Repeat MitraClip Procedures
In Search of the Perfect Grasp*

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The MitraClip (Abbott Vascular, Santa Clara, California) procedure is simple in concept. A small “clip” with moveable arm and gripper elements is used singly or in multiples to grasp the leading edges of the anterior and posterior mitral leaflets, bringing them closer together and improving coaptation. Although the basic design of the MitraClip and catheter delivery system have not changed significantly since the first human implant in 2003, our understanding of MitraClip positioning and manipulation has improved considerably. Every knob on the MitraClip delivery system has a function that can improve clip alignment, orientation, and grasping. In addition, intraprocedural imaging of the mitral valve apparatus has advanced, especially with the availability of real-time 3-dimensional transesophageal echocardiography (TEE). The ultimate goal of any MitraClip procedure is to obtain a “perfect grasp” (Figure 1). In an ideal situation, both the anterior and posterior leaflets are clearly imaged on TEE, then they are securely grasped by the MitraClip and brought together as the clip is tightened. Despite the reliable mechanical performance of the MitraClip device, there are many procedural challenges to actually grasping the leaflets, especially in patients with severe mitral regurgitation (MR). By definition, the gap between leaflets is larger in severe MR. The leaflets themselves may flail with excessive motion, or they may be restricted in movement and highly tethered. There may be leaflet thickening, calcification, deep leaflet scallops or clefts, or potential mitral stenosis—all of which make grasping the leaflets more challenging. There can be inherent limitations to intraprocedural TEE imaging. Some patients have poor ultrasound “windows,” making visualization a challenge. Despite an adequate grasp, native leaflet pathology or ventricular function can change over time, affecting the durability of MitraClip repair. Finally, it is possible to lose leaflet insertion over time. This phenomenon has been given several names including “partial clip detachment” and “single leaflet device attachment” (SLDA).

As clinicians, we care about achieving a durable result with MitraClip therapy. Discussions regarding the management of patients with recurrent MR after MitraClip therapy began during the landmark EVEREST (Endovascular Valve Edge-to-Edge Repair Study) I and II trials. In these trials, clinical experience with the device was still early, and procedural outcomes showed a learning curve. In the EVEREST phase I clinical trial, 27 patients were enrolled with only 18 patients (67%) having ≤2+ MR at discharge, and 3 patients having partial clip detachment from 1 leaflet (1). In the EVEREST II trial, procedural efficacy improved with per-protocol success rates of 72% for the primary endpoint of freedom from death, surgery, or MR 3 to 4+. Partial clip detachment was also reduced to 9 of 184 patients (4.9%) randomized to MitraClip therapy (2). In the EVEREST trials, repeat MitraClip procedures were not allowed and procedural failures were treated with surgical intervention. Many patients in EVEREST II who were referred for surgery after MitraClip procedures had successful mitral valve repair, but others required mitral valve replacement. The need for replacement was related in part to baseline complex anterior mitral valve pathology and was not necessarily due to the previous MitraClip attempt or inadequate grasping per se (3). In recent real-world registries, the rates of
SLDA are low. In the ACCESS-EU (A Two-Phase Observational Study of the MitraClip System in Europe) study, a European prospective, multicenter, post-approval registry of 567 patients at 14 centers (71% with functional MR), 27 patients had an SLDA event (4.8%), with all but 1 diagnosed within 6 months of the index procedure. Of these 27 patients, 10 had additional MitraClip procedures, 6 underwent mitral valve surgery, and 11 had no additional therapy (4). Finally, in the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) MitraClip registry of 564 patients treated at 61 U.S. hospitals (86% with degenerative MR), the 30-day reported SLDA rate was only 1.1% (5).

In this issue of JACC: Cardiovascular Interventions, Kreidel et al. (6), from a high volume MitraClip center in Germany, report on their fascinating experience with 21 patients (of 410 total patients treated with MitraClip) undergoing a second MitraClip procedure for recurrent MR at a mean of 6.3 months after the index procedure. Patients in this series received an average of 1.4 clips, mostly placed centrally and medially along the mitral valve coaptation plane. The investigators present their results in the context of TEE findings at the time of the index procedure versus at follow-up. A novel aspect of their analysis is their introduction of the term “LLI,” referring to “loss of leaflet insertion.” They have defined LLI as loss of leaflet attachment or insertion into the clip arms in follow-up due to either of the following situations: 1) increased leaflet mobility at the grasping site (through possible leaflet tear or perforation); or 2) complete separation of the leaflet from the clip (partial clip detachment). If patients did not have any evidence of LLI, they were defined as having “adequate leaflet insertion.”

When analyzing their follow-up procedures, the main conclusions of the investigators are as follow: 1) although repeat MitraClip procedures are feasible, the success rate of repeat MitraClip procedures (61.9%) is lower than the index treatment success (90.8%); 2) patients who returned for repeat procedures with LLI had success rates of 25% (2 of 8) versus 85% (11 of 13) for those patients with adequate leaflet insertion; 3) survival is worse for those patients who require repeat procedures. It was encouraging that only 8 of 410 patients treated (1.95%) had evidence of LLI on follow-up, reinforcing that this is an infrequent event, much like SLDA as described in other registries.

An intriguing aspect of the report by Kreidel et al. (6) is that loss of leaflet insertion was only partially responsible for recurrent MR. The majority of patients in this series had functional MR (71.4%) with systolic heart failure and depressed left ventricular (LV) ejection fractions. Importantly, in the patients with adequate leaflet insertion who developed recurrent MR, LV volume increased substantially over time, supporting the idea that recurrent MR can be related to progressive LV dilation despite successful leaflet grasping. This underscores the adage that functional mitral regurgitation is a ventricular disease. It is also interesting that most repeat clips were placed lateral to the original clips. This would also suggest progressive LV dysfunction with annular septal lateral dilation as opposed to primary clip failure. Why some patients developed progressive LV enlargement over time despite a successful index procedure, whereas others did not, is not known.

In summary, this report is of importance because there is a paucity of data available on the outcomes of patients who undergo repeat MitraClip procedures. In the final analysis, it would appear that recurrent MR after MitraClip procedures could be due to multiple mechanisms in spite of adequate leaflet grasping at the initial procedure. Patients who develop recurrent MR due to LLI likely have inherent complex leaflet pathology to begin with, and this may predispose them to progressive leaflet degeneration over time. Of course, obtaining the best possible grasp at the index procedure is of paramount importance and the investigators provide some clear examples of how to measure leaflet insertion quantitatively. At our center, we have a “grasp vote” as a team, and
only release the clip when all participants in the procedure (echocardiographer and interventionalist) agree that the grasp is adequate. The decision to release the MitraClip depends on a collective review of quantitative techniques to measure leaflet insertion in the LV outflow tract, bicommissural, 4-chamber, 3-dimensional, and occasionally transgastric echocardiographic views. We also record the entire grasping sequence (up to a 15-second acquisition loop) for subsequent review, frame by frame if needed, to assess leaflet insertion. Finally, we must all remember that MR can arise from numerous aberrations of the mitral valve apparatus, and that durable reduction of MR will depend not only on adequate leaflet grasping, but also on careful attention to guideline-directed medical therapy for heart failure, resynchronization therapy when appropriate, maintenance of sinus rhythm, and preservation of LV function.

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