# Clinical Insights

SUMMARY OF CLINICAL DATA

**MITRACLIP™ TRANSCATHETER EDGE-TO-EDGE REPAIR**

# CARDIOVASCULAR PHYSIOLOGY IN MITRAL REGURGITATION

## What you need to know

### ESSENTIAL HIGHLIGHTS

- The MitraClip™ can effectively perform valve leaflet coaptation to reduce MR under TEE and color doppler guidance. However, this approach provides, at best, semi-quantitative physiologic data
- When left uncorrected, chronic mitral valve regurgitation (MR) can lead to ventricular volume overload and increased risk of decompensated heart failure
- Left atrial pressure (LAP) is elevation is proportional to the severity of mitral regurgitation. Reduction in LAP and improved forward flow are key measures of successful MR repair
- Continuous LAP monitoring allows hemodynamic and functional feedback during MC placement to optimally reduce regurgitation severity and risk of inducing mitral stenosis

### ACRONYMS

| | |
|---|---|
| **LAP** | *Left atrial pressure* |
| **LAmP** | *left atrial mean pressure* |
| **LAmPI** | *Left atrial mean pressure index* |
| **LAvP** | *Left atrial v-wave pressure* |
| **LAvPI** | *Left atrial v-wave pressure index* |
| **LAv height** | *Left atrial v-wave height* |
| **LVEDP** | *Left ventricle end diastolic pressure* |
| **LVSP** | *Left ventricular systolic pressure* |
| **MC** | *MitraClip* |
| **MR** | *Mitral regurgitation* |
| **PMR** | *Primary mitral regurgitation* |
| **SMR** | *Secondary mitral regurgitation* |
| **sBP** | *Systemic blood pressure* |
| **TEE** | *Transesophageal echocardiography* |
| **TMVR** | *Transcatheter mitral valve repair* |

### BASIC CARDIOVASCULAR PHYSIOLOGY AND MITRAL REGURGITATION (MR)[2]

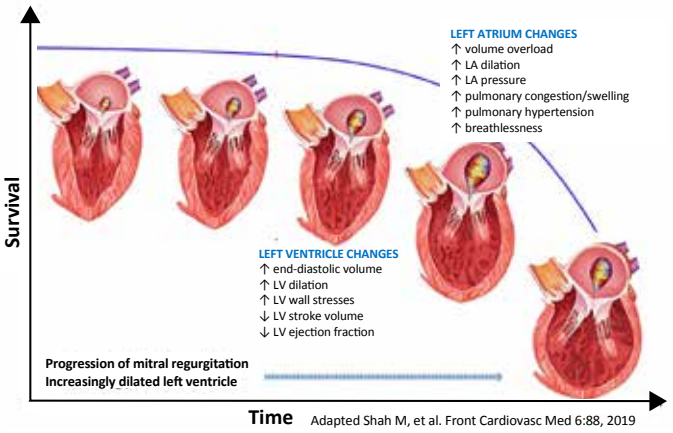
**Mitral regurgitation (MR)** refers to retrograde blood flow from the left ventricle back up to the left atrium during ventricular contraction, which can be a consequence of:

- Degenerative mitral valve abnormalities (**Primary MR**), or
- Ventricular dilatation and distortions from ischemic or idiopathic cardiomyopathy leading to displacement of the papillary muscles and leaflet tethering (**Secondary MR**)

**Primary MR (PMR)** begins with an abnormal mitral valve apparatus but mostly functional left ventricle.

1. During systole (contraction), higher regurgitant flow increases left atrial pressure (LAP)
2. During diastole (relaxation), regurgitant blood repeatedly flows back to the left ventricle, resulting in increasingly larger diastolic volumes and subsequently **higher left ventricular end diastolic pressures.** The heart initially compensates by pumping harder.
3. With chronic MR however, the left ventricle eventually becomes overloaded in diastole. Increased wall stress induces cardiac remodeling with dilation of the ventricle. The heart eventually decompensates into critical left ventricular dysfunction and clinical symptoms of heart failure [Figure 1].

**FIGURE 1: PROGRESSION OF MR ON DETERIORATION OF LEFT HEART FUNCTION**




Source: Front Cardiovasc Med. 6:88, 2019

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*The goal of PMR repair is to avoid this process of decompensation early on in PMR.*

**Secondary (functional) MR** begins with an already weak and dilated left ventricle, which alters mitral valve geometry, causing regurgitation. Chronic SMR quickly follows the pattern of decompensated MR described in step 3 of PMR. *The goal of SMR repair is to avoid further exacerbation of heart failure by improving cardiac output*

**In both cases, clinical heart failure ensues because:**

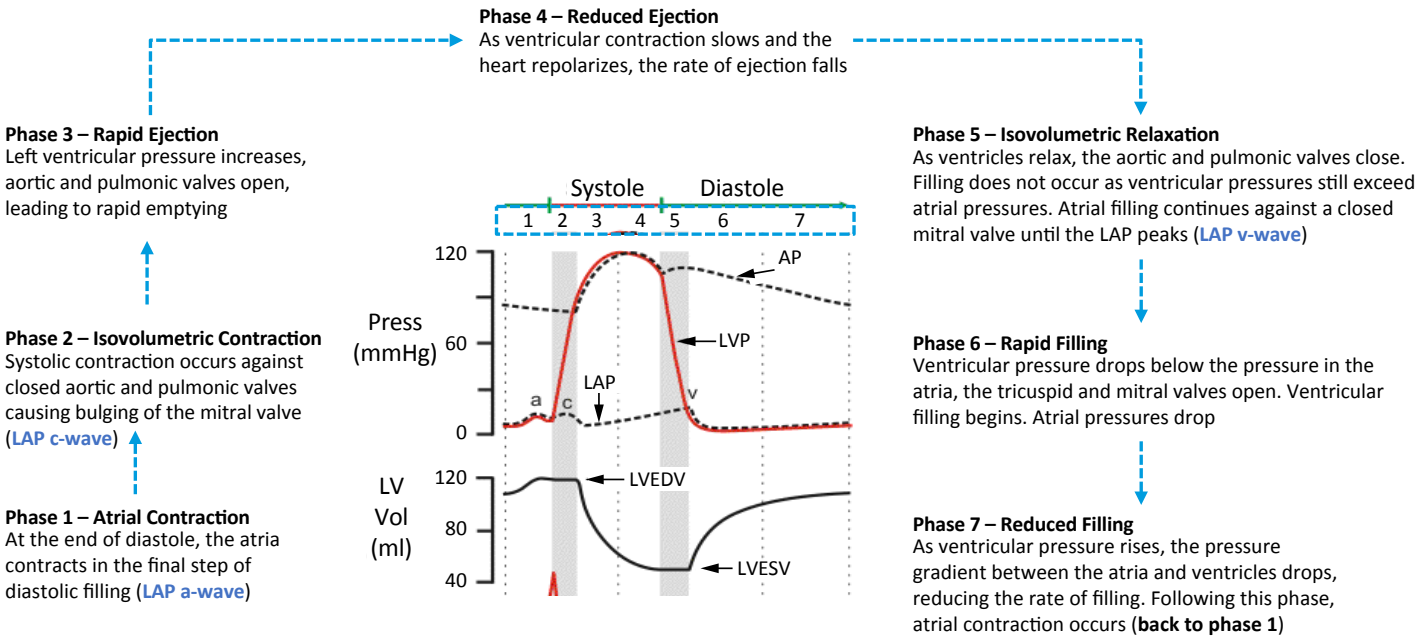
- Cardiac output is diminished, lowering renal blood flow. The kidneys interpret this as a low volume state and inappropriately stimulate water retention in an attempt to maintain blood volume and end organ perfusion.
- Abnormal water retention further stresses an already failing heart. Volume overload causes blood to back up into the pulmonary circuit, causing pulmonary edema (swelling) and dyspnea (breathlessness).
- Over time pulmonary pressures increase to compensate for volume overload, causing increased right ventricular stress and ultimately right-sided heart failure and peripheral volume overload

## PHASES OF THE CARDIAC CYCLE

An understanding of the cardiac cycle underscores hemodynamic changes that occur in MR [Figure 2].

**FIGURE 2: PHASES AND PRESSURES OF THE CARDIAC CYCLE IN THE LEFT HEART UNDER NORMAL CONDITIONS**[3]

AP: aortic pressure; LAP: left atrial pressure; LV: left ventricle; LVEDV: left-ventricular end diastolic pressure; LVESV: left ventricular end systolic volume




Source: Klabunde R. Cardiovascular Physiology Concepts. https://www.cvphysiology.com/Heart%20Disease/HD005

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## LEFT ATRIAL PRESSURE AND MITRAL REGURGITATION[3]

Normal mean LAP is **6-12 mmHg**. In chronic MR, repetitive regurgitant flow increases atrial filling during phases 3-4 [Figure 2]. At the end of phase 5, the LAP can increase to as high as **25 mmHg** depending on MR etiology and severity, and patient state[3]. Visually, this is seen as a **tall v-wave**, the height of which [Figure 3], especially relative to the baseline, is an indicator of MR severity.

More sophisticated parameters can be used to quantify regurgitant flow in MR. These include:

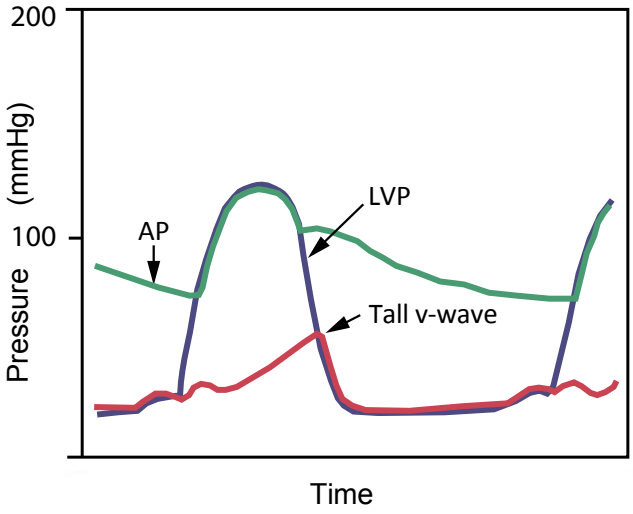
- **LAmP:** Mean pressure in the left atrium throughout the cardiac cycle
- **LAvP:** Peak LA v-wave pressure on the LAP tracing
- **LAv height:** Difference between the peak LA v-wave and the minimum LAP.

Ideally, LAmP, LAvP, and LAvheight would all decrease after mitral valve repair to alleviate MR. However, this is not always the case. Paradoxical Instances of reduction in v-wave height with LAmP increase can happen. Continuous LAP monitoring during mitral valve repair is thus important to track such subtle changes.

LAP is also influenced by systemic blood pressure (sBP). In two MR patients with identical hearts but different blood pressures, the patient with a higher sBP (hypertensive) will have an increased left ventricular systolic pressures (LVSP), more regurgitation (as blood will take the path of least resistance), and higher left atrial pressures, though the underlying valvular disorder is the same. Thus, changes in LVSP can affect LAP independent of underlying MR severity. To normalize for differences in LVSP, the LAP pressures can be "indexed" or normalized to the LVSP:

- **LAmPi:** LAmP indexed to (divided by) LVSP
- **LAvPI:** LAvP indexed to (divided by) LVSP

**FIGURE 3: MR CONDITION: LEFT ATRIAL PRESSURE TRACING WITH TALL V-WAVE[3]**




Source: Klabunde R. Cardiovascular Physiology Concepts. https://www.cvphysiology.com/Heart%20Disease/HD005

## WHY PERFORM CONTINUOUS LAP MEASUREMENT DURING MITRACLIP PLACEMENT?

The MitraClip alleviates MR by coapting two leaflets, a procedure that currently relies on qualitative and semi-quantitative determination of residual MR based primarily on visualizing the regurgitant jets under color doppler echocardiography. While effective, it limits assessment of any potential iatrogenic mitral stenosis. Real time continuous LAP monitoring during MitraClip placement can provide adjunctive objective data to complement intraprocedural decision making, and establish optimal post-procedure MR reduction with minimal stenosis risks.

## REFERENCES


1. Leonard, L. S. (2016). Pathophysiology of Heart Disease. A collaborative Project of Medical Students and Faculty. Wolters Kluwer, Philadelphia.
2. Shah M, Jorde UP. (2019) Percutaneous Mitral Valve Interventions (Repair): Current Indications and Future Perspectives. Front Cardiovasc Med. https://www.frontiersin.org/articles/10.3389/fcvm.2019.00088/full
3. Klabunde, R. (2011) Cardiovascular Physiology Concepts. Lippincott Williams & Wilkins, Philadelphia. https://www.cvphysiology.com/Heart%20Disease/HD005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**Rx ONLY**
**IMPORTANT SAFETY INFORMATION**
**MITRACLIP™ CLIP DELIVERY SYSTEM**

**Indications for Use**

- The MitraClip™ G4 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™ G4 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 American Society 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 symptoms and 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 G4 System is contraindicated in patients with the following conditions: Patients who cannot tolerate, including allergy or hypersensitivity to, procedural anticoagulation or post procedural anti-platelet regime; Patients with known hypersensitivity to clip components (nickel / titanium, cobalt, chromium, polyester), or with contrast sensitivity; Active endocarditis of the mitral valve; Rheumatic mitral valve disease; Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus

**Potential Complications and Adverse Events**

The following ANTICIPATED EVENTS have been identified as possible complications of the MitraClip G4 procedure: Allergic reactions or hypersensitivity to latex, contrast agent, anaesthesia, device materials (nickel / titanium, cobalt, chromium, polyester), and drug reactions to anticoagulation, or antiplatelet drugs, Vascular access complications which may require transfusion or vessel repair including: wound dehiscence, catheter site reactions, Bleeding (including ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage), Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture, vascular occlusion, Emboli (air thrombotic material, implant, device component); Peripheral Nerve Injury; Lymphatic complications; Pericardial complications which may require additional intervention, including: Pericardial effuse on, Cardiac tamponade, Pericarditis; Cardiac complications which may require additional interventions or emergency cardiac surgery, including: Cardiac perforation, Atrial septal defect; Mitral valve complications, which may complicate or prevent later surgical repair, including: Chordal entanglement / rupture, Single Leaflet Device Attachment (SLDA), Thrombosis, Dislodgement of previously implanted devices, Tissue damage, Mitral valve stenosis, Persistent or residual mitral regurgitation, Endocarditis; Cardiac arrhythmias (including conduction disorders, atrial arrhythmias, ventricular arrhythmias); Cardiac ischemic conditions (including myocardial infarction, myocardial ischemia, and unstable / stable angina); Venous thromboembolism (including deep vein thrombosis, pulmonary embolism, post procedure pulmonary embolism); Stroke / Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA); System organ failure: Cardio-respiratory arrest, Worsening heart failure, Pulmonary congestion, Respiratory dysfunction / failure / atelectasis, Renal insufficiency or failure, Shock (including cardiogenic and anaphylactic); Blood cell disorders (including coagulopathy, hemolysis, and Heparin Induced Thrombocytopenia (HIT)); Hypotension / hypertension; Infection including: Urinary Tract Infection (UTI), Pneumonia, Septicemia; Nausea / vomiting; Chest pain; Dyspnea; Edema; Fever or hyperthermia; Pain; Death; Fluoroscopy, Transesophageal echocardiogram (TEE) and Transthoracic echocardiogram (TTE) -related complications: Skin injury or tissue changes due to exposure to ionizing radiation, Esophageal irritation; Esophageal perforation, Gastrointestinal bleeding

See Important Safety Instructions referenced within.

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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