Left Ventricular Reverse Remodeling Post-MitraClip: Results from the EXPANDed Studies

Mirjam Keßler, Gilbert Tang, Sebastien Deferm, Rodrigo Estevez-Loureiro, Wolfgang Rottbauer, Federico M. Asch, Jose L. Zamorano, Janani Aiyer, Rong Huang, Evelio Rodriguez, Francesco Maisano, Ralph Stephan von Bardeleben

The EXPANDed studies (EXPAND + EXPAND G4) are sponsored by Abbott.

Potential conflicts of interest

Speaker's name : Mirjam Kessler

☑ I do not have any potential conflict of interest to declare

Background

- Mitral transcatheter edge-to-edge repair (M-TEER) with the MitraClip device has been used to treat over 200,000 patients with mitral regurgitation (MR).

- The EXPANDed (EXPAND and EXPAND G4) studies were conducted to evaluate real-world clinical experience and outcomes associated with use of the 3rd and 4th generation MitraClip systems.

- Studies have shown that post-MitraClip treatment, patients with secondary MR experience beneficial left ventricular reverse remodeling (LVRR).[1-3]

The objective of this analysis is to report the impact of early (30-day) LVRR on clinical outcomes in subjects with primary and secondary MR and identify independent associations with early LVRR in the EXPANDed studies.

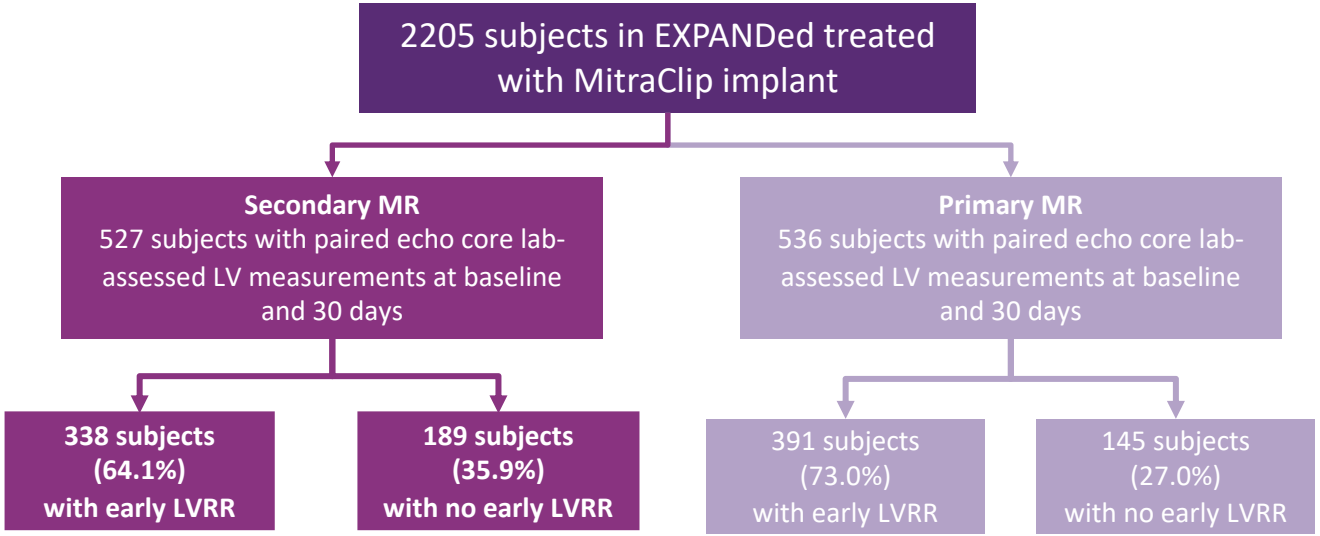
[1]Megaly et al, SHJ, Volume 2, Issue 6, p541-547, 2018
[2]Brouwer et al, EHJ CVI, 2019; 20(3):307-313
[3]Kessler et al, EuroPCR 2022

Analysis of Early LVRR in Secondary MR

Early LVRR

Defined as >10% reduction[1,2] in any of the following from baseline to 30 days:

- **LVEDV**
- **LVEDD**
- **LVESV**
- **LVESD**



1142 subjects were excluded due to missing etiology or lack of paired LV measurements

Analysis Methodology in SMR Subjects:

- MR severity through 1 year was compared between subjects with early vs no early LVRR
- Composite outcome of all-cause mortality or heart-failure hospitalizations (HFH) through 1 year was compared between subjects with early vs no early LVRR
- Multivariable analysis was used to identify clinical and echocardiographic associations with early LVRR

LVEDV: Left ventricular end diastolic volume, LVESV: Left ventricular end systolic volume, LVEDD: Left ventricular end diastolic dimension, LVESD: Left ventricular end systolic dimension

[1]Nita et al, CCI, 2020;96(3):687-97
[2]Bano et al, J. Cardiology, 2016;68(1):57-63

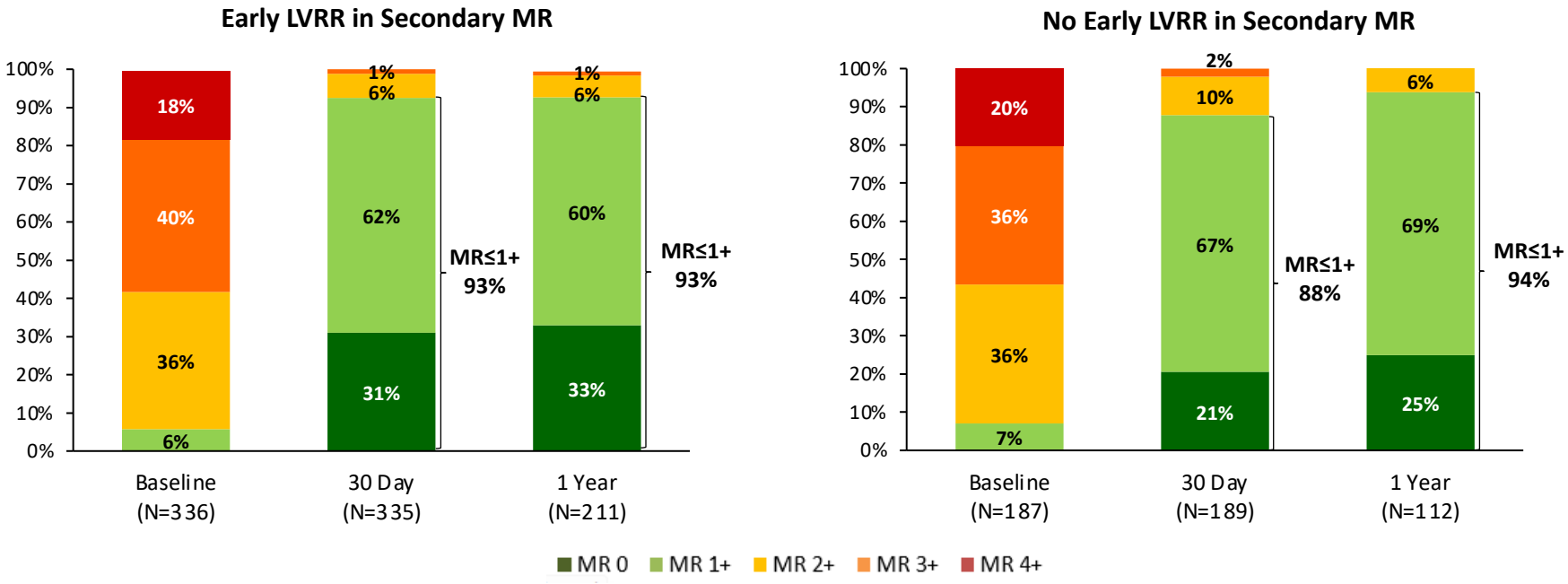
Secondary MR - Baseline Characteristics

Subjects with SMR who did not experience early LVRR had larger ventricles, lower EF, and a higher prevalence of prior cardiac surgery and pacemakers.

Demographics, Comorbidities, and Echo Measures in SMR Subjects	Early LVRR (n=338)	No Early LVRR (n=189)	P-Value
Age (years)	74.9±9.5	74.1±10.2	0.69
Female	42.6% (144)	36.5% (69)	0.17
STS Repair Score (%)	6.2±6.1	6.5±7.1	0.88
Hypertension	**86.0% (289)**	**77.0% (144)**	**<0.01**
Renal Failure	36.2% (122)	37.2% (70)	0.74
Prior Cardiac Surgeries	**27.2% (92)**	**41.3% (78)**	**<0.001**
CRT/CRT-D/ICD/Permanent Pacemaker	**19.2% (65)**	**30.7% (58)**	**0.003**
A-P Diastolic Annular Dimension (APDAD, cm)	3.46±0.49	3.42±0.49	0.37
Left Ventricular Ejection Fraction (LVEF, %)	**41.0±13.9**	**37.5±13.4**	**0.006**
Left Ventricular End Systolic Volume (LVESV, mL)	**104.0±61.1**	**121.2±72.4**	**0.001**
Left Ventricular End Diastolic Volume (LVEDV, mL)	168.0±72.4	184.4±85.3	0.05
Left Ventricular End Systolic Dimension (LVESD, cm)	**4.78±1.1**	**5.13±1.22**	**0.002**
Left Ventricular End Diastolic Dimension (LVEDD, cm)	**5.88±0.88**	**6.13±1.02**	**0.008**

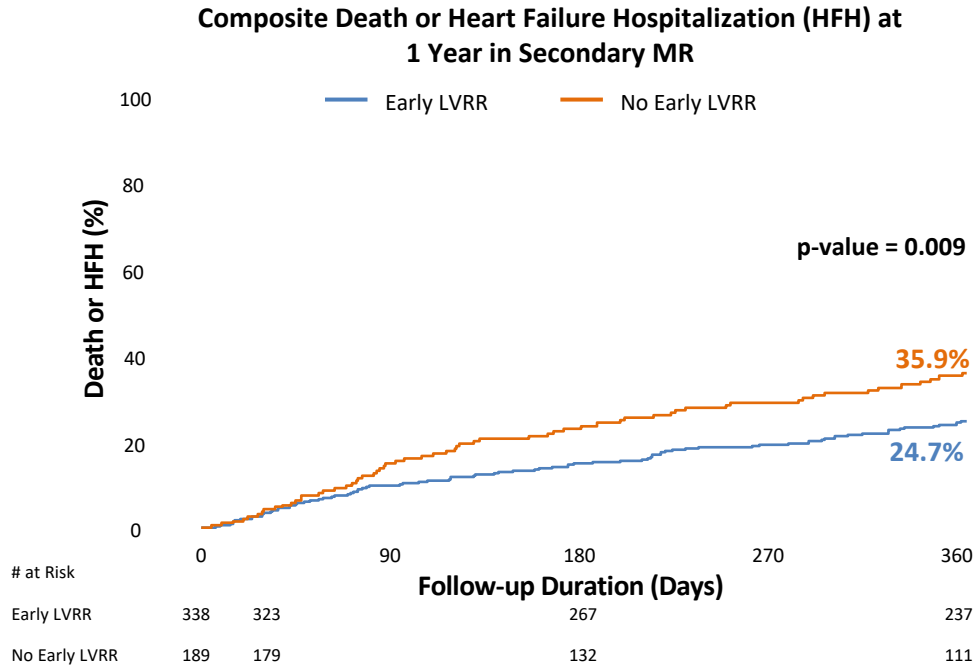
Secondary MR – MR Severity

Subjects with SMR experienced significant MR reduction regardless of early LVRR.



Secondary MR – Composite Death or HFH

Subjects with SMR who experienced early LVRR had significantly lower death/HFH rates than those who did not undergo early LVRR.



Secondary MR – Associations with Early LVRR

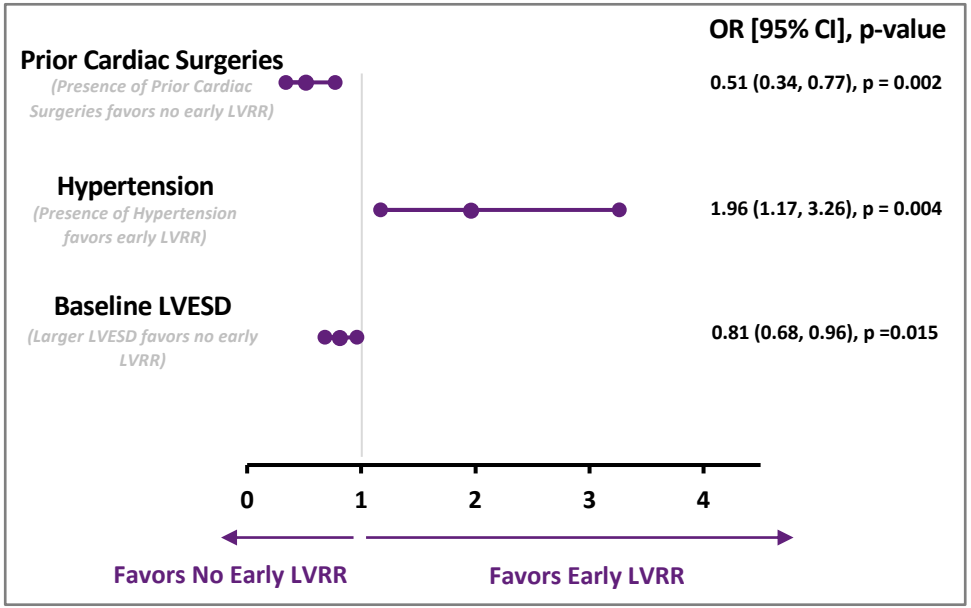
The presence of hypertension was associated with early LVRR while prior cardiac surgery and larger LVESD was associated with no early LVRR.

Univariable Analysis

Event	Odds Ratio (95% CI)	P-value
LV End Systolic Dimension (cm)	0.77 (0.65, 0.90)	<0.001
Prior cardiac surgeries	0.53 (0.37, 0.77)	0.001
CRT/ CRT-D/ ICD/ Permanent Pacemaker	0.54 (0.36, 0.81)	0.003
LV End Diastolic Dimension (cm)	0.75 (0.62, 0.91)	0.004
LV Ejection Fraction (%)	1.02 (1.01, 1.03)	0.006
LV End Systolic Volume (ml)	0.96 (0.94, 0.99)	0.006
Hypertension	1.84 (1.16, 2.91)	0.01
LV End Diastolic Volume (ml)	0.97 (0.95, 1.00)	0.02
Discharge AP Diastolic Annular Dimension (cm)	0.73 (0.51, 1.04)	0.08

Additional Variables Included in Univariable Analyses: Age, Female sex, STS Score Repair and Replacement, Diabetes, Renal Failure, CLD, COPD, Prior HFH, Home O2, Peripheral Arterial Disease, NYHA III/IV, Baseline and Discharge MR>1+ and >2+, Baseline TR>1+, SLDAD, APDAD, EROA, Mean gradient at baseline and discharge, PASP, Baseline and Discharge MVA, MV Peak E

Multivariable Analysis

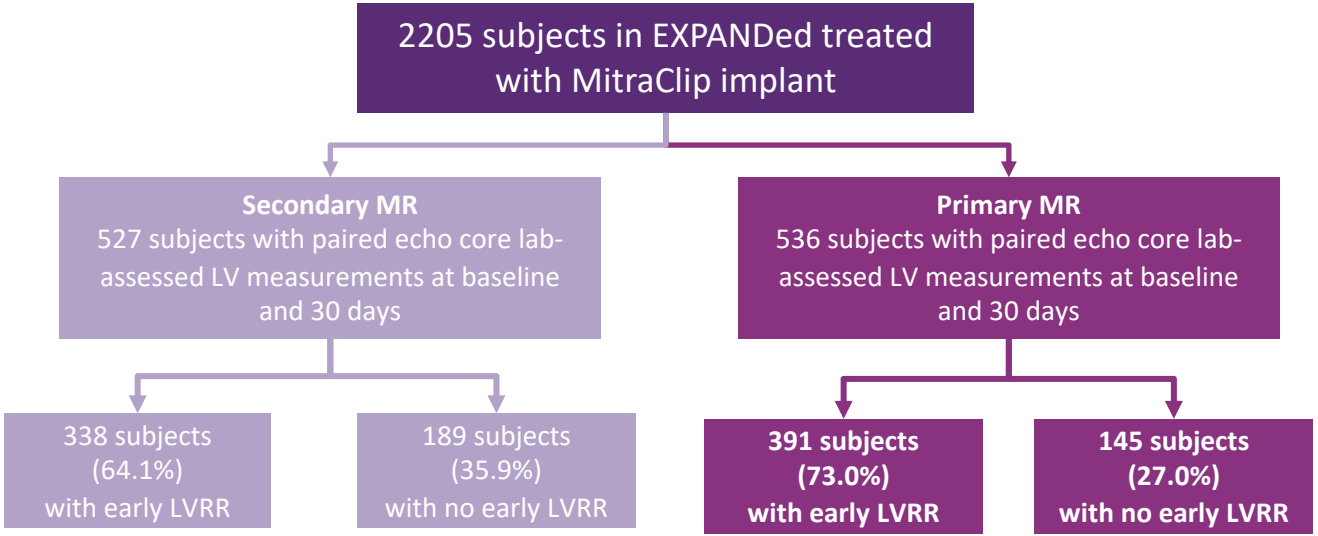


Analysis of LVRR in Primary MR

Early LVRR

Defined as >10% reduction[1,2] in any of the following from baseline to 30 days:

- **LVEDV**
- **LVEDD**
- **LVESV**
- **LVESD**



1142 subjects were excluded due to missing etiology or lack of paired LV measurements

Analysis Methodology in PMR Subjects:

- MR severity through 1 year was compared between subjects with early vs no early LVRR
- Composite outcome of all-cause mortality or heart-failure hospitalizations (HFH) through 1 year was compared between subjects with early vs no early LVRR

LVEDV: Left ventricular end diastolic volume, LVESV: Left ventricular end systolic volume, LVEDD: Left ventricular end diastolic dimension, LVESD: Left ventricular end systolic dimension

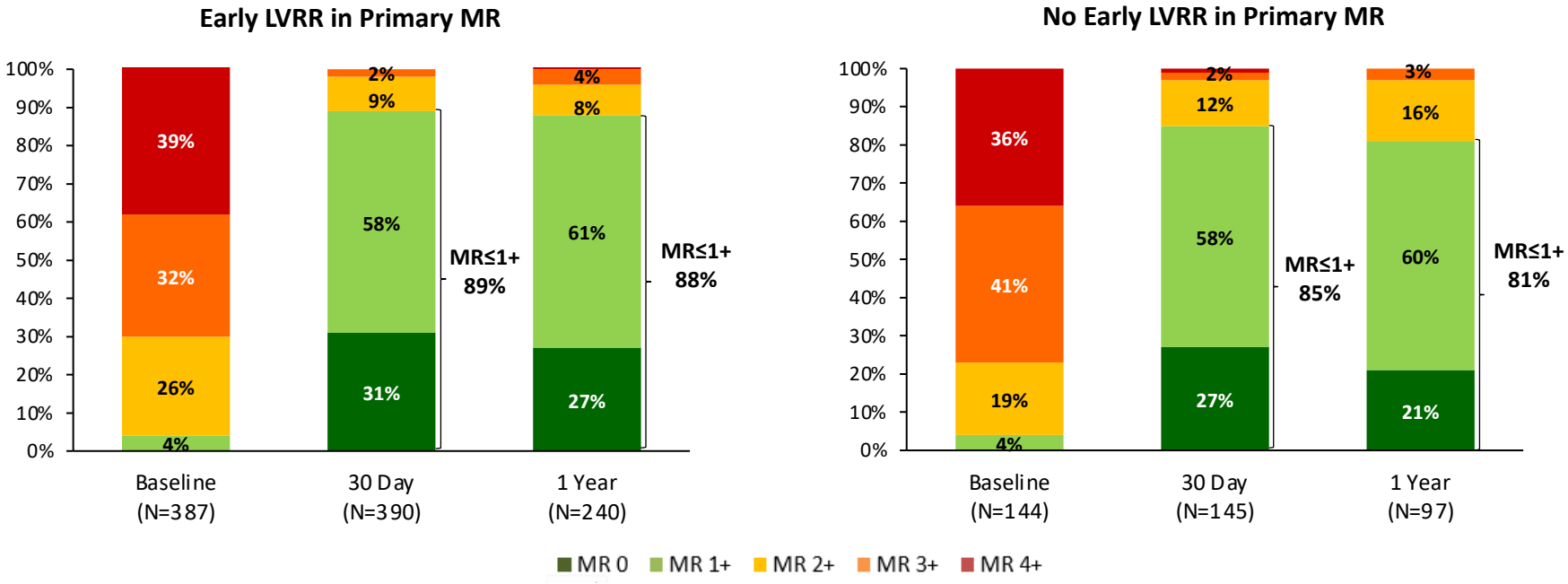
Primary MR - Baseline Characteristics

Subjects with PMR who underwent early LVRR had larger ventricles than those who did not.

Demographics, Comorbidities, and Echo Measures in PMR Subjects	Early LVRR (n=391)	No Early LVRR (n=145)	P-Value
Age (years)	79.5±8.8	80.0±8.7	0.60
Female (n, %)	45.3% (177)	49.7% (72)	0.37
STS Repair Score (%)	5.0±4.3	5.6±6.1	0.28
Hypertension (n, %)	75.4% (294)	80.6% (116)	0.21
Renal Failure (n, %)	36.2% (122)	37.6% (70)	0.74
Prior Cardiac Surgeries (n, %)	16.6% (65)	18.6% (27)	0.59
Prior Mitral Valve Procedure (n, %)	**7.7% (30)**	**2.8% (4)**	**0.04**
A-P Diastolic Annular Dimension (APDAD, cm)	3.29±0.53	3.23±0.54	0.24
Left Ventricular Ejection Fraction (LVEF, %)	61.1±9.9	60.3±11.1	0.72
Left Ventricular End Systolic Volume (LVESV, mL)	**49.1±27.0**	**46.5±30.2**	**0.04**
Left Ventricular End Diastolic Volume (LVEDV, mL)	**123.3±45.0**	**111.9±43.8**	**0.004**
Left Ventricular End Systolic Dimension (LVESD, cm)	**3.57±0.79**	**3.42±0.82**	**0.01**
Left Ventricular End Diastolic Dimension (LVEDD, cm)	5.19±0.7	5.13±0.69	0.39

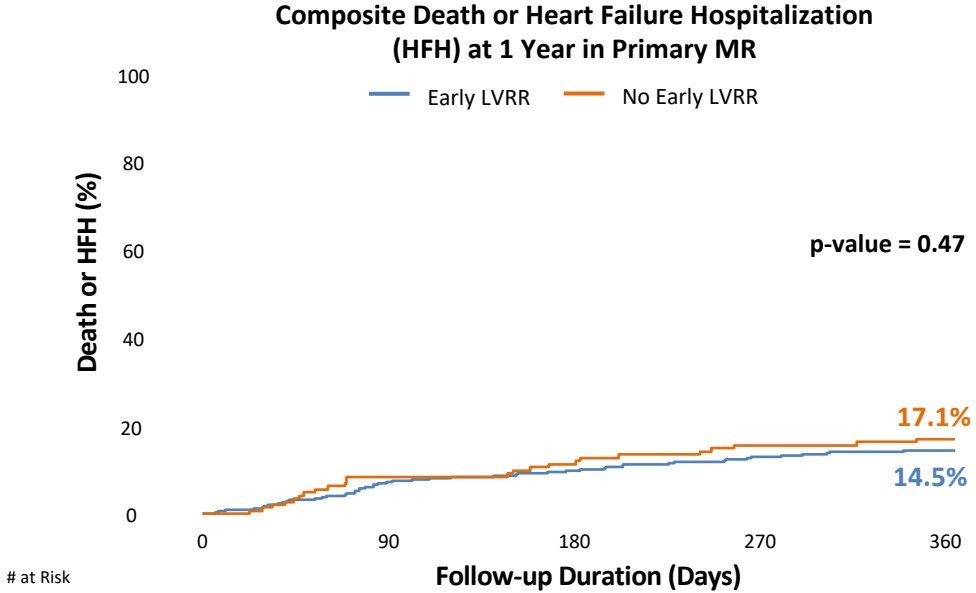
Primary MR – MR Severity

Subjects with PMR experienced significant MR reduction regardless of early LVRR.



Primary MR – Composite Death or HFH

Early LVRR did not impact the outcome of death/HFH in subjects with PMR.



Why is this important?

Results from the EXPANDed study show that MitraClip therapy effectively treats MR and results in LV reverse remodeling.

- A high proportion of subjects experienced early (30-day) LVRR (64% in SMR, 73% in PMR).
- Regardless of MR etiology, subjects in the early and no LVRR groups experienced significant MR reduction.
- Subjects with SMR who experienced early LVRR had a lower composite rate of death or HFH.
- The presence of hypertension in SMR was associated with early LVRR while prior cardiac surgery and larger LVESD was associated with no early LVRR.

Results from the EXPANDed studies demonstrate that MitraClip therapy can provide optimal clinical benefit to patients with SMR who are treated prior to significant disease progression.

PCR

PCRonline.com

For US audience, see Important Safety Information referenced within. For audiences outside of the U.S.: always check the regulatory status of the device in your region.

For US audience only

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

For US audience, see Important Safety Information referenced within. For audiences outside of the U.S.: always check the regulatory status of the device in your region.

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

Illustrations are artist's representations only and should not be considered as engineering drawings or photographs. Photos on file at Abbott.

Abbott 3200 Lakeside Dr., Santa Clara, CA. 95054 USA, Tel: 1.800.277.9902

www.structuralheart.abbott

Abbott