Clinicopathological insights from early structural valve deterioration of a surgical and transcatheter valve-in-valve mitral bioprotheses

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Abstract

Introduction: Transcatheter mitral valve replacement (TMVR) is indicated in case of degenerated bioprosthesis in high-risk patients. However, durability of these valves still represents an important issue.

Methods: Early severe structural valve deterioration of a mitral porcine surgical bioprosthesis and of a subsequent bovine TMVR, both at 4 years follow-up, is here presented.

Results: Gross, histopathologic, and X-ray examination revealed massive calcification of both devices and fibrous tissue overgrowth involving the TMVR stent.

Conclusions: Careful clinical evaluation and strict follow-up are mandatory to identify early signs of dysfunction and to intervene in a timely manner.

KEYWORDS
cardiovascular pathology, valve repair/replacement

1 | INTRODUCTION

Structural valve deterioration (SVD) is a well-known complication that involves bioprostheses within 10–15 years after implantation, with a prevalence of 35% for bioprosthetic mitral valve replacement (MVR). The gold-standard therapy for this condition is still represented by surgical reoperation, but in case of inoperable or high-risk patients valve-in-valve transcatheter mitral valve replacement (TMVR) has been introduced as the alternative therapy. Nevertheless, it has been recently demonstrated that percutaneous heart valves may undergo SVD similarly to surgical bioprostheses. Herein, we report the results of pathologic analysis of both surgical bioprosthesis and subsequent valve-in-valve TMVR affected by early SVD.

2 | CASE REPORT

2.1 | Clinical data

In 2009, a 55-year-old woman with diabetes, thalassemia, and hyperuricemia underwent surgical MVR with a 29 mm porcine Epic Mitral Valve (St. Jude Medical) for rheumatic mitral valve disease...
causing severe stenosis and moderate–severe regurgitation at our institution. The decision to implant a xenograft was based on serious concerns over patient compliance to the anti-coagulation regimen and was also influenced by patient choice. The postoperative period was uneventful, and the patient was discharged with oral anticoagulant therapy for the first 3 months, and then with antiplatelet therapy, as recommended. Four years later, she came back with signs of heart failure and evidence of increased mitral gradients (50/27 mmHg, effective orifice area: 0.7 cm²) and severe calcification of the prosthetic cusps at the computed tomography (CT), without signs of thrombosis. After Heart-Team discussion, the patient was scheduled for trans-apical valve-in-valve (ViV) TMVR due to severe comorbidities (high surgical risk: STS score 14.2%, especially due to severe pulmonary arterial hypertension, previous cardiac surgery, and urgent indication) and also for patient’s choice. A 29 mm Edwards Sapien XT valve (Edwards Lifescience) was implanted. The postoperative period was uneventful, and the patient was discharged with acetylsalicylic acid associated with warfarin as antithrombotic strategy. Echocardiography at discharge demonstrated slightly increased trans-prosthetic gradients (23/11 mmHg), without paravalvular leak. Clinical and echocardiographic 1-year follow-up confirmed good prostheses function. Four years later, the patient was admitted again for acute heart failure. A trans-thoracic and trans-esophageal echocardiography showed severe mitral ViV prosthesis SVD. In particular, Sapien XT cusps appeared thickened, hyper-echogenic and unpliable leading to severe mitral stenosis (medium gradient: 19 mmHg; planimetry area at 3D imaging: 0.5 cm²) and moderate regurgitation. Angio-CT revealed extensive conal-shaped calcifications involving both the mitral prostheses and the subvalvular apparatus (Figure 1). Surgical reoperation with removal of the two prostheses and the implantation of a 31 mm Epic valve was considered the only therapeutic chance despite the society of thoracic surgeons predictive risk of mortality 30.5%. Visual inspection revealed: dystrophic calcification of the transcatheter valve, in particular of its posterior cusp; fusion of papillary muscles’ apex with calcific degeneration of the posterior one and fusion of the Sapien XT stent with both papillary muscles. At 2-year follow-up she is still in good clinical conditions, without signs of functional impairment.

2.2 | Pathological examination

Explanted valves were fixed in 10% neutral buffer formalin and examined by two experienced cardiovascular pathologists/biologists (C. B., M. D. B.). Before processing, the two valves were photographed and radiographed, to identify any frame fractures and calcification of the cusps. The cusps of the Epic bioprosthesis were mashed in open position and characterized by massive dystrophic calcification and tears in the commissures and in the belly, due to both the iatrogenic effects of the ViV prosthesis implantation and the calcium-related valve degeneration (Figure 2). The X-ray calcium score was 4/4. The Sapien XT ViV bioprosthesis showed nodular calcifications of the cusps’ surface, especially in the posterior one, whereas the commissures were free from calcific deposits. Moreover, fibrous tissue overgrowth involved the metallic stent and the ventricular surface of the posterior commissure. The X-ray calcium score was 3/4.

Samples of the Epic surgical mitral valve and of the Sapien XT bioprosthesis cusps, in correspondence of nodular calcific deposits underwent histological investigation with Haematoxylin–eosin, Azan Mallory Heidenhein modified, Elastic Weigert-van Gieson, Alcian blue-PAS, and von Kossa stains. In the cusps of both the Epic and Sapien XT bioprostheses conspicuous, intrinsic nodular calcific deposits were found; collagen fibers, close to mineralization deposits, were disrupted and not oriented.

3 | DISCUSSION

Early occurrence of severe SVD both in a porcine-stented surgical bioprosthesis and then in a bovine TMVR device is herein reported. Patient’s age is recognized to represent a strong risk factor for a limited valve longevity, despite advances in fixation and anti-mineralization processes. In addition, it is well-known from data of surgical MVR that prostheses in mitral position have a higher rate of degeneration than those in aortic position, because of their exposition to a systolic pressure gradient that increases hemodynamic stress.

In contrast of the previous St. Jude mitral valve, the Biocor valve, the Epic bioprosthesis is treated with Linx AC technology to improve long-term performance and valve durability. Analyses of the Linx AC treatment have demonstrated resistance to calcification by extracting lipids, reducing free aldehydes, minimizing cholesterol uptake, and stabilizing leaflet collagen. Lehmann et al. reported freedom from SVD of 95.8 ± 1.5% after 5 years and of 93.8 ± 2.4% after 10 years in Epic valves. However, this was in a cohort of patients with...
a mean age of 73 years. Our report confirms that implantation of biological valves in patients <65 years is associated with early valve degeneration, despite advanced anticalcification treatments.

As far as transcatheter bioprostheses are concerned, limited data exist regarding their application for patients with failed MVR. Some of the larger series of TMVR does not report any structural valve degeneration, but their results are limited to 1-year follow-up. In this case we have reported degeneration of TMVR after 4 years. Thus, a longer term follow-up of TMVR procedures may bright to light more cases of valve failure. Besides classical issues of anticalcification treatment and patient-related risk factors, additional device-related factors need to be discussed to explain TMVR SVD. Microscopic lesions as collagen fiber fragmentation and disruption, despite normal macroscopic cusps appearance, immediately after valve deployment, probably due to crimping/deployment procedures, have been already reported in the literature. It is difficult to say at the present time whether these lesions will have an impact on prosthesis durability, but long-term data of TVMR will be helpful. Another possible explanation for the Sapien XT early SVD can be its suboptimal hemodynamic condition due to the “tube graft” shape created by the ViV procedure in the left ventricle: in fact, the second valve continuously holds open the first one, creating a “tube graft” into the subvalvular apparatus and in some cases interfering with the left ventricular outflow tract. Possible consequences can be represented by suboptimal (as in our case) or high residual gradients, which may have a significant impact for valve durability. Furthermore, the transcatheter valve showed fibrous tissue overgrowth (or “pannus”), especially on the ventricular surface of the posterior commissure. Pannus can form as part of a host’s reaction to procedural trauma, a foreign body, or as the end product of organized thrombus formation. In our case, pannus involved the posterior commissure, while anterior cusps and commissures were unaffected. The anterior part of the valve faces the left ventricle outflow tract where the blood flow runs at a higher velocity, probably preventing thrombus deposition and consequent pannus formation. In contrast, in the posterior part blood flow is likely to be of lower velocity and without clear run-off, favoring thrombus deposition. Despite no signs of thrombus formation, it might organize as fibrous pannus, as to reduce cusps mobility. We can suggest that in our case the combo antithrombotic therapy was not enough to prevent its formation.

**CONCLUSION**

In conclusion, early SVD after mitral ViV is a potential occurrence, especially in young patients. Therefore, a strict clinical and echocardiographic follow-up is mandatory to identify this complication and to intervene in a timely manner.
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CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

ETHICS STATEMENT
This manuscript and all its content meet the ethical guidelines, including adherence to the legal requirements of the study country. Patient’s informed consent for the procedures and for data collection for scientific purposes was always collected.

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