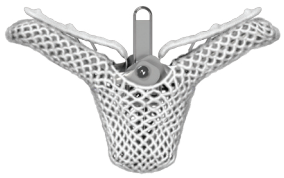
Clinical Insights

SUMMARY OF CLINICAL DATA

MITRACLIP™ TRANSCATHETER MITRAL VALVE REPAIR

HEMODYNAMIC MONITORING DURING MITRACLIP™ PROCEDURES

Early Data, Future Promise



PERSPECTIVE

- MitraClip™ safely and effectively reduces mitral regurgitation (MR) with excellent procedural and clinical outcomes demonstrated in over 100,000 cases world-wide.
- Today, most MitraClip procedures are guided solely by echocardiography which is highly dependent on operator experience (transducer position, acoustic shadows, eccentric jets), and standardized MR assessment post-MitraClip is difficult due to split regurgitant jets.
- Adding intraprocedural hemodynamic monitoring to complement echocardiography/color doppler may help further optimize clip placement and improve clinical outcomes.

KEY HIGHLIGHTS

Hemodynamic monitoring of left atrial pressure (LAP) is an emerging area of interest. Its inclusion can potentially improve post-MitraClip outcomes. When used in combination with echocardiography/color doppler, LAP monitoring facilitates optimal MR reduction while minimizing the risk of iatrogenic stenosis. Importantly, preliminary data has shown continuous LAP monitoring to be:

- An important adjunct to echocardiography/color doppler for guiding clip placement
- Associated with clinically meaningful outcomes: improved heart failure rehospitalizations, symptom status, and exercise capacity
- Feasible in a clinical setting

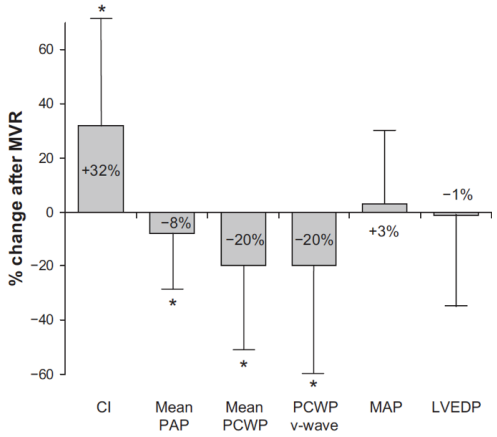
WHY INTRODUCE HEMODYNAMIC MONITORING WITH MITRACLIP?

Hemodynamic monitoring has a well-established role in Transcatheter Aortic Valve Replacement (TAVR) where transaortic pressure is a key index of procedural success. By contrast, reporting of hemodynamic parameters pre-, during, and post-MitraClip is a relatively new practice.

MitraClip placement is conventionally guided by transesophageal echocardiography (TEE) with color doppler imaging (CDI). While effective, both approaches do have limitations. MR assessment, defined by vena contracta, PISA, and other TEE measures, is challenging post-clipping due to double orifice valve. Similarly, regurgitant jet assessed by CDI is operator-dependent, transducer location-dependent, and lacks standardized quantitative metrics. Jet demarcation by color doppler reflects flow topography rather than the true regurgitant volume, presenting further challenges to interpretation[1].

Importantly, the tissue approximation by the clip reduces MR and also narrows the mitral valve orifice, thereby inducing a risk of elevated transmitral pressure gradients[2]. Hence, continuous monitoring of LAP during a MitraClip procedure can supplement echocardiography to optimize MR reduction with minimal risk of stenosis[2].

FIGURE 1: PCWP AND HENCE LAP CHANGES ARE SENSITIVE TO MR CHANGES WITH MITRACLIP[3]



CI, cardiac index; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; MAP mean arterial pressure; LVEDP, left ventricular end diastolic pressure.
Source: Circulation 2013;127(9):1018–27.

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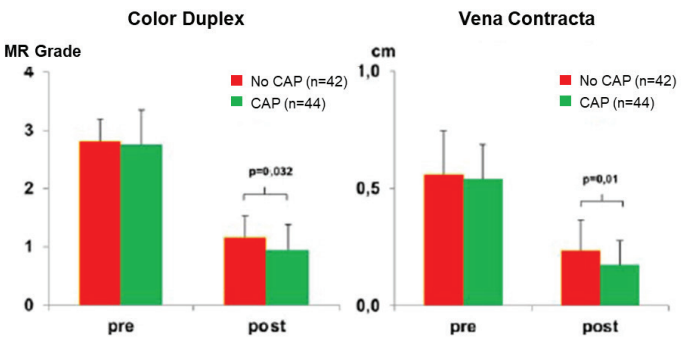
FIGURE 2: CONTINUOUS LAP WITH ECHOCARDIOGRAPHY



Continuous LAP with echocardiography reduced MR grade and Vena Contracta after MitraClip compared to only echocardiography. **Source: Catheterization and Cardiovascular Interventions 2016;88(7):1134–43.**

DOES CONTINUOUS LAP MONITORING HAVE A CLINICALLY MEANINGFUL IMPACT?

Early observational studies showed improvement in multiple hemodynamic parameters following MitraClip, specifically pulmonary capillary wedge pressure, a surrogate of LAP [Figure 1][3,4]. Subsequent studies reported improved clinical outcomes with continuous LAP monitoring:

- **Lower post-procedural regurgitation, without a significant increase in procedural duration or complication rate** [Figure 2][5]
  In a study of 86 patients undergoing MitraClip, continuous LAP monitoring (CAP, n=44) was compared with intermittent measurement (n=42). A greater reduction in MR grade was observed in the group who underwent CAP compared to the intermittent measurement group (2.8→0.9 vs. 2.8→1.3, p=0.03) which persisted through discharge.

- **Improved exercise tolerance assessed by six minute walk distance (6MWD** [Figures 3 and 4]**)**[6]
  In a single center study of 50 patients, change in LAP v-wave was independently associated with longer 6MWD and improved New York Heart Association (NYHA) class at 30 days. Additionally, each 5 mmHg decrease in mean V-wave was associated with a 49% increase in the likelihood of improved 6MWD (OR=1.49, 95% CI: 1.01-2.18, p=0.04). Patients with V-wave drop of > 11 mmHg (median) were 3.8x more likely to improve their 6MWD (p=0.05)

- **Reduced heart failure rehospitalization (HFH) and NYHA III/IV** [Figure 5][7]
  In a sub-study of 50 patients from the MitraSwiss registry, higher indexed mean LAP (LAMPi, mean LAP adjusted to LV systolic pressure) was associated with
  - re-hospitalization for heart failure [Figure 5] (log rank p=0.001), and
  - worsening NYHA III/IV (multivariate HR 1.5, 95%CI 1.01-2.10, p=0.005)

Residual MR by doppler echo failed to show these relationships, further supporting the adjunctive value of hemodynamics in deciding clip placement and/or repositioning.

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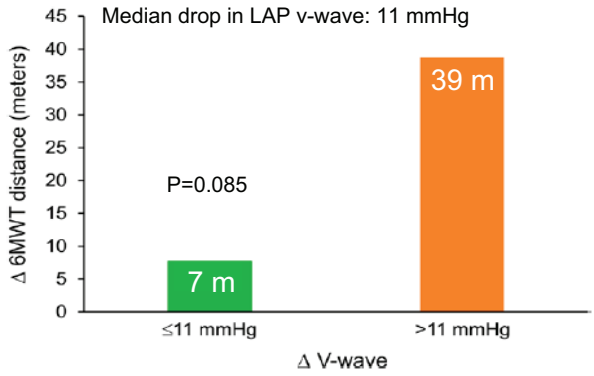
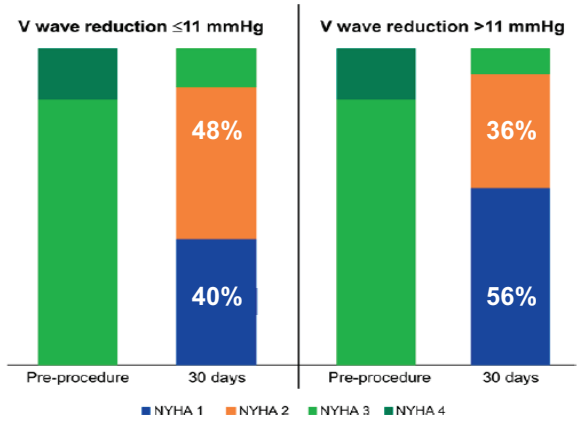
FIGURE 3: 6MW TEST – PATIENTS WITH LAP V-WAVE DECREASE



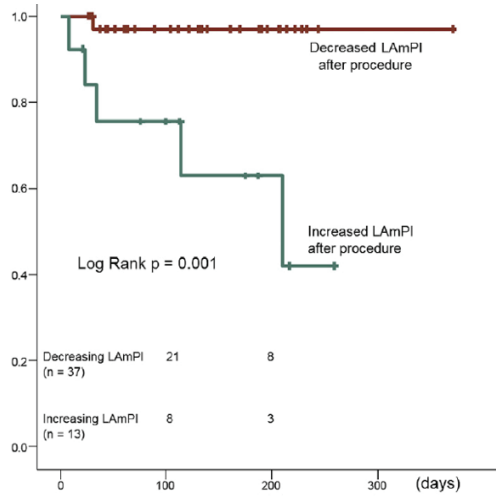
In the 6MW test, patients with a LAP v-wave decrease > 11 mmHg could walk substantially further after receiving a MitraClip than those with < 11 mmHg change. **Source: Cardiovascular Interventions 2017;10(4):e004856.**

FIGURE 4: PATIENTS WITH LAP V-WAVE DECREASE



Patients with a LAP v-wave decrease > 11 mmHg had a higher proportion of NYHA I/II after MitraClip compared to those with < 11 mmHg change. **Source: Cardiovascular Interventions 2017;10(4):e004856.**

FIGURE 5: HEART FAILURE REHOSPITALIZATION



Freedom from heart failure rehospitalization is statistically associated with a decrease in the indexed mean left atrial pressure (LAmPI). **Source: JACC: Cardiovascular Interventions 2019;12(2):127–36.**

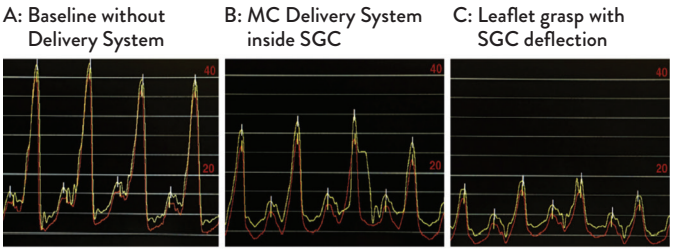
HOW IS INTRAPROCEDURAL LAP MONITORING DONE AND IS IT FEASIBLE IN A CLINICAL SETTING?

Pulmonary capillary wedge pressure (PCWP) is frequently used as an indirect surrogate for LAP, and has a well-established prognostic role in mitral stenosis[8], heart failure and mitral regurgitation[9]. In healthy states, the LAP and PCWP are well correlated (r=0.95)[10]. However in mitral regurgitation, the correlation is less evident (r=0.79)[11]. Instead, direct LAP measurements are more accurate and is thus preferable to guide clip implantations.

LAP can be measured using a separate (buddy) catheter delivered transseptally to the left atrium but this approach increases complexity, risks, and procedural time[12]. Instead, some users continuously transduced LAP through the steerable guide catheter (SGC) of the original MitraClip and the MitraClip NT and NTR/XTR systems. Flow inhibition within the SGC by the MitraClip delivery catheter (CDS) during clip placement can create problems.

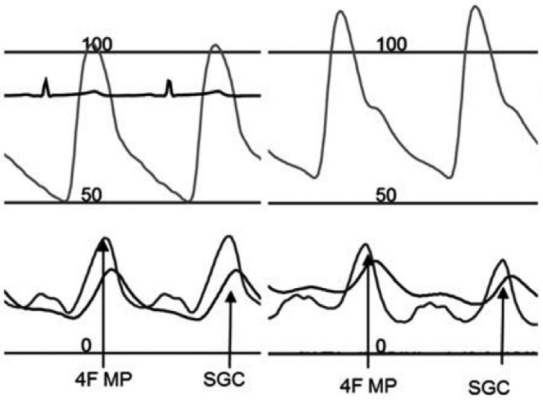
When blood flow in the SGC is unimpeded, continuous monitoring occurs **[Figure 6]**[13] but the SGC waveforms are overdamped compared to those obtained with the buddy catheter **[Figure 7]**[12]. When flow is insufficient, the signal is sporadic, overdamped, or drops off completely especially when the CDS rotates down to cross the mitral valve[2,12]. A redesign of the SGC in the next generation MitraClip G4 will mitigate these issues and enable continuous tracking of the LAP with accuracy and consistency.

FIGURE 6: LEFT ATRIAL PRESSURE TRACINGS[13]



Consistency and reproducible of left atrial pressure tracings transduced from the side-hole buddy catheter (red line) and via the SGC (yellow line) at key stages of the MitraClip procedure (5 cases). Mean and maximum observed difference in mean LA pressure between the SGC and side-hole catheter were 1.3 and 3.0 mm Hg, respectively. **Source: JACC: Cardiovascular Interventions 2017;10(14):1466–7**

FIGURE 7: THE SGC LAP WAVEFORM[12]



The SGC LAP waveform (SGC) is overdamped and slightly lagging that from a dedicated pigtail catheter (4F MP). **Source: Catheterization and Cardiovascular Interventions 2018;92(2):374–8.**

SUMMARY

- Adjunctive continuous LAP monitoring with standard color doppler imaging provides important objective data for proceduralists to optimize MR reduction while minimizing risks for iatrogenic mitral stenosis during MitraClip placement
- Continuous LAP monitoring has the potential to positively impact clinical outcomes by reducing heart failure rehospitalization, improving functional symptoms, and increasing exercise capacity.
- Continuous LAP monitoring is feasible clinically, though the promising early data will need to be confirmed in larger studies to establish optimal monitoring criteria.

REFERENCES

1. Lin BA, Forouhar AS, Pahlevan NM, et al. Color Doppler Jet Area Overestimates Regurgitant Volume when Multiple Jets are Present. J Am Soc Echocardiogr 2010;23(9):993–1000.
2. Tang GHL, Ong LY, Kaple R, et al. Continuous invasive hemodynamic monitoring using steerable guide catheter to optimize mitraclip transcatheter mitral valve repair: A multicenter, proof-of-concept study. J Intervent Cardiol 2018;31(6):907–15.
3. Gaemperli O, Moccetti M, Surder D, et al. Acute haemodynamic changes after percutaneous mitral valve repair: relation to mid-term outcomes. Heart 2012;98(2):126–32.
4. Gaemperli Oliver, Biaggi Patric, Gugelmann Remo, et al. Real-Time Left Ventricular Pressure-Volume Loops During Percutaneous Mitral Valve Repair With the MitraClip System. Circulation 2013;127(9):1018–27.
5. Horstkotte J, Kloeser C, Beucher H, Schwarzlaender E, Bardeleben RS von, Boekstegers P. Intraprocedural assessment of mitral regurgitation during the mitraclip procedure: Impact of continuous left atrial pressure monitoring. Catheter Cardiovasc Interv 2016;88(7):1134–43.
6. Maor Elad, Raphael Claire E., Panaich Sidakpal S., et al. Acute Changes in Left Atrial Pressure After MitraClip Are Associated With Improvement in 6-Minute Walk Distance. Circ Cardiovasc Interv 2017;10(4):e004856.
7. Kuwata S, Taramasso M, Czopak A, et al. Continuous Direct Left Atrial Pressure: Intraprocedural Measurement Predicts Clinical Response Following MitraClip Therapy. JACC Cardiovasc Interv 2019;12(2):127–36.
8. Nagy AI, Venkateshvaran A, Dash PK, et al. The pulmonary capillary wedge pressure accurately reflects both normal and elevated left atrial pressure. Am Heart J 2014;167(6):876–83.
9. Ritzema Jay, Melton Iain C., Richards A. Mark, et al. Direct Left Atrial Pressure Monitoring in Ambulatory Heart Failure Patients. Circulation 2007;116(25):2952–9.
10. Walston A, Kendall ME. Comparison of pulmonary wedge and left atrial pressure in man. Am Heart J 1973;86(2):159–64.
11. Chen L, Mantri N, Eng ML, et al. Intraprocedural direct left atrial and wedge pressure correlation during transcatheter mitral valve repair: Results from a single center registry. Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv 2019;94(1):165–70.
12. Eleid MF, Reeder GS, Rihal CS. Comparison of left atrial pressure monitoring with dedicated catheter versus steerable guiding catheter during transcatheter mitral valve repair. Catheter Cardiovasc Interv 2018;92(2):374–8.
13. Gajjar M, Yadlapati A, Van Assche, LMR, et al. Real-Time Continuous Left Atrial Pressure Monitoring During Mitral Valve Repair Using the MitraClip NT System. JACC Card. Interv 2017;10(14):1466-67.

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IMPORTANT SAFETY INFORMATION

MITRACLIP CLIP DELIVERY SYSTEMS

Rx ONLY

INDICATION FOR USE

- The MitraClip™ NTR/XTR Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.
- The MitraClip™ NTR/XTR Clip Delivery System, when used with maximally tolerated guideline-directed medical therapy (GDMT), is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) mitral regurgitation (MR; MR ≥ Grade III per AmericanSociety of Echocardiography criteria) in patients with a left ventricular ejection fraction (LVEF) ≥20% and ≤ 50%, and a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptomsand MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of heart failure and mitral valve disease.

CONTRAINDICATIONS

The MitraClip™ NTR/XTR Clip Delivery System is contraindicated in patients with the following conditions:

- Patients who cannot tolerate procedural anticoagulation or post procedural antiplatelet regimen
- Active endocarditis of the mitral valve
- Rheumatic mitral valve disease
- Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus

WARNINGS

- **DO NOT use MitraClip™ outside of the labeled indication.**
- The MitraClip™ Implant should be implanted with sterile techniques using fluoroscopy and echocardiography (e.g., transesophageal [TEE] and transthoracic [TTE]) in a facility with on-site cardiac surgery and immediate access to a cardiac operating room.
- Read all instructions carefully. Failure to follow these instructions, warnings and precautions may lead to device damage, user injury or patient injury. Use universal precautions for biohazards and sharps while handling the MitraClip™ System to avoid user injury.
- Use of the MitraClip™ should be restricted to those physicians trained to perform invasive endovascular and transseptal procedures and those trained in the proper use of the system.
- The Clip Delivery System is provided sterile and designed for single use only. Cleaning, re-sterilization and / or reuse may result in infections, malfunction of the device or otherserious injury or death.
- Use caution when treating patients with hemodynamic instability requiring inotropic support or mechanical heart assistance due to the increased risk of mortality in this patient population. The safety and effectiveness of MitraClip™ in these patients has not been evaluated.

PRECAUTIONS

- Note the product "Use by" date specified on the package.
- Inspect all product prior to use. Do not use if the package is open or damaged, or if product is damaged.
- Prohibitive Risk Primary (or degenerative) Mitral Regurgitation
  - Prohibitive risk is determined by the clinical judgment of a heart team, including a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, due to the presence of one or more of the following documented surgical risk factors:
    - 30-day STS predicted operative mortality risk score of
      - ≥8% for patients deemed likely to undergo mitral valve replacement orr
      - ≥6% for patients deemed likely to undergo mitral valve repair
  - Porcelain aorta or extensively calcified ascending aorta.
  - Frailty (assessed by in-person cardiac surgeon consultation)
  - Hostile chest
  - Severe liver disease / cirrhosis (MELD Score > 12)
  - Severe pulmonary hypertension (systolic pulmonary artery pressure > 2/3 systemic pressure)
  - Unusual extenuating circumstance, such as right ventricular dysfunction with severe tricuspid regurgitation, chemotherapy for malignancy, major bleeding diathesis, immobility, AIDS, severe dementia, high risk of aspiration, internal mammary artery (IMA) at high risk of injury, etc.
  - Evaluable data regarding safety or effectiveness is not available for prohibitive risk DMR patients with an LVEF < 20% or an LVESD > 60 mm. MitraClip™ should be used only when criteria for clip suitability for DMR have been met.
  - The heart team should include a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease and may also include appropriate physicians to assess the adequacy of heart failure treatment and valvular anatomy.
- Secondary Mitral Regurgitation
  - Evaluable data regarding safety or effectiveness is not available for secondary MR patients with an LVEF < 20% or an LVESD > 70 mm.
  - The multidisciplinary heart team should be experienced in the evaluation and treatment of heart failure and mitral valve disease and determine that symptoms and MR severity persist despite maximally tolerated GDMT. rohibitive Risk Primary (or degenerative) Mitral Regurgitation

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

The following ANTICIPATED EVENTS have been identified as possible complications of the MitraClip™ procedure.

Death; Allergic reaction (anesthetic, contrast, Heparin, nickel alloy, latex); Aneurysm or pseudo-aneurysm; Arrhythmias; Atrial fibrillation; Atrial septal defect requiring intervention; Arterio-venous fistula; Bleeding; Cardiac arrest; Cardiac perforation; Cardiac tamponade / Pericardial Effusion; Chordal entanglement / rupture; Coagulopathy; Conversion to standard valve surgery; Deep venous thrombus (DVT); Dislodgement of previously implanted devices; Dizziness; Drug reaction to anti-platelet / anticoagulation agents / contrast media; Dyskinesia; Dyspnea; Edema; Emboli (air, thrombus, MitraClip™ Implant); Emergency cardiac surgery; Endocarditis; Esophageal irritation; Esophageal perforation or stricture; Failure to deliver MitraClip™ to the intended site; Failure to retrieve MitraClip™ System components; Fever or hyperthermia; Gastrointestinal bleeding or infarct; Hematoma; Hemolysis; Hemorrhage requiring transfusion; Hypotension / hypertension; Infection; Injury to mitral valve complicating or preventing later surgical repair; Lymphatic complications; Mesenteric ischemia; MitraClip™ Implant erosion, migration or malposition; MitraClip™ Implant thrombosis; MitraClip™ System component(s) embolization; Mitral stenosis; Mitral valve injury; Multi-system organ failure; Myocardial infarction; Nausea / vomiting; Pain; Peripheral ischemia; Prolonged angina; Prolonged ventilation; Pulmonary congestion; Pulmonary thrombo-embolism; Renal insufficiency or failure; Respiratory failure / atelectasis / pneumonia; Septicemia; Shock, Anaphylactic or Cardiogenic; Single leaflet device attachment (SLDA); Skin injury or tissue changes due to exposure to ionizing radiation; Stroke or transient ischemic attack (TIA); Urinary tract infection; Vascular trauma, dissection or occlusion; Vessel spasm; Vessel perforation or laceration; Worsening heart failure; Worsening mitral regurgitation; Wound dehiscence

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CAUTION: This product is intended for use by or under the direction of a physician. Prior to use, reference the Instructions for Use, inside the product carton (when available) or at eifu.abbottvascular.com or at medical.abbott/manuals for more detailed information on Indications, Contraindications, Warnings, Precautions and Adverse Events.

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