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Case Series

A Case Series of Proliferative Deterioration in Adjacent Mitral Valve Tissue after Mitral Transcatheter Edge-to-Edge Repair in Patients with Degenerative Mitral Regurgitation

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ABSTRACT

There has been growing success in treating patients with functional mitral regurgitation (FMR) due to the expanding role of mitral transcatheter edge-to-edge repair (mTEER) systems. While similar success exists for mTEER in higher, or greater, surgical risk patient with degenerative MR (DMR), clinical and technical markers of success have not reached the levels seen in FMR patients. In this case series we will examine cases of DMR treated with the commercially available MitraClip system who later developed recurrence of 3+, or greater, mitral regurgitation (MR).

We present three cases of recurrent DMR and postulate the continued proliferation of degeneration can be attributed to the flagpole effect. This effect derives its name from the deterioration found at weak points along a flag as it connects to the flagpole tethered on one side. The damage is caused by the chronic effects of adjacent pressure loading placed by excess forces at the weak points of the flag in its attachment to the fixed flagpole. In the transcatheter mitral space, we propose the Waggoner-Flagpole Effect (WFE) as an etiology for proliferation of degeneration in certain DMR patients post mTEER by tethering adjacent degenerative mitral segments with a fixation point causing excess loading pressure on neighboring diseased mitral tissue leading to premature and accelerated tissue breakdown.

Keywords: Mitral transcatheter edge-to-edge repair . MitraClip . Waggoner-Flagpole Effect . Degenerative mitral regurgitation . Mitral regurgitation.

Introduction

The results of the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional MR (COAPT) trial and the Endovascular Valve Edge-to-Edge Repair Study II trial (EVEREST II) led to an expanding role for mitral transcatheter edge-to-edge repair (mTEER) systems. Successful implantation rates within these two trials were excellent at 96-98% of cases [1,2]. Closer inspection of the EVEREST II trial shows lower success rates for patients with degenerative MR (DMR) compared to those with functional MR (FMR). Freedom from death, mitral valve surgery, and grade 3-4+ MR were similar between mTEER and surgical patients with FMR. However, for DMR patients, rates were significantly lower with only 56% of these patients meeting the primary endpoint compared to 82% in surgical arm patients [1]. Many patients with DMR have a component of fibroelastic deficiency (FED) with the most severe cases falling under the Barlow's disease diagnosis. Conventional surgery can be difficult due to the co-existing dilated annulus, redundant myxomatous tissue, chordal elongation, and/or chordal rupture making many of these patient poor

surgical candidates [3]. The presence of a dilated annulus, redundant myxomatous tissue, chordal elongation, and/or chordal rupture also creates challenges for successful mTEER results [4-7].

We suggest, beyond technical reasons for suboptimal results, their exists anatomical and physiological explanations for the recurrent MR sometimes seen after mTEER therapy in patients with DMR. Many of these patients have some component of FED and through mechanical shear stress placed on tissue adjacent to the clip there is further myxomatous degeneration of the tissue leading to valve redundancy and mal-coaptation. We term this the Waggoner-Flagpole Effect (WFE).

The Waggoner-Flagpole Effect derives its name from damage found at weak points along a flag as it connects to the flagpole. The damage is caused by the chronic effects of wind placing excess forces at such points [8]. In the mitral space, the flagpole can be likened to the mTEER device as they both create a fixation point. The flag can be likened to the adjacent mitral tissue with the weak points being the degenerated mitral valve tissue of which the failure rates can be exaggerated by the existence of FED.

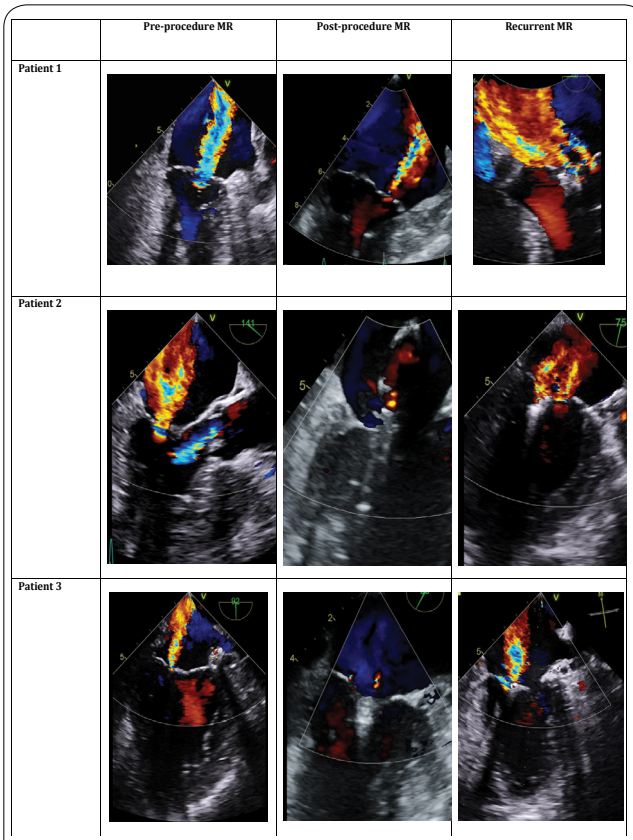

Figure 1: Two-dimensional transesophageal echocardiogram imaging in the mid-esophageal window of patient 1 *(top)*, patient 2 *(middle)*, and patient 3 *(bottom)* showing pre-procedural *(left)*, post-procedural *(middle)*, and recurrent MR (*right)*.

Case Presentation

Case 1:

The first case is an 87-year-old male with a past medical history significant for paroxysmal atrial fibrillation (PAF), hypertension, and hyperlipidemia presenting with progressive dyspnea on exertion and fatigue. Cardiac catheterization demonstrated non-obstructive coronary artery disease. Transesophageal echocardiogram (TEE) demonstrated preserved left ventricular ejection fraction, mild FED of the mitral valve tissue, severe (3 to 4+) DMR, with mild mitral valve prolapse involving the posterior leaflet (P2 segment). The structural heart team determined the patient to be high-risk based on advanced age, frailty, and favorable percutaneous anatomy. In addition, the patient had favorable percutaneous anatomy given the central leaflet pathology with adequate leaflet length and coaptation gap.

During the index procedure, a single XTW MitraClip was placed on the A2/P2 scallops and felt to have adequate leaflet insertions with healthy mitral tissue bridging. Subsequently, significant MR was seen lateral to the initial MitraClip. It was elected to place a second NT MitraClip at this time. This resulted in further reduction of MR with mild (1+) residual regurgitation noted on post procedure echocardiography imaging (Figures 1 and 2).

Approximately five months later, the patient presented with New York Heart Association (NYHA) class III heart failure symptoms. TEE at this time showed preserved left ventricular ejection fraction, stable MitraClip positioning, and severe (4+) MR adjacent to the index MitraClip devices. The MR was eccentrically directed with both the medial and lateral jets (Figures 1 and 2). Additionally, there was moderate mitral valve prolapse of the P1 and P3 leaflet segments (Figures 1 and 2).

Case 2:

The second case is an 86-year-old male with a past medical history significant for coronary artery disease (CAD), PAF with prior left atrial appendage closure by the commercially available Watchman device, hypertension, and hyperlipidemia who presented with progressive fatigue and worsening lower extremity edema. Cardiac catheterization demonstrated 70% stenosis of the proximal and mid left anterior descending artery with successful percutaneous intervention performed resulting in no residual stenosis. TEE demonstrated preserved left ventricular ejection fraction, moderate FED,

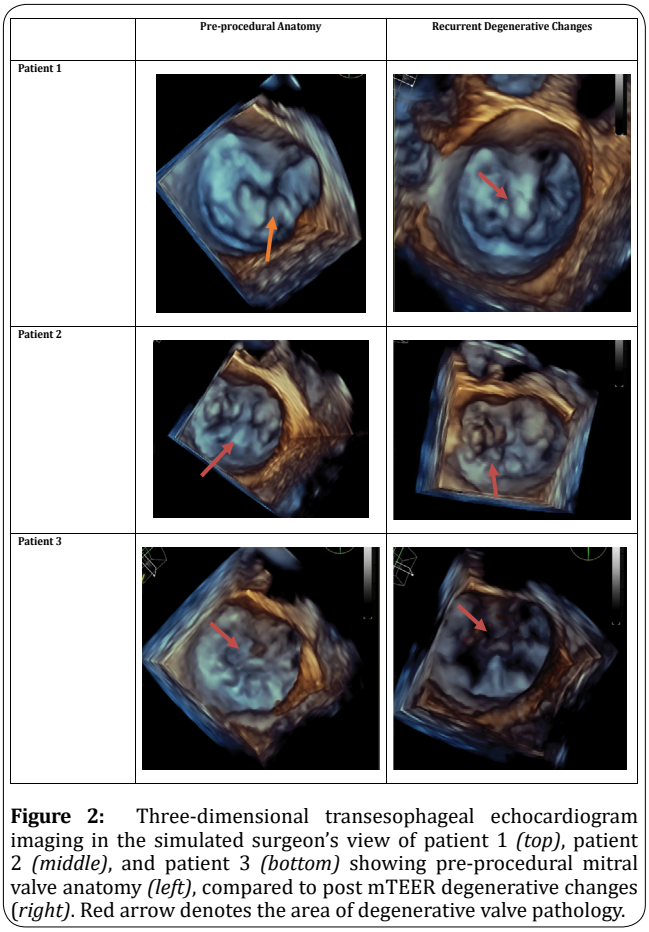

Figure 2: Three-dimensional transesophageal echocardiogram imaging in the simulated surgeon's view of patient 1 *(top)*, patient 2 *(middle)*, and patient 3 *(bottom)* showing pre-procedural mitral valve anatomy *(left)*, compared to post mTEER degenerative changes (*right)*. Red arrow denotes the area of degenerative valve pathology.

moderate to severe (3+) DMR, with mild mitral valve prolapse involving the P2 leaflet segment. The structural heart team determined the patient to be high-risk based on advanced age, frailty, history of transient ischemic attack (TIA), and favorable percutaneous anatomy. During the index procedure, a single NTW clip was successfully placed on the A2/P2 scallops resulting in mild (1+) residual regurgitation. Again, there was adequate insertion and tissue bridging during the index procedure (Figures 1 and 2).

Approximately ten months later, the patient presented with a NYHA IV heart failure symptoms. TEE at this time showed preserved left ventricular ejection fraction, stable MitraClip positioning on A2/P2, and recurrence of 3+ MR with a prominent medial and lateral jet. Moderate mitral valve prolapsing of the A1 and A3 anterior leaflet segments were also noted (Figures 1 and 2).

Case 3:

The final case is a 71-year-old female with a past medical history of CAD with coronary artery bypass graft, hypertension, hyperlipidemia with progressive dyspnea on exertion. Cardiac catheterization demonstrated complex CAD with a 70% proximal left anterior descending artery stenosis, 90% stenosed ostial calcified left circumflex artery, non-dominant right coronary artery, patent LIMA to LAD, and occluded SVG to OM. Successful percutaneous intervention was performed of both the proximal LAD and ostial left circumflex with no residual stenosis and TIMI 3 flow. TEE several months later demonstrated preserved left ventricular ejection fraction, mild FED, moderate to severe (3+) MR, and mild mitral valve prolapse of the A2 anterior leaflet segment. The structural heart team determined the patient to be high-risk based on advanced age, frailty, re-do sternotomy, history of left sided breast cancer, and favorable percutaneous anatomy given the central pathology with acceptable leaflet length and coaptation gap.

A single NTW clip was placed successfully on the A2/P2 scallops with acceptable leaflet grasping, insertion, and tissue bridging. This resulted in mild (1+) residual MR (Figures 1 and 2). Approximately four months later, the patient presented with worsening shortness of breath and NYHA III heart failure symptoms. TEE at this time showed preserved LVEF, stable MitraClip positioning on A2/P2, moderate to severe MR with a predominant medially directed jet (Figures 1 and 2).

Discussion

The cases discussed all demonstrate technical and clinical failures of mTEER in patients with concomitant 3 or 4+ DMR despite acceptable mTEER results during the index procedure. We posit these three cases of recurrent MR can be attributed to WFE. The presence of an mTEER device with surrounding degenerative mitral valve tissue and residual MR may allow shear stress to exert itself on the unhealthy tissue potentially leading to further degeneration and acceleration of DMR. This effect can be exacerbated by the co-existence of FED, present in each case discussed. Further research is needed to better understand mTEER failures in patients with degenerative MR. The concept needs further histologic validation at the tissue level to fully understand and describe this process. As technology continues to advance and more percutaneous options become available, better understanding of this anatomy may help lead to better treatment planning, especially in those at high or prohibitive risk for surgical options.

Conclusion

Continued deterioration of the mitral valve leaflets

after mTEER is a poorly understood phenomenon. Future research is needed to understand the physics and histology surrounding the mTEER failure in degenerative mitral valve tissue. We hope the cases presented here will bring light to this ever-growing problem and eventually lead to better techniques and technologies to combat it.

Acknowledgments

All authors contributed equally.

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