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Late Calcific Mitral Stenosis After MitraClip Procedure in a Dialysis-Dependent Patient

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Abstract

The EVEREST II trial investigated the MitraClip (Abbott Vascular, Menlo Park, CA) in patients with severe mitral regurgitation (MR) undergoing surgical procedures. Although mitral stenosis was not reported in this cohort, this trial excluded patients receiving dialysis. We report a case of a 43-year-old HIV-positive, dialysis-dependent patient with nonischemic cardiomyopathy and severe MR, who was considered at high operative risk because of frailty. She was treated with a MitraClip as part of the REALISM high-risk registry. Her symptomatic MR improved but severe symptomatic mitral stenosis developed 28 months after the MitraClip procedure. At that point, she was felt to be a better operative candidate but required open mitral valve replacement. Pathologic examination demonstrated significant calcification of the leaflets around the MitraClip devices.

The MitraClip (Abbott Vascular, Menlo Park, CA) procedure is under investigation as an alternative to surgical mitral valve repair for high-risk patients with mitral regurgitation (MR). Patients with end-stage renal disease represent a particularly high operative risk and have a well-documented history of calcific valvular disease. To date, no literature exists describing the safety of the MitraClip in this high-risk patient population.

A 43-year-old woman with HIV-associated cardiomyopathy and renal failure who had been receiving hemodialysis for 6 years presented with New York Heart Association class III heart failure and cardiac cachexia. She had a history of atrial fibrillation treated with catheter ablation and an implantable cardiac defibrillator. She was found to have severe functional mitral regurgitation (MR) with normal leaflet mobility and an ejection fraction of 25%. Because of her physical state, she was believed to be a high-risk operative candidate by her cardiologist, the physician treating her heart failure, and her cardiac surgeon. She was then enrolled in the nonrandomized high-risk registry of REALISM trial and underwent the MitraClip procedure with placement of 2 devices. She had a successful procedure with reduction in her MR from severe to mild and a mean mitral gradient of 7 mm Hg. She had dramatic symptom improvement with resolution of her dyspnea and cardiac cachexia. She regained her healthy weight and started daily exercise. Her serum calcium levels remained within normal limits and her serum phosphate levels remained elevated (6–8 mg/dL) despite

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treatment with oral phosphate binders. She was noted to have progressively worsening gradients across her mitral valve by echocardiography and ultimately presented 28 months after the MitraClip procedure with increasing dyspnea. Transesophageal echocardiography (TEE) demonstrated severe mitral stenosis (Fig 1) with a pulmonary artery systolic pressure of 90 mm Hg and an ejection fraction of 55%. At this point she was thought to be a better operative candidate and subsequently underwent a mitral valve operation. Intraoperatively, the 2 leaflets (A2 and P2 segments) were seen to be severely calcified around the MitraClip devices and the devices were unable to be extracted without damage to the A2 and P2 segments of the valve (Fig 2). She underwent placement of a 29-mm St. Jude mechanical valve (St. Jude Medical, St. Paul, MN), with preservation of the remaining cords, along with tricuspid valve repair and primary closure of her atrial septal defect. Postoperatively, she did well with no complications and acute correction of her pulmonary artery pressure. She was seen in follow-up at 4 months and was doing well.

Comment

The MitraClip procedure is based on Alfieri's technique, which involves suturing the anterior and posterior leaf-lets at the point of maximal regurgitation to reduce the regurgitant jet. Results after open Alfieri-type edge-to-edge repair have shown a small decrease in the mitral valve area without evidence of significant mitral stenosis [1]. The first edge-to-edge repair studies (EVEREST trials) examined the efficacy of a percutaneous device (MitraClip), which creates coaptation from the leaflet edges, to address regurgitation of the mitral valve [2]. In the EVEREST I and II trials, echocardiographic and hemodynamic measurements after MitraClip placement were examined and found to show no evidence of significant mitral stenosis both immediately after placement and at 12-month follow up [2, 3].

The EVEREST II trial demonstrated superior MR reduction with surgical intervention, whereas the MitraClip demonstrated a superior safety profile compared with open repair, although most of the benefit was due to a reduction in blood transfusion [3]. However, patients with creatinine levels greater than 3.0 mg/dL or those who received dialysis were excluded from both of these trials. Moreover, to our knowledge, no currently published studies have analyzed the durability of the surgical Alfieri repair in patients receiving dialysis.

Procedural success during MitraClip placement is defined by the reduction in MR by TEE. If this does not occur after single-clip placement, a second MitraClip is often placed in the area of greatest residual regurgitation. Before and after release of each device, a transvalvular gradient is measured by direct catheter measurements and by TEE to prevent the development of hemodynamically significant mitral stenosis. In our patient, there was no evidence of an elevated transmitral gradient at the time of first or second device placement, and the patient showed clinical and echocardiographic improvement for several months after clip placement.

The dystrophic calcification associated with end-stage renal disease has a known deleterious effect on cardiac valves, with a prevalence of events as high as 4.5% [4]. In particular, the

progression of aortic stenosis occurs more rapidly in patients with uremia [5]. This phenomenon is likely secondary to the derangement of calciumphosphate metabolism in this patient population, and the calcium-phosphate product has been shown to be the best predictor of valvular calcification in asymptomatic patients receiving hemodialysis [4]. This effect may even be partially reversible, as improvement in mitral stenosis after renal transplantation has been reported [6]. We propose that this mechanism may explain our patient's development of calcific mitral stenosis. Calcium deposition in this location only and not in the mitral annulus may be due to inflammation around the clip.

The ability to repair valves after the MitraClip procedure has been reported and is has high as 54% [7]. In this case, the patient's original mitral valve would likely have been amenable to repair, although she was felt to be at high operative risk at the time. However because of the development of calcific leaflet mitral stenosis after the MitraClip procedure, the patient required mitral valve replacement. It should be noted that conventional mitral valve annuloplasty for nonischemic MR has been shown to have a 16% recurrence rate at late follow-up (4 years) despite good early postoperative results [8].

Percutaneous edge-to-edge repair with the MitraClip is not a US Food and Drug Administration–approved procedure but is currently under investigation in highrisk patients. Preoperative renal dysfunction represents an independent and significant risk factor for morbidity and mortality after cardiac operations. Although percutaneous edge-to-edge mitral valve repair may be a reasonable choice in patients at high operative risk, the long-term sequelae of this technique are unknown in this patient population. In fact, based on our experience, we caution the use of the MitraClip in patients receiving dialysis, in which the risk of dystrophic calcification is higher. Further investigation of this procedure in patients who receive dialysis is warranted.

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Fig 1. Transesophageal echocardiography (TEE) at time of operation 28 months after MitraClip device implantation, demonstrating severe calcific mitral stenosis.

Fig 2.
(A) Intraoperative photograph of severely stenotic and calcified mitral valve 28 months after placement of 2 MitraClip devices for symptomatic MR. (B) Side view of Mitra-Clip after extraction, with adherent calcified leaflets. Suture marks posterior attachment. Both devices had similar calcification to the leaflets and were difficult to extract.