Acute Mitral Regurgitation Secondary to Papillary Muscle Tear

Is Transcatheter Edge-to-Edge Mitral Valve Repair a New Paradigm?

Javier A. Valle, MD, MSCS; Rhonda L. Miyasaka, MD; John D. Carroll, MD

Severe mitral regurgitation (MR) secondary to papillary muscle tear is an infrequent but overwhelmingly morbid and often fatal complication of acute myocardial infarction occurring in 1% to 3% of patients.[1] In-hospital mortality without surgical correction can approach 80%[2]; however, even with surgical correction, papillary muscle tear carries a mortality rate between 19% and 53%.[2–5] While consideration of emergent surgical correction continues to be indicated[6] with undeniable impact on mortality, outcomes have remained poor over time, with a mortality of nearly 40% in a contemporary evaluation of clinical outcomes.[5] Additionally, over 50% of patients with severe MR complicating acute myocardial infarction are declined for surgical intervention because of ongoing instability, shock, or the presence of comorbidities that make surgery of prohibitive risk.[2] Thus, although mitral valve repair is necessary for these patients, surgical correction remains an imperfect and incomplete solution.

The emergence of percutaneous interventions for valvular heart disease have offered opportunities for many patients that previously were without therapeutic options.[7–9] Specifically, in patients with severe chronic MR with elevated surgical risk, the development and advancement of the MitraClip has offered an alternative to high or prohibitive-risk surgical intervention. With MitraClip as a viable alternative to mitral valve replacement or repair for high-risk patients with chronic MR, is it time to consider its possible use in the setting of those high-risk patients with acute MR secondary to myocardial infarction? If so, an optimal approach for decision-making and management of these patients needs to be developed, incorporating procedural aspects and considerations of percutaneous versus surgical repair.

We describe a clinical case of a patient with severe MR after acute myocardial infarction and discuss the management for such patients in the current era of percutaneous intervention for valvular heart disease.

Case Presentation

An 84-year-old man with a past medical history of remote coronary artery bypass grafting, hypertension, and dyslipidemia presented with acute-onset chest pain and inferior ST-segment elevations. He underwent emergent angiography, demonstrating occlusion of a saphenous vein graft to the posterior descending artery (Figure 1; Movie I in the Data Supplement) and proceeded to receive percutaneous intervention to the vein graft with a drug-eluting stent. Despite revascularization, on hospital day 2, the patient developed progressive respiratory distress, and echocardiography demonstrated severe MR with a partial tear of the posteromedial papillary muscle and a resultant large eccentric posteriorly directed regurgitant jet (Figure 2; Movie IIA through IIC in the Data Supplement) in the setting of mildly reduced left ventricular function. The patient underwent aggressive medical management to achieve stability but, however, developed oliguric renal failure, hepatic dysfunction, and hypoxic respiratory failure. Because of ongoing instability and progressive multiorgan failure, he was transferred between hospitals for evaluation of mitral valve intervention.

On transfer, the patient was evaluated by interventional cardiology and cardiothoracic surgery. Based on history of prior sternotomy, multiorgan failure, and the presence of a patent left internal mammary artery graft, the patient was felt to be at high risk for surgical intervention. After discussion with the patient and family, the decision was made to attempt percutaneous edge-to-edge mitral valve repair with the MitraClip system.

The patient was urgently brought to the cardiac cath laboratory and intubated for escalating oxygen requirements. Fluoroscopy and transesophageal echocardiography (TEE)–guided transseptal puncture was performed crossing the septum primum in a posterior location that yielded a midatrial position for the guiding catheter, 4 cm from leaflet coaptation. Left atrial pressure was measured at baseline, with a mean left atrial pressure of 29 mm Hg with V waves of 59 mm Hg.

TEE-guided MitraClip percutaneous edge-to-edge mitral valve repair was performed, deploying 3 clips in a zipper approach and producing a single residual lateral orifice. The first clip was deployed at the most medial aspect of the MR jet approximating the edge of the flail segment to facilitate delivery of the following clip, which was placed at the lateral aspect of the jet. Repeat TEE measurements demonstrated a

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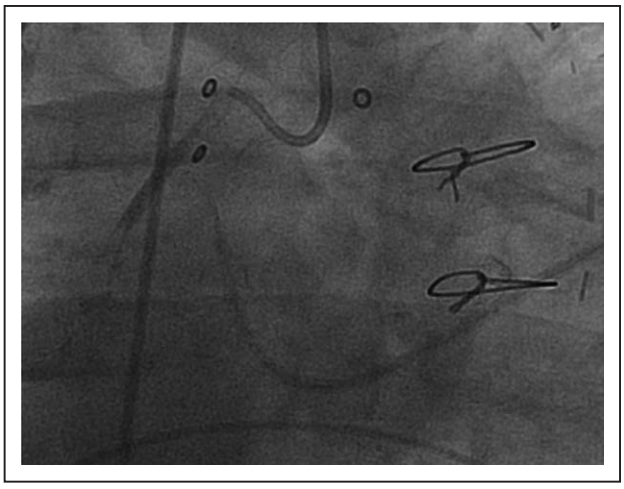

Figure 1. Occluded saphenous vein graft to posterior descending artery.

gradient of 5 mm Hg across the mitral valve with residual 2+ MR. Finally, a third clip was placed between the medial and lateral (first and second) clips, with significant reduction in echocardiographic MR (1+) and no change in mitral gradient (Figure 3; Movie IIIA through IIIC in the Data Supplement). Hemodynamic evaluation confirmed significant improvement in left atrial pressure, with a reduction to a mean pressure of 14 mm Hg and a V wave of 20 mm Hg. Furthermore, after clip placement, the partially torn papillary muscle appeared to have been stabilized, as demonstrated by significantly reduced mobility of the papillary muscle by echocardiography (Figure 4; Movie IVA and IVB in the Data Supplement).

Discussion

Surgery Has Been the Only Treatment for Correcting Severe MR Involving Papillary Muscle Dysfunction Post-MI. What Alternative Therapeutic Strategies Might be Considered?

Dr Carroll: In this patient, we all felt that he had prohibitive risk for surgery in his state upon transfer, and therefore, alternatives should be considered. A traditional alternative approach would have involved intra-aortic balloon counterpulsation or other forms of LV assistance. This combined with nitroprusside might have stabilized the patient and improved his chances of surviving surgery. Yet this approach may or may not have succeeded and, furthermore, he still would have been a man of advanced age with a prior sternotomy, and with a patent left internal mammary arterial graft. Therefore, we considered his case in the context of currently approved indications in for MitraClip in the US The mechanism of his mitral regurgitation could be considered degenerative with a flail segment. He was severely symptomatic and in the final stages of decompensated heart failure with multiorgan dysfunction. Despite the lack of predictability from this transcatheter approach being used in a partial rupture of a papillary muscle, we thought this was his only hope of survival. We were encouraged by his overall LV systolic function not being severely depressed. Reduction in the severity of his mitral regurgitation therefore had a good chance of changing his clinical course. After long discussions with the patient and his family we proceeded.

What Have Been the Outcomes for Patients Like This Undergoing Surgical Mitral Valve Repair? Have These Patients Been Included in Surgical Case Series and Analyses?

Dr Valle: Surgical outcomes for severe mitral regurgitation following acute myocardial infarction have consistently been suboptimal with high rates of mortality (Table).[2,5,10–16] Furthermore, many patients (like this one) are considered to be too high risk for surgery[2] because of their clinical instability and multiorgan failure. In this patient, with a percutaneous approach, the perils of initiating cardiopulmonary bypass in such an unstable patient was able to be avoided, as well as the sequelae of a repeat sternotomy for this patient with previous coronary artery bypass grafting and patent left internal mammary conduit to his left anterior descending.

Are There Other Case Reports of MitraClip Being Used to Treat Severe MR in the Setting of Papillary Muscle Dysfunction-Rupture? How Is This Case Unique?

Dr Carroll: Yes, there have been isolated case reports, and we studied these before performing this procedure with the caveat

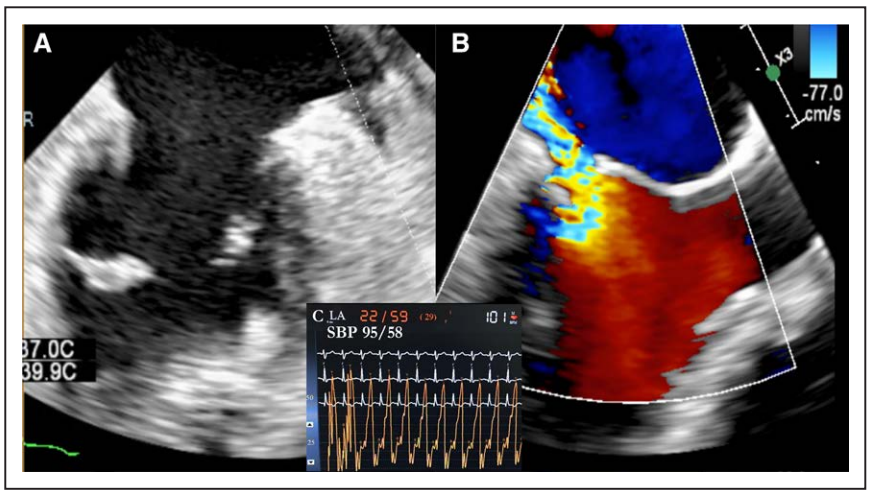

Figure 2. Partial rupture of posteromedial papillary muscle (**A**) with severe mitral regurgitation (**B**) and left atrial pressure at baseline (**C**).

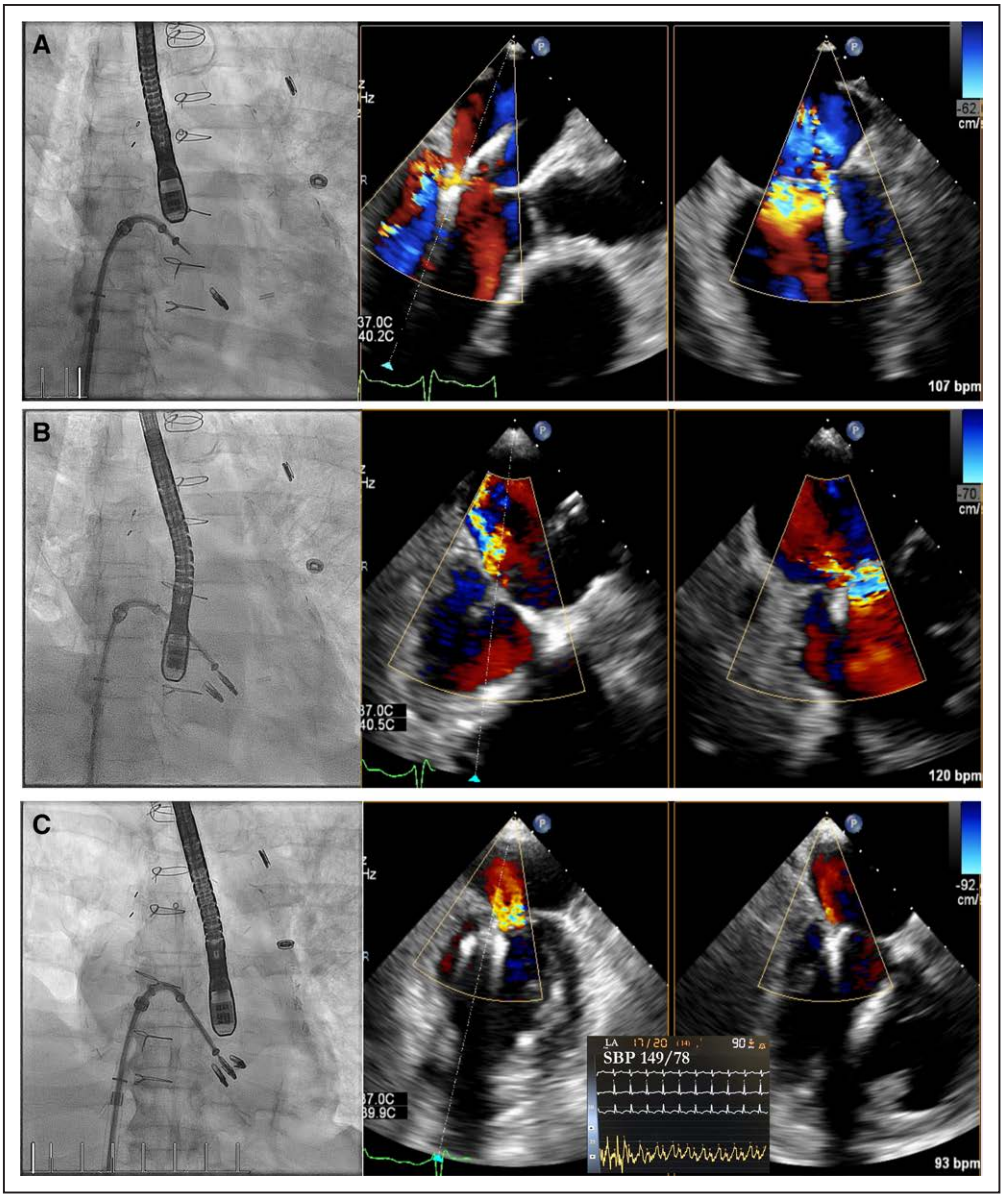

Figure 3. Successive clip deployment: Zipper approach (**A**, fluoroscopy and doppler transesophageal echocardiography [TEE] after first clip deployment; **B**, fluoroscopy and doppler TEE after second clip deployment; **C**, fluoroscopy and doppler TEE after third and final clip deployment).

of publication bias: successful outcomes are much more likely to be reported than failures. There have been cases described of MitraClip being used to treat acute severe MR,[17–22] with three cases in the setting of papillary muscle rupture with cardiogenic shock following acute myocardial infarction.[17,19,20] Between 1 and 3 MitraClips were placed and the patients recovered. The first case reported was from Turkey, and the other two were from German and Canadian centers.

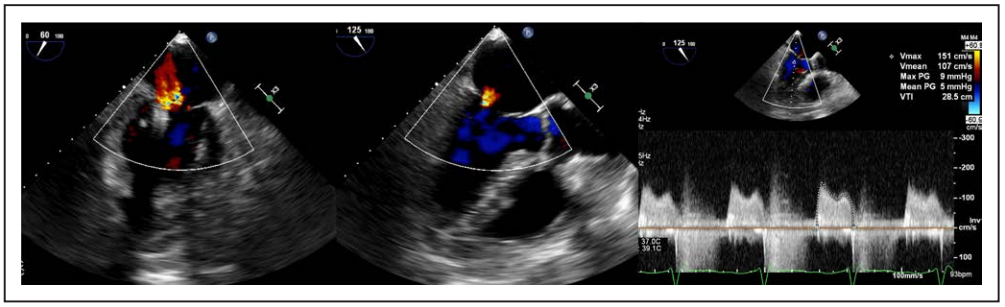

Figure 4. Final transesopheageal echocardiographic evaluation of mitral regurgitation.

Table. Outcomes of Mitral Valve Surgery for Severe Mitral Regurgitation After Acute Myocardial Infarction

Authors	Year of Publication	Number of Patients Undergoing Surgery	Patient Population	Surgical Timing	Outcome
Nishimura et al[10]	1986	7	Patients undergoing surgery for papillary muscle rupture, case series	100% within 4 days	42% mortality at 1 y
Kishon et al[11]	1992	22	Patients undergoing surgery for papillary muscle rupture, case series	19 (87%) within 3 wk	27% mortality at 30 days; 47% mortality at 7 y
Thompson et al[2]	2000	43 patients (of 1190 patients with post-AMI cardiogenic shock, 98 with severe MR)	Post-MI patients with cardiogenic shock (SHOCK registry)	NA	39% in-hospital mortality
Gillinov et al[12]	2001	482	Patients undergoing valve surgery for ischemic MR, Cardiovascular Information Registry	95 (19.7%) within 14 d	11% in-hospital mortality; 23% mortality at 1 y; 45% mortality at 5 y
Minami et al[13]	2004	6	Patients undergoing valve surgery for papillary muscle rupture	6 (100%) within 19 days	33% perioperative mortality
Russo et al[15]	2008	54	Patients undergoing valve surgery for papillary muscle rupture	48 (83%) within 30 days	18.5% perioperative mortality; 35% mortality at 5 y
Lorusso et al[14]	2008	126 (of 279 patients)	Patients undergoing emergent surgery for acute severe mitral regurgitation, multicenter study	100%	27.3% perioperative mortality (30 days); 40% at 3 y
Schroeter et al[5]	2013	28	Patients undergoing surgery for papillary muscle rupture	25 (89%) within 21 days	39% mortality at 30 days
Bouma et al[16]	2014	48	Patients undergoing surgery for papillary muscle rupture	100%	Intraoperative mortality 4.2%; In-hospital mortality 25.0%

AMI indicates acute myocardial infarction; MI, myocardial infarction; MR, mitral regurgitation; and SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock.

This case is unique in several regards. This case adds to a small but growing base of evidence supporting the use of MitraClip in acute mitral regurgitation, and specifically in the setting of papillary muscle tear. Additionally, having been performed in the United States, as mandated by the Food and Drug Administration (FDA) and Centers for Medicare & Medicaid Services (CMS), this patient's data were entered in the STS-ACC TVT Registry (The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy). This case also was performed using 3D TEE imaging with fusion of ultrasound and fluoroscopic images to provide procedural guidance. Finally, this case demonstrates the successful implantation of three MitraClips that not only reduced the degree of MR but also stabilized the partial rupture of the papillary muscle by restricting the motion and torque placed on the muscle by the flail leaflet.

How Does Having 3D TEE Imaging and Echocardiographic-Fluoroscopic Fusion Help in the Performance of MitraClip?

Dr Miyasaka: We have found that the use of 3D TEE imaging and echocardiographic-fluoroscopic fusion allows for more accurate and timely feedback during the guidance of MitraClip implantation.

While 2D echocardiographic imaging is the standard approach for the majority of the procedure, this modality provides only a small slice of information compared to the complexity of the three-dimensional interactions of the MitraClip system with left atrial structures and the mitral valve apparatus. Having a full three-dimensional understanding of the pathology was crucial in the current case, as we needed to minimize unnecessary interactions with the mitral valve and subvalvular apparatus to avoid destabilizing the partially ruptured papillary muscle. Furthermore, when relying on 2D imaging alone, there is inherent lag time during adjustment of the probe, omniplane angle, and viewing sector to follow the catheters as they slide in and out of our imaging plane. With the use of 3D TEE, we are able to recreate the surgeon's view of the mitral valve, including key left atrial structures in addition to the valve itself, providing continuous feedback during the procedure. This reliable and reproducible working view can be used for multiple portions of the procedure, including initial advancement of the wire into the pulmonary vein after transseptal puncture, crossing the interatrial septum with the guide catheter, and advancing the MitraClip toward the mitral valve while clearing the warfarin ridge.

Similarly, echocardiographic-fluoroscopic fusion facilitates communication between the echocardiographer and interventionalist. Using EchoNav (Philips HealthCare, Best, the Netherlands), the ability to overlay echocardiographic and fluoroscopic images allows for real-time feedback and response between the echocardiographer and interventionalist. Catheter manipulation in relation to probe and image plane position (and vice versa) can be visually demonstrated despite the complex geometric relationships that occur within the heart. Fusion of the echocardiographic imaging familiar to the echocardiographer with the fluoroscopic imaging most familiar to the interventionalist can facilitate improved communication about spatial relationships and decision-making

on approaches for the complex motions and steps required in these procedures (ie, determining optimal transseptal location and crossing the valve plane). Additionally, this fusion allows for anticipation of the fine imaging adjustments needed to guide the procedure, allowing the case to proceed as expeditiously as possible. This was vitally important in the current case given the critical illness of the patient.

MitraClip Is Thought of As an Elective Procedure in Stable Patients. How Was the Procedure Impacted in This Very Different Clinical Situation? What Were Your Concerns at the Start of the Procedure?

Dr Carroll: We decided to proceed with emergency MitraClip therapy immediately upon transfer. Patients who have entered multiorgan failure and approaching the need for intubation are in danger of further rapid deterioration. A strategy of stabilization could have been tried but we felt that treating the primary cause of the patient's deterioration had the best chance of success. We drew from our experience in aortic stenosis that when patients are admitted with refractory pulmonary edema with cardiogenic shock, it is key to reduce the severity of the underlying valvular abnormality, that is, perform emergency aortic balloon valvuloplasty, since other supportive measures are likely to fail.

He was unstable in the cardiac catheterization laboratory primarily from difficulties in oxygenation. The cardiac anesthesiologist employed bursts of high positive pressure ventilation to maintain him at a low normal degree of oxygenation. We attempted to reduce his pulmonary edema with intravenous diuretics but these had minimal effect until we started reducing the severity of his mitral regurgitation.

I was concerned that we may have considerable difficulty in grasping the leaflets and that we would then fail to reduce his mitral regurgitation. We therefore started with placing a clip where the distance between the two leaflets was not too great. This foundation clip then allowed us to place a clip where the mitral regurgitate jet was largest. We received immediate intraprocedural feedback, with each MitraClip placement improving his systemic blood pressure, ultimately allowing us to reduce and subsequently eliminate vasopressor support.

A second concern was that we could convert the partial rupture to a complete rupture by navigating the clip delivery system unto the left ventricle and trying to grasp leaflets. Complete rupture could make the procedure technically impossible and also lead to the immediate death of the patient. Having 3D visualization greatly helped in navigating the clip delivery system. Having image fusion allowed me to use fluoroscopy in avoiding going too deep into the left ventricle.

At the End of the Procedure What Were the Major Echocardiographic Findings and What Was Unexpected?

Dr Miyasaka: At the end of the procedure, the patient demonstrated only 1+ residual mitral regurgitation. This was greater MR reduction than what was expected given the severity of the valvular abnormality. Furthermore, we noticed that the MitraClips seemed to have stabilized the partially ruptured papillary muscle. At the start of the case, we noticed that with each systole, the anterior leaflet would flail into the left atrium and pull on the partially ruptured papillary muscle. There was concern that, over time, this strain would eventually lead to a complete tear. After the MitraClips were placed, it appeared that the anterior leaflet gained support from the posterior leaflet, thereby redistributing the tension off of the papillary muscle. Visually the papillary muscle appeared more stable, and we hope that this will clinically translate into a decreased chance of progression to a complete rupture. The MitraClips essentially served a dual purpose of mitral regurgitation reduction and papillary muscle stabilization.

What Further Steps Are Needed for This Patient? Should Patients Like This Be Considered for Subsequent Mitral Valve Surgery, or Should This Be Considered a Stand-Alone Procedure?

Dr Valle: This is a critical question that must be addressed on a patient-to-patient basis until more definitive data exist to guide management. Whether these patients may require a surgical intervention for their valvular disease after initial stabilization with a percutaneous approach is just one of the questions that call for collection of these cases and experiences, with subsequent analysis of acute and medium-term outcomes in order to optimally inform future care.

Case Studies Are Useful but Anecdotal. How Can the Cardiovascular Community Gather Evidence Regarding This Treatment Option's Success, Failures, Complications, and Outcomes?

Dr Carroll: The STS-ACC TVT Registry[23,24] is a vehicle for the accumulation of comprehensive data on all US commercial MitraClip cases. For these unusual cases the TVT registry provides a means to assemble an adequate number of cases from multiple centers that represent a comprehensive overview of the US experience including both in-hospital but also medium-term outcomes. Linkages with the CMS database increase the likelihood of capturing longer-term outcomes include the rehospitalization rates and crossover to surgery. Thus, a multicenter experience may be accumulated to develop and distribute best practices. Finally, in alignment with recent FDA draft guidance document,[25] these registry data may be used as real-world evidence to support regulatory decision-making. Otherwise individual case studies as this one will serve only a limited educational focus and no regulatory purpose. Single centers will never accumulate an adequate case series to identify and share best practices, facilitate quality improvement throughout the cardiovascular community, and contribute to the regulatory process of expanding indications of approved devices.

Clinical Outcome

Post-procedure, the clinical improvement was immediate and dramatic, with improved hemodynamics and diuretic-responsiveness. The patient was extubated the day of the procedure with minimal oxygen requirements. Repeat transthoracic echocardiography demonstrated ongoing significant reduction in mitral regurgitation to a mild degree. Over the next 3 days, his acute kidney injury and hepatic dysfunction resolved.

He was transferred to a short-term rehab center and within a week was discharged to home on dual antiplatelet

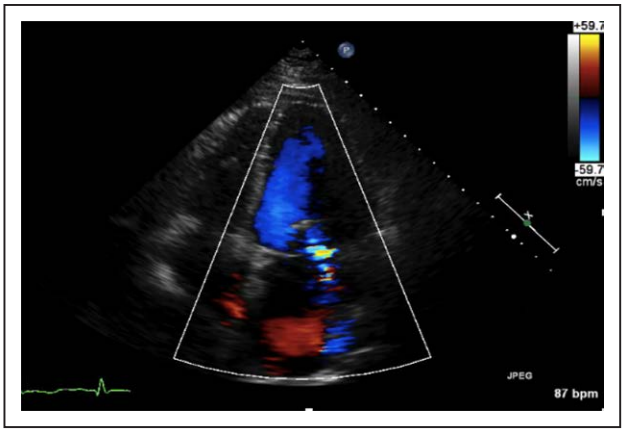

Figure 5. Follow-up transthoracic echocardiographic evaluation of mitral regurgitation.

therapy with aspirin and clopidogrel, as well as atorvastatin, metoprolol, lisinopril, and 80 mg of furosemide daily. At 6 weeks' follow-up, he has resumed some of his normal activities as a rancher with New York Heart Association Class 2 symptoms and 1 to 2 plus residual MR on echocardiography performed 1 month post-discharge (Figure 5; Movie V in the Data Supplement). He still requires diuretic therapy to be free of edema.

Disclosures

Dr Carroll receives research support from and serves as a consultant for Philips HealthCare. Drs Valle and Miyasaka report no conflicts.

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Is Transcatheter Edge-to-Edge Mitral Valve Repair a New Paradigm?

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Severe mitral regurgitation (MR) secondary to papillary muscle tear is an infrequent but overwhelmingly morbid and often fatal complication of acute myocardial infarction occurring in 1% to 3% of patients.[1] In-hospital mortality without surgical correction can approach 80%[2]; however, even with surgical correction, papillary muscle tear carries a mortality rate between 19% and 53%.[2–5] While consideration of emergent surgical correction continues to be indicated[6] with undeniable impact on mortality, outcomes have remained poor over time, with a mortality of nearly 40% in a contemporary evaluation of clinical outcomes.[5] Additionally, over 50% of patients with severe MR complicating acute myocardial infarction are declined for surgical intervention because of ongoing instability, shock, or the presence of comorbidities that make surgery of prohibitive risk.[2] Thus, although mitral valve repair is necessary for these patients, surgical correction remains an imperfect and incomplete solution.

The emergence of percutaneous interventions for valvular heart disease have offered opportunities for many patients that previously were without therapeutic options.[7–9] Specifically, in patients with severe chronic MR with elevated surgical risk, the development and advancement of the MitraClip has offered an alternative to high or prohibitive-risk surgical intervention. With MitraClip as a viable alternative to mitral valve replacement or repair for high-risk patients with chronic MR, is it time to consider its possible use in the setting of those high-risk patients with acute MR secondary to myocardial infarction? If so, an optimal approach for decision-making and management of these patients needs to be developed, incorporating procedural aspects and considerations of percutaneous versus surgical repair.

We describe a clinical case of a patient with severe MR after acute myocardial infarction and discuss the management for such patients in the current era of percutaneous intervention for valvular heart disease.

Case Presentation

An 84-year-old man with a past medical history of remote coronary artery bypass grafting, hypertension, and dyslipidemia presented with acute-onset chest pain and inferior ST-segment elevations. He underwent emergent angiography, demonstrating occlusion of a saphenous vein graft to the posterior descending artery (Figure 1; Movie I in the Data Supplement) and proceeded to receive percutaneous intervention to the vein graft with a drug-eluting stent. Despite revascularization, on hospital day 2, the patient developed progressive respiratory distress, and echocardiography demonstrated severe MR with a partial tear of the posteromedial papillary muscle and a resultant large eccentric posteriorly directed regurgitant jet (Figure 2; Movie IIA through IIC in the Data Supplement) in the setting of mildly reduced left ventricular function. The patient underwent aggressive medical management to achieve stability but, however, developed oliguric renal failure, hepatic dysfunction, and hypoxic respiratory failure. Because of ongoing instability and progressive multiorgan failure, he was transferred between hospitals for evaluation of mitral valve intervention.

On transfer, the patient was evaluated by interventional cardiology and cardiothoracic surgery. Based on history of prior sternotomy, multiorgan failure, and the presence of a patent left internal mammary artery graft, the patient was felt to be at high risk for surgical intervention. After discussion with the patient and family, the decision was made to attempt percutaneous edge-to-edge mitral valve repair with the MitraClip system.

The patient was urgently brought to the cardiac cath laboratory and intubated for escalating oxygen requirements. Fluoroscopy and transesophageal echocardiography (TEE)–guided transseptal puncture was performed crossing the septum primum in a posterior location that yielded a midatrial position for the guiding catheter, 4 cm from leaflet coaptation. Left atrial pressure was measured at baseline, with a mean left atrial pressure of 29 mm Hg with V waves of 59 mm Hg.

TEE-guided MitraClip percutaneous edge-to-edge mitral valve repair was performed, deploying 3 clips in a zipper approach and producing a single residual lateral orifice. The first clip was deployed at the most medial aspect of the MR jet approximating the edge of the flail segment to facilitate delivery of the following clip, which was placed at the lateral aspect of the jet. Repeat TEE measurements demonstrated a

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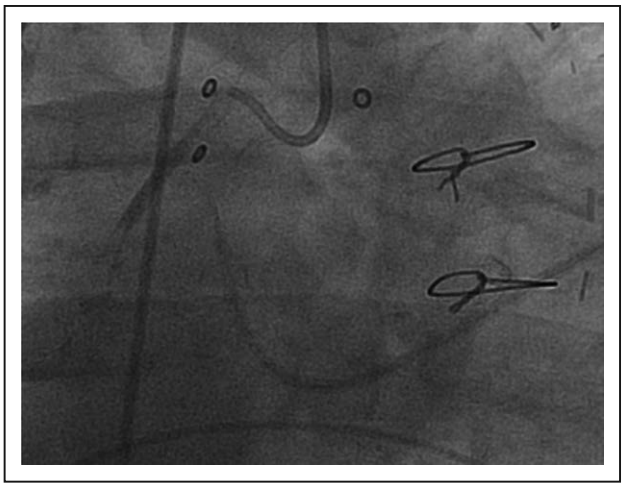

Figure 1. Occluded saphenous vein graft to posterior descending artery.

gradient of 5 mm Hg across the mitral valve with residual 2+ MR. Finally, a third clip was placed between the medial and lateral (first and second) clips, with significant reduction in echocardiographic MR (1+) and no change in mitral gradient (Figure 3; Movie IIIA through IIIC in the Data Supplement). Hemodynamic evaluation confirmed significant improvement in left atrial pressure, with a reduction to a mean pressure of 14 mm Hg and a V wave of 20 mm Hg. Furthermore, after clip placement, the partially torn papillary muscle appeared to have been stabilized, as demonstrated by significantly reduced mobility of the papillary muscle by echocardiography (Figure 4; Movie IVA and IVB in the Data Supplement).

Discussion

Surgery Has Been the Only Treatment for Correcting Severe MR Involving Papillary Muscle Dysfunction Post-MI. What Alternative Therapeutic Strategies Might be Considered?

Dr Carroll: In this patient, we all felt that he had prohibitive risk for surgery in his state upon transfer, and therefore, alternatives should be considered. A traditional alternative approach would have involved intra-aortic balloon counterpulsation or other forms of LV assistance. This combined with nitroprusside might have stabilized the patient and improved his chances of surviving surgery. Yet this approach may or may not have succeeded and, furthermore, he still would have been a man of advanced age with a prior sternotomy, and with a patent left internal mammary arterial graft. Therefore, we considered his case in the context of currently approved indications in for MitraClip in the US The mechanism of his mitral regurgitation could be considered degenerative with a flail segment. He was severely symptomatic and in the final stages of decompensated heart failure with multiorgan dysfunction. Despite the lack of predictability from this transcatheter approach being used in a partial rupture of a papillary muscle, we thought this was his only hope of survival. We were encouraged by his overall LV systolic function not being severely depressed. Reduction in the severity of his mitral regurgitation therefore had a good chance of changing his clinical course. After long discussions with the patient and his family we proceeded.

What Have Been the Outcomes for Patients Like This Undergoing Surgical Mitral Valve Repair? Have These Patients Been Included in Surgical Case Series and Analyses?

Dr Valle: Surgical outcomes for severe mitral regurgitation following acute myocardial infarction have consistently been suboptimal with high rates of mortality (Table).[2,5,10–16] Furthermore, many patients (like this one) are considered to be too high risk for surgery[2] because of their clinical instability and multiorgan failure. In this patient, with a percutaneous approach, the perils of initiating cardiopulmonary bypass in such an unstable patient was able to be avoided, as well as the sequelae of a repeat sternotomy for this patient with previous coronary artery bypass grafting and patent left internal mammary conduit to his left anterior descending.

Are There Other Case Reports of MitraClip Being Used to Treat Severe MR in the Setting of Papillary Muscle Dysfunction-Rupture? How Is This Case Unique?

Dr Carroll: Yes, there have been isolated case reports, and we studied these before performing this procedure with the caveat

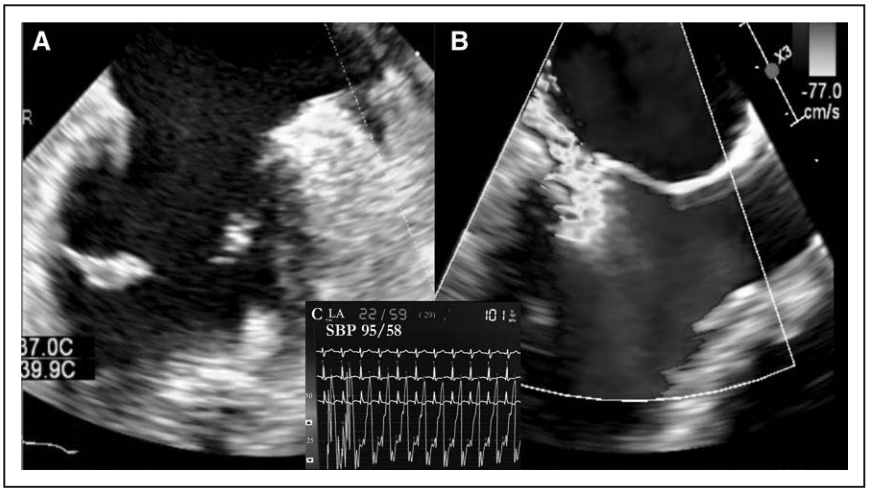

Figure 2. Partial rupture of posteromedial papillary muscle (**A**) with severe mitral regurgitation (**B**) and left atrial pressure at baseline (**C**).

Figure 3. Successive clip deployment: Zipper approach (**A**, fluoroscopy and doppler transesophageal echocardiography [TEE] after first clip deployment; **B**, fluoroscopy and doppler TEE after second clip deployment; **C**, fluoroscopy and doppler TEE after third and final clip deployment).

of publication bias: successful outcomes are much more likely to be reported than failures. There have been cases described of MitraClip being used to treat acute severe MR,[17–22] with three cases in the setting of papillary muscle rupture with cardiogenic shock following acute myocardial infarction.[17,19,20] Between 1 and 3 MitraClips were placed and the patients recovered. The first case reported was from Turkey, and the other two were from German and Canadian centers.

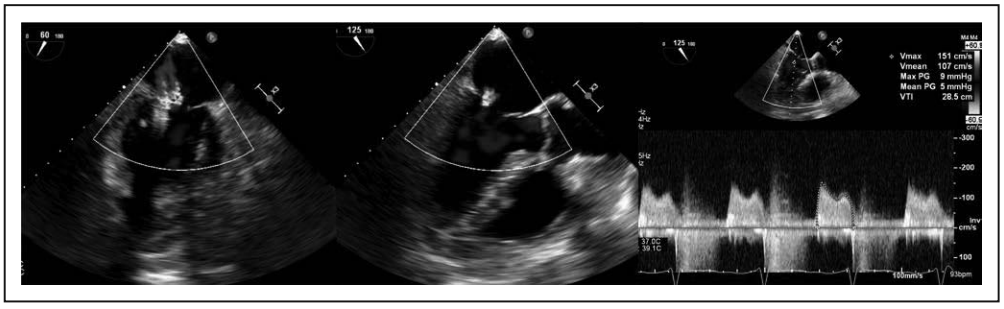

Figure 4. Final transesopheageal echocardiographic evaluation of mitral regurgitation.

Table. Outcomes of Mitral Valve Surgery for Severe Mitral Regurgitation After Acute Myocardial Infarction

Authors	Year of Publication	Number of Patients Undergoing Surgery	Patient Population	Surgical Timing	Outcome
Nishimura et al[10]	1986	7	Patients undergoing surgery for papillary muscle rupture, case series	100% within 4 days	42% mortality at 1 y
Kishon et al[11]	1992	22	Patients undergoing surgery for papillary muscle rupture, case series	19 (87%) within 3 wk	27% mortality at 30 days; 47% mortality at 7 y
Thompson et al[2]	2000	43 patients (of 1190 patients with post-AMI cardiogenic shock, 98 with severe MR)	Post-MI patients with cardiogenic shock (SHOCK registry)	NA	39% in-hospital mortality
Gillinov et al[12]	2001	482	Patients undergoing valve surgery for ischemic MR, Cardiovascular Information Registry	95 (19.7%) within 14 d	11% in-hospital mortality; 23% mortality at 1 y; 45% mortality at 5 y
Minami et al[13]	2004	6	Patients undergoing valve surgery for papillary muscle rupture	6 (100%) within 19 days	33% perioperative mortality
Russo et al[15]	2008	54	Patients undergoing valve surgery for papillary muscle rupture	48 (83%) within 30 days	18.5% perioperative mortality; 35% mortality at 5 y
Lorusso et al[14]	2008	126 (of 279 patients)	Patients undergoing emergent surgery for acute severe mitral regurgitation, multicenter study	100%	27.3% perioperative mortality (30 days); 40% at 3 y
Schroeter et al[5]	2013	28	Patients undergoing surgery for papillary muscle rupture	25 (89%) within 21 days	39% mortality at 30 days
Bouma et al[16]	2014	48	Patients undergoing surgery for papillary muscle rupture	100%	Intraoperative mortality 4.2%; In-hospital mortality 25.0%

AMI indicates acute myocardial infarction; MI, myocardial infarction; MR, mitral regurgitation; and SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock.

This case is unique in several regards. This case adds to a small but growing base of evidence supporting the use of MitraClip in acute mitral regurgitation, and specifically in the setting of papillary muscle tear. Additionally, having been performed in the United States, as mandated by the Food and Drug Administration (FDA) and Centers for Medicare & Medicaid Services (CMS), this patient's data were entered in the STS-ACC TVT Registry (The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy). This case also was performed using 3D TEE imaging with fusion of ultrasound and fluoroscopic images to provide procedural guidance. Finally, this case demonstrates the successful implantation of three MitraClips that not only reduced the degree of MR but also stabilized the partial rupture of the papillary muscle by restricting the motion and torque placed on the muscle by the flail leaflet.

How Does Having 3D TEE Imaging and Echocardiographic-Fluoroscopic Fusion Help in the Performance of MitraClip?

Dr Miyasaka: We have found that the use of 3D TEE imaging and echocardiographic-fluoroscopic fusion allows for more accurate and timely feedback during the guidance of MitraClip implantation.

While 2D echocardiographic imaging is the standard approach for the majority of the procedure, this modality provides only a small slice of information compared to the complexity of the three-dimensional interactions of the MitraClip system with left atrial structures and the mitral valve apparatus. Having a full three-dimensional understanding of the pathology was crucial in the current case, as we needed to minimize unnecessary interactions with the mitral valve and subvalvular apparatus to avoid destabilizing the partially ruptured papillary muscle. Furthermore, when relying on 2D imaging alone, there is inherent lag time during adjustment of the probe, omniplane angle, and viewing sector to follow the catheters as they slide in and out of our imaging plane. With the use of 3D TEE, we are able to recreate the surgeon's view of the mitral valve, including key left atrial structures in addition to the valve itself, providing continuous feedback during the procedure. This reliable and reproducible working view can be used for multiple portions of the procedure, including initial advancement of the wire into the pulmonary vein after transseptal puncture, crossing the interatrial septum with the guide catheter, and advancing the MitraClip toward the mitral valve while clearing the warfarin ridge.

Similarly, echocardiographic-fluoroscopic fusion facilitates communication between the echocardiographer and interventionalist. Using EchoNav (Philips HealthCare, Best, the Netherlands), the ability to overlay echocardiographic and fluoroscopic images allows for real-time feedback and response between the echocardiographer and interventionalist. Catheter manipulation in relation to probe and image plane position (and vice versa) can be visually demonstrated despite the complex geometric relationships that occur within the heart. Fusion of the echocardiographic imaging familiar to the echocardiographer with the fluoroscopic imaging most familiar to the interventionalist can facilitate improved communication about spatial relationships and decision-making

on approaches for the complex motions and steps required in these procedures (ie, determining optimal transseptal location and crossing the valve plane). Additionally, this fusion allows for anticipation of the fine imaging adjustments needed to guide the procedure, allowing the case to proceed as expeditiously as possible. This was vitally important in the current case given the critical illness of the patient.

MitraClip Is Thought of As an Elective Procedure in Stable Patients. How Was the Procedure Impacted in This Very Different Clinical Situation? What Were Your Concerns at the Start of the Procedure?

Dr Carroll: We decided to proceed with emergency MitraClip therapy immediately upon transfer. Patients who have entered multiorgan failure and approaching the need for intubation are in danger of further rapid deterioration. A strategy of stabilization could have been tried but we felt that treating the primary cause of the patient's deterioration had the best chance of success. We drew from our experience in aortic stenosis that when patients are admitted with refractory pulmonary edema with cardiogenic shock, it is key to reduce the severity of the underlying valvular abnormality, that is, perform emergency aortic balloon valvuloplasty, since other supportive measures are likely to fail.

He was unstable in the cardiac catheterization laboratory primarily from difficulties in oxygenation. The cardiac anesthesiologist employed bursts of high positive pressure ventilation to maintain him at a low normal degree of oxygenation. We attempted to reduce his pulmonary edema with intravenous diuretics but these had minimal effect until we started reducing the severity of his mitral regurgitation.

I was concerned that we may have considerable difficulty in grasping the leaflets and that we would then fail to reduce his mitral regurgitation. We therefore started with placing a clip where the distance between the two leaflets was not too great. This foundation clip then allowed us to place a clip where the mitral regurgitate jet was largest. We received immediate intraprocedural feedback, with each MitraClip placement improving his systemic blood pressure, ultimately allowing us to reduce and subsequently eliminate vasopressor support.

A second concern was that we could convert the partial rupture to a complete rupture by navigating the clip delivery system unto the left ventricle and trying to grasp leaflets. Complete rupture could make the procedure technically impossible and also lead to the immediate death of the patient. Having 3D visualization greatly helped in navigating the clip delivery system. Having image fusion allowed me to use fluoroscopy in avoiding going too deep into the left ventricle.

At the End of the Procedure What Were the Major Echocardiographic Findings and What Was Unexpected?

Dr Miyasaka: At the end of the procedure, the patient demonstrated only 1+ residual mitral regurgitation. This was greater MR reduction than what was expected given the severity of the valvular abnormality. Furthermore, we noticed that the MitraClips seemed to have stabilized the partially ruptured papillary muscle. At the start of the case, we noticed that with each systole, the anterior leaflet would flail into the left atrium and pull on the partially ruptured papillary muscle. There was concern that, over time, this strain would eventually lead to a complete tear. After the MitraClips were placed, it appeared that the anterior leaflet gained support from the posterior leaflet, thereby redistributing the tension off of the papillary muscle. Visually the papillary muscle appeared more stable, and we hope that this will clinically translate into a decreased chance of progression to a complete rupture. The MitraClips essentially served a dual purpose of mitral regurgitation reduction and papillary muscle stabilization.

What Further Steps Are Needed for This Patient? Should Patients Like This Be Considered for Subsequent Mitral Valve Surgery, or Should This Be Considered a Stand-Alone Procedure?

Dr Valle: This is a critical question that must be addressed on a patient-to-patient basis until more definitive data exist to guide management. Whether these patients may require a surgical intervention for their valvular disease after initial stabilization with a percutaneous approach is just one of the questions that call for collection of these cases and experiences, with subsequent analysis of acute and medium-term outcomes in order to optimally inform future care.

Case Studies Are Useful but Anecdotal. How Can the Cardiovascular Community Gather Evidence Regarding This Treatment Option's Success, Failures, Complications, and Outcomes?

Dr Carroll: The STS-ACC TVT Registry[23,24] is a vehicle for the accumulation of comprehensive data on all US commercial MitraClip cases. For these unusual cases the TVT registry provides a means to assemble an adequate number of cases from multiple centers that represent a comprehensive overview of the US experience including both in-hospital but also medium-term outcomes. Linkages with the CMS database increase the likelihood of capturing longer-term outcomes include the rehospitalization rates and crossover to surgery. Thus, a multicenter experience may be accumulated to develop and distribute best practices. Finally, in alignment with recent FDA draft guidance document,[25] these registry data may be used as real-world evidence to support regulatory decision-making. Otherwise individual case studies as this one will serve only a limited educational focus and no regulatory purpose. Single centers will never accumulate an adequate case series to identify and share best practices, facilitate quality improvement throughout the cardiovascular community, and contribute to the regulatory process of expanding indications of approved devices.

Clinical Outcome

Post-procedure, the clinical improvement was immediate and dramatic, with improved hemodynamics and diuretic-responsiveness. The patient was extubated the day of the procedure with minimal oxygen requirements. Repeat transthoracic echocardiography demonstrated ongoing significant reduction in mitral regurgitation to a mild degree. Over the next 3 days, his acute kidney injury and hepatic dysfunction resolved.

He was transferred to a short-term rehab center and within a week was discharged to home on dual antiplatelet

Figure 5. Follow-up transthoracic echocardiographic evaluation of mitral regurgitation.

therapy with aspirin and clopidogrel, as well as atorvastatin, metoprolol, lisinopril, and 80 mg of furosemide daily. At 6 weeks' follow-up, he has resumed some of his normal activities as a rancher with New York Heart Association Class 2 symptoms and 1 to 2 plus residual MR on echocardiography performed 1 month post-discharge (Figure 5; Movie V in the Data Supplement). He still requires diuretic therapy to be free of edema.

Disclosures

Dr Carroll receives research support from and serves as a consultant for Philips HealthCare. Drs Valle and Miyasaka report no conflicts.

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