi 2012; Bajaj 2008], and inappropriate surgical operation in 1 case [Gualis 2009]. The Table summarizes all reported cases of EBF and the cause of failure.

### DISCUSSION

Bioprosthesis failure is inevitable, but most failure of bioprosthesis occurs more than 12 years after implantation [Bach 2007]. Currently, little research has been done in EBF and the concrete mechanism of it is unclear. We recognize that EBF is a complicated process with many regulation factors involved.

Leaflet adhesion is an important cause of EBF. A leaflet can occur between the bioprosthesis and preserved valvular apparatus or the bioprosthesis itself. Preserving the subvalvular apparatus during mitral valve replacement (MVR) or TVR is suggested and the superiority of it has been demonstrated [Natsuaki 1996]. But it may require early explantation because of EBF. Bianchi et al [Bianchi 2013] and Robertson et al [Robertson 2008] reported three EBF cases after MVR because of the fusion of the papillary muscle and chordae remnants with the bioprosthetic leaflets. For this complication, Bianchi advises folding the spared posterior leaflet [Bianchi 2013] and Robertson advises using an alternate method of preserving the subvalvular apparatus [Robertson 2008]. We also advise confirming the position between the bioprosthesis and the native leaflets. Preserved valvular apparatus adhesion

## Overview of Published Cases of Early Bioprosthesis Failure

Reference	Sex	Age, y	Operating method	Valve type	Time of EBF Occurrence after First Operation	Cause of EBF
Al Kindi	Female	75	AVR	Medtronic 3F	5 months	Immuno-inflammatory responses
Bajaj M	Male	61	MVR	Medtronic Mosaic	9 months	Immuno-inflammatory responses
Bianchi G	Female	73	MVR	St. Jude	3 years	Leaflet adhesion
Fasol R	Male	69	MVR	Carpentier-Edward	8 days	Early thrombotic occlusion
Glaser N (Case 1)	Male	25	MVR	Edwards Perimount Magna	1 month	Leaflet adhesion
Glaser N (Case 2)	Male	65	MVR	Edwards Perimount Magna	4 days	Leaflet adhesion
Gualis J	Male	61	AVR	Mitroflow	6 months	Inappropriate surgical operation
Gutierrez M	unknown	unknown	unknown	unknown	4 months	Early thrombotic occlusion
Ito Y	Male	75	AVR	Carpentier-Edward	39 months	MS
Izutani H	Female	80	AVR	Carpentier-Edward	29 months	MS
Robertson JO (Case 1)	Male	77	MVR	Bovine prosthesis	5 years	Leaflet adhesion
Robertson JO (Case 2)	Male	75	MVR	unknown	3.5 years	Leaflet adhesion
Takeda K	Female	42	MVR	Carpentier-Edward	4 years	Leaflet adhesion
Wiedemann D	Male	61	AVR	St. Jude	8 months	MS

EBF indicates early bioprosthesis failure; AVR, aortic valve replacement; MVR, mitral valve replacement; MS, metabolic syndrome.

to the bioprosthesis should be avoided by removing excess valvular tissue. Glaser et al [Glaser 2013] reported two EBF cases with extracorporeal membrane oxygenation (ECMO) support after MVR due to fusion of the bioprosthetic leaflets; they thought the probable mechanism causing the leaflets to fuse was the low flow over the prosthesis during ECMO support, resulting in little or no motion of the cusps.

MS can result in EBF. It is reported that MS is independently associated with faster bioprosthetic valve degeneration [Briand 2006; Nollert 2003; Antonini-Canterin 2003]. Boeken et al observed accelerated bioprosthetic valve calcification in patients with end-stage RF who had a high level of blood calcium [Boeken 2010]. We and Wiedemann et al [Wiedemann 2010] reported 2 EBF cases after AVR, all with MS. It may be that MS can accelerate bioprosthetic valve calcification. MS should be corrected after bioprosthetic valve replacement in order to avoid EBF.

Early thrombotic occlusion is another cause of EBF. We and Gutierrez et al [Gutierrez 1996] reported 2 EBF cases after AVR, and Fasol et al [Fasol 2000] reported 1 EBF case after MVR; all three cases were due to early thrombotic occlusion. Fasol et al reported early thrombotic occlusion due to the preservation of the posterior mitral valve leaflet in their case [Fasol 2000]. But the other 2 EBF cases did not have this problem. So we believe that anticoagulation is very important in the early stage after bioprosthetic valve replacement.

Immuno-inflammatory responses can result in EBF. Bajaj et al [Bajaj 2008] reported an EBF case after MVR because of bioprosthetic mitral stenosis; they believe the stenosis was

a result of diffuse idiopathic inflammation and deposition of fibroconnective tissue. Al Kindi et al [Al Kindi 2012] reported an EBF case after AVR. During reoperation, they found a fibrous band in the subvalvular apparatus linking the inter-ventricular septum to the free wall of the left ventricle, resulting in significant left ventricular outflow tract obstruction; the fibrous band may have resulted from a cell-mediated inflammatory reaction [Al Kindi 2012]. Until now, to our knowledge there are no systematic studies on immuno-inflammatory responses after bioprosthetic valve replacement.

Surgical technique is also a cause of EBF. Gualis et al [Gualis 2009] reported an EBF case after AVR because of suture distribution; the suture distribution resulted in stent deformation and then severe prosthetic aortic stenosis. They advised sutures must be distributed cautiously and equidistantly along the mitroflow prosthetic Dacron rim to prevent stent deformation.

EBF is a rare but possible complication. Our review summarizes causes of EBF, including leaflet adhesion, MS, early thrombotic occlusion, immuno-inflammatory responses, and surgical technique. Appropriate measures should be taken to avoid EBF such as alternate methods of preserving the subvalvular apparatus, correct MS, anticoagulation, anti-inflammatory measures, and equal sutures.

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