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INTERMEDIATE

CASE REPORT: CLINICAL CASE

# MitraClip Implantation for Functional Mitral Regurgitation With Coaptation Gap Facilitated by Levosimendan Treatment

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## ABSTRACT

A patient with severe, symptomatic functional mitral regurgitation was initially considered not suitable for MitraClip (Abbott Vascular, Abbott Park, Illinois) implantation because of non-coapting mitral leaflets. Repeated levosimendan infusions in combination with intensive diuresis induced sufficient valve coaptation, thus allowing MitraClip implantation to be performed. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:862–5) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

## HISTORY OF PRESENTATION

A 74-year-old patient was admitted to our cardiology department for heart failure symptoms with dyspnea (New York Heart Association functional class III) and bilateral pitting leg edema. Hemodynamic status was stable, with blood pressure of 111/67 mm Hg, heart rate of 61 beats/min, no fever, and 95% oxygen saturation. The electrocardiogram showed sinus rhythm with ventricular pacing. A transthoracic echocardiogram (TTE) showed a left ventricular (LV) ejection fraction (LVEF) of 45% with inferior and lateral wall hypokinesia, severe functional mitral regurgitation (MR), and tricuspid regurgitation (TR).

### LEARNING OBJECTIVES

- To understand that functional MR is a dynamic phenomenon.
- To demonstrate that levosimendan may influence the severity and morphology of MR by altering hemodynamic and loading conditions.

## MEDICAL HISTORY

The patient's medical history included type 2 diabetes, hypertension, chronic kidney disease (estimated glomerular filtration rate 49 ml/min/m$^2$), myocardial infarction with angioplasty of the left circumflex artery 4 four years before the current admission, pacemaker implantation for atrioventricular block, and left anterior descending artery angioplasty 1 year before admission as a result of positive stress echocardiography. His treatment included bisoprolol (2.5 mg), ramipril (2.5 mg), spironolactone (25 mg), atorvastatin (40 mg), aspirin (75 mg), clopidogrel (75 mg), furosemide (60 mg), and insulin.

## DIFFERENTIAL DIAGNOSIS

The differential diagnosis of dyspnea is broad and includes the majority of cardiopulmonary

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diseases such as heart failure, coronary artery and valvular disease, pulmonary embolism, and infection. In our case, the most probable diagnosis was decompensated heart failure in the context of severe MR.

## INITIAL INVESTIGATIONS

A blood sample showed a hemoglobin level of 12 g/l, a serum creatinine level of 143 μmol/l, elevated N-terminal pro-B-type natriuretic peptide levels (3,557 pg/ml), and normal troponin levels. The chest radiograph showed pulmonary congestion. The TTE showed LV dilatation (end-diastolic volume 156 ml, 82 ml/m$^2$) with moderate LV dysfunction (LVEF, 45%) related to inferolateral and inferior wall hypokinesia and severe functional MR (effective regurgitant orifice area [EROA] 0.35 cm$^2$) and TR (EROA 0.4 cm$^2$). The left atrium (52 ml/m$^2$) and tricuspid annulus (44 mm) were dilated. The right ventricular (RV) systolic function was reduced (tricuspid annular plane systolic excursion = 15 mm; RV fractional area change 22%) and the pulmonary pressure was estimated at 76 mm Hg. A transesophageal echocardiogram (TEE) was also performed, confirming the severe functional MR (EROA 0.56 cm$^2$) with a coaptation defect (2 mm) and short posterior leaflet length (8 mm) (Video 1).

## MANAGEMENT AND INTERVENTIONS

The initial medical strategy was to treat heart failure symptoms with intravenous diuretic agents. However, despite adequate depletion, the severity of MR and TR remained unchanged on TTE. A coronary angiogram was performed to exclude an ischemic origin, and it showed patent left anterior descending artery and left circumflex artery stents. After heart team discussion, the surgical option was excluded because of the operative risk (European System for Cardiac Operative Risk Evaluation [EuroSCORE] II of 8%, in addition to tricuspid surgery with RV dysfunction). Cardiac resynchronization was not indicated because the LVEF was >35%. MitraClip (Abbott Vascular, Abbott Park, Illinois) implantation was considered, but the TEE showed a severe coaptation defect (2 mm) at the level of $A_2$-$P_2$ segment with a short posterior leaflet length. It was therefore proposed to administer repeated levosimendan infusions in combination with diuretic treatment. The patient underwent 3 levosimendan infusions (every 2 weeks) at a dose of 0.2 μg/kg/min over 24 h (without a loading dose). The infusions were well tolerated, and the patient felt clinically improved. TTE and TEE examinations performed after the third infusion showed a significant decrease in MR severity (EROA, 0.56 cm$^2$

### ABBREVIATIONS AND ACRONYMS

**EROA** = effective regurgitant orifice area

**LVEF** = left ventricular ejection fraction

**MC** = MitraClip

**MR** = mitral regurgitation

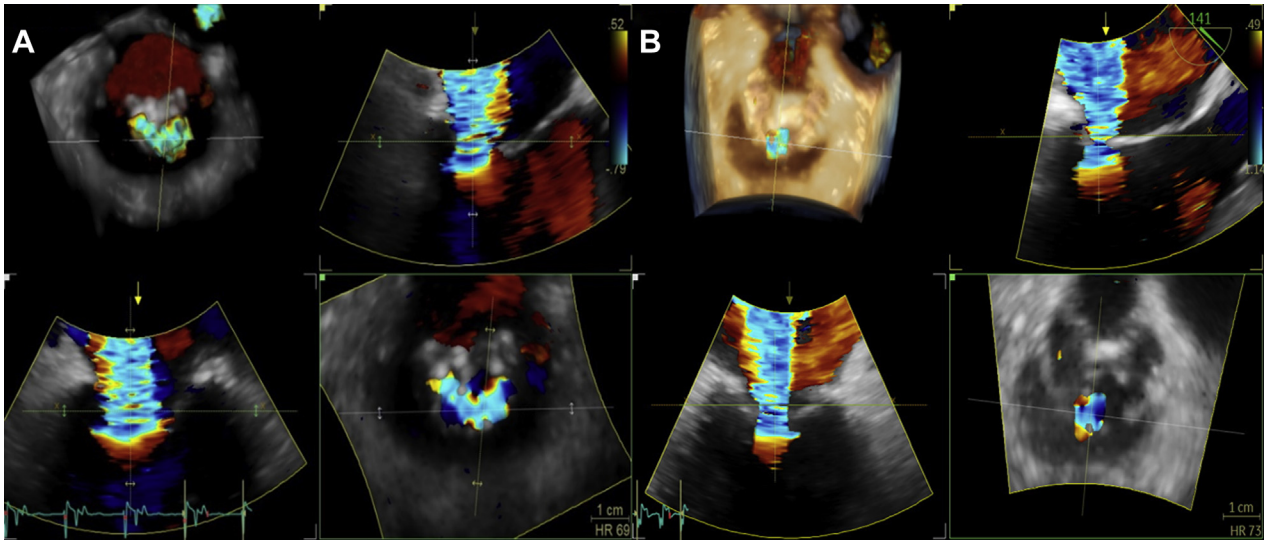
**RV** = right ventricular

**TEE** = transesophageal echocardiogram

**TTE** = transthoracic echocardiogram

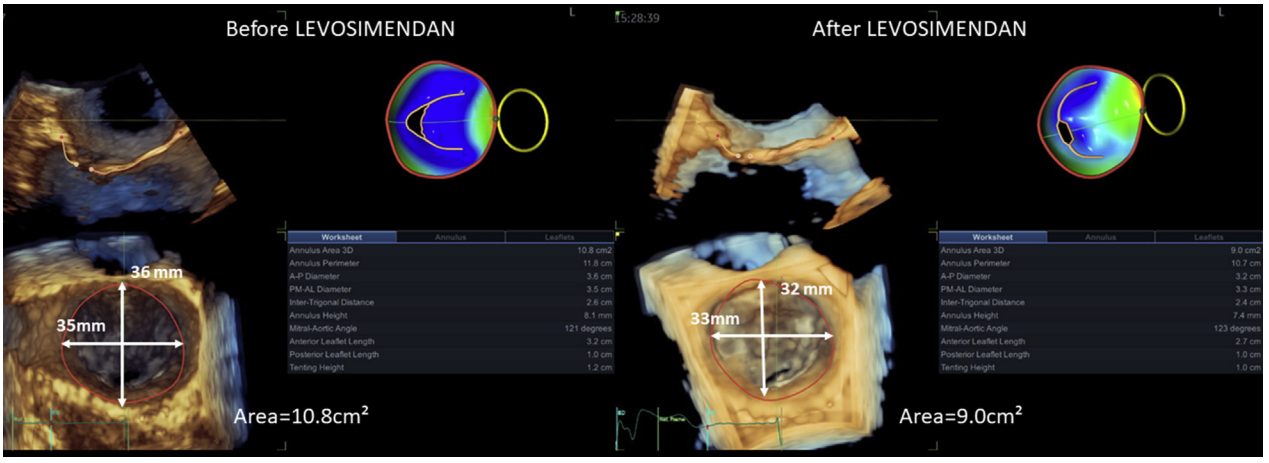
**TR** = tricuspid regurgitation

**FIGURE 1** Mitral Regurgitation Before and After Levosimendan




3-dimensional transesophageal echocardiography **(A)** pre-levosimendan. and **(B)** post-levosimendan. Notice the reduction in mitral regurgitation severity.

**FIGURE 2 Mitral Annular Dimensions and Area Before and After Levosimendan**




3-dimensional transesophageal echocardiography. Annular dimensions and surface **(left)** pre-levosimendan and **(right)** post-levosimendan. A-P = anteroposterior; PM-AL = posteromedial-anterolateral.

vs. 0.27 $cm^2$) (**Figures 1A and 1B**, Video 2) associated with a reduction in left atrial volume (43 $ml/m^2$ vs. 52 $ml/m^2$) and mitral annulus size (**Figure 2**). Most importantly, coaptation improved (Videos 3 and 4), and TR almost disappeared (Videos 5 and 6). The RV and tricuspid annulus sizes were both reduced, whereas tricuspid annular plane systolic excursion and LVEF remained unchanged (**Table 1**). The MC procedure was successfully performed 1 month after the last levosimendan infusion. Two clips were implanted with no residual regurgitation or stenosis on control TTE (Video 7).

**TABLE 1 Echocardiographic Parameters Pre- and Post-Levosimendan Treatment**

| | Before Levosimendan | After Levosimendan |
|---|---|---|
| MR severity (TEE values) | | |
| EROA ($cm^2$) | 56 | 27 |
| PISA radius (mm) | 11 | 7 |
| Regurgitant volume (ml) | 82 | 49 |
| LV end-diastolic volume (ml) | 156 | 151 |
| LV end-systolic volume (ml) | 76 | 80 |
| Left atrial volume ($ml/m^2$) | 52 | 43 |
| Mitral annular diameter (mm) | 35 | 33 |
| Mitral annular area ($cm^2$) | 10.8 | 9 |
| Tricuspid annular diameter (mm) | 44 | 35 |
| TAPSE (mm) | 15 (with severe TR) | 15 (with minimal TR) |

EROA = effective regurgitant orifice area; LV = left ventricular; MR = mitral regurgitation; PISA = proximal isovelocity surface area; TAPSE = tricuspid annular plane systolic excursion; TEE = transesophageal echocardiography; TR = tricuspid regurgitation.

## DISCUSSION

The MC procedure is an alternative to cardiac surgery in patients with severe symptomatic secondary MR who are receiving optimal medical treatment (1). In our case, MR severity (EROA >0.4 $cm^2$) was disproportionate to LV dysfunction (LVEF 45%) and dilatation (end-diastolic volume 82 $ml/m^2$). Patients with disproportionate MR seem to benefit from mechanical interventions (2). Although clinical criteria were fulfilled for an MC procedure, anatomic criteria were not met. The ideal valve morphology for successful MC implantation includes a coaptation length >2 mm and a coaptation depth <11 mm (3).

However, secondary MR is dynamic, and these criteria may be modified by loading conditions and LV contractility. In a recent study, the use of an intra-aortic balloon pump in patients with unfavorable valve anatomy fostered better anatomic conditions and permitted uneventful performance of MC implantation (4).

To our knowledge, this is the first case report describing the use of levosimendan to facilitate a MC procedure in a patient with unfavorable anatomy. Levosimendan is a long-acting inotrope with vasodilatory effects. Levosimendan also improves ventriculoarterial coupling, decreases LV afterload, and interferes with neurohormonal mechanisms, such as decreasing the levels of natriuretic peptides (5,6). The foregoing mechanisms usually participate in LV remodeling, which determines MR severity. Small

sample studies suggested that levosimendan may reduce functional MR in patients with chronic heart failure and may improve the short-term results of the MC procedure (7–9). However, these studies were performed in patients with mitral anatomy that was suitable for MC implantation, and the dose of levosimendan used (0.01 μg/kg/min) was 20 times lower than the dose usually used in heart failure trials (10). In our case, a conventional dose of levosimendan combined with diuretic treatment seemed to be superior to diuretic therapy alone for modifying loading conditions and obtaining more favorable valve coaptation. RV elasticity properties and sensitivity to levosimendan may explain the complete and sustained regression of TR.

Even though MR improved after levosimendan infusions, we decided to proceed with the MC procedure for 2 reasons. First, MR still remained significant, with an EROA of 0.27 $cm^2$. A secondary MR with an EROA >0.20 $cm^2$ is considered severe according to the European Society of Cardiology guidelines, and this was also the cutoff used in the MITRA-FR (Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral Regurgitation) (1,11). Second, levosimendan is an inotrope with a duration of action of 7 to 15 days (5). There are no data on the long-term effect of the drug in the context of severe functional MR, so the possibility that MR could become reaggravated had to be taken into account.

## FOLLOW-UP

The patient was clinically stable at 3-month follow-up, without signs of congestion during low-dose diuretic treatment. The control TTE and TEE were also satisfying, showing the presence of 2 residual jets with mild to moderate MR (Video 8).

## CONCLUSIONS

In this case report a patient with secondary MR and initially unfavorable anatomy for MC was managed with levosimendan infusions that enabled leaflet coaptation and subsequent MC implantation.

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**KEY WORDS** heart failure, levosimendan, MitraClip, mitral regurgitation

**APPENDIX** For supplemental videos, please see the online version of this paper.