Clinical Insights

SUMMARY OF CLINICAL DATA

MITRACLIP[™] TRANSCATHETER MITRAL VALVE 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

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.

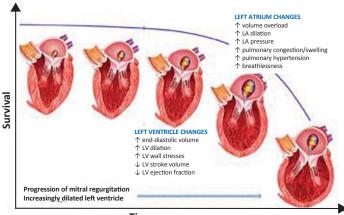
- 1. During systole (contraction), higher regurgitant flow increases left atrial pressure (LAP)
- 2. During diastole (relaxation), regurgitant blood repeatedly flows back to the left ventricle, resulting in increasingly larger diastolic volumes and subsequently **higher left ventricular end diastolic 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].



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

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



Time Adapted Shah M, et al. Front Cardiovasc Med 6:88, 2019

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:

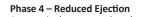
- Cardiac output is diminished, lowering renal blood flow. The kidneys interpret this as a low volume state and inappropriately stimulate water retention in an attempt to maintain blood volume and end organ perfusion.
- Abnormal water retention further stresses an already failing heart. Volume overload 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 CONDITIONS³

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

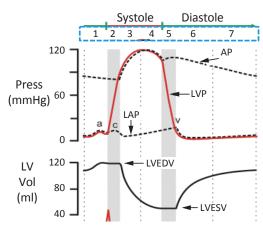


As ventricular contraction slows and the - heart repolarizes, the rate of ejection falls

Phase 3 – Rapid Ejection Left ventricular pressure increases, aortic and pulmonic valves open, leading to rapid emptying

Phase 2 – Isovolumetric Contraction Systolic contraction occurs against closed aortic and pulmonic valves causing bulging of the mitral valve (LAP c-wave)

Phase 1 – Atrial Contraction At the end of diastole, the atria contracts in the final step of diastolic filling (LAP a-wave)



Phase 5 – Isovolumetric Relaxation

As ventricles relax, the aortic and pulmonic valves close. Filling does not occur as ventricular pressures still exceed atrial pressures. Atrial filling continues against a closed mitral valve until the LAP peaks (LAP v-wave)

Phase 6 – Rapid Filling

Ventricular pressure drops below the pressure in the atria, the tricuspid and mitral valves open. Ventricular filling begins. Atrial pressures drop

Phase 7 – Reduced Filling

As ventricular pressure rises, the pressure gradient between the atria and ventricles drops, reducing the rate of filling. Following this phase, atrial contraction occurs (**back to phase 1**)

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

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LEFT ATRIAL PRESSURE AND MITRAL REGURGITATION³

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 state³. 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:

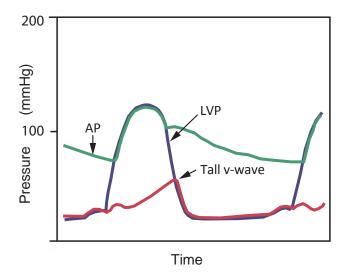
- LAmP: Mean pressure in the left atrium throughout the cardiac cycle
- LAvP: Peak LA v-wave pressure on the LAP tracing
- **LAv height:** Difference between the peak LA v-wave and the minimum LAP.

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-WAVE³



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 semiquantitative 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.
- 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/fcrun.2019.00088/full
- Klabunde, R. (2011) Cardiovascular Physiology Concepts. Lippincott Williams & Wilkins, Philadelphia. https://www.cvphysiology.com/Heart%20Disease/HD005

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