

Mitral Regurgitation in the MitraClip Era

Patient selection for MitraClip Therapy

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FACULTÉ DE MÉDECINE
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ESC Heart Failure 2012 Guidelines



European Heart Journal
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES



ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

“ In patients with an indication for valve repair but judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order to improve symptoms ” (page 48 from ESC 2012 guidelines)

Source: ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 published on ESC web-site: <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/acute-chronic-heart-failure.aspx?hit=dontmiss>

ESC/EACTS 2012 Guidelines on the Management of Valvular Heart Disease



European Heart Journal
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES 



Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

“ **Indication for primary MR:** Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C). ” (page 21)

“ **Indication for secondary MR:** The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C). ” (page 25)

Source: <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/valvular-heart-disease.aspx>

A patient with ischemic MR

History of the disease

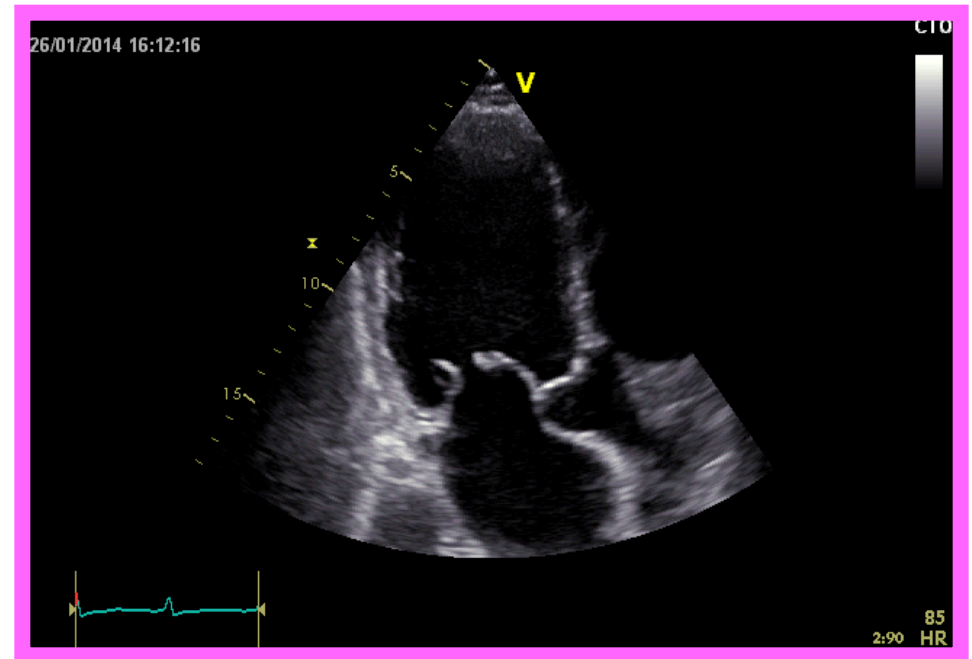
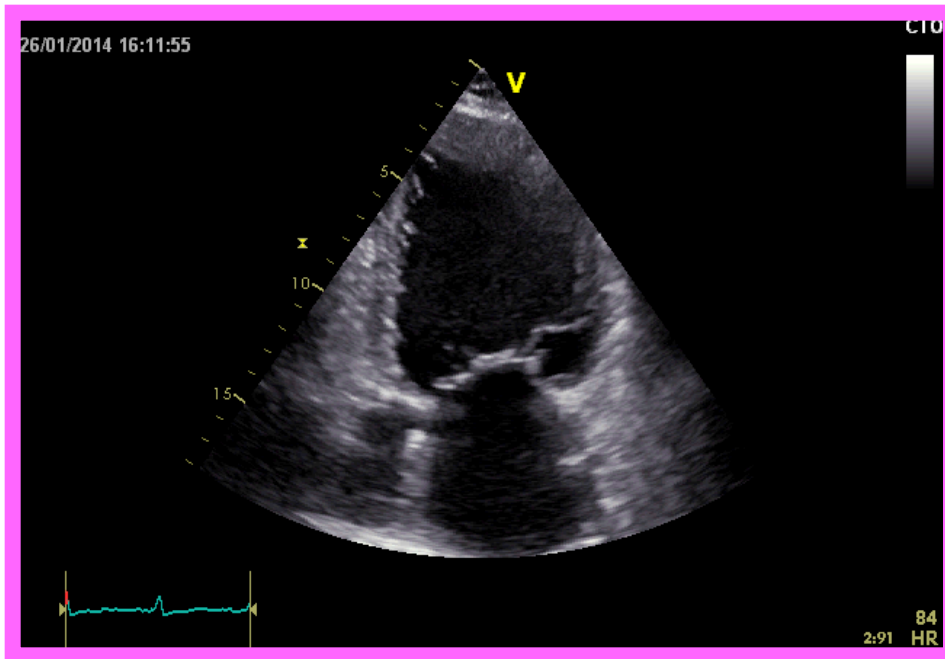
- ◆ 74 year-old man,
- ◆ diabetic ischemic cardiomyopathy
- ◆ multiple coronary stentings, 3-vessel disease
- ◆ previous inferior MI
- ◆ severe chronic renal failure
- ◆ paroxysmal AF
- ◆ repeat episodes of CHF

Clinical examination

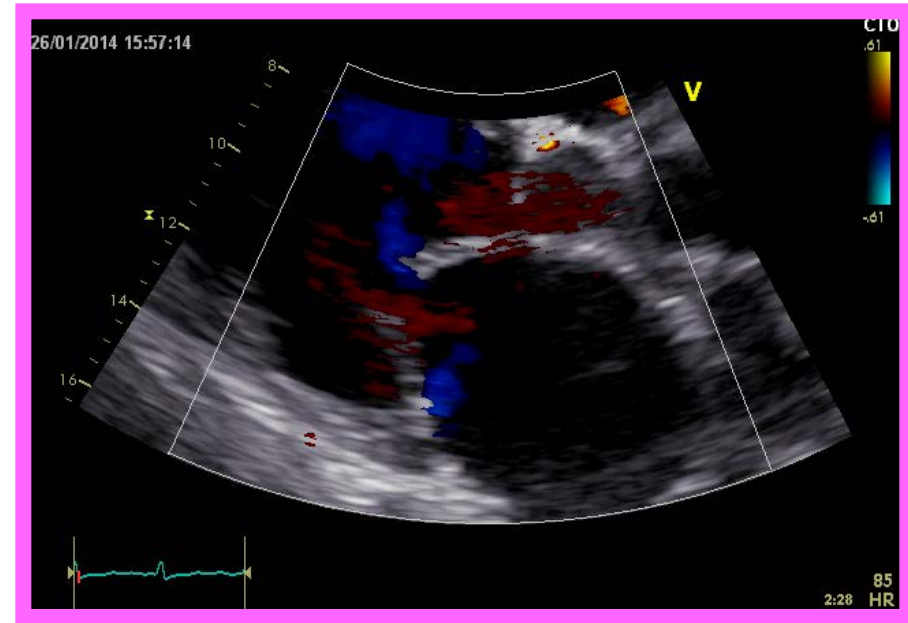
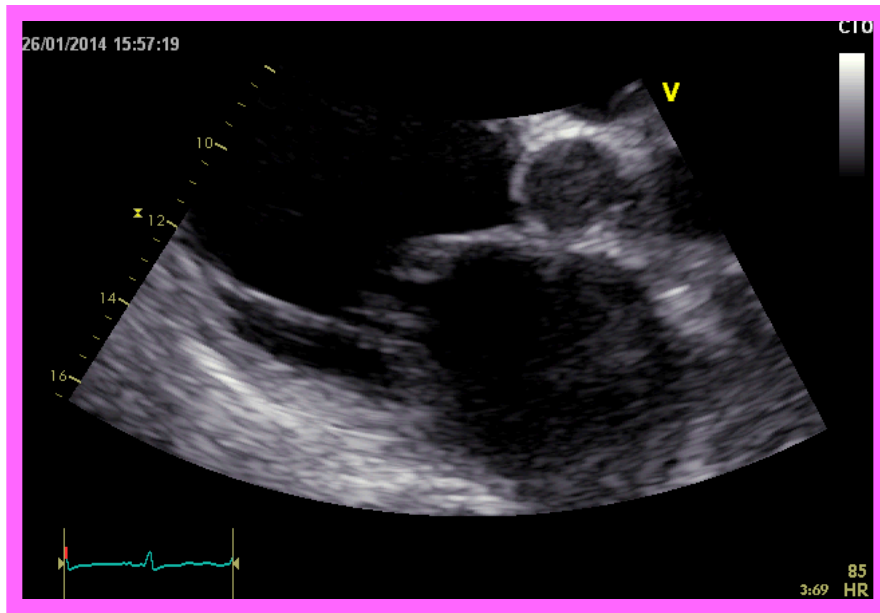
- ◆ NYHA IV
- ◆ mitral systolic murmur 2/6
- ◆ arterial pressure: 90 / 60 mmHg



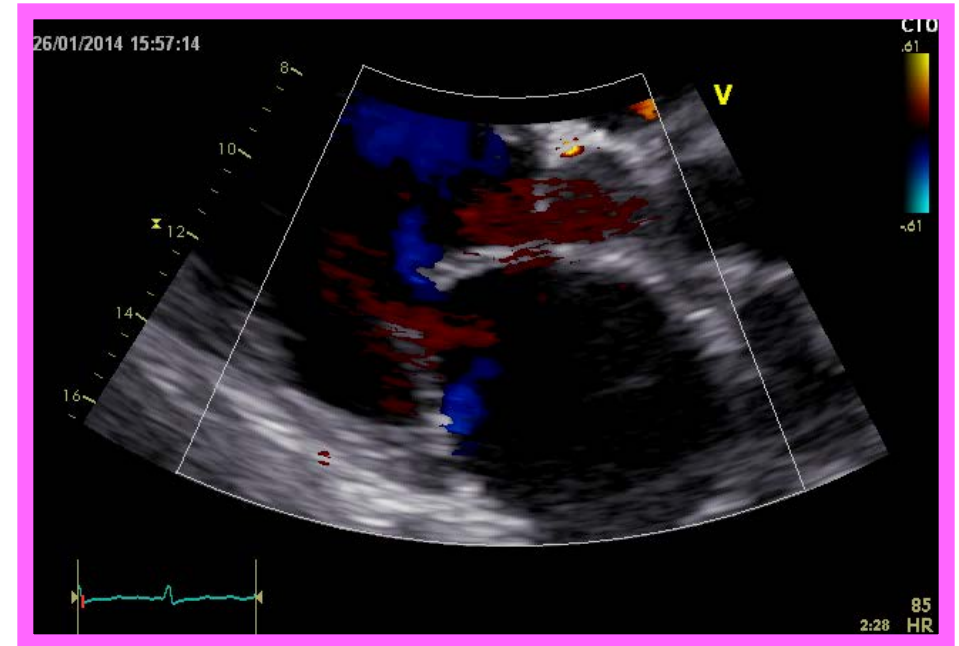
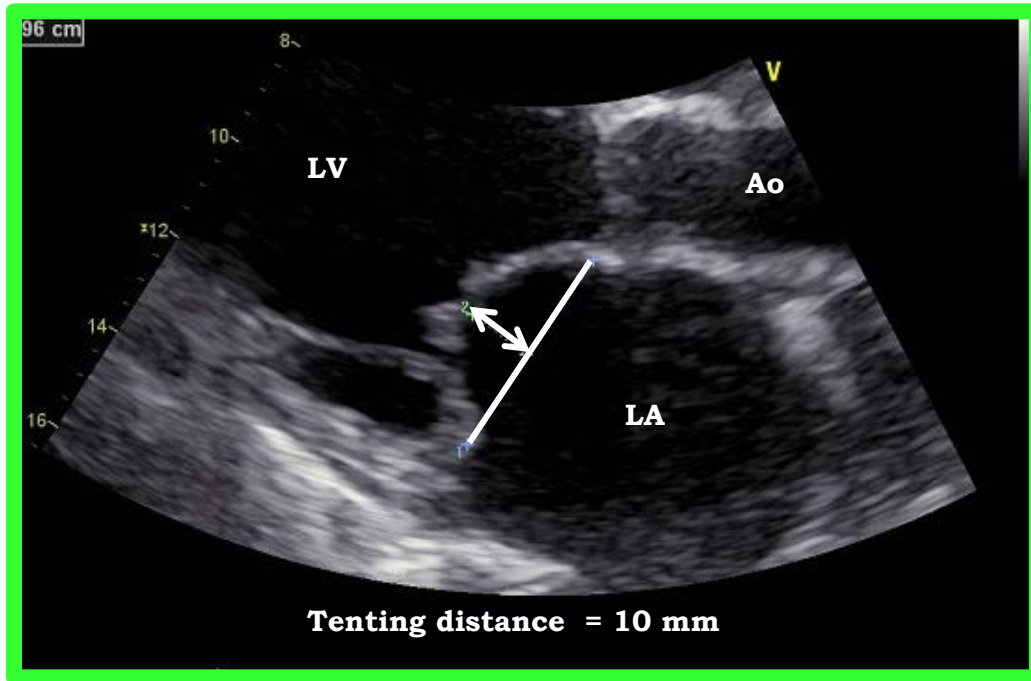
LVEF = 24%



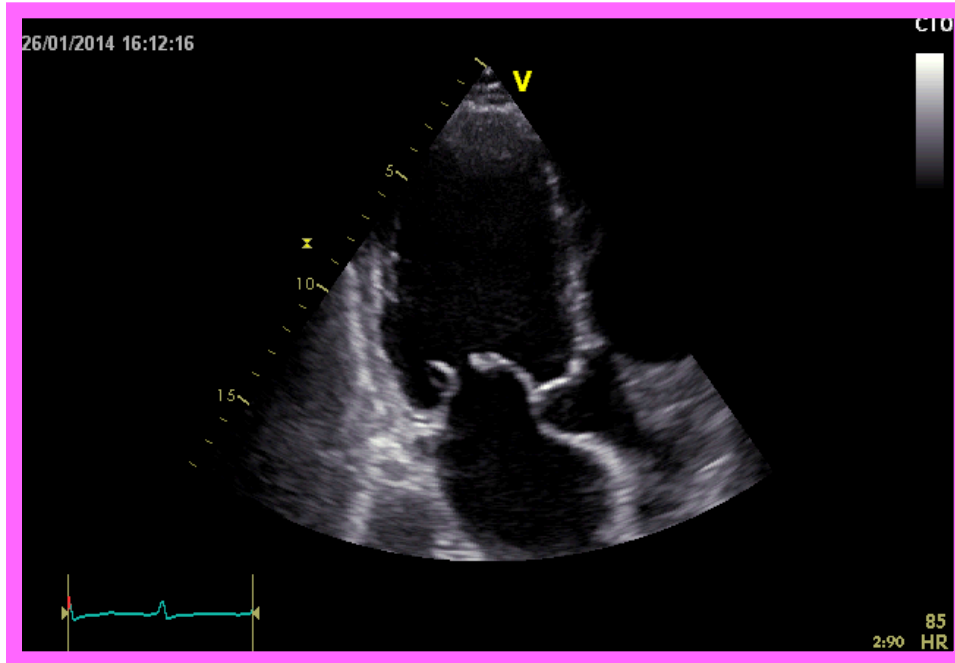
TTE: mitral regurgitation



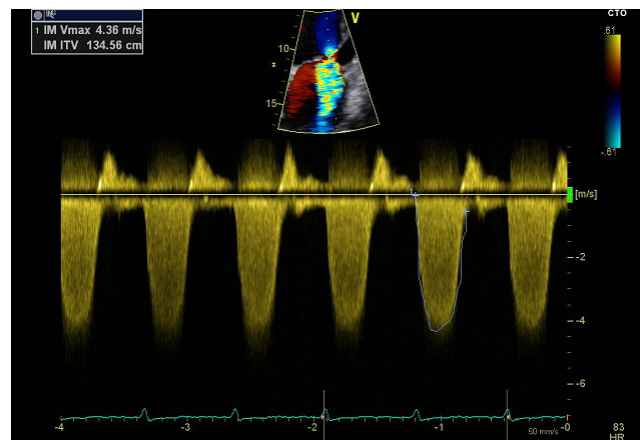
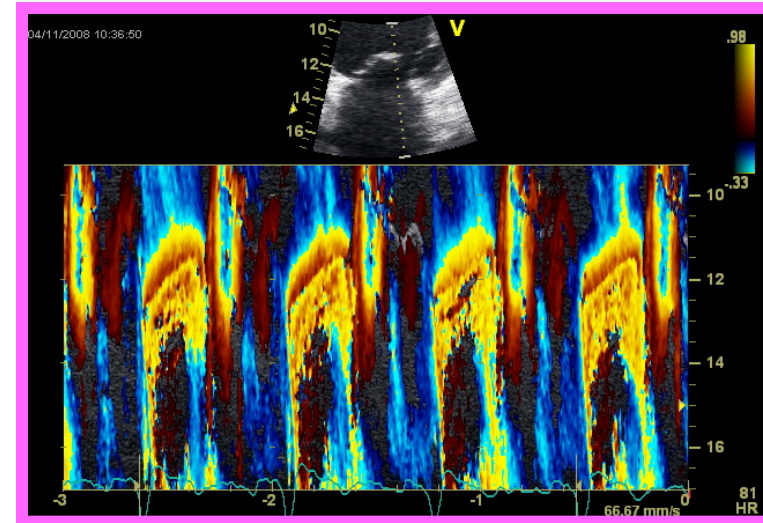
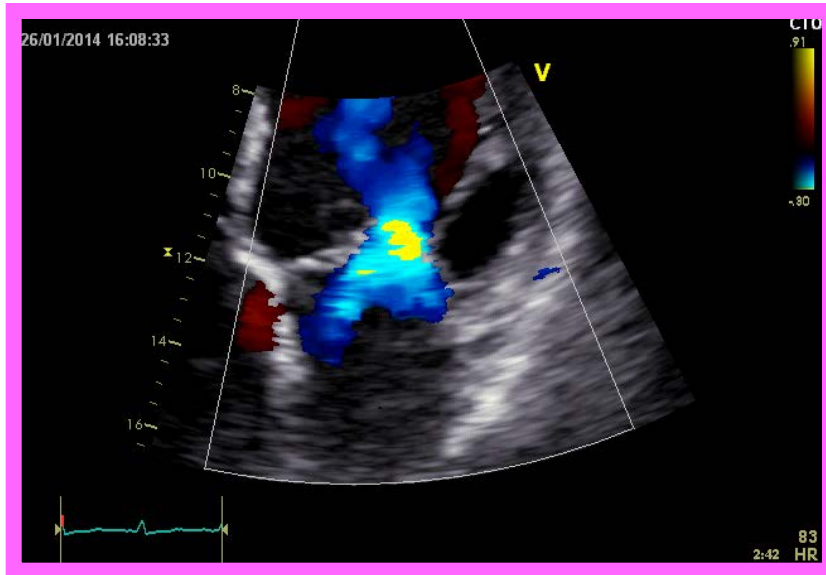
TTE: mitral regurgitation



TTE: severe MR



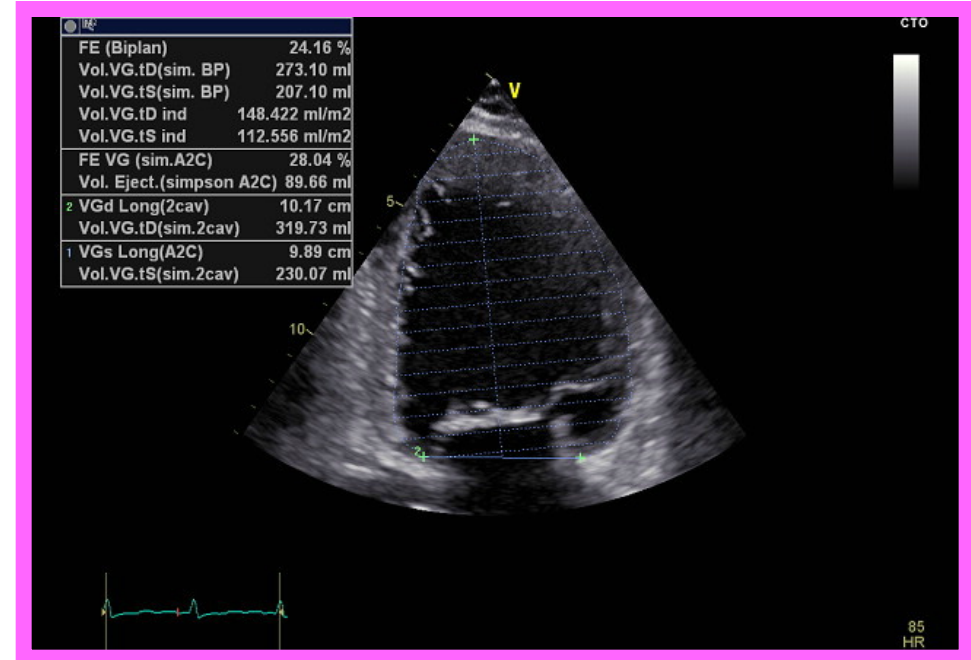
TTE: severe MR



- mitral ERO = 40 mm²
- regurgitant volume = 60 ml

Patient case: summary

- LVEF = 24%
- LVEDD = 78 mm
- LVESD = 60 mm
- LVEDV = 273 ml (148 ml/m²)
- LVESV = 207 ml (112 ml /m²)
- severe mitral regurgitation: ERO = 40 mm²
- regurgitant volume = 60 ml



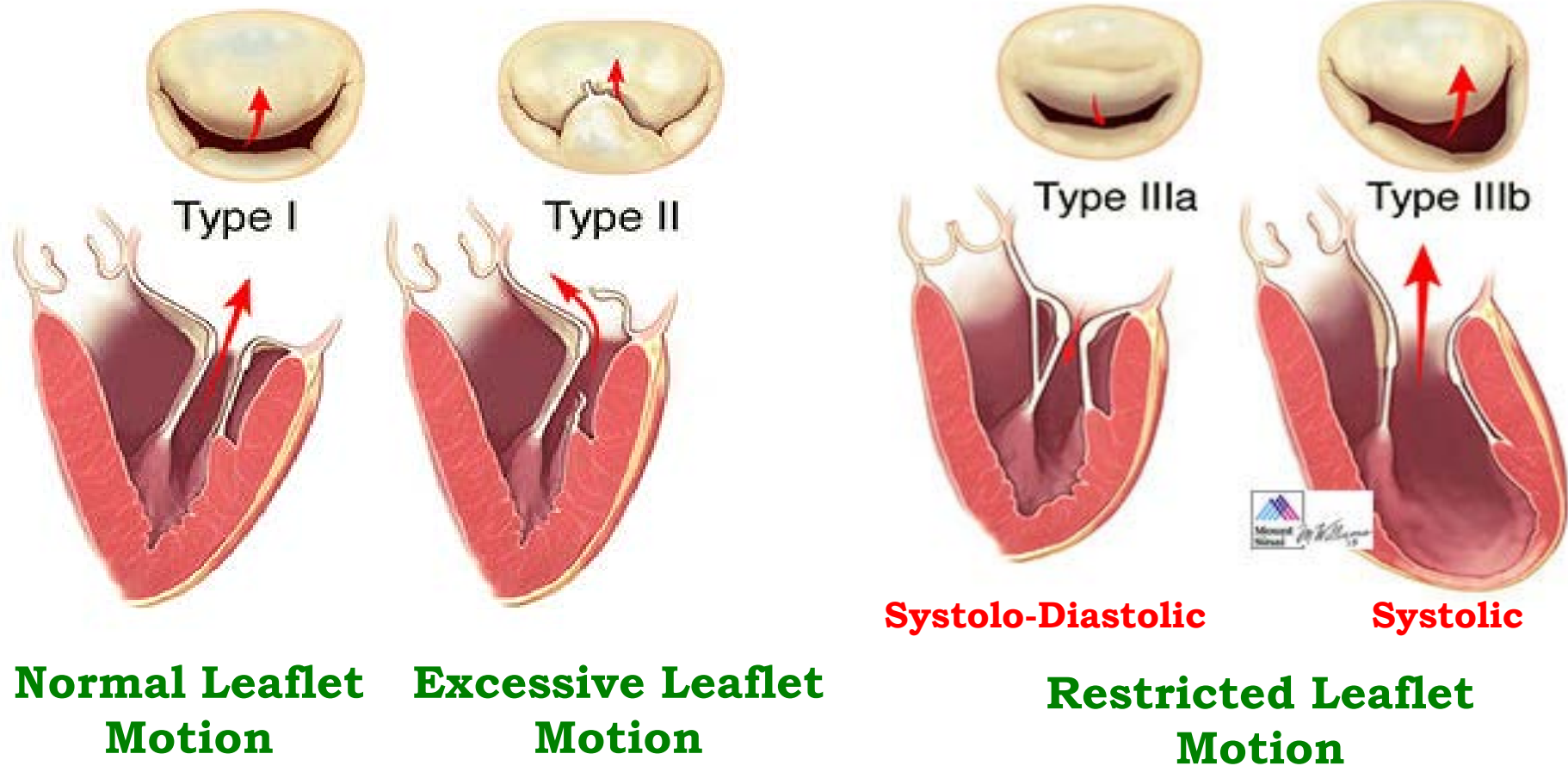
Assessment of Mitral Regurgitation

- 1. Mechanism**
- 2. Quantification**
- 3. Suitability for MitraClip**

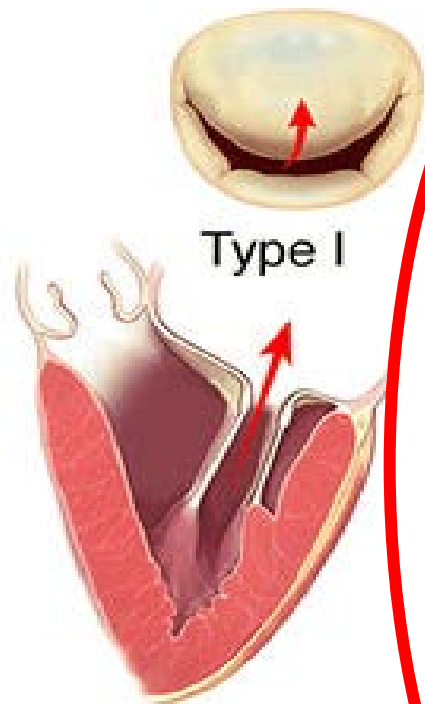
Assessment of Mitral Regurgitation

1. *Mechanism*
2. **Quantification**
3. **Suitability for MitraClip**

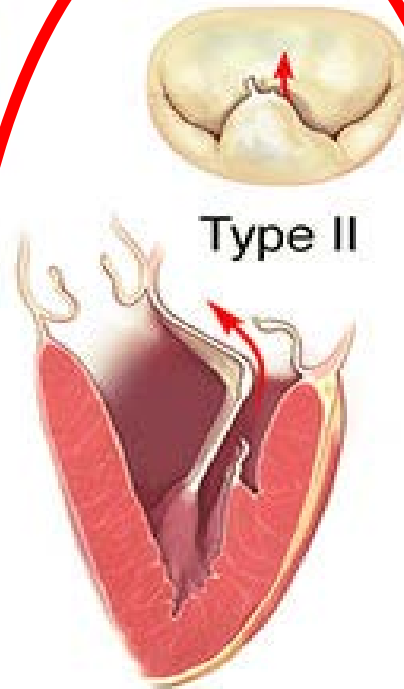
Carpentier's classification



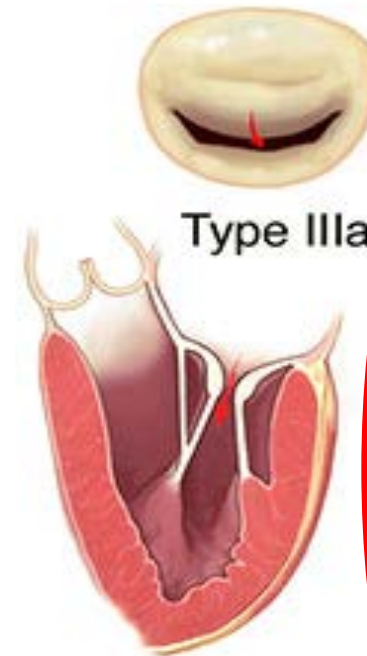
Carpentier's classification



Normal Leaflet Motion

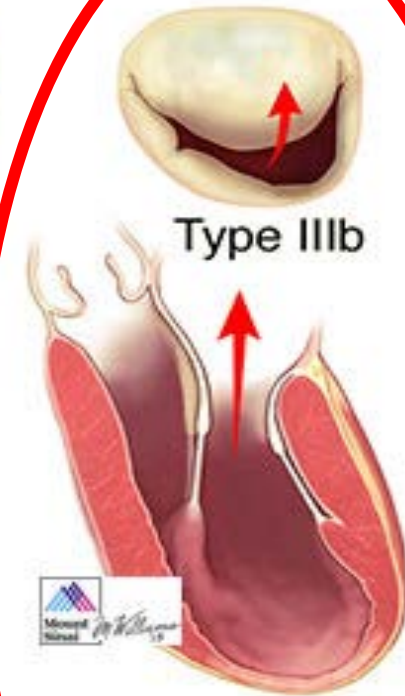


Excessive Leaflet Motion



Systolo-Diastolic

Restricted Leaflet Motion



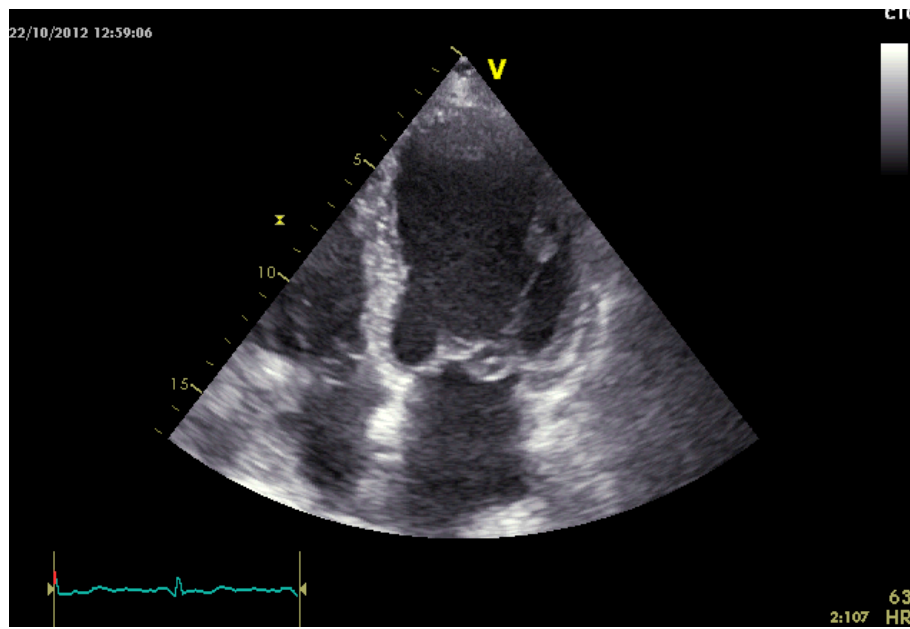
Systolic



Chronic mitral regurgitation

**Organic MR
(primary) type II**

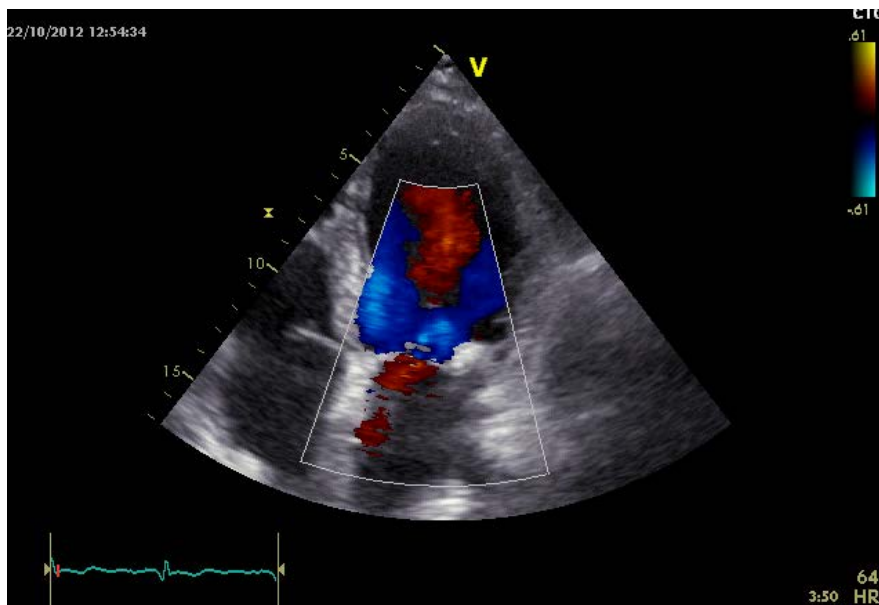
**Functional MR
(secondary) type IIIb**



Chronic mitral regurgitation

**Organic MR
(primary) type II**

**Functional MR
(secondary) type IIIb**



Chronic mitral regurgitation

**Organic MR
(primary) type II**

**Functional MR
(secondary) type IIb**

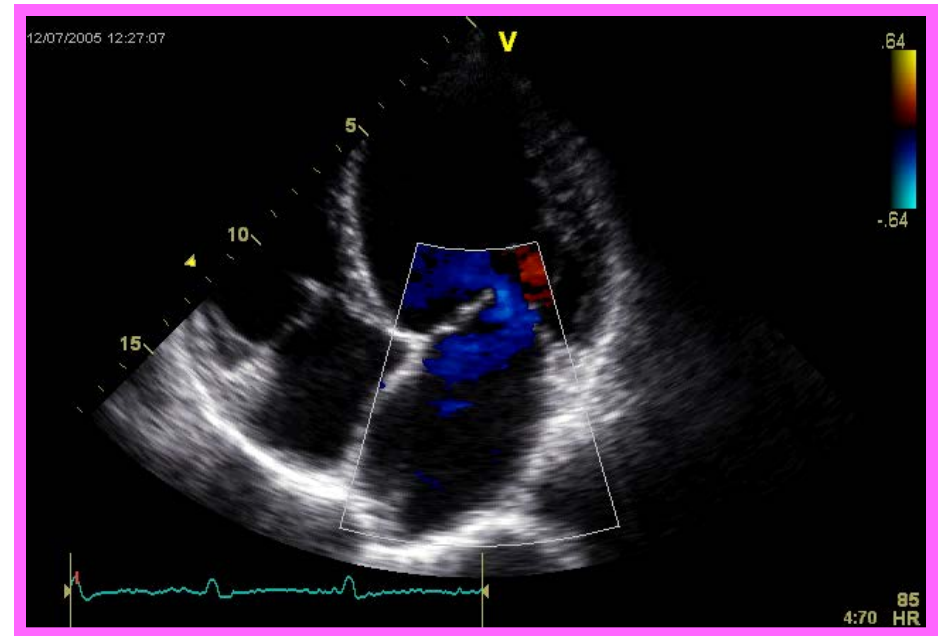
- ischemic CM
- non ischemic CM



Chronic mitral regurgitation

**Organic MR
(primary) type II**

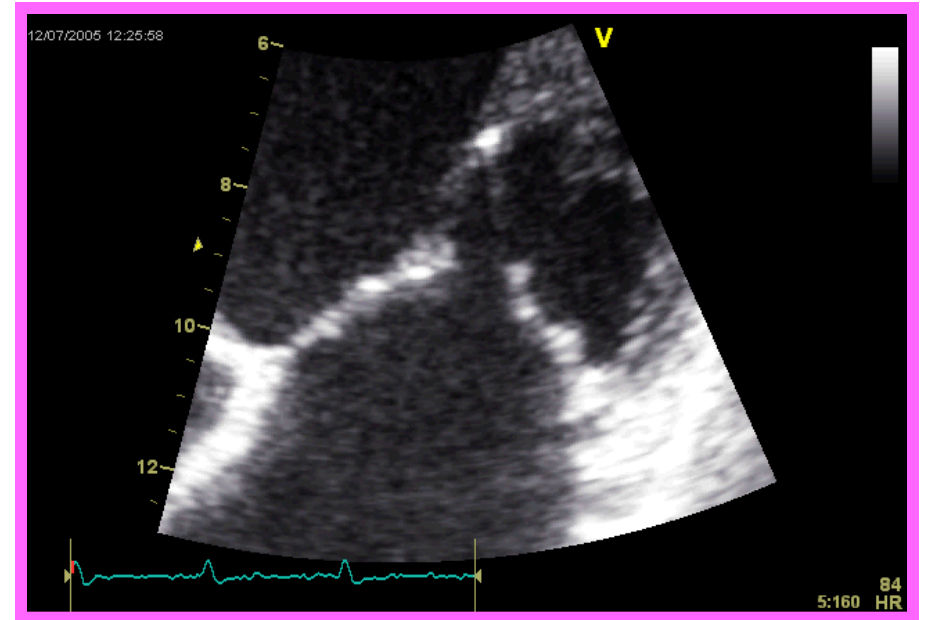
**Functional MR
(secondary) type IIIb**



Chronic mitral regurgitation

**Organic MR
(primary) type II**

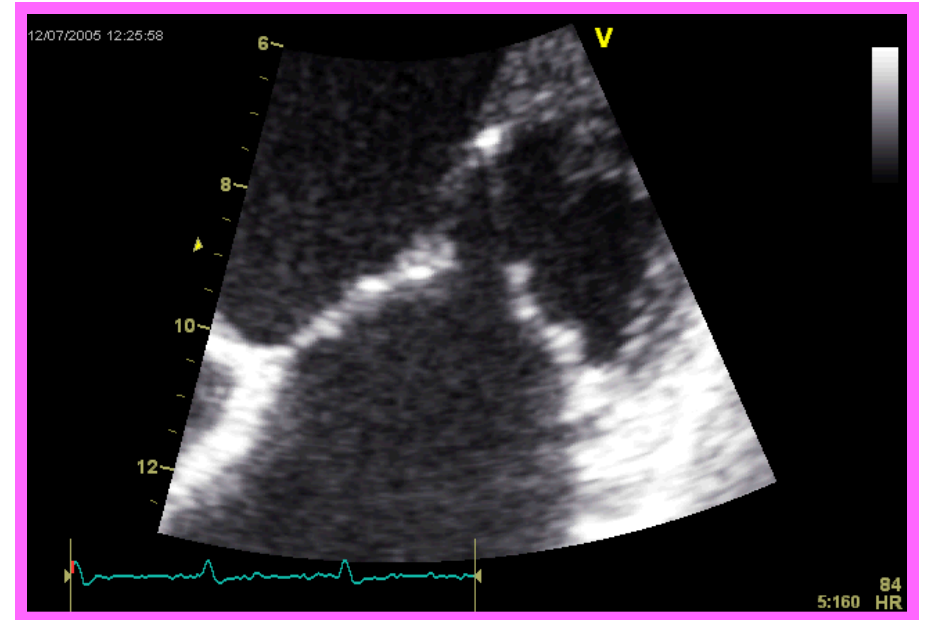
**Functional MR
(secondary) type IIIb**



Chronic mitral regurgitation

**Organic MR
(primary) type II**

**Functional MR
(secondary) type IIIb**



Mechanism of ischemic MR

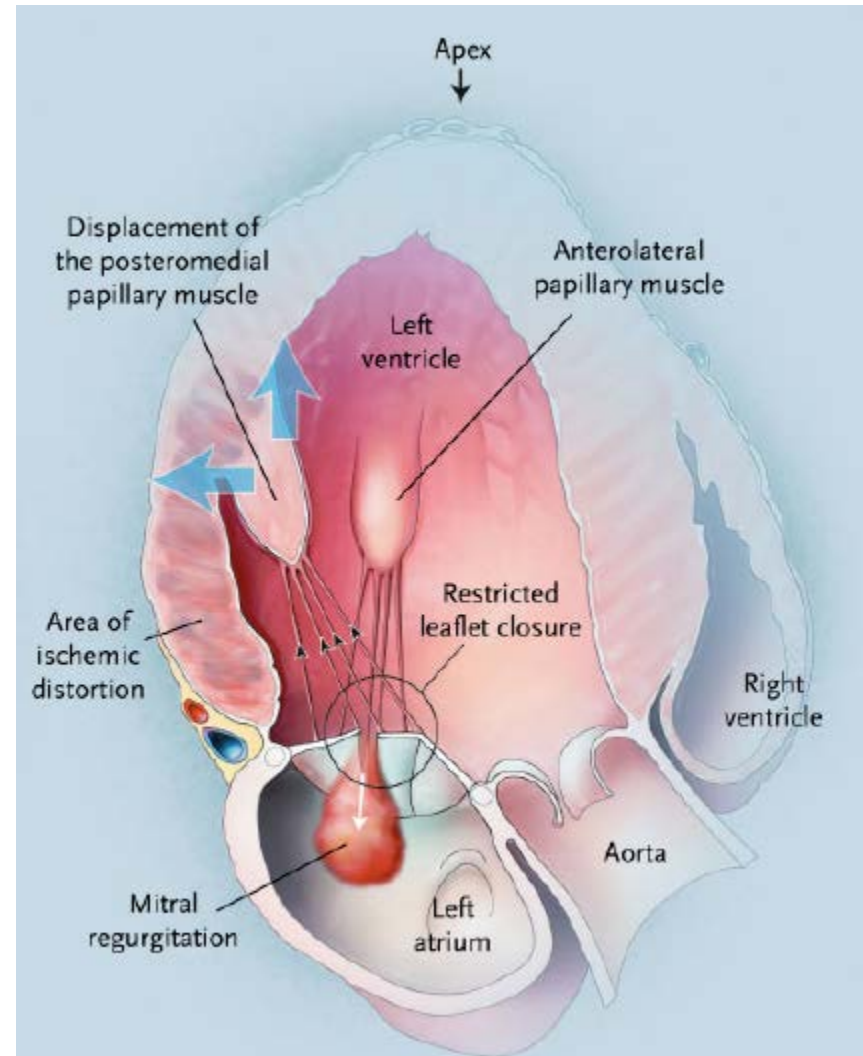
Levine R – N Eng J Med 2004

1. apical displacement of PLPM

- tethering of mitral leaflets
- tenting of the mitral valve
- restriction of leaflet closure
- mitral regurgitation

2. other mechanisms

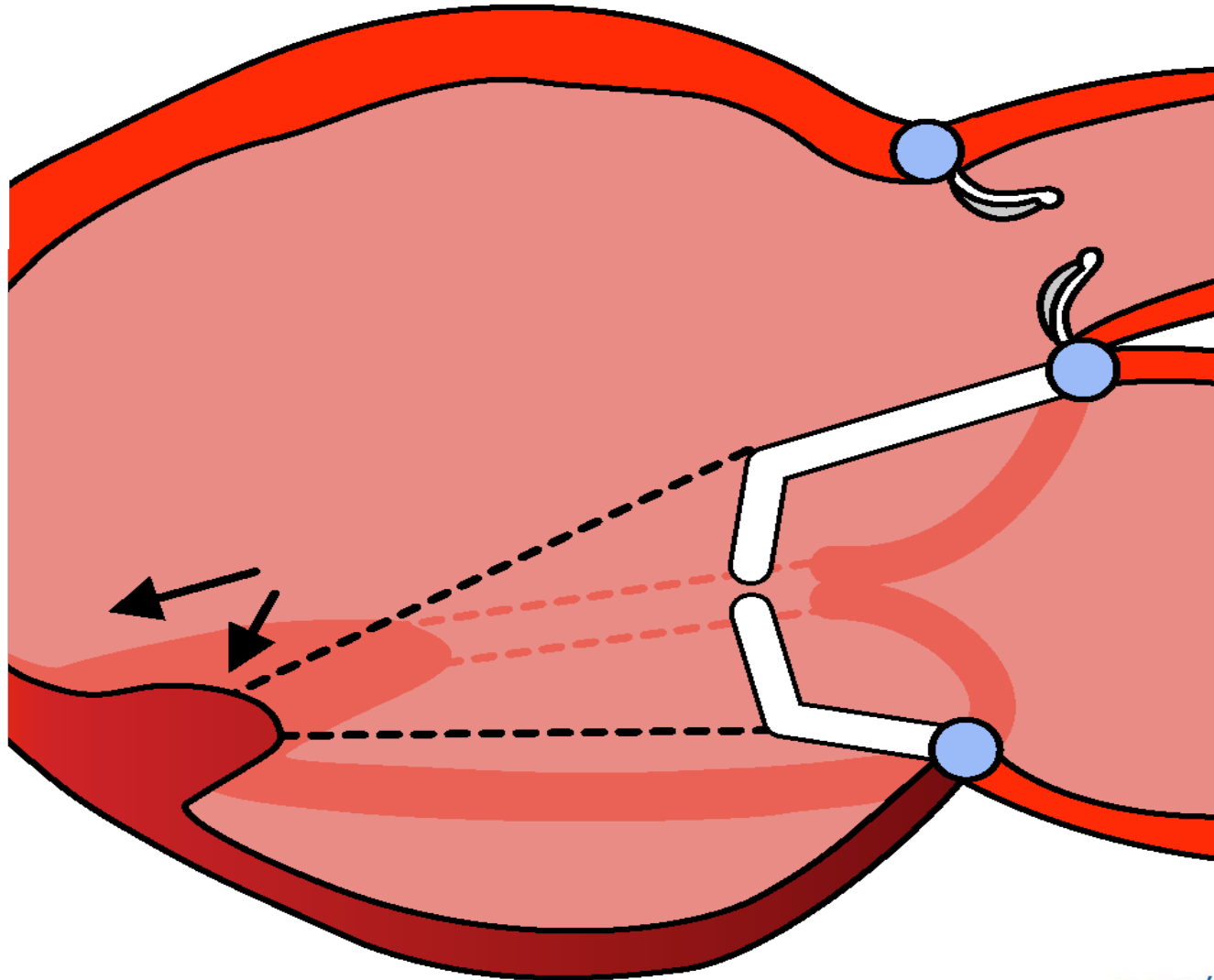
- annular dilatation / loss of contractility
- LV asynchrony



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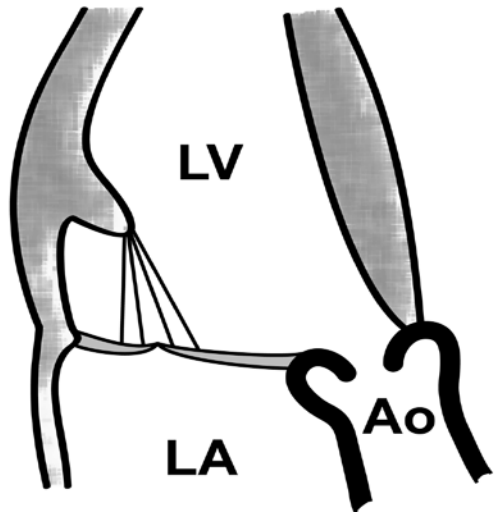


Mechanism of functional MR

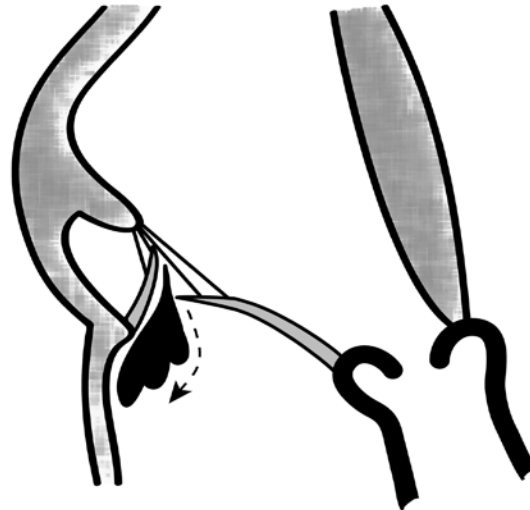


Symmetric vs Asymmetric functional MR

Normal Valve

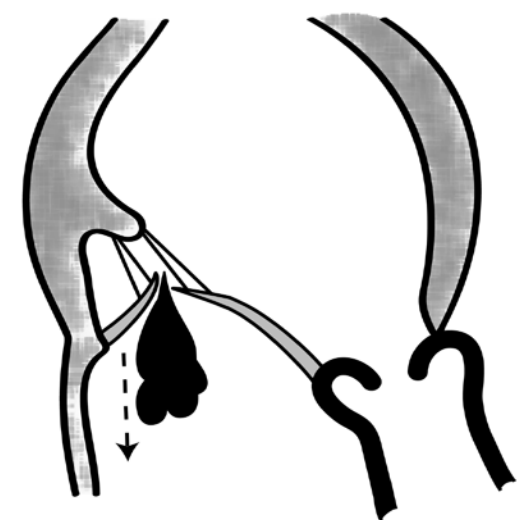


Asymmetric Tethering



**Inferior and/or posterior MI
Regional remodeling
Predominant posterior leaflet restriction**

Symmetric Tethering



**Anterior MI
Regional remodeling
Both leaflet restriction**

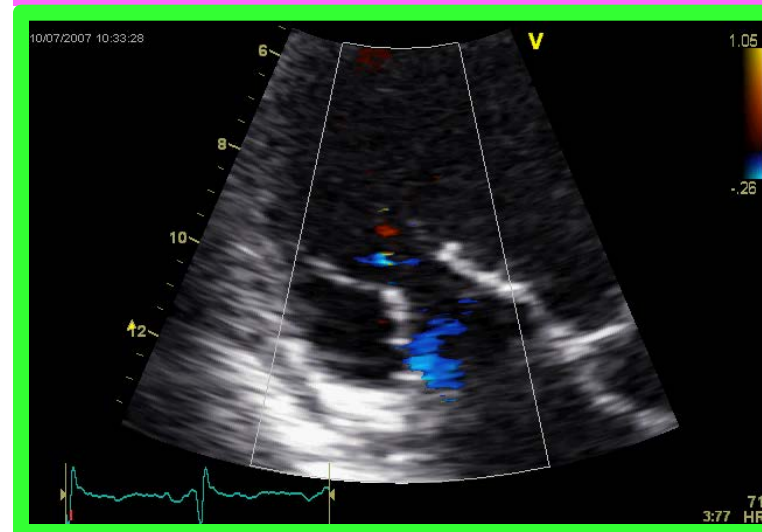
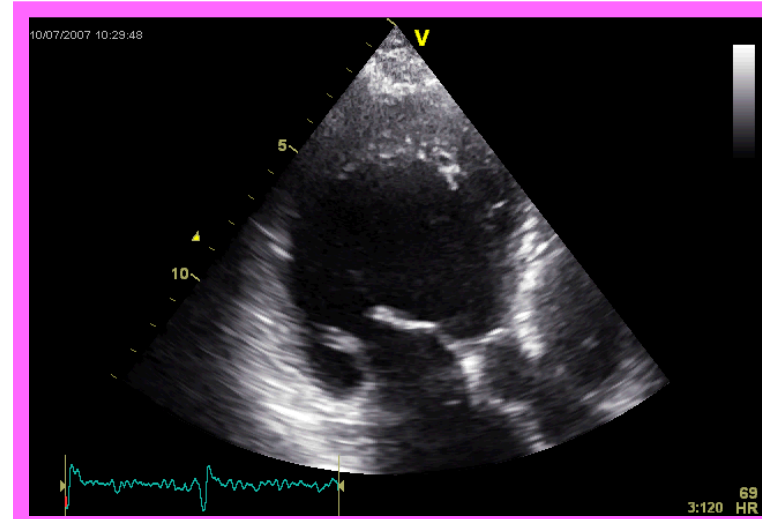
Agricola et al. EJE, 2004

Magne et al. Circulation, 2007



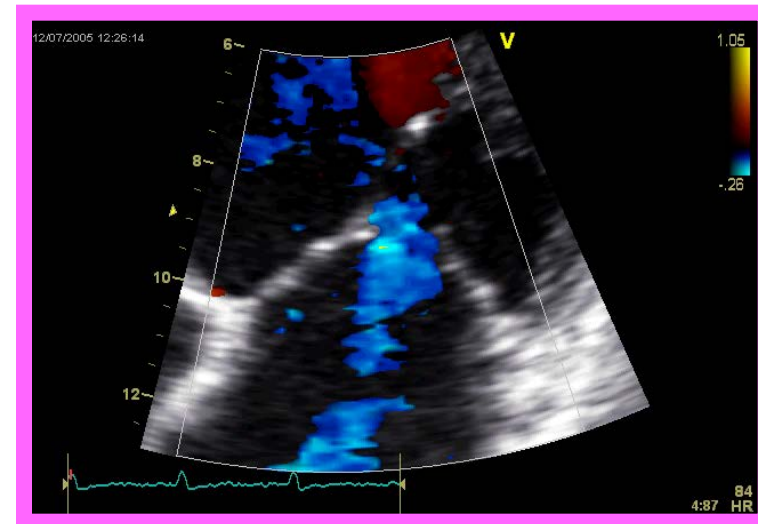
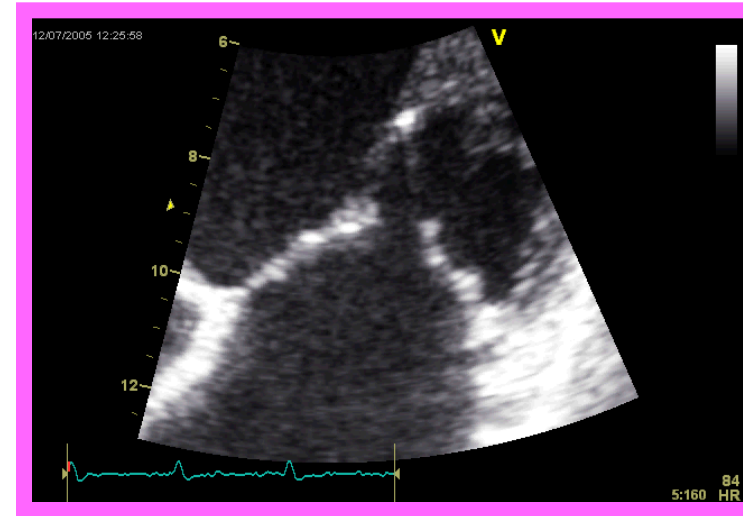
Asymmetric functional MR

- inferior MI
- local remodelling
- posterior leaflet tethering
- tenting MV
- eccentric jet

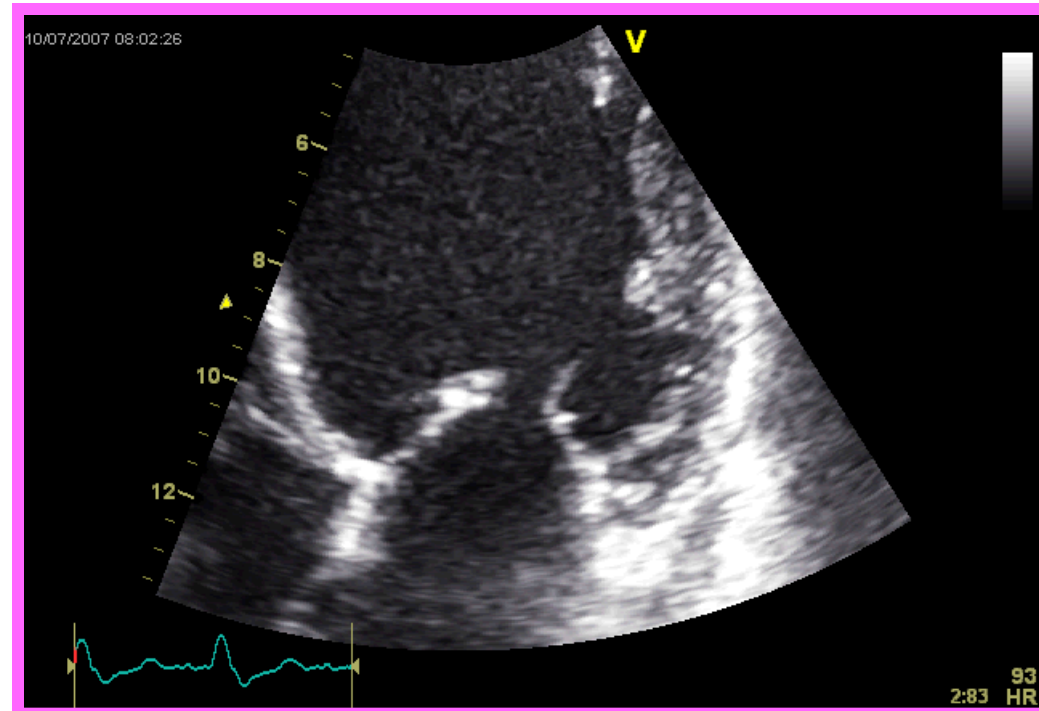
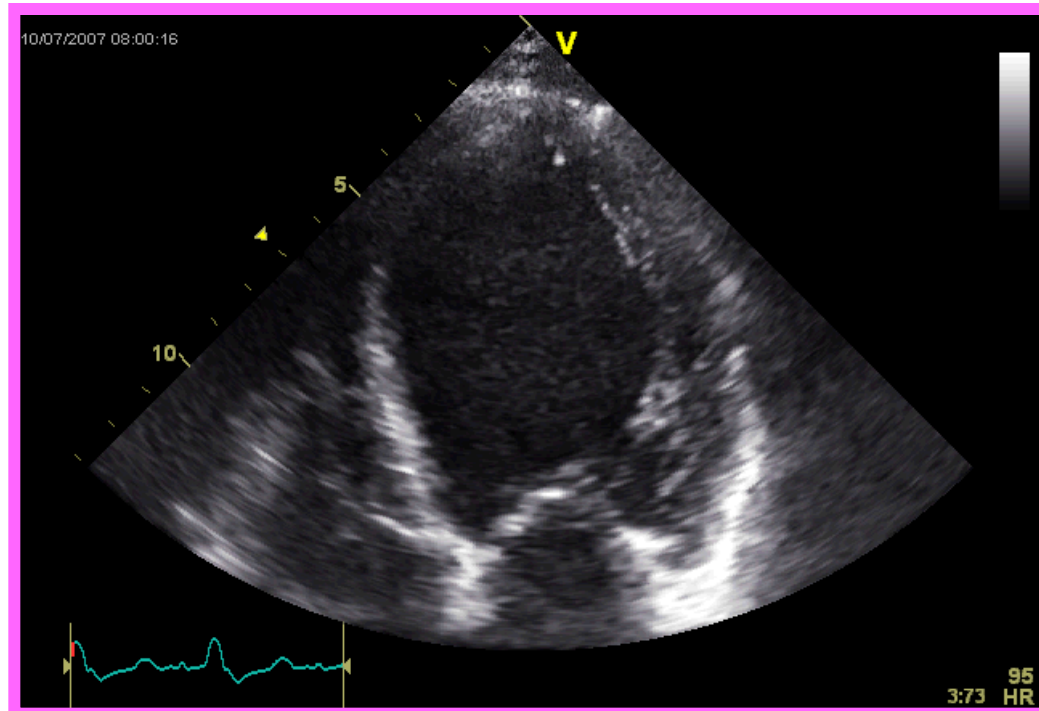


Symmetric functional MR

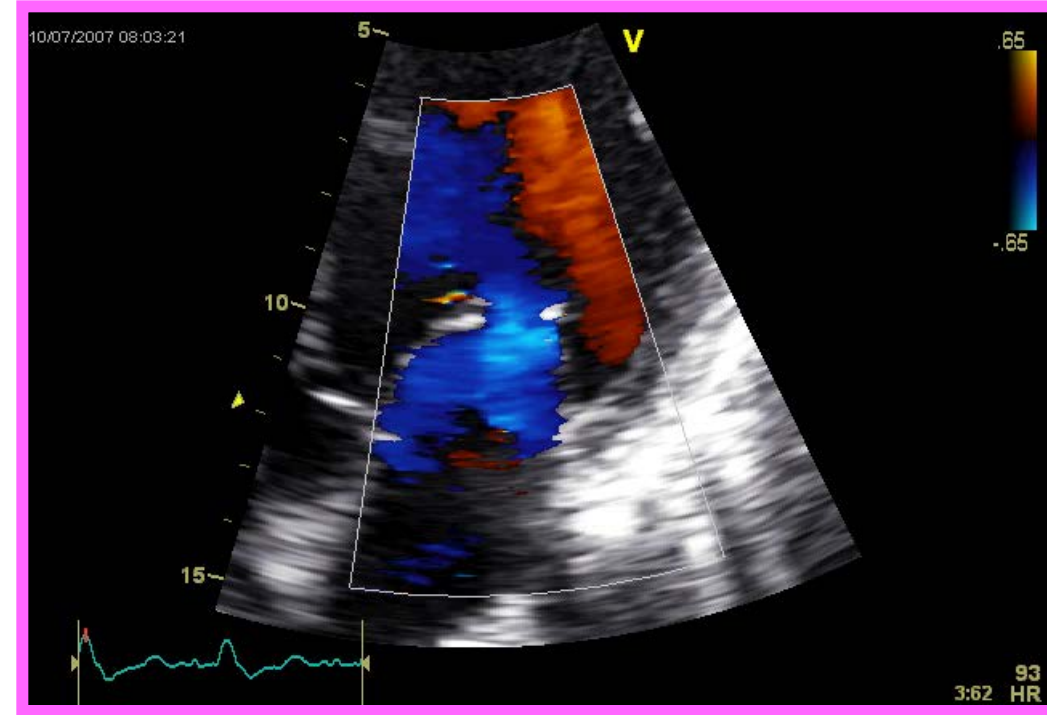
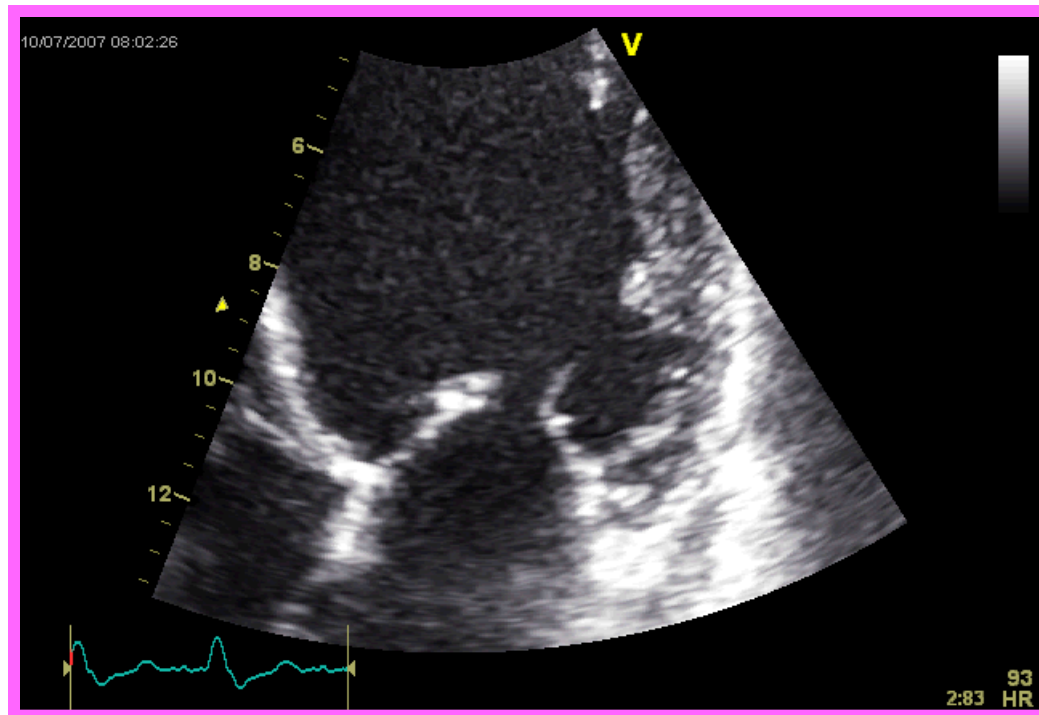
- **anterior MI**
- **non ischemic CM**
- **local and global remodeling**
- **apical leaflet tethering**
- **tenting MV**
- **central jet**
- **annular dilatation and flattening**



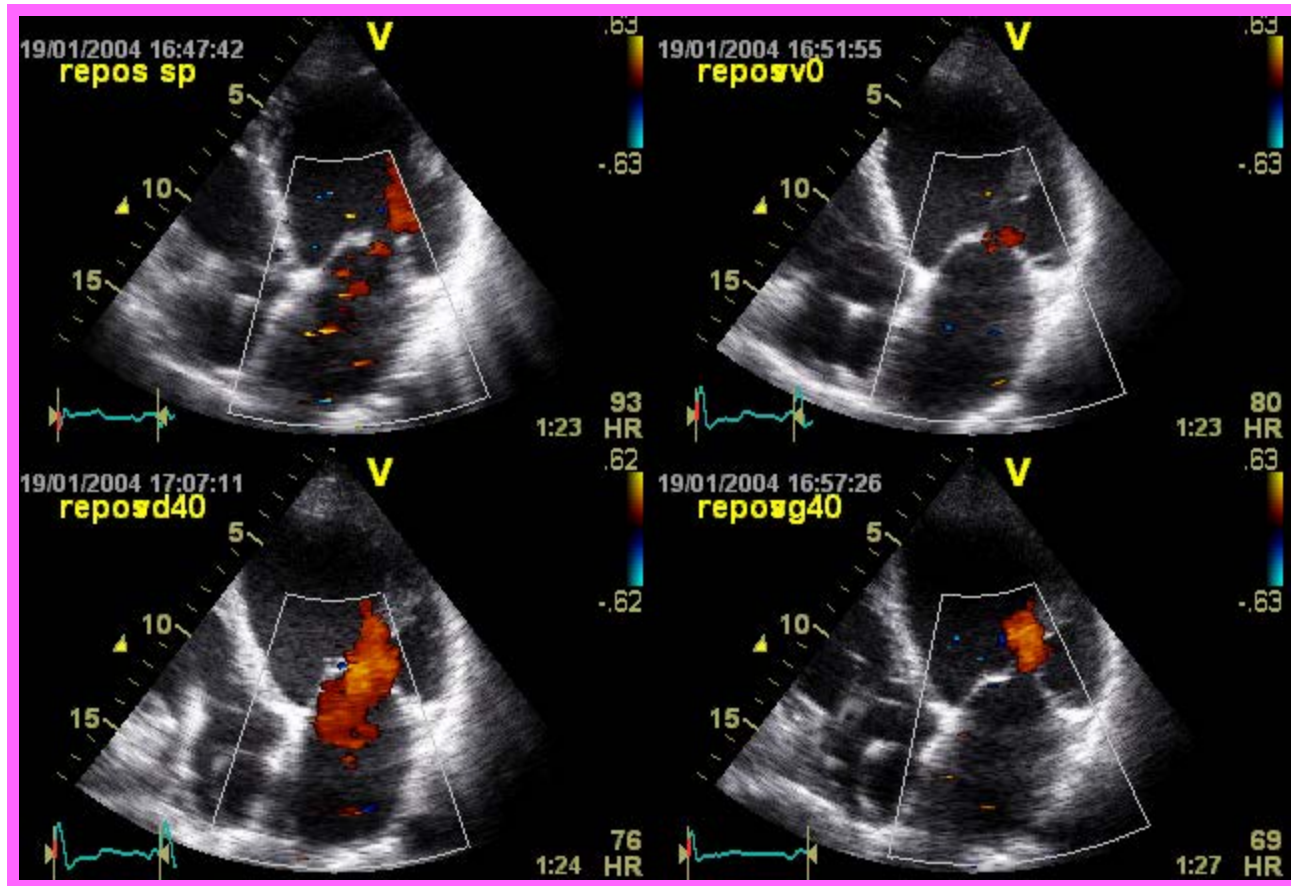
Role of intra LV asynchrony



Role of intra LV asynchrony



Cardiac resynchronization therapy



Courtesy of Stéphane Lafitte



Evaluation of Mitral Regurgitation

1. Mechanism
2. *Quantification*
3. Suitability for MitraClip

EAE guidelines 2010

Table 3 Grading the severity of organic mitral regurgitation

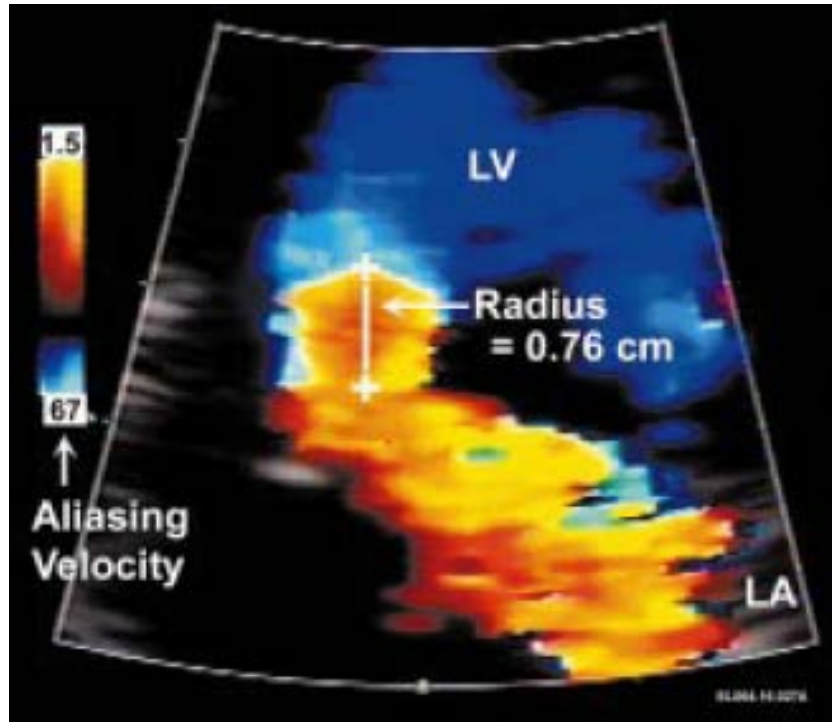
Parameters	Mild	Moderate	Severe
Qualitative			
MV morphology	Normal/Abnormal	Normal/Abnormal	Flail leaflet/Ruptured PMs
Colour flow MR jet	Small, central	Intermediate	Very large central jet or eccentric jet adhering, swirling and reaching the posterior wall of the LA
Flow convergence zone ^a	No or small	Intermediate	Large
CW signal of MR jet	Faint/Parabolic	Dense/Parabolic	Dense/Triangular
Semi-quantitative			
VC width (mm)	<3	Intermediate	≥7 (>8 for biplane) ^b
Pulmonary vein flow	Systolic dominance	Systolic blunting	Systolic flow reversal ^c
Mitral inflow	A wave dominant ^d	Variable	E wave dominant (>1.5 cm/s) ^e
TVI mit /TVI Ao	<1	Intermediate	>1.4
Quantitative			
EROA (mm ²)	<20	20–29; 30–39 ^f	≥40
R Vol (mL)	<30	30–44; 45–59 ^f	≥60
+ LV and LA size and the systolic pulmonary pressure ^g			

EAE guidelines 2010

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What is a severe MR ?



RV
(ml)

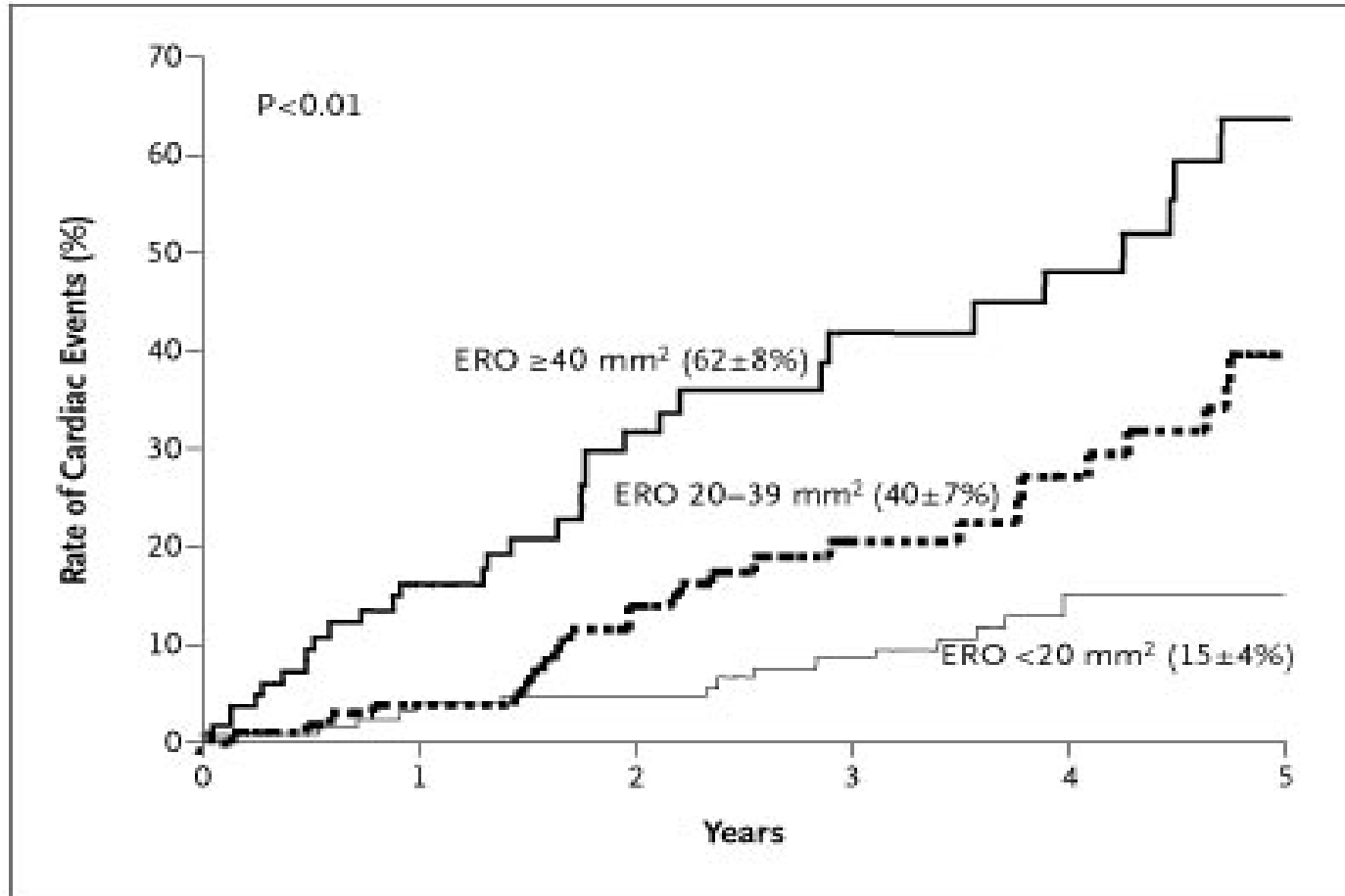
RO
(mm²)

≥60

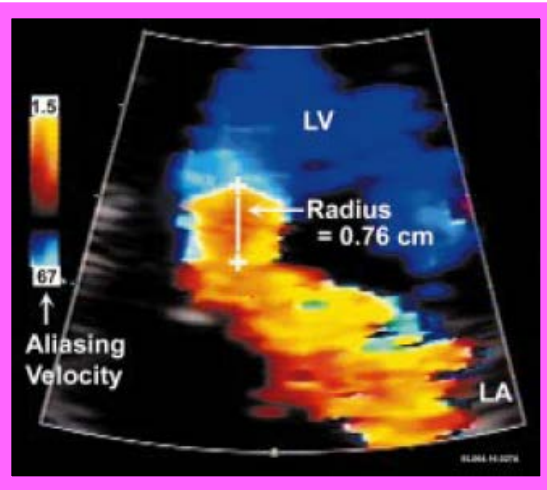
≥40

Prognosis of asymptomatic MR

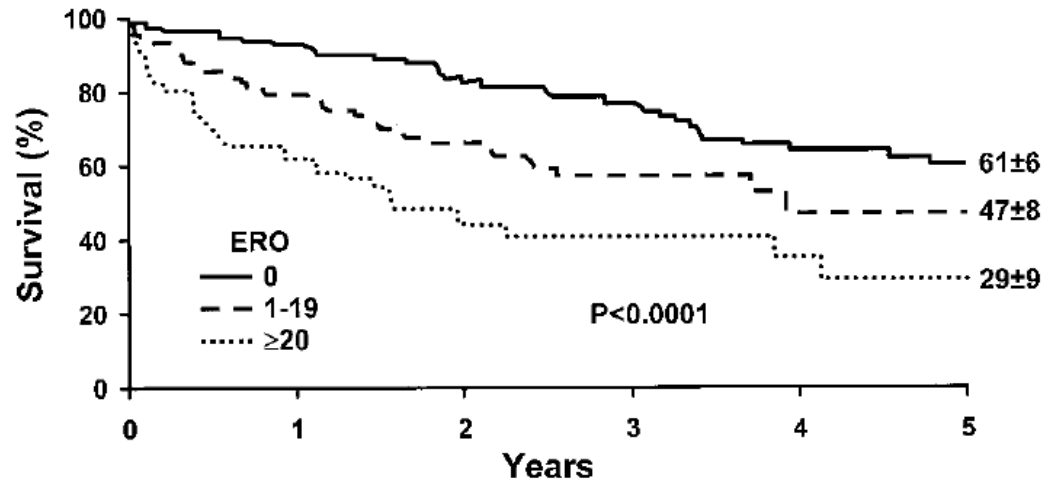
Sarano – NEJM 2005



What is a severe ischemic MR?



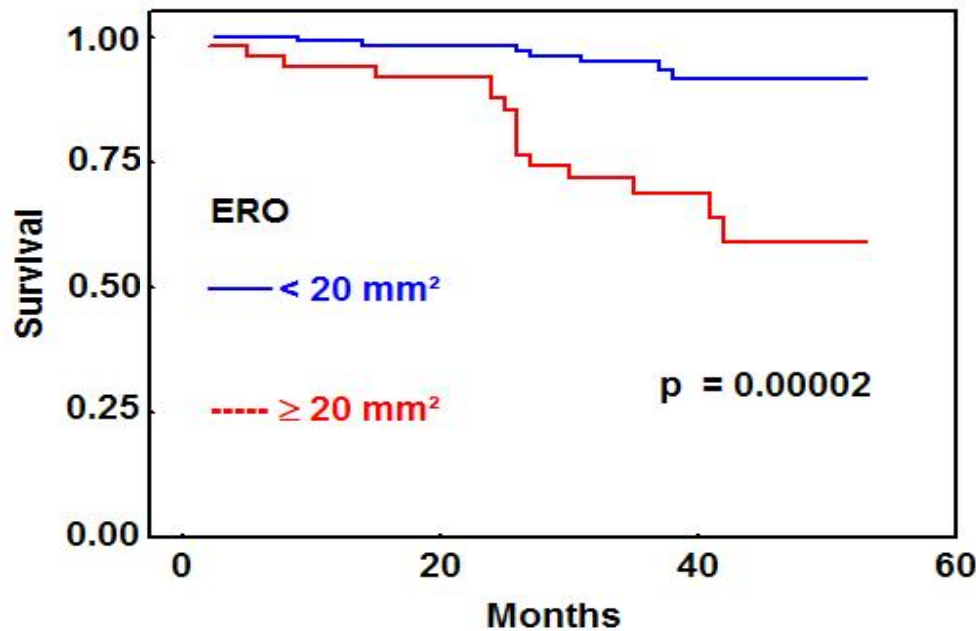
- Reg Vol > 30 ml
- ERO > 20 mm²



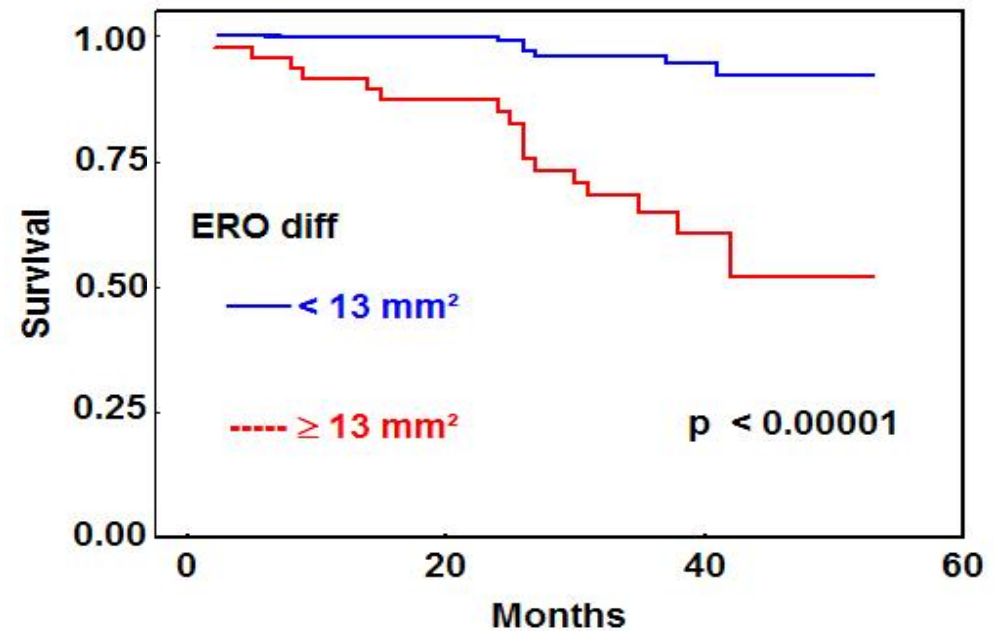
Grigioni F – Circulation 2001

Prognostic value of exercise echo

Lancellotti P - Eur Heart J 2005 ; 28 : 1528 - 32



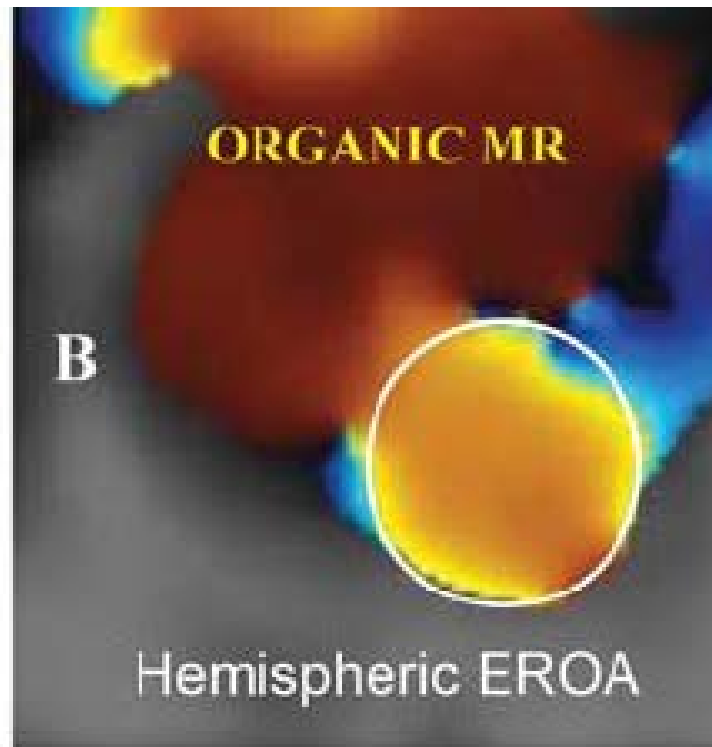
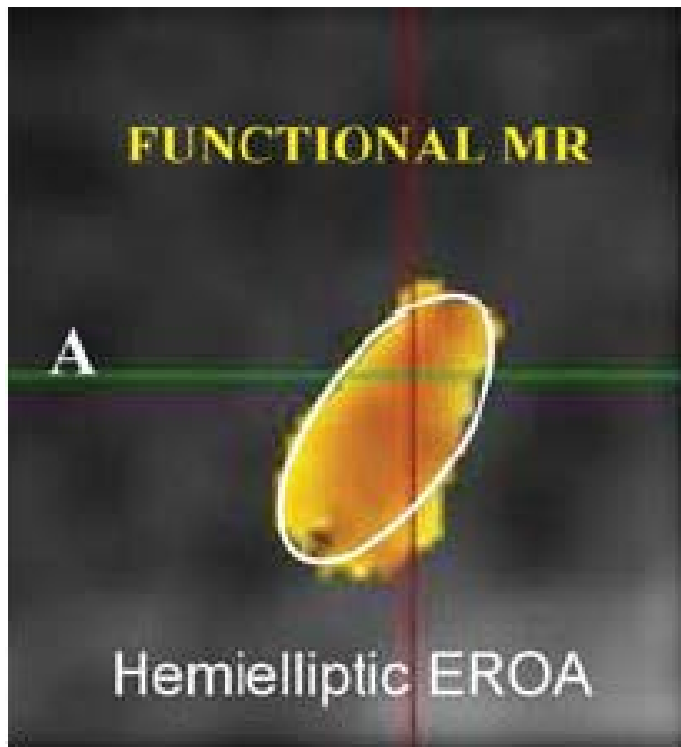
ERO at rest



Increase in ERO during exercise



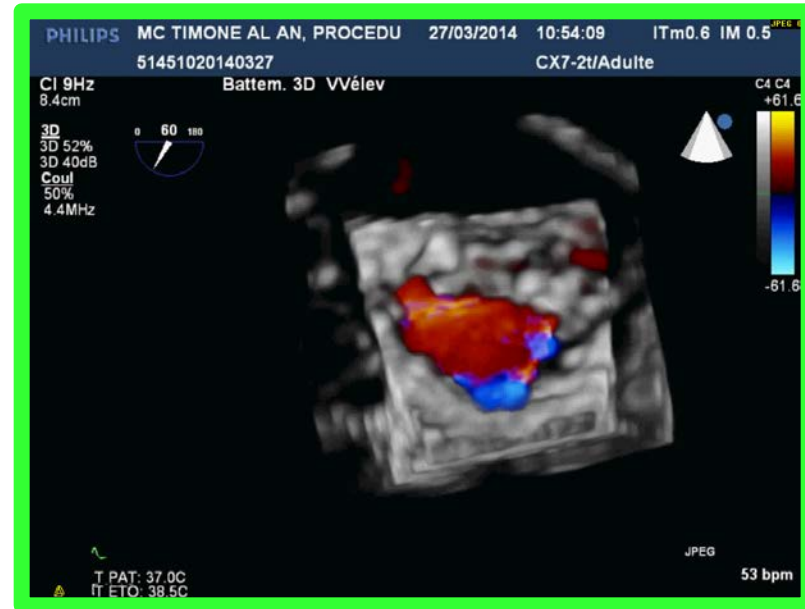
Limitations of PISA method



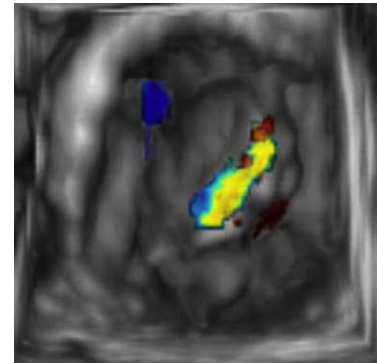
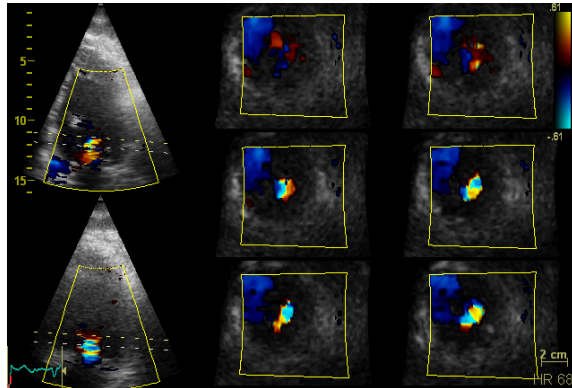
- PISA shape affected
 - by the aliasing velocity
 - in case of non-circular orifice
 - by systolic changes in regurgitant flow
 - by adjacent structures (flow constraintment)
- PISA is more a hemi-ellipse
- Errors in PISA radius measurement are squared
- Inter-observer variability
- Not valid for multiple jets

Continued

Hemielliptic ERO in functional MR



3d quantification of MR



**Khanna Echocardiography
2004**

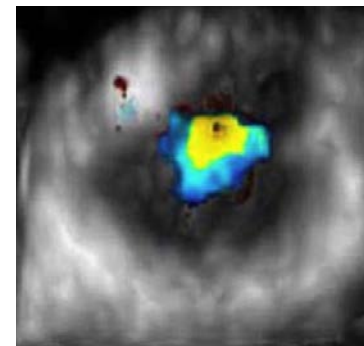
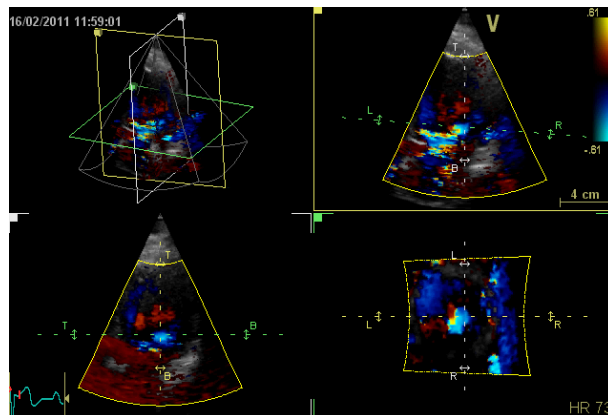
Lange Int J Cardiol 2002

Valocik Eur J Echo 2005

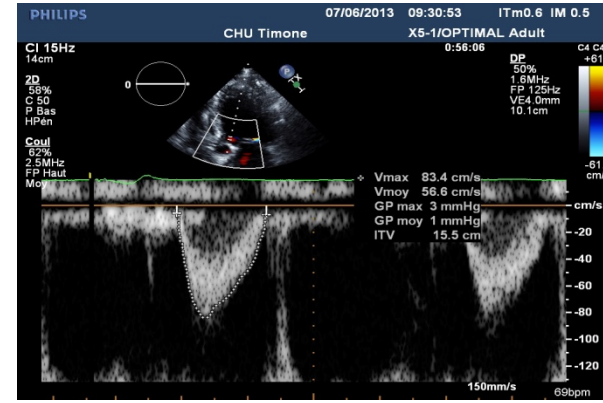
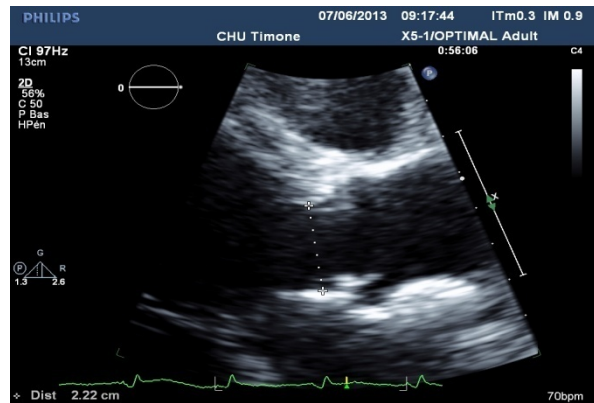
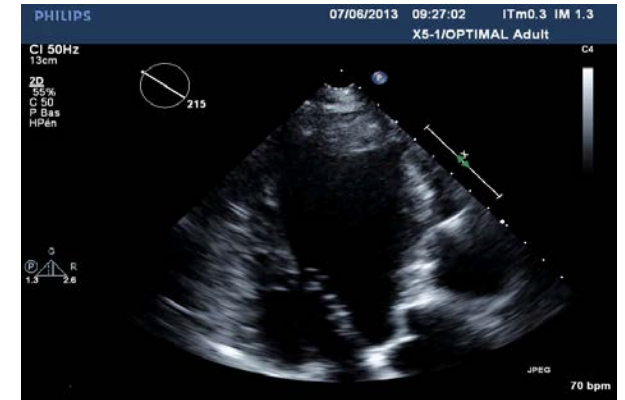
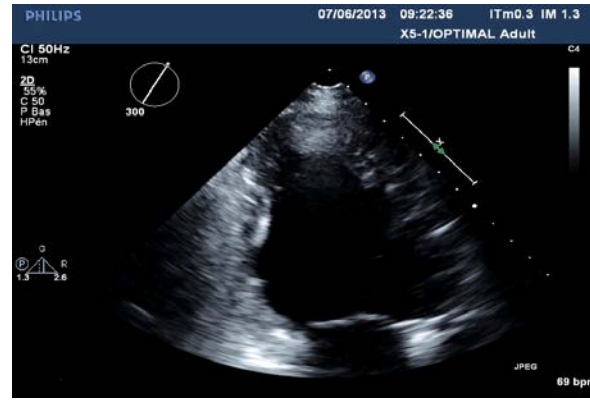
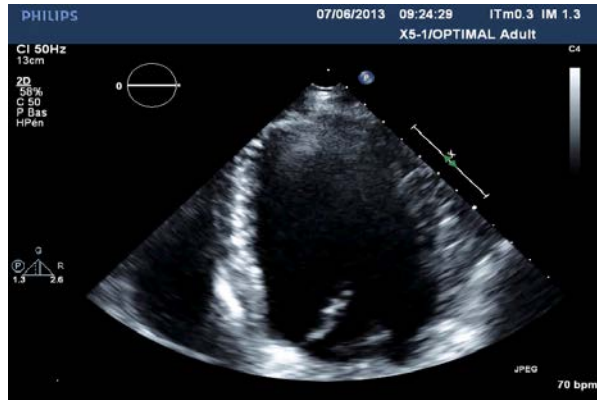
Breburda JACC 1998

Stiges JASE 2003

Matsumura AHJ 2008



Quantitative 2D echocardiography



Evaluation of Mitral Regurgitation

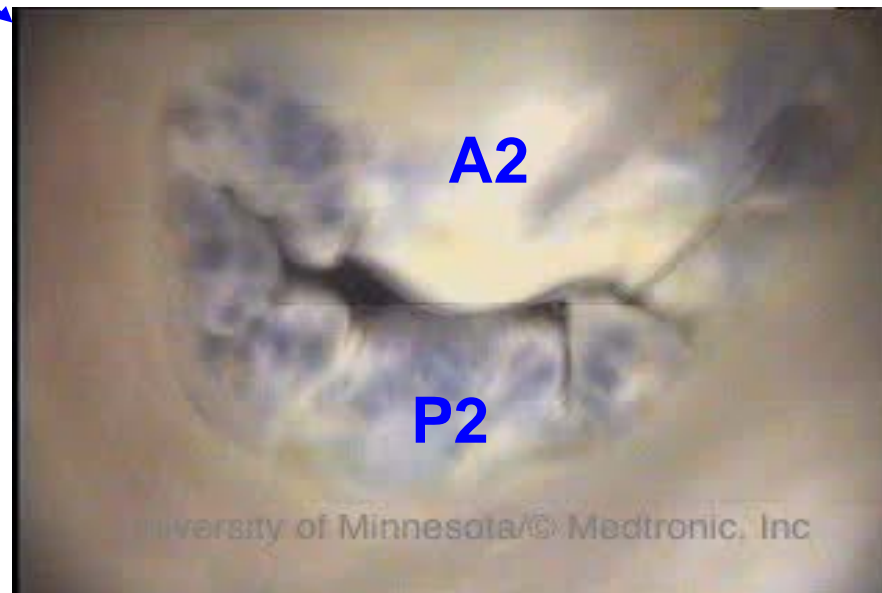
1. **Mechanism**
2. **Quantification**
3. ***Suitability for MitraClip***

P2 / A2 localization

Anterolateral
commissure

Anterior leaflet

Posteromedial
commissure

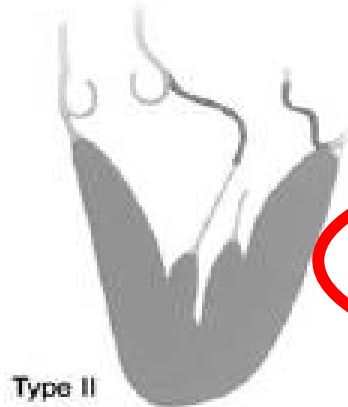


Posterior leaflet

Carpentier's nomenclature

Type I: normal valvular motion

Annular dilatation, valve perforation



Type II: excessive leaflet motion

Mitral prolapse



Type IIIa: restricted leaflet motion both in systole and diastole

Leaflet thickening/shortened chordae

Type IIIb: restricted leaflet motion in systole

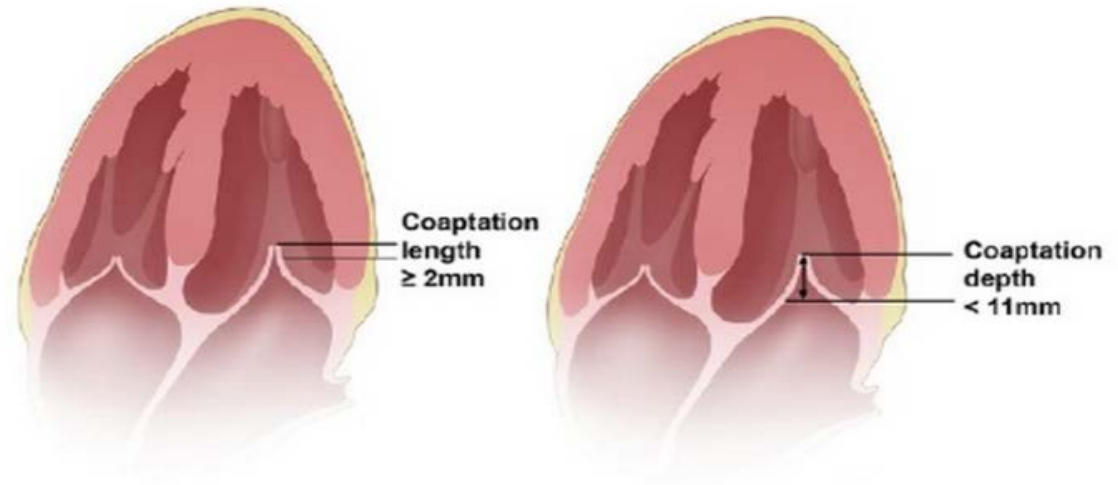
Ischaemic, functional MR

Ideal valve morphology for Mitraclip

Recommended criteria

Functional MR

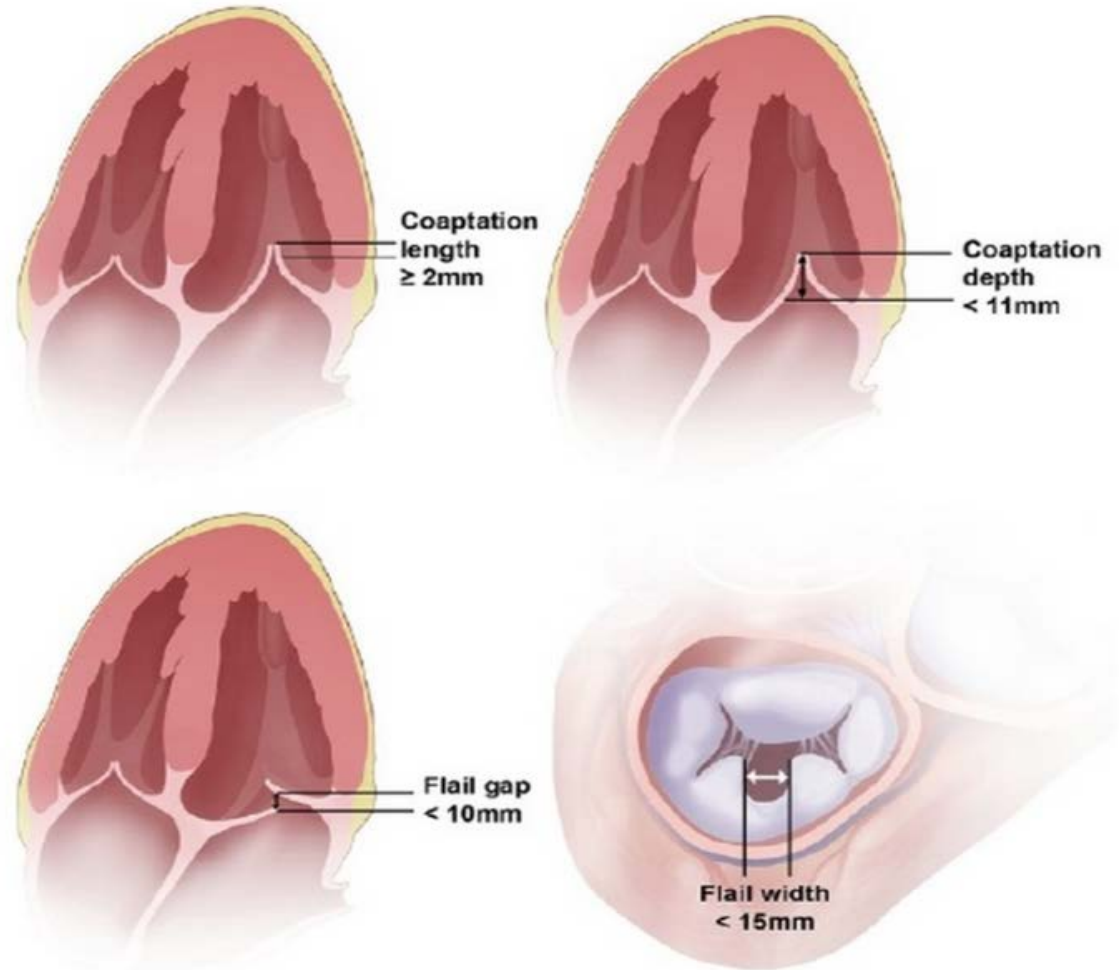
- moderate to severe MR
- pathology in the A2-P2 area
- coaptation length > 2 mm
- coaptation depth < 11 mm
- mitral valve orifice > 4 cm²
- posterior leaflet length > 10 mm



Ideal valve morphology for Mitraclip

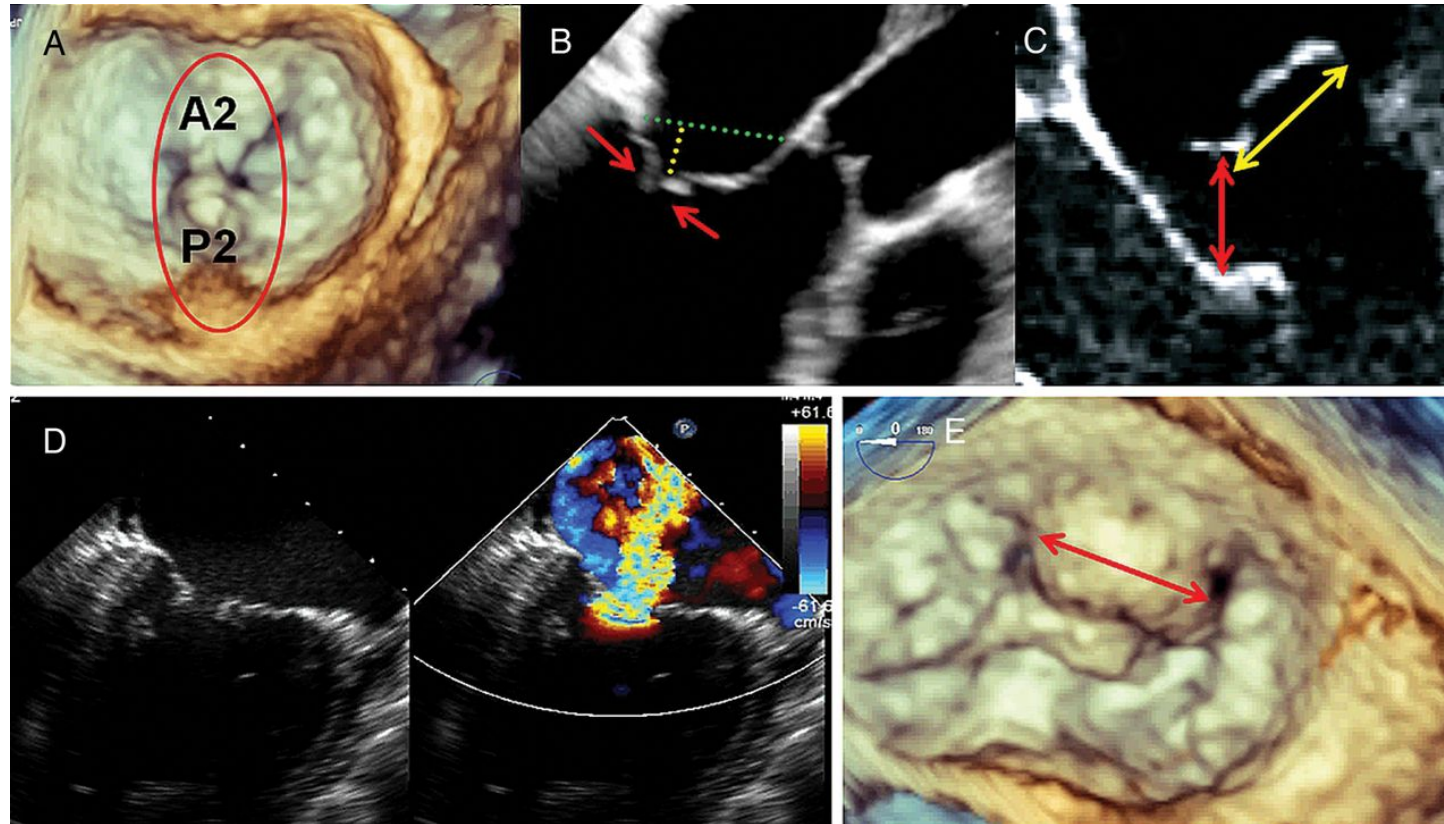
Recommended criteria¹

- Moderate to severe MR (Grade 3 or more out of 4 grades)
- Pathology in A2-P2 area
- Coaptation length > 2 mm (depending on leaflet mobility)
- Coaptation depth < 11 mm
- Flail gap < 10 mm
- Flail width < 15 mm
- Mitral valve orifice area $> 4\text{cm}^2$ (depending on leaflet mobility)
- Mobile leaflet length > 1 cm



Ideal cases for Mitraclip

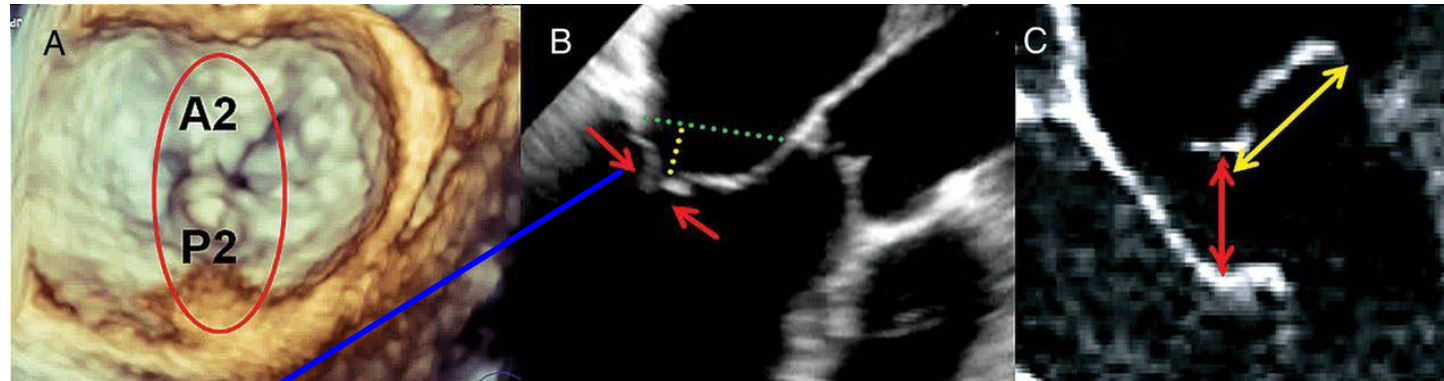
Wunderlich NC , Siegel RJ EHJCVI 2013



Ideal morphologies for a MitraClip implantation.

Ideal cases for Mitraclip

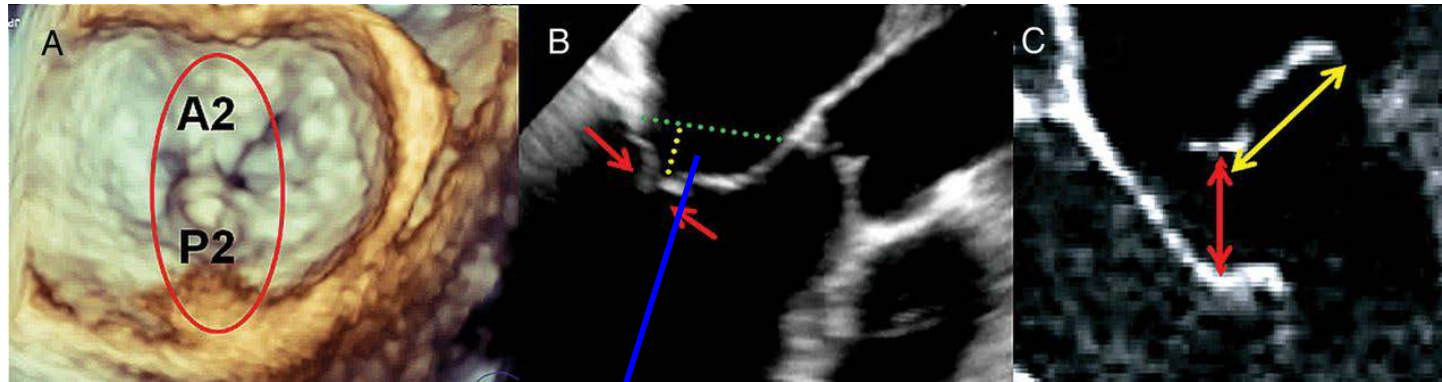
Wunderlich NC , Siegel RJ EHJCVI 2013



Coaptation length > 2 mm

Ideal cases for Mitraclip

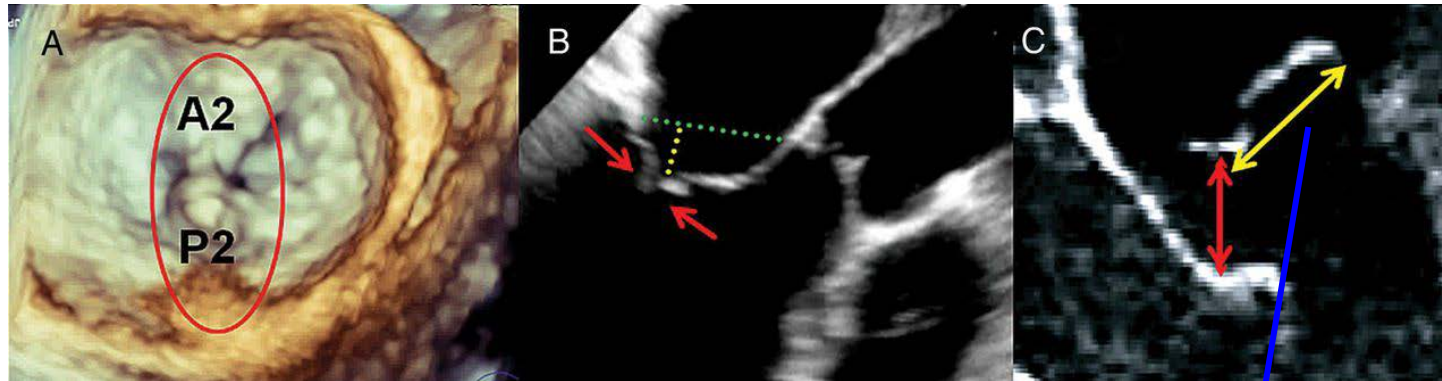
Wunderlich NC , Siegel RJ EHJCVI 2013



Coaptation depth < 11 mm

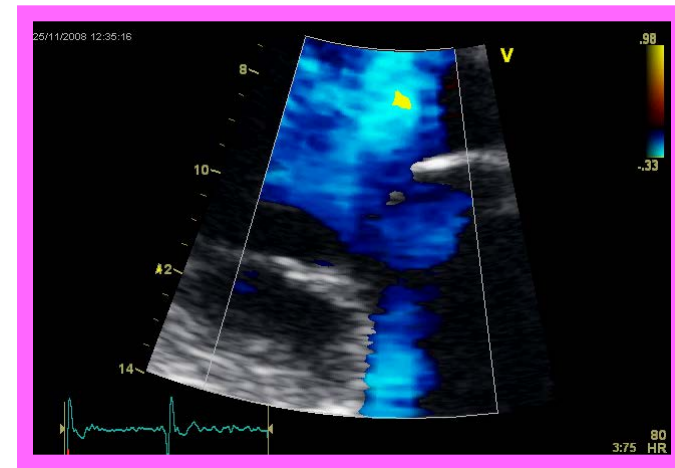
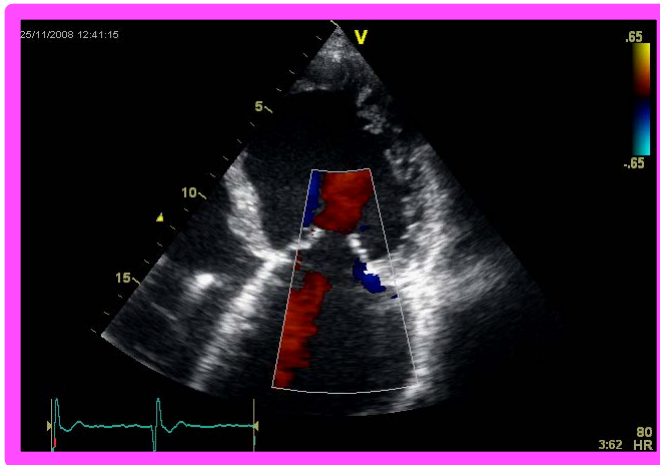
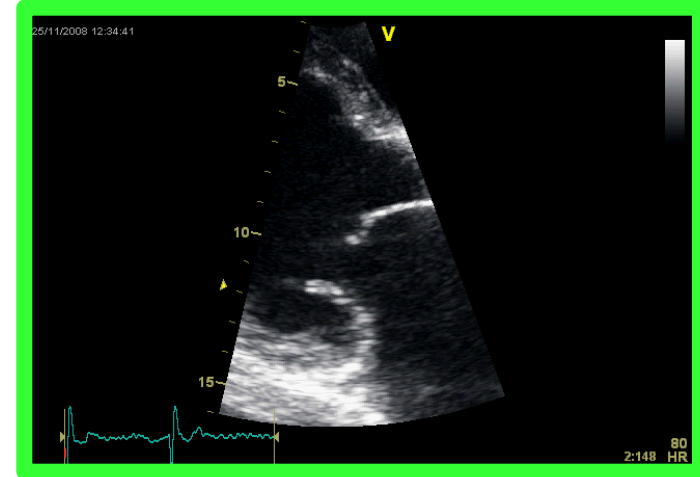
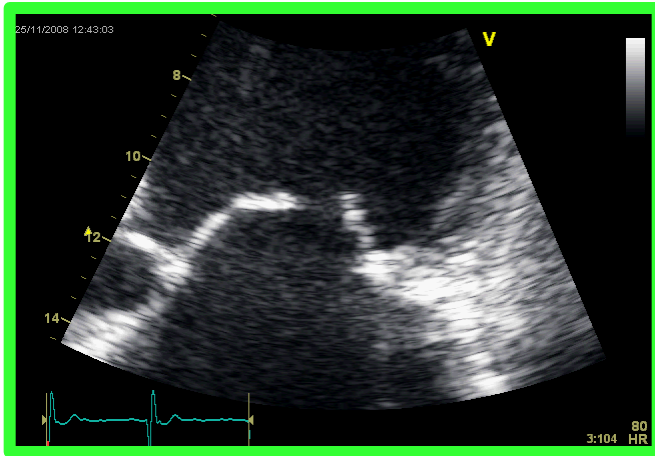
Ideal cases for Mitraclip

Wunderlich NC , Siegel RJ EHJCVI 2013

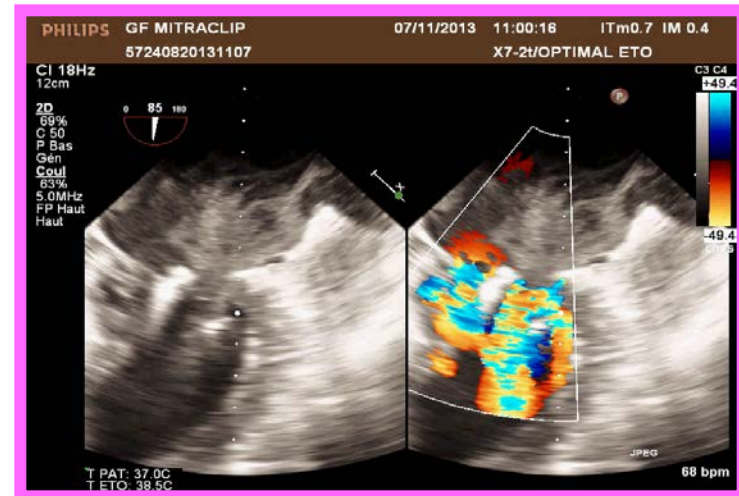
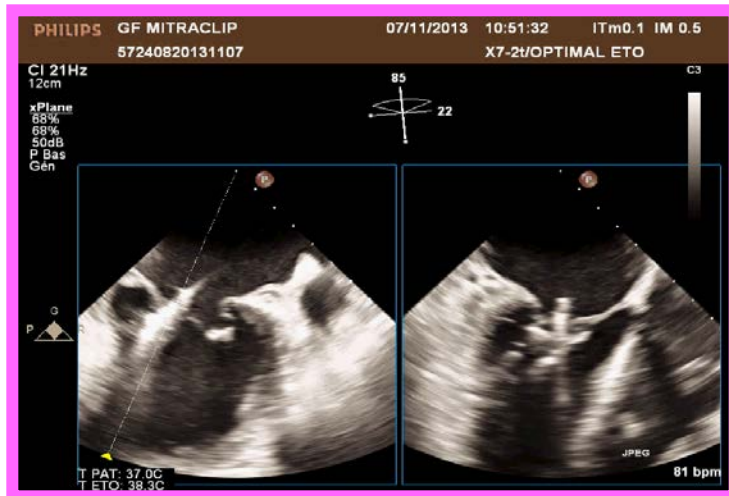
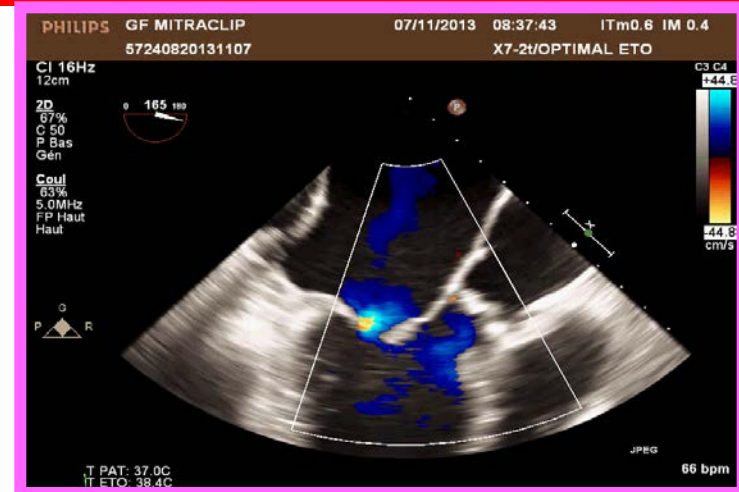
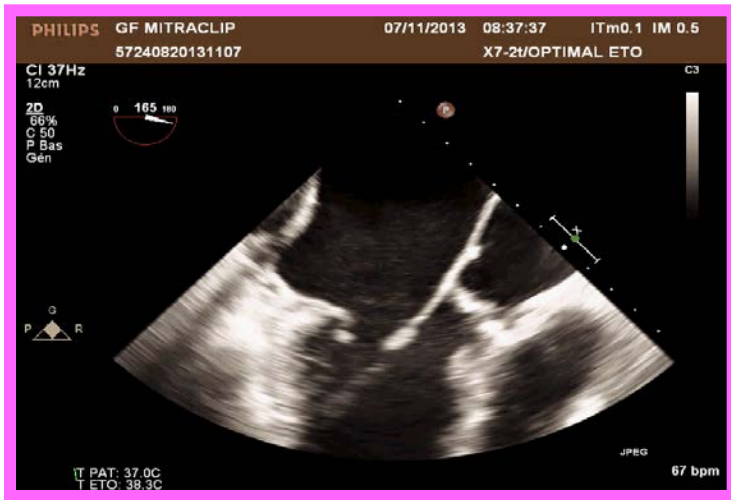


Posterior leaflet tissue > 10 mm

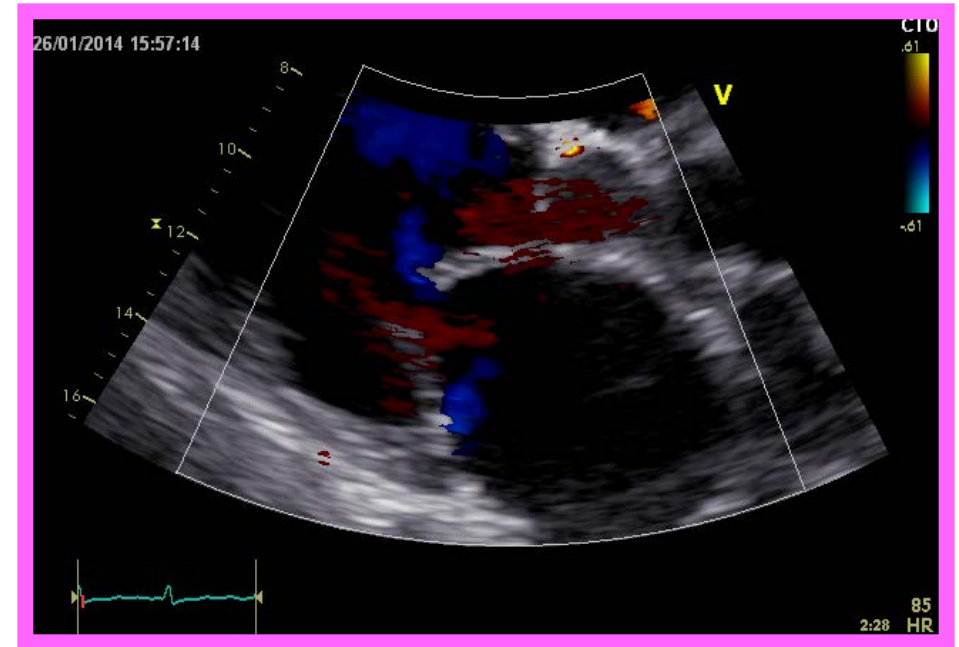
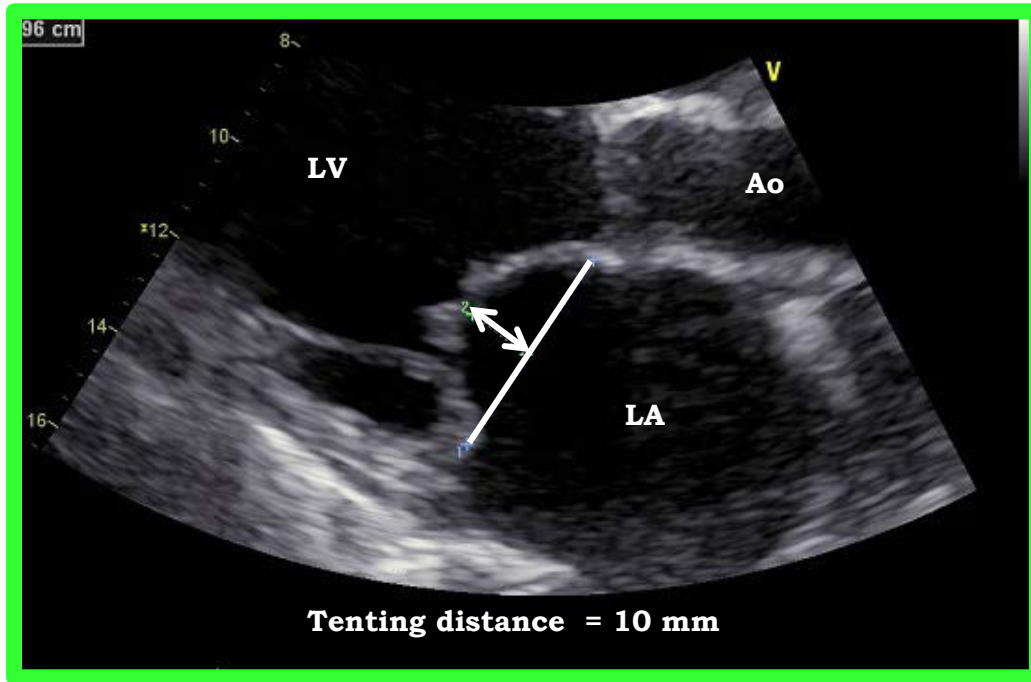
Difficult cases for Mitraclip



Difficult cases for Mitraclip



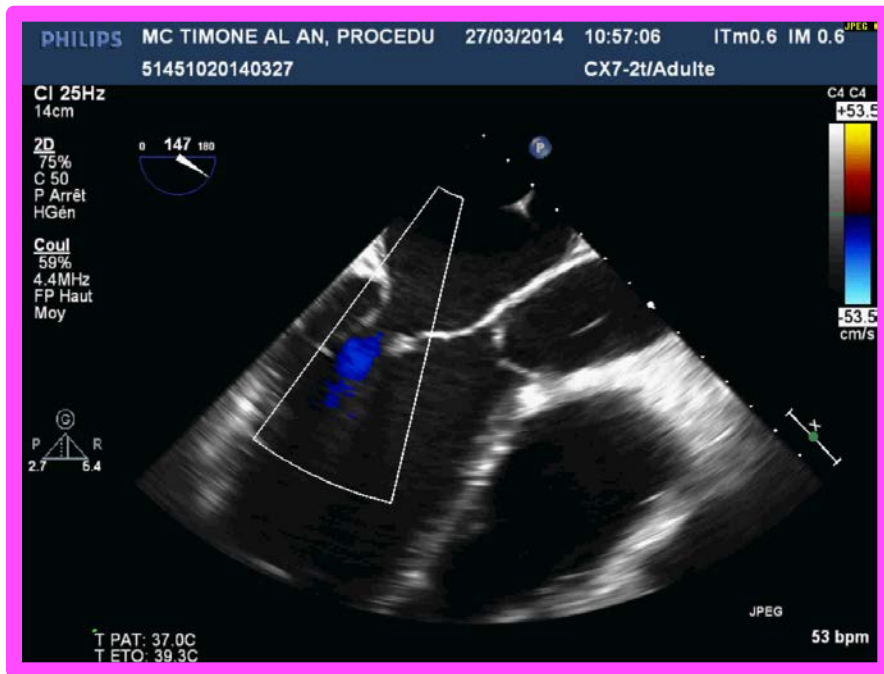
Good candidate for Mitraclip



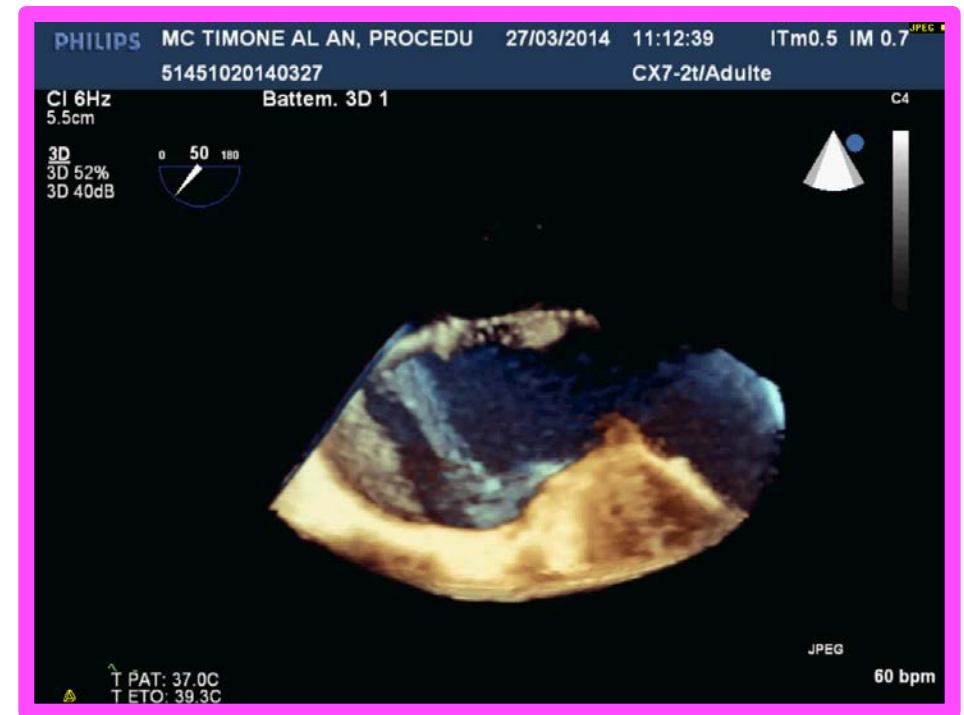
Typical Mitraclip procedure for functional MR



Per-procedural assessment



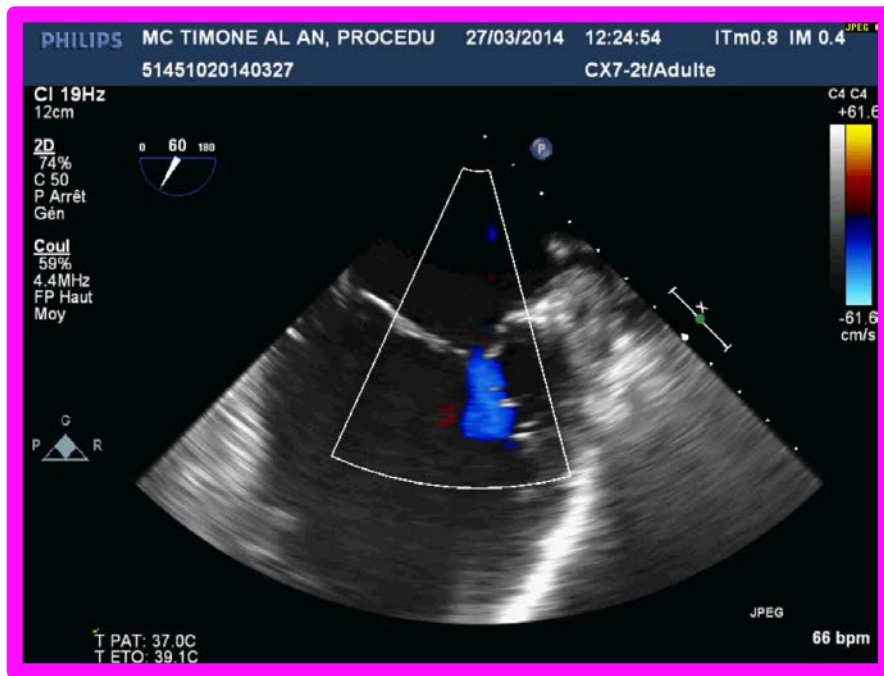
Atrial septal puncture



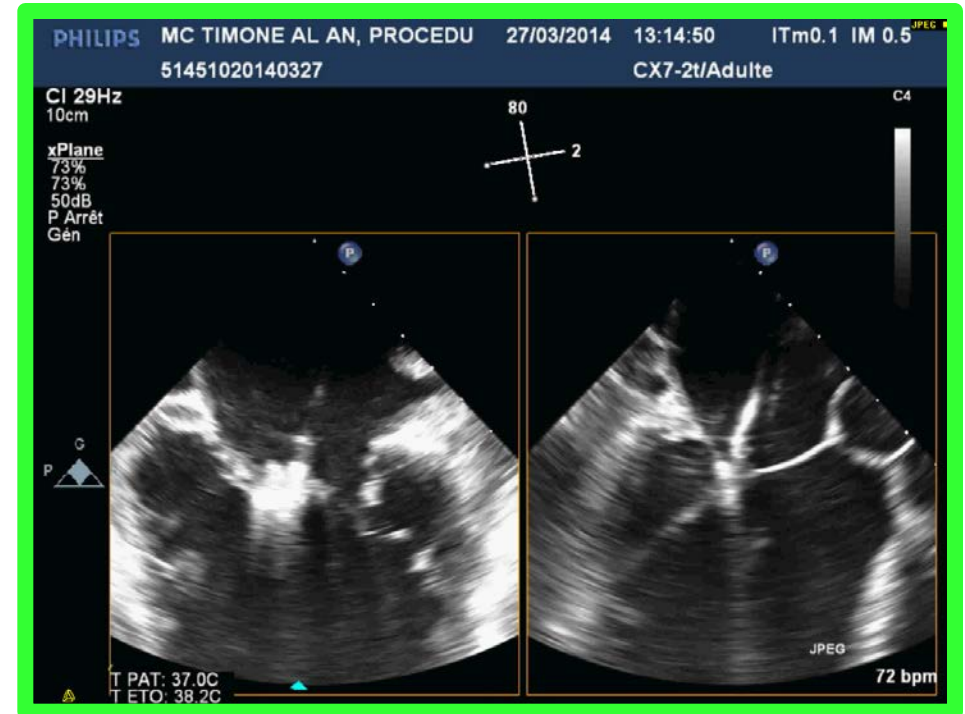
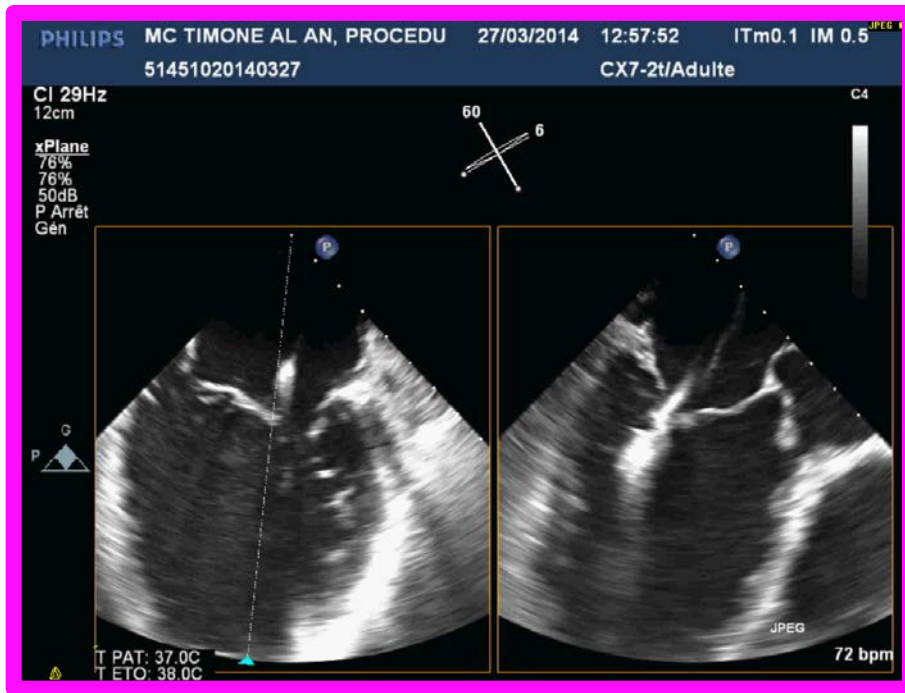
1st clip positionning



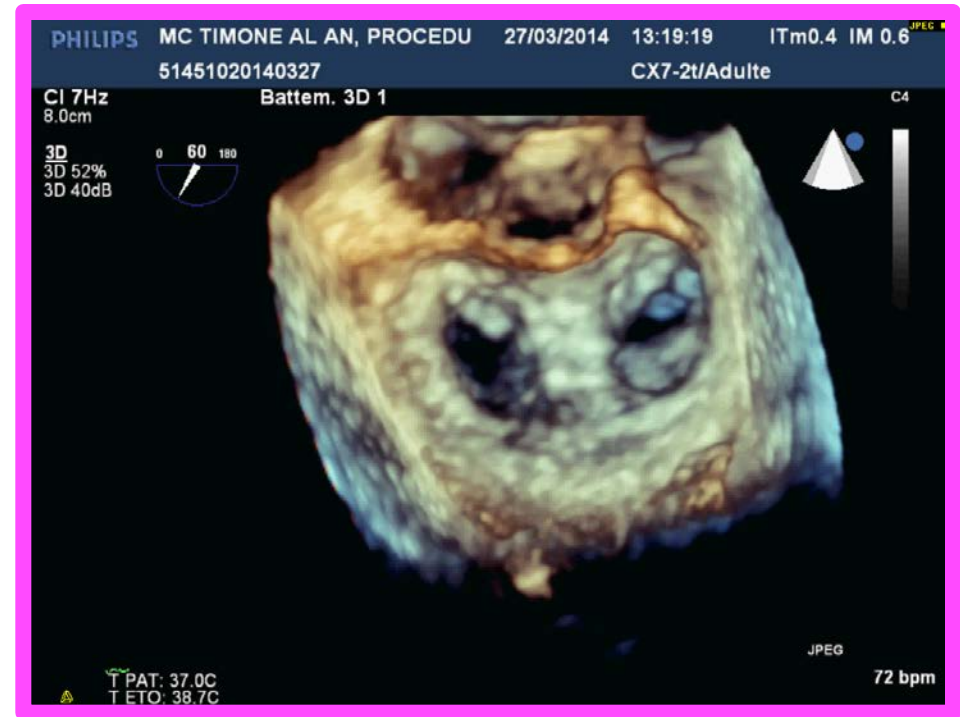
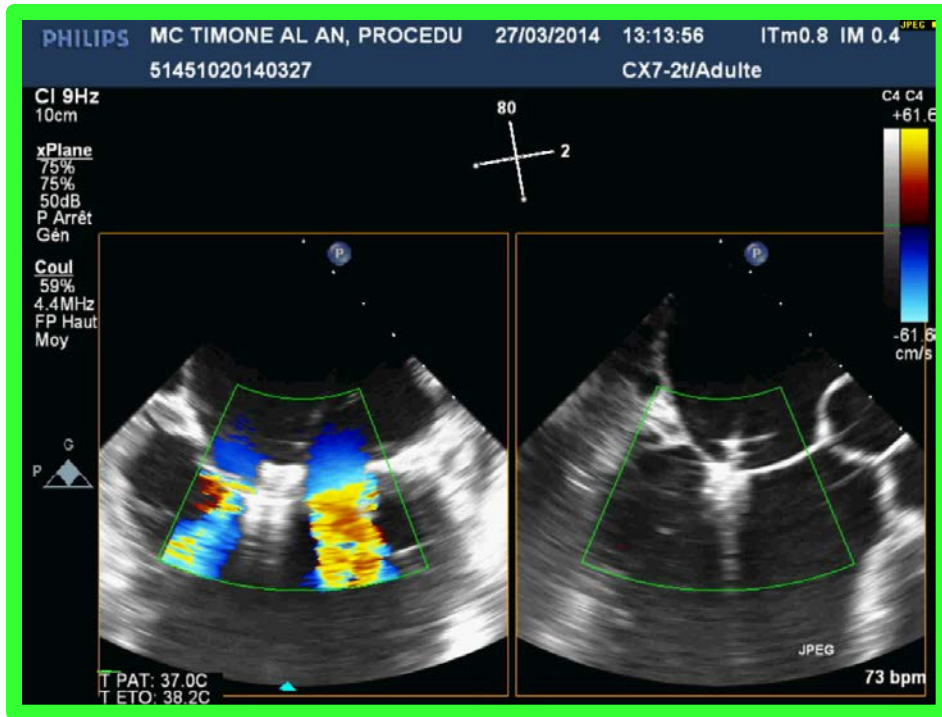
Residual MR after 1st clip



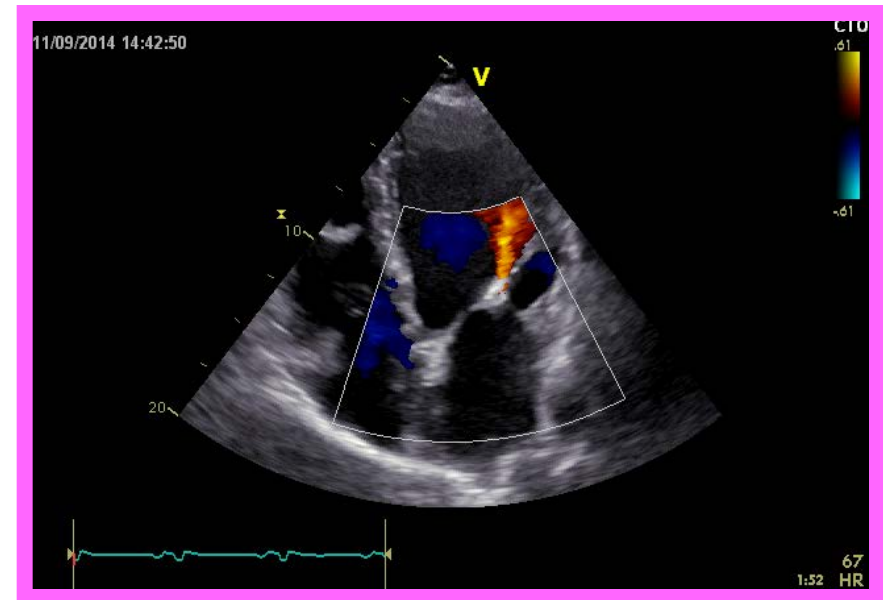
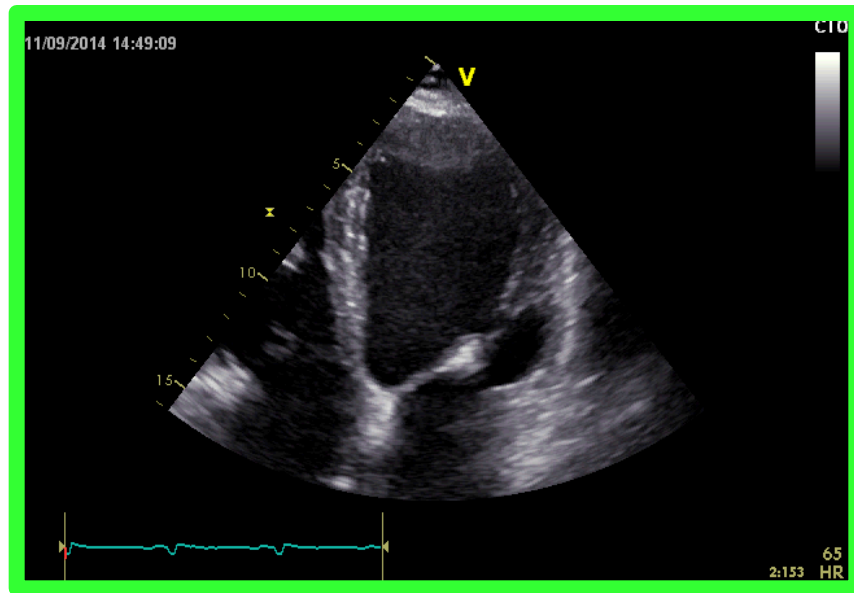
2nd clip placement



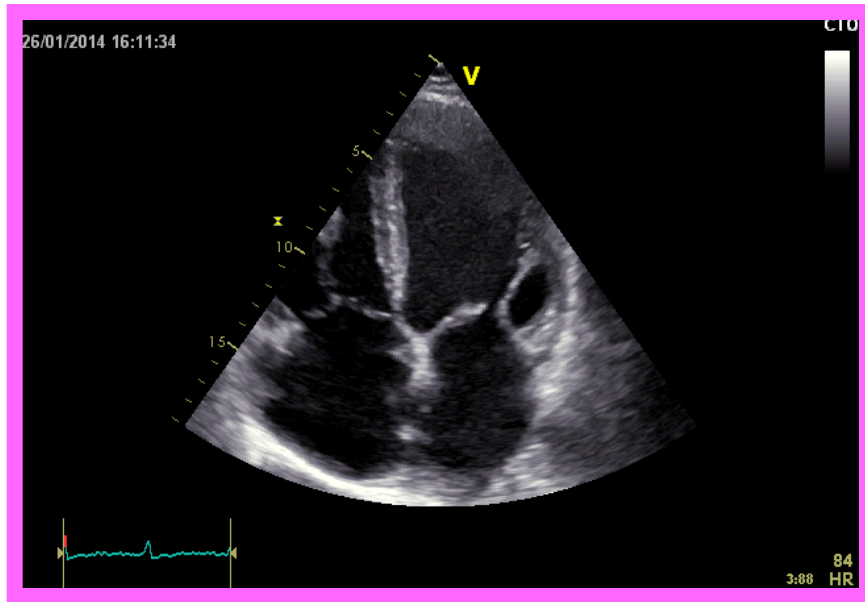
Final Result after 2 clips



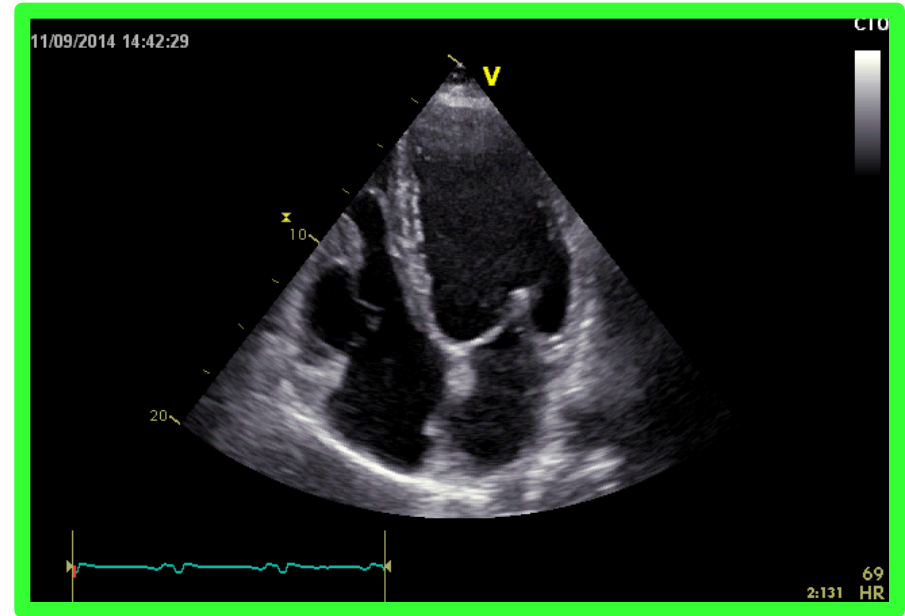
6-months Follow-up



6-months Follow-up



January 2014



September 2014

Evaluation of Mitral Regurgitation

1. Pre-interventional assessment

- mechanism
- quantification
- suitability for surgical or interventional repair

2. Per-interventional assessment

- intra-operative echocardiography
- monitoring of catheterization procedures





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ACC/AHA 2014 Guidelines for the Management of Patients With Valvular Heart Disease

*‘move the timing of intervention earlier in the disease course with the goal of preventing irreversible LV dysfunction, arrhythmias and pulmonary hypertension due to longstanding LV volume overload.’ **

Nishimura, RA et al.
2014 AHA/ACC Valvular Heart Disease Guideline

MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1% when performed at a Heart Valve Center of Excellence	IIa	B	(149, 203, 205-209)
MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure >50 mm Hg)	IIa	B	(154, 205, 210-215)
Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications	IIa	C	N/A
MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤30% (stage D)	IIb	C	N/A
MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable	IIb	B	(194, 202, 203)
Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B	(216)
MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful	III: Harm	B	(195-198)

Source : <http://circ.ahajournals.org/content/early/2014/02/27/CIR.000000000000029.citation> / * Nishimura RA, et al. Heart June 2014 Vol 100 No 12; 905-7



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Indications for mitral valve surgery in secondary mitral regurgitation

	Class	Level
Surgery is indicated in patients with severe MR undergoing CABG, and LVEF > 30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG.	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF < 30%, option for revascularization, and evidence of viability.	IIa	C
Surgery may be considered in patients with severe MR, LVEF > 30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

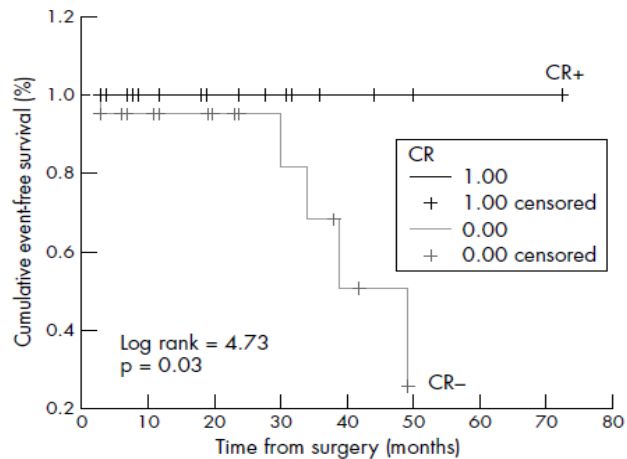
ESC/EACTS 2012 GUIDELINES

European Association of Echocardiography Recommendations on Stress-echo

Degenerative MR

Key point

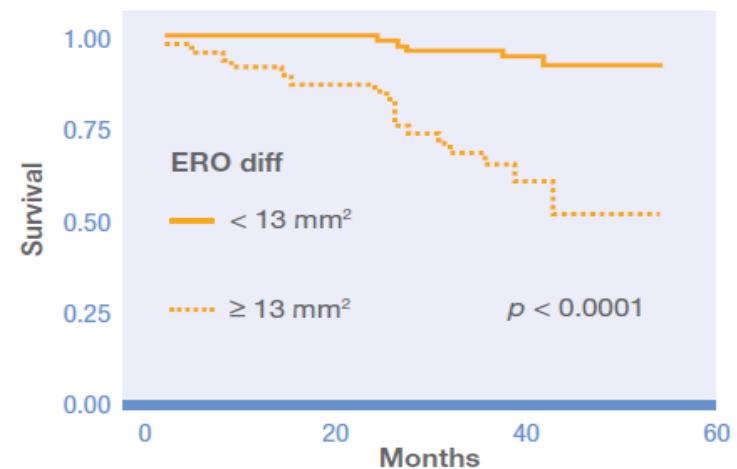
Exercise echocardiography is useful in asymptomatic patients with severe organic MR and borderline values of LV ejection fraction (60–65%) or LV end-systolic diameter (closed to 40 mm or 22 mm/m²). The absence of contractile reserve could identify patients at increased risk of cardiovascular events. Moreover, exercise echocardiography may also be helpful in patients with equivocal symptoms out of proportion of MR severity at rest.



Functional MR

Key point

Exercise echocardiography is useful in patients with functional ischaemic MR and chronic LV systolic dysfunction to unmask the dynamic behaviour of MR. Patients with an increase in EROA by ≥ 13 mm² are patients at increased risk of cardiovascular events. In these patients, exercise echocardiography also helps to identify the presence and extent of viable myocardium at jeopardy.



Source: Lancellotti et al., European Journal of Echocardiography (2010) 11, 307-332. Patrizio Lancellotti, Paul L. Gérard, and Luc A. Piérard, Long-term outcome of patients with heart failure and dynamic functional mitral regurgitation, European Heart Journal (2005) 26, 1528-1532. R Lee, B Haluska, D Y Leung, C Case, J Mundy, T H Marwick. Functional and prognostic implications of left ventricular contractile reserve in patients with asymptomatic severe mitral regurgitation, Heart 2005;91:1407-1412

ESC/EACTS 2012 GUIDELINES

As ischaemic MR is a dynamic condition: stress testing may play a role in its evaluation. Echocardiographic quantification of MR during exercise is feasible, provides a good demonstration of dynamic characteristics and has prognostic importance. An exercise-induced increase of $\geq 13 \text{ mm}^2$ of the EROA has been shown to be associated with a large increase in the relative risk of death and hospitalization for cardiac decompensation.¹⁴³ The

- Application of stress echo for measurement of dynamic MR as seen in IMR
- Increase in EROA associated with increase in mortality and hospitalization

Table 13 Indications for mitral valve surgery in chronic secondary mitral regurgitation

	Class ^a	Level ^b
Surgery is indicated in patients with severe MR ^c undergoing CABG, and LVEF >30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG. ^d	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability.	IIa	C
Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

CABG = coronary artery bypass grafting; CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; SPAP = systolic pulmonary artery pressure.

^aClass of recommendation.

^bLevel of evidence.

^cThe thresholds for severity (EROA $\geq 20 \text{ mm}^2$; R Vol > 30 ml) differ from that of primary MR and are based on the prognostic value of these thresholds to predict poor outcome: see Table 5.¹⁷

^dWhen exercise echocardiography is feasible, the development of dyspnoea and increased severity of MR associated with pulmonary hypertension are further incentives to surgery.

ESC/EACTS 2012 GUIDELINES

- Asymptomatic patients
- Preserved LV function
- Surgical candidates
- LA dilation
- Pulmonary hypertension with exercise

Table 12 Indications for surgery in severe primary mitral regurgitation

	Class ^a	Level ^b	Ref ^c
Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: <ul style="list-style-type: none">• left atrial dilatation (volume index ≥ 60 ml/m² BSA) and sinus rhythm, or• pulmonary hypertension on exercise (SPAP ≥ 60 mmHg at exercise).	IIb	C	

MitraClip in Specific Patient Populations

Patient groups in which significant clinical benefits have been reported:

- Degenerative MR, declined for surgery¹
- Severe LV dysfunction refractory to medical therapy²
- Severe Heart Failure, despite optimal medical therapy³
- CRT non-responders⁴
- Bivalvular Disease: Severe Aortic Stenosis and Mitral Regurgitation⁵

The following parameters should be taken into consideration by the Heart Team⁶:

- Moderate to severe or severe MR (Functional or Degenerative)
- Echocardiographic criteria for eligibility
- Level of surgical risk
- Greater than one year life expectancy

1. Reichenspurner, H. et al. Clinical Outcomes through 12 months in patients with Degenerative Mitral Regurgitation treated with the MitraClip device in the ACCESS-Europe Phase I trial. *Eur J Cardiothoracic Surgery*. 2013; 44:e 280-288. 2. Franzen O, Baldus S, Rudolph V, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: Emphasis on adverse valve morphology and severe left ventricular dysfunction. *Eur Heart J*. 2010; 31:1373-1381. 3. Franzen et al. MitraClip Therapy In Patients With End-Stage Systolic Heart Failure. *Eur J Heart Failure*. 2011; 13: 569-576. 4. Auricchio et al. Correction of Mitral Regurgitation in Nonresponders To Cardiac Resynchronization Therapy By MitraClip Improves Symptoms And Promotes Reverse Remodeling. *JACC* 2011; 58: 2183-2189. 5. Rudolph V, Schirmer J, Franzen O, Schlüter M, Seiffert M, Treede H, Reichenspurner H, Blankenberg S, Baldus S. Bivalvular transcatheter treatment of high-surgical-risk patients with coexisting severe aortic stenosis and significant mitral regurgitation. *Int J Cardiol*. 2013; 167(3):716-20. 6. ESC/EACTS 2012 Guidelines on the management of valvular heart disease. *Eur Heart J* (2012) 33, 2451–2496.

Step 1 Selection of the patient

The first basic step in patient selection is clinical and global echo evaluation

Predicted surgical procedural mortality risk >12% (STS calculated or Surgeon estimated based on pre-specified co-morbidities)

Symptomatic 3+ or 4+ MR

Degenerative or Functional

KEY exclusion criteria

EF \leq 20% and/or LVESD >60mm

MVA <4cm²

Leaflet anatomy unsuitable for MitraClip Device