
# Primary MR phenotypes/stages: what do they offer?

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HART LONG
CENTRUM LEIDEN


# FACULTY DISCLOSURE

I disclose the following financial relationships:

Receiving grant/research support from Alnylam, Pfizer, Novartis, Pie Medical

Paid speaker for GE Healthcare, Philips Utrasound, Abbott Vascular, Omron, Pfizer

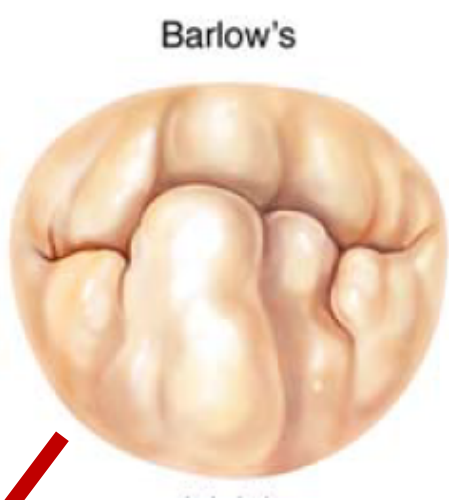
# Why should we phenotype/stage?

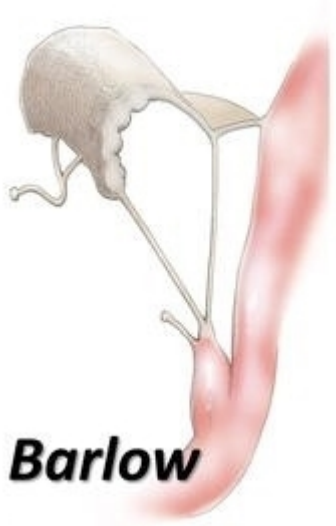
- Improve risk stratification
- Impact on management: follow-up or choice of treatment

# How?

- Segmental analysis of the MV for detailed assessment of mechanism and anatomical lesions
- Looking beyond the MV

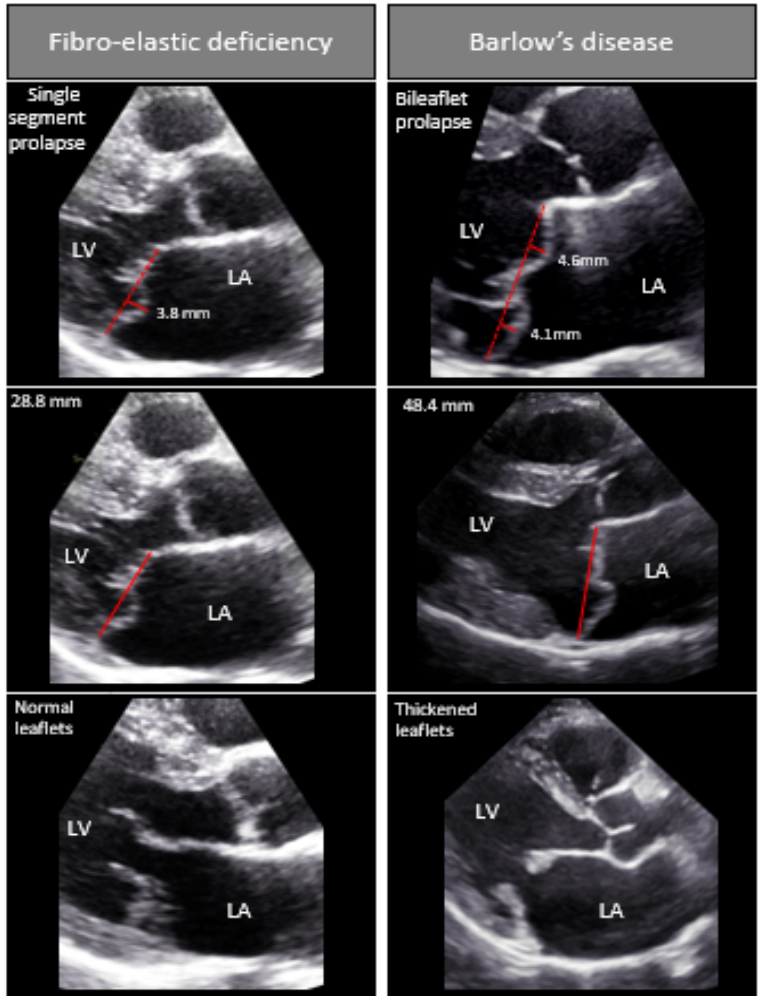
# Phenotypes of Mitral Valve Prolapse

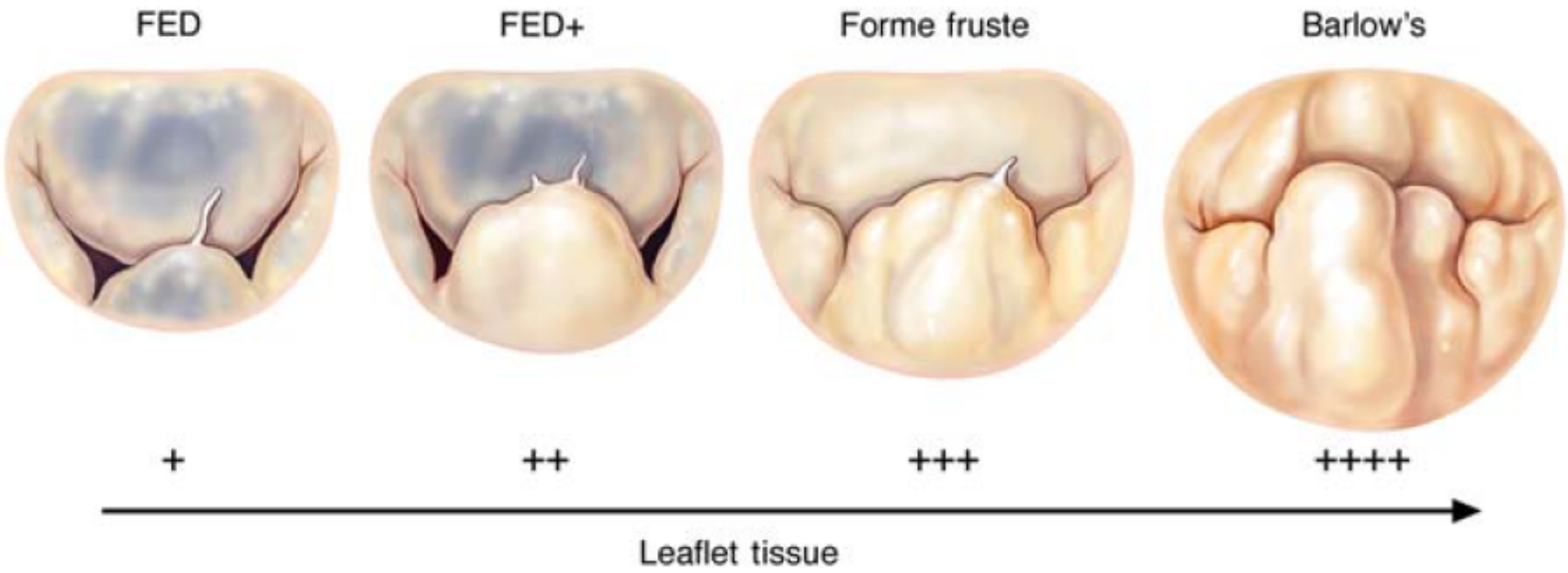

# Mitral Valve Prolapse

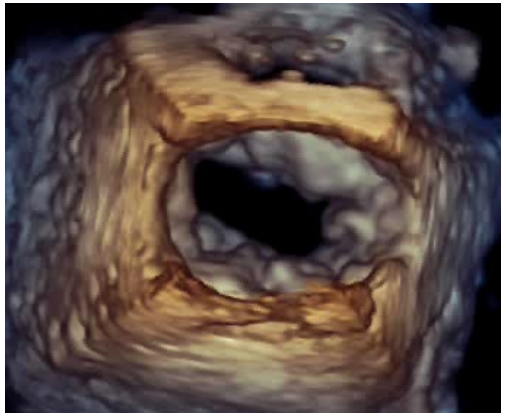
| | Fibroelastic deficiency | Barlow's disease |
|---|---|---|
| **Clinical characteristics** | | |
| Age of onset | Older (≥60 years) | Younger (<60 years) |
| History | No history of murmur | Usually long history of murmur |
| Duration of the disease | Months (likely <5 years) | Years to decades |
| Auscultation | Holosystolic murmur | Mid-systolic click and late systolic murmur |
| **Echocardiographic characteristics** | | |
| Leaflets | No excessive valve tissue<br>Thin leaflets and no billowing in noninvolved segments<br>Single segment involvement | Excessive valve tissue<br>Thickened leaflets<br>Leaflet billowing<br>Multiple segments involvement |
| Annulus | Normal of moderate dilatation<br>No calcifications | Severe annular dilatation<br>Calcifications could be present |
| Chordae | Ruptured | Elongated, ruptured |
| **Surgical observation** | | |
| Annulus | Normal or mildly dilated annulus | Severe annular dilatation; calcifications |
| Leaflets | Thin translucent leaflets without excess tissue<br>Single segment involved, which often shows leaflet thickening<br>No billowing of other segments | Thick leaflets with excess tissue<br>Multiple segments involved, often bi-leaflet<br>Multi-segmental billowing |

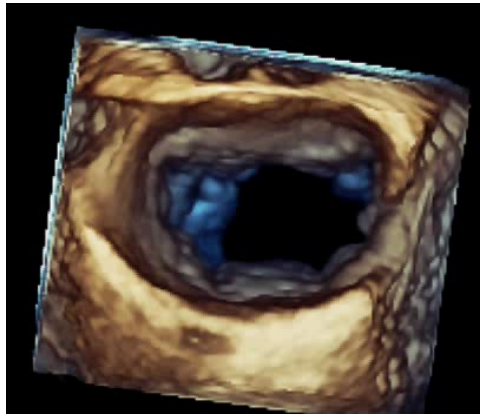


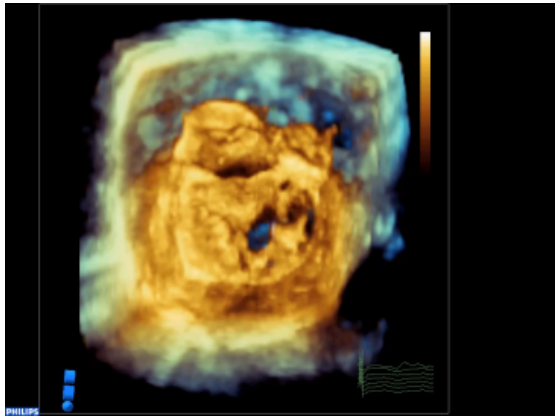

Van Wijngaarden et al, JCDD 2021

# Mitral Valve Prolapse



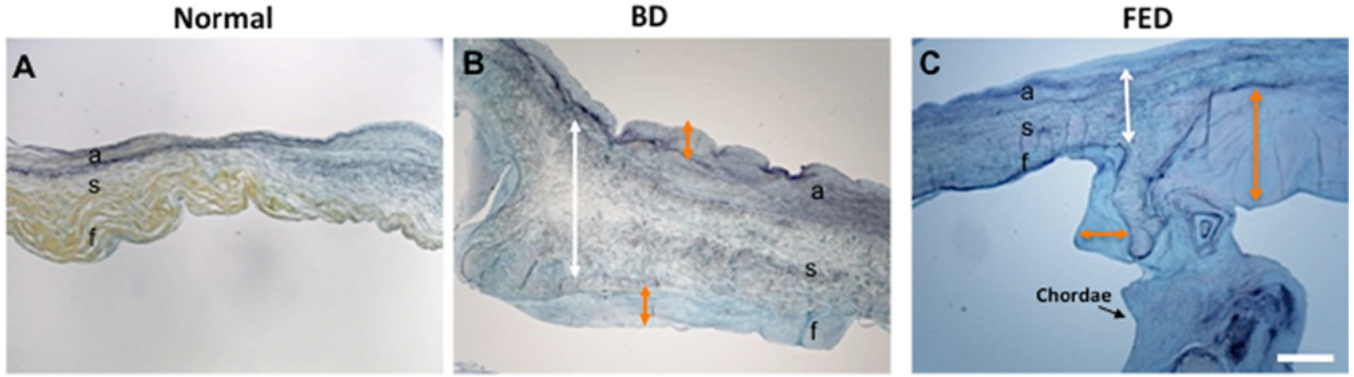





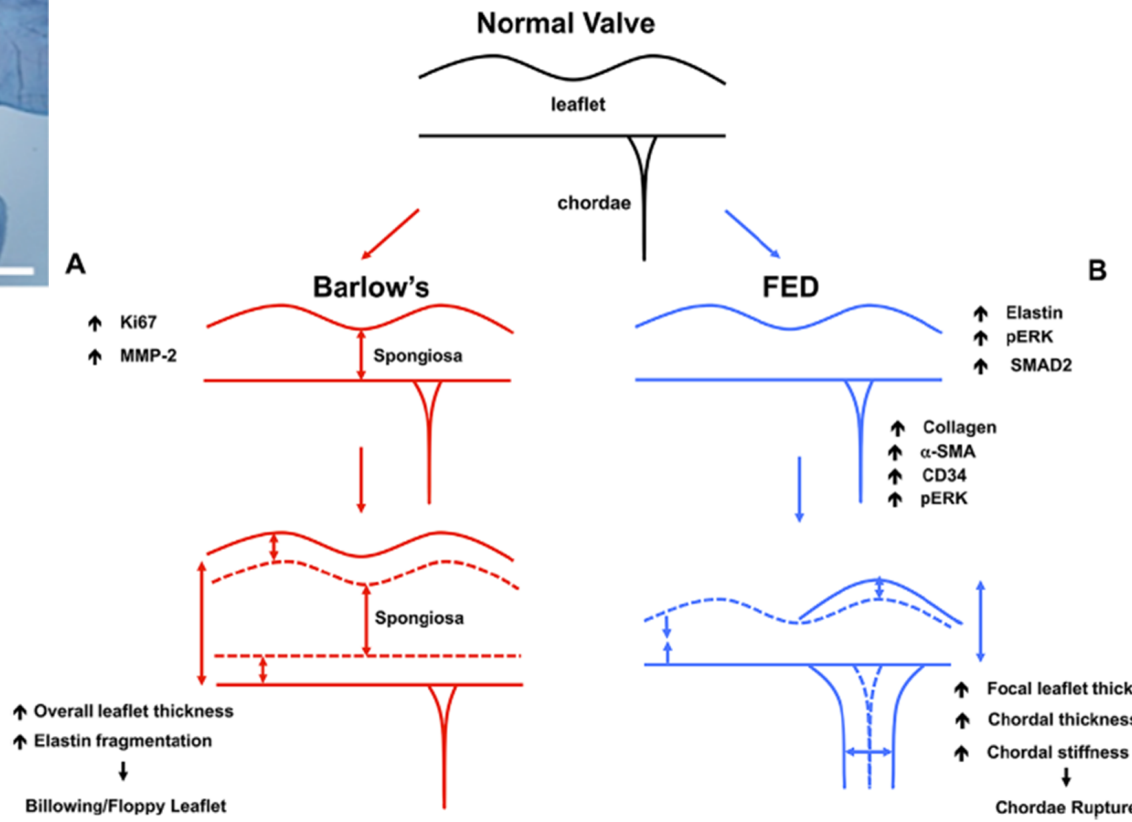


# Comparative Histopathological Analysis of Mitral Valves in Barlow Disease and Fibroelastic Deficiency

*Jesper Hjortnaes, MD, PhD,[*,†] Josh Keegan, BS,[*] Patrick Bruneval, MD,[‡,§,¶] Eugenia Schwartz, BS,[*] Frederick J. Schoen, MD, PhD,[#] Alain Carpentier, MD,[‡,¶,**] Robert A. Levine, MD,[††] Albert Hagège, MD,[‡,¶,‡‡] and Elena Aikawa, MD, PhD[*,§§]*



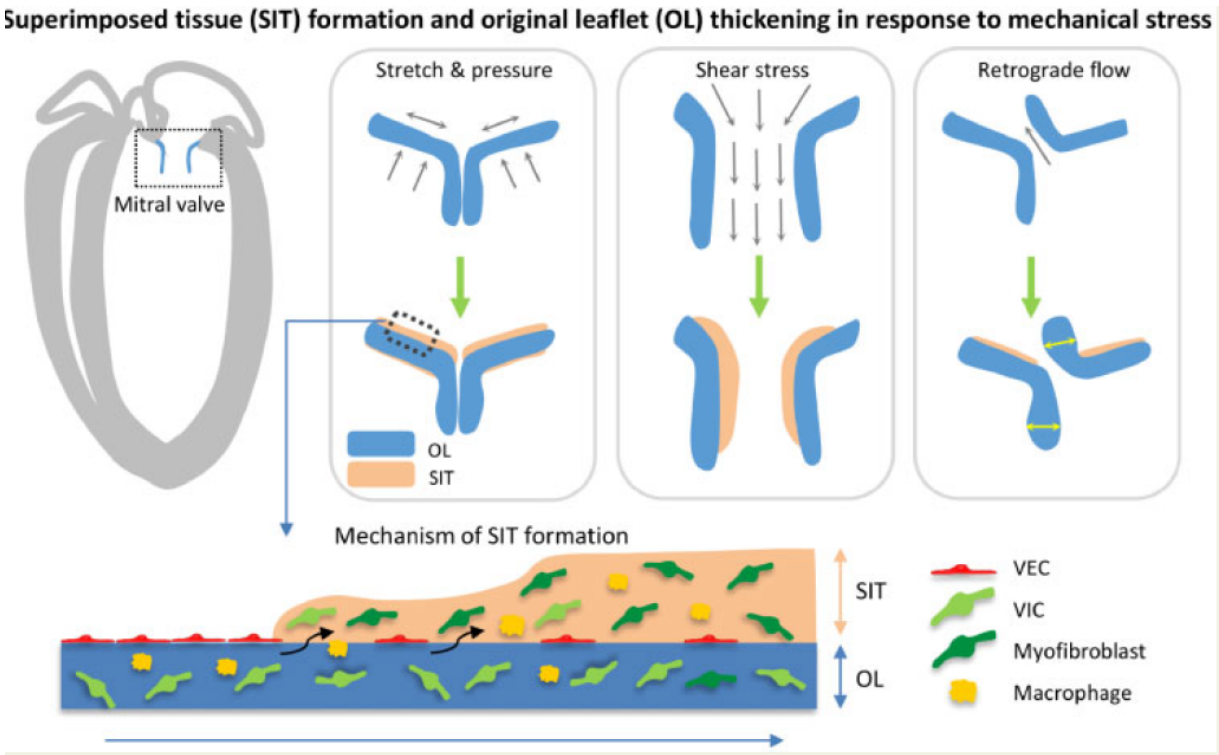

**Collagen and elastin fibers are fragmented and the spongiosa layer expands due to the accumulation of proteoglycans, characteristic of the myxomatous degeneration, and infiltrates the fibrosa layer**

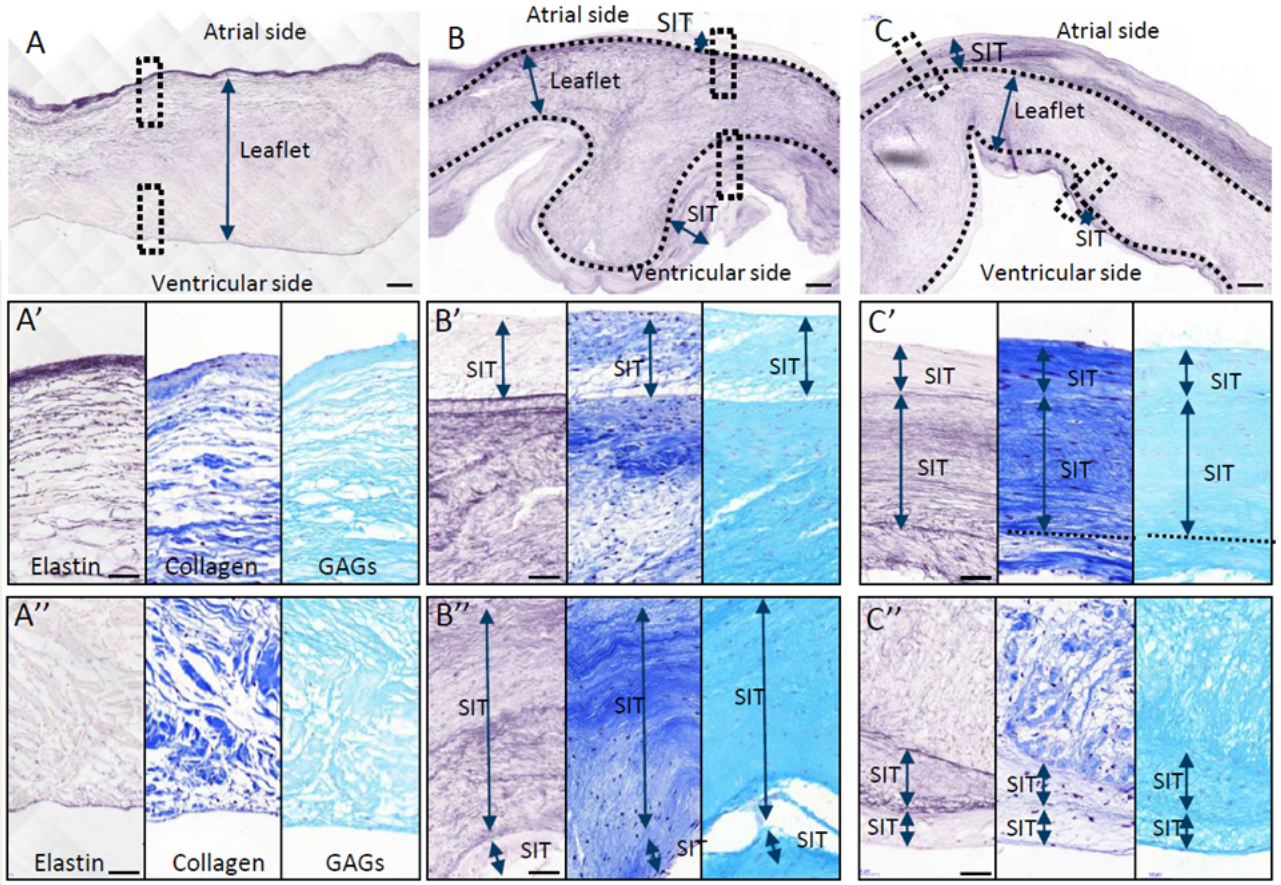


ESC European Society of Cardiology
Cardiovascular Research (2020) **116**, 931–943
doi:10.1093/cvr/cvz204

# Stress-induced remodelling of the mitral valve: a model for leaflet thickening and superimposed tissue formation in mitral valve disease

**Boudewijn P.T. Kruithof [1,2,3]*, Laura Paardekooper [2], Yasmine L. Hiemstra[1], Marie-José Goumans [2], Meindert Palmen [4], Victoria Delgado[1], Robert J.M. Klautz[4], and Nina Ajmone Marsan[1]**




Roberts et al , JACC 2014

# Mitral Valve Prolapse: Primary Aetiology

- **Aging?**
- **Developmental?**



Published in final edited form as:
*Circulation*. 2015 January 20; 131(3): 263–268. doi:10.1161/CIRCULATIONAHA.114.012594.

## Familial Clustering of Mitral Valve Prolapse in the Community

**Francesca N. Delling, MD[1,2], Jian Rong, PhD[1,3], Martin G. Larson, ScD[1,4], Birgitta Lehman, RDCS[1], Ewa Osypiuk, MD[1], Plamen Stantchev, MD[1], Susan A. Slaugenhaupt, PhD[5], Emelia J. Benjamin, MD, ScM[1,6,7], Robert A. Levine, MD[8], and Ramachandran S. Vasan, MD[1,6,7]**

**Parental mitral valve prolapse was associated with a higher prevalence of mitral valve prolapse in their offspring**

European Journal of Preventive Cardiology
ESC European Society of Cardiology

*Full research paper*

European Journal of Preventive Cardiology
2020, Vol. 27(3) 272–280

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DOI: 10.1177/2047487319874148
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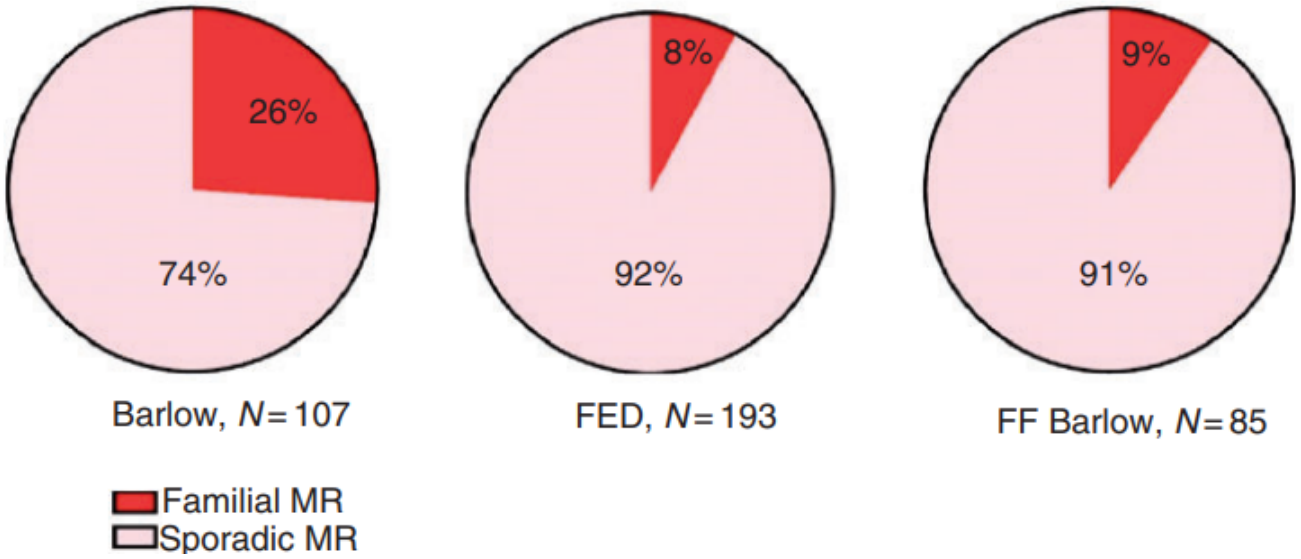
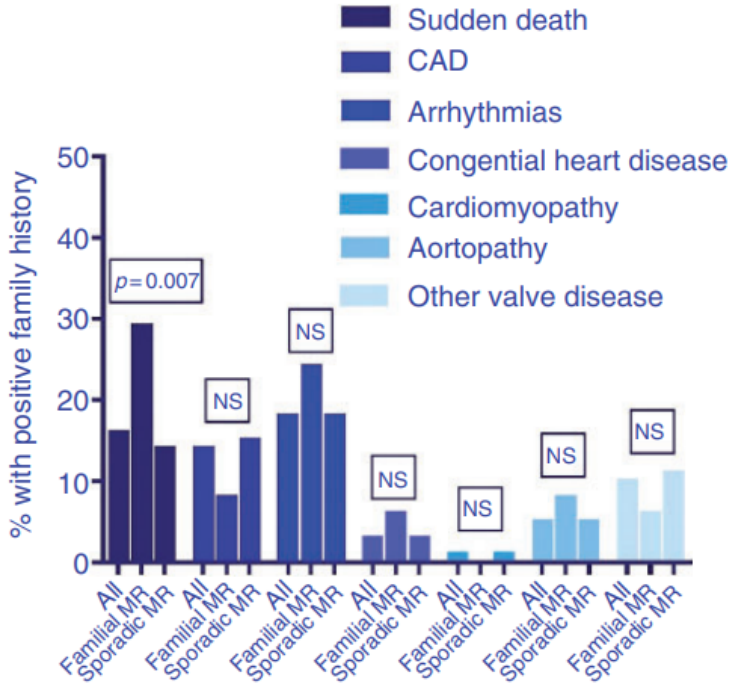
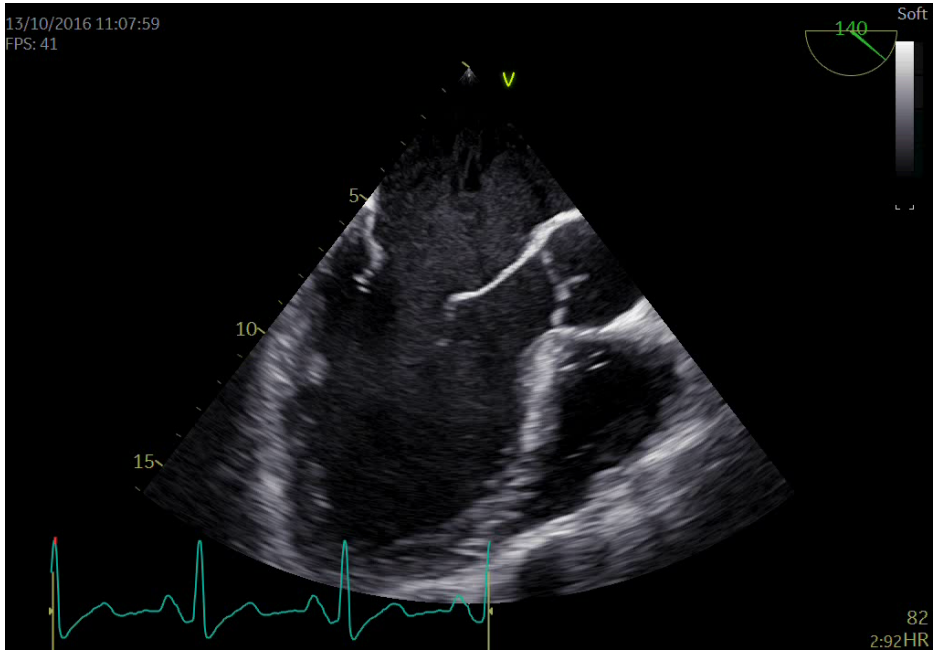
# Familial occurrence of mitral regurgitation in patients with mitral valve prolapse undergoing mitral valve surgery

**Yasmine L Hiemstra[1], Aniek L van Wijngaarden[1], Mathilde W Bos[1], Martin J Schalij[1], Robert JM Klautz[2], Jeroen J Bax[1], Victoria Delgado[1], Daniela QCM Barge-Schaapveld[3] and Nina Ajmone Marsan[1]**



# The Father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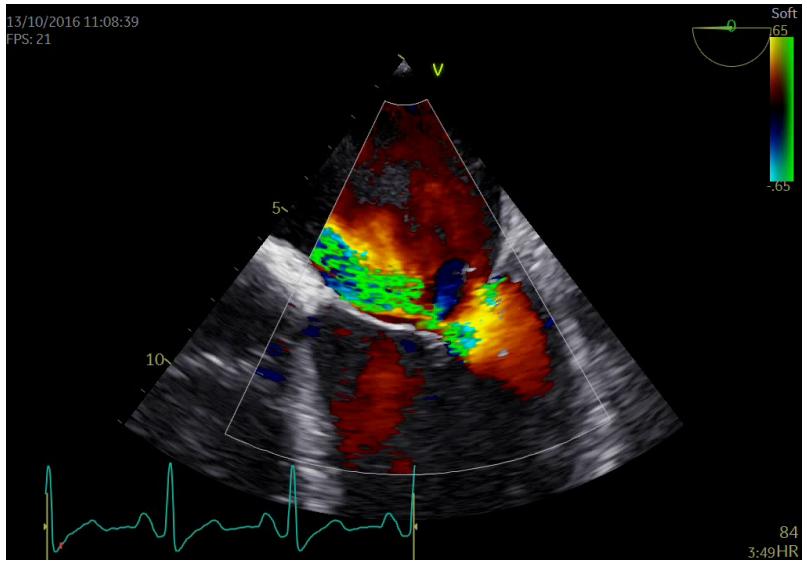
140
5
10
15
82
2:92HR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Soft
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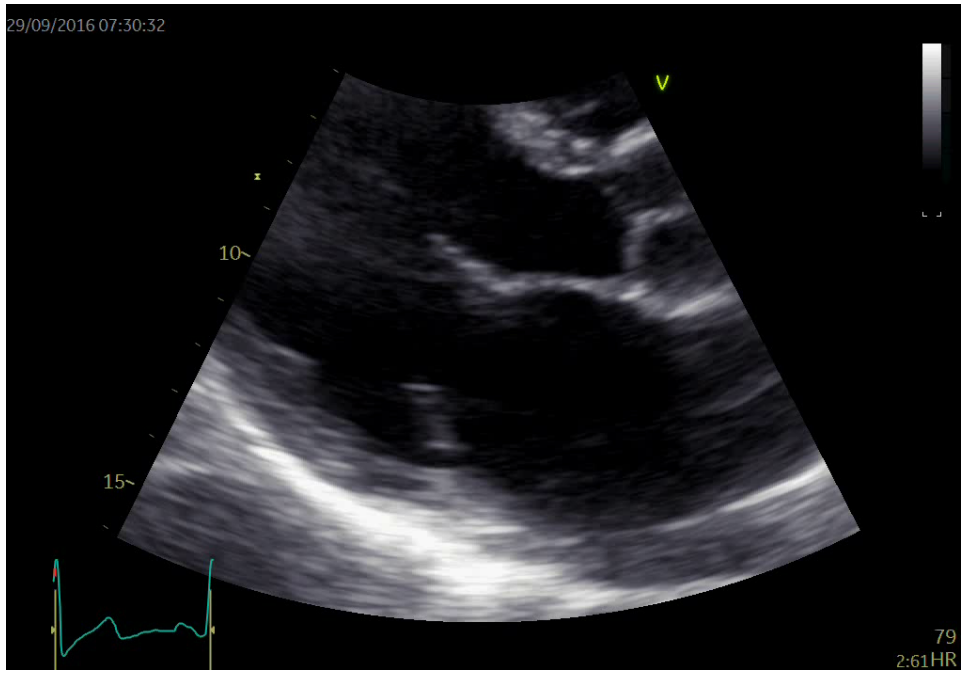
-65
5
10
84
3:49HR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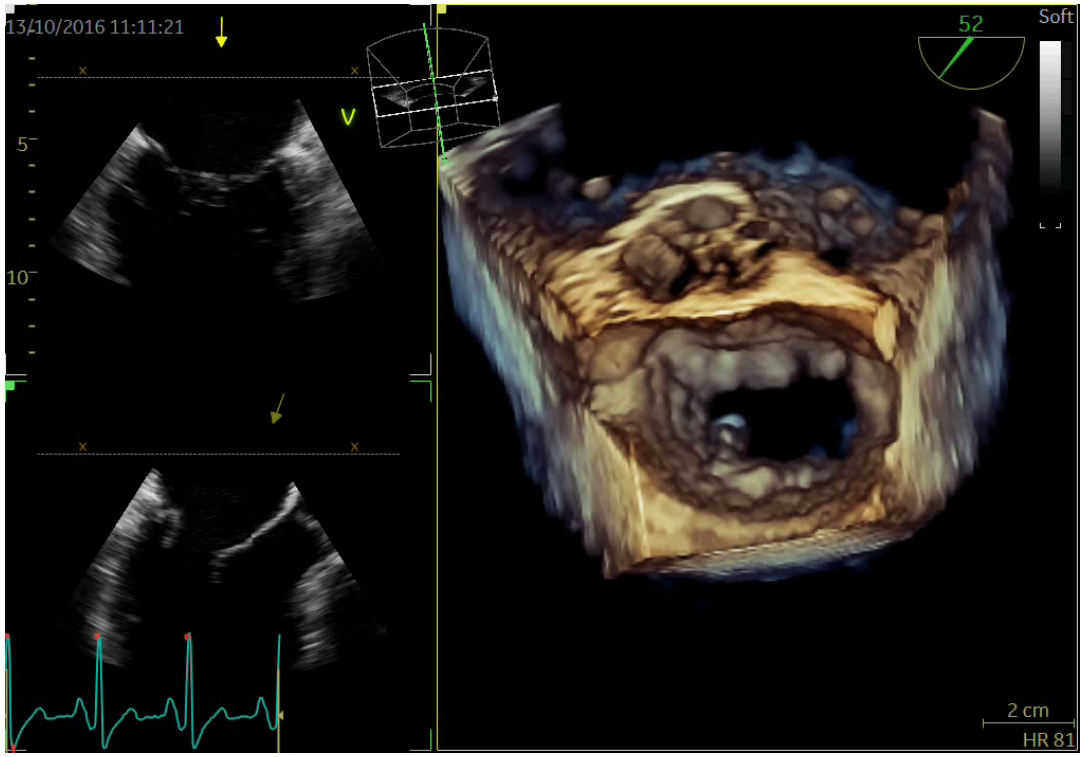
10
15
79
2:61HR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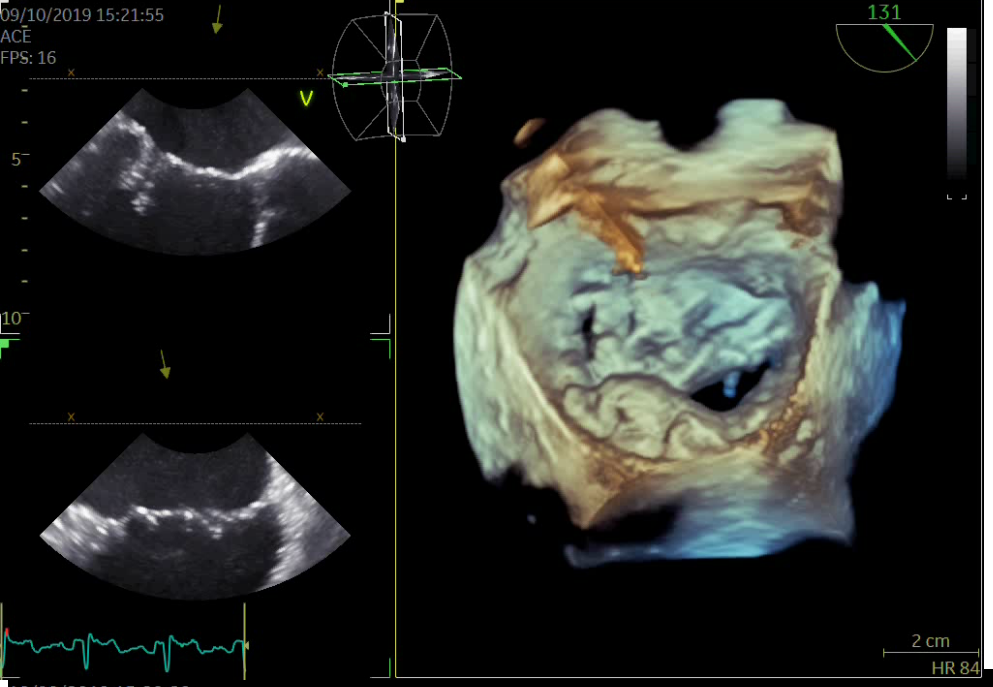
Soft
52
5
10
2 cm
HR 81

# The Son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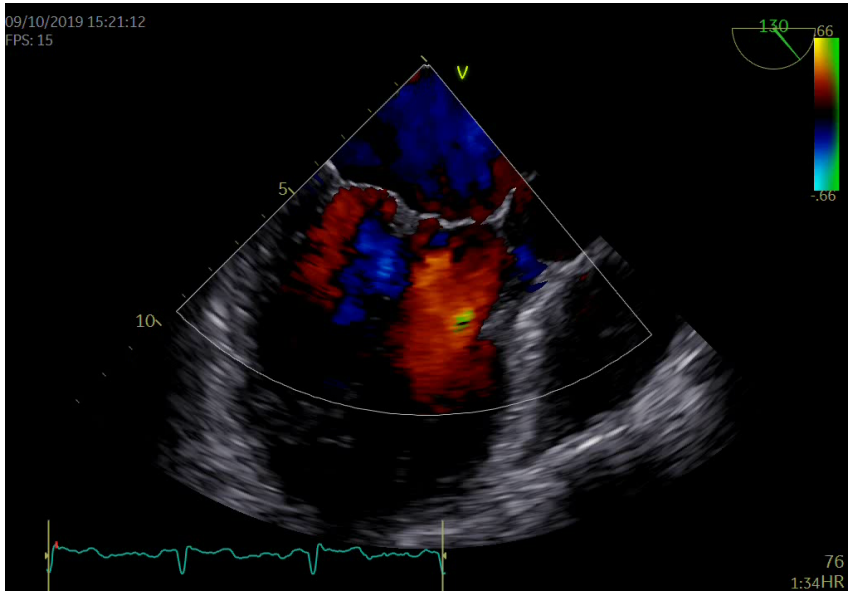
ACE
FPS: 16
131
2 cm
HR 84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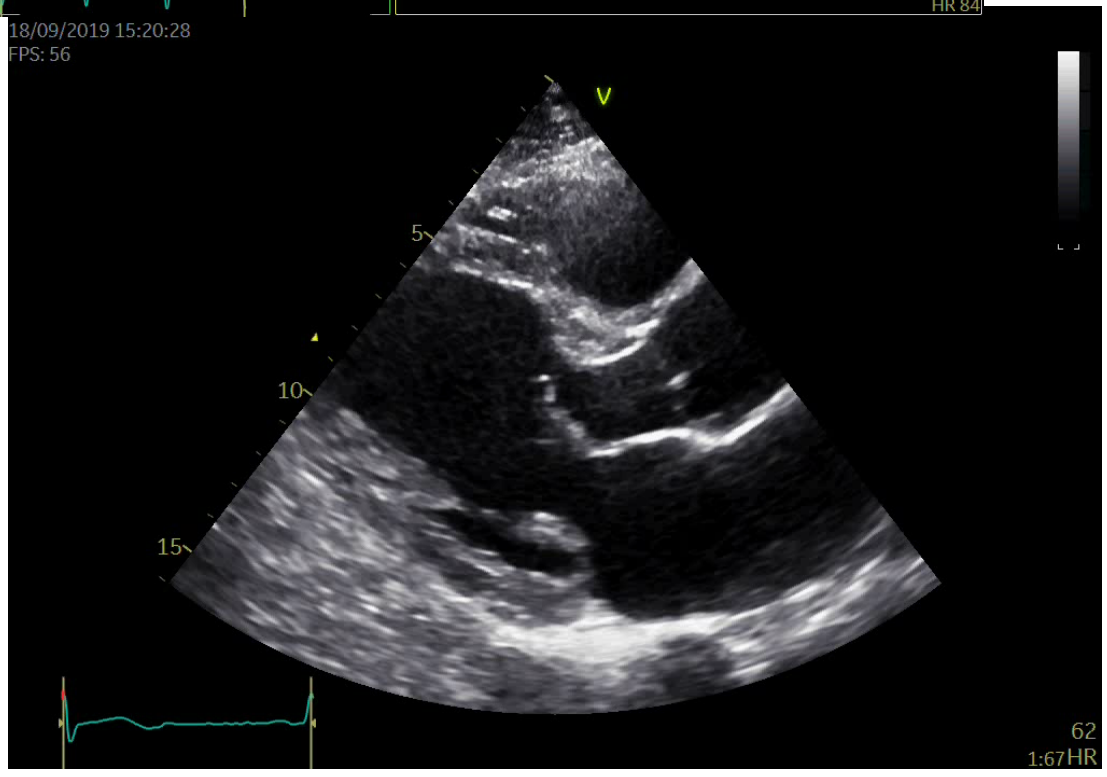
FPS: 15
130
.66
-.66
76
1:34HR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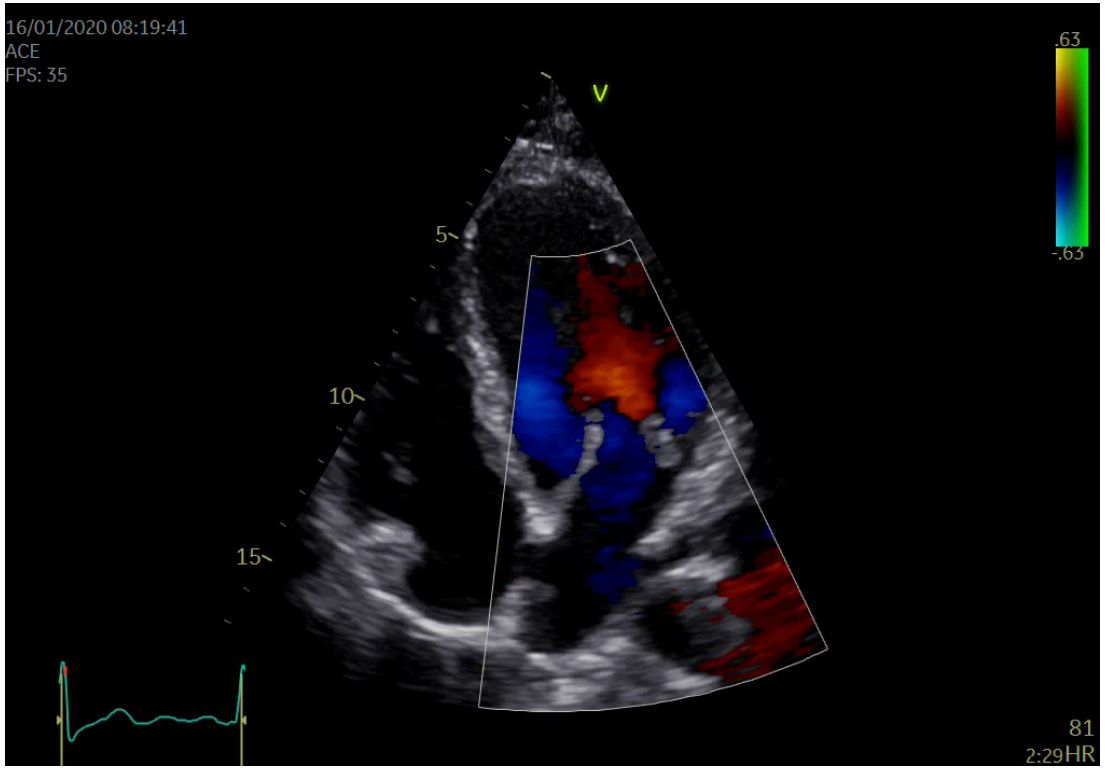
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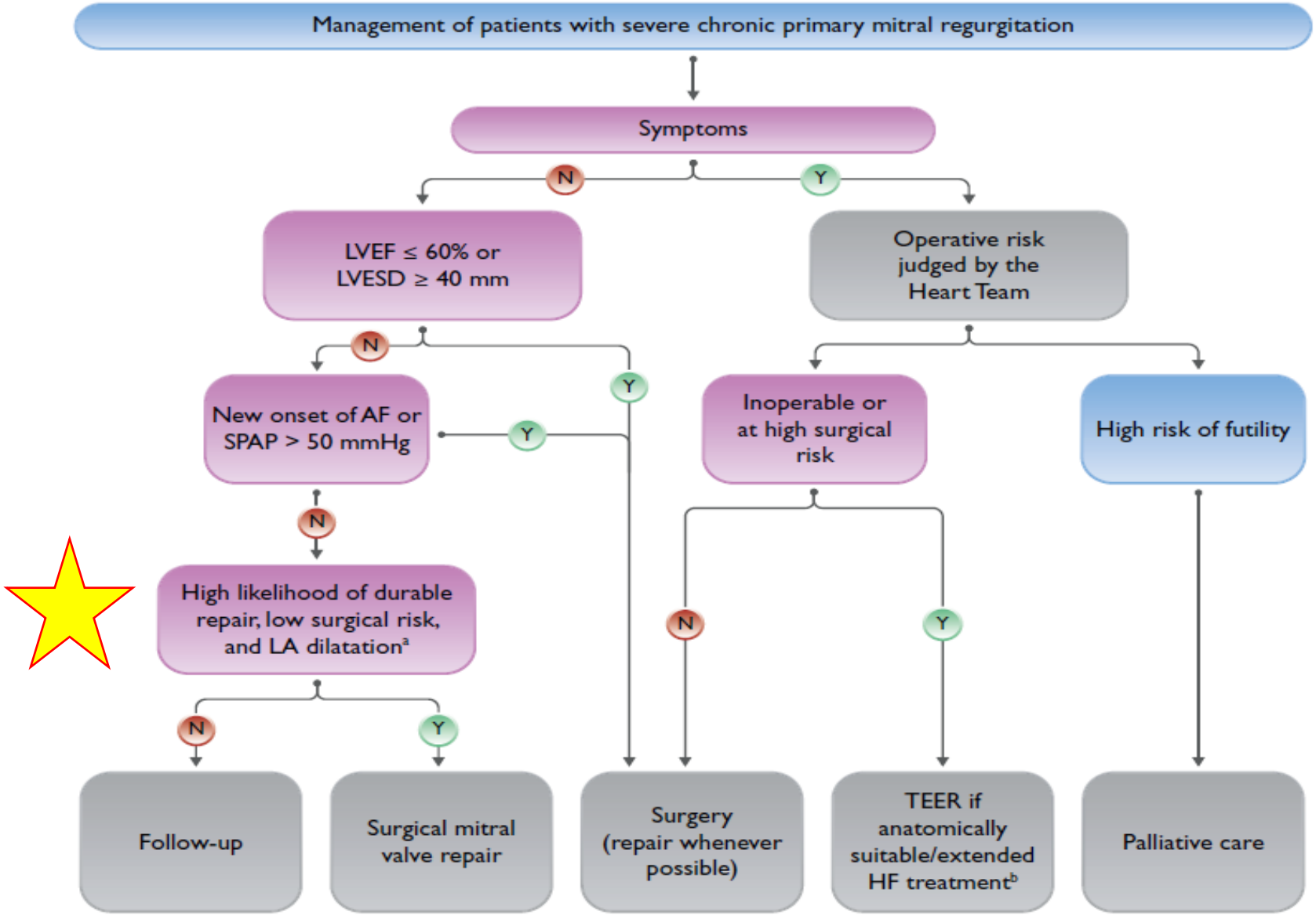
ACE
FPS: 35
.63
-.63
81
2:29HR

# Indication for surgery



# Probability of mitral valve repair

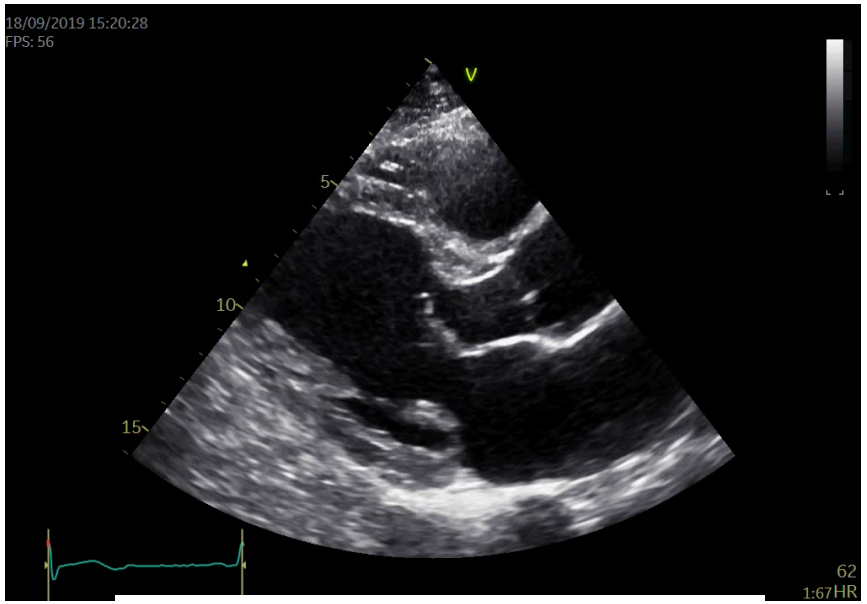
**Table 11** Probability of successful surgical mitral valve repair in MR based on echo findings

| Aetiology | Dysfunction | Calcification | Mitral annulus dilatation | Probability of repair |
|---|---|---|---|---|
| Degenerative | II: Localized prolapse (P2 and/or A2) | No/localized | Mild/moderate | **Feasible** |
| Secondary | I or IIIb | No | Moderate | **Feasible** |
| Barlow | II: Extensive prolapse (≥3 scallops, posterior commissure) | Localized (annulus) | Moderate | **Difficult** |
| Rheumatic | IIIa but pliable anterior leaflet | Localized | Moderate | **Difficult** |
| Severe Barlow | II: Extensive prolapse (≥ 3 scallops, anterior commissure) | Extensive (annulus + leaflets) | Severe | **Unlikely** |
| Endocarditis | II: Prolapse but destructive lesions | No | No/mild | **Unlikely** |
| Rheumatic | IIIa but stiff anterior leaflet | Extensive (annulus + leaflets) | Moderate/severe | **Unlikely** |
| Secondary | IIIb but severe valvular deformation | No | No or severe | **Unlikely** |

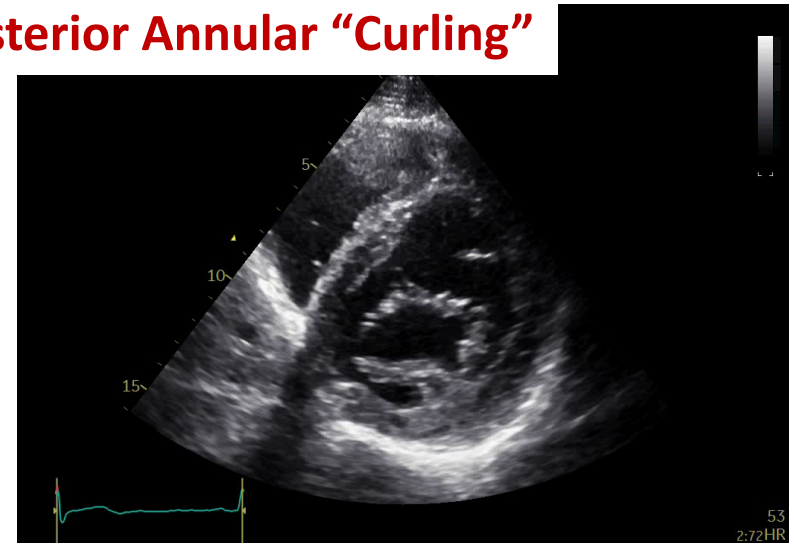
**"Detailed MV segmental analysis And referral to Heart Valve Center"**

*Lancellotti et al, EHJ CVI 2022*

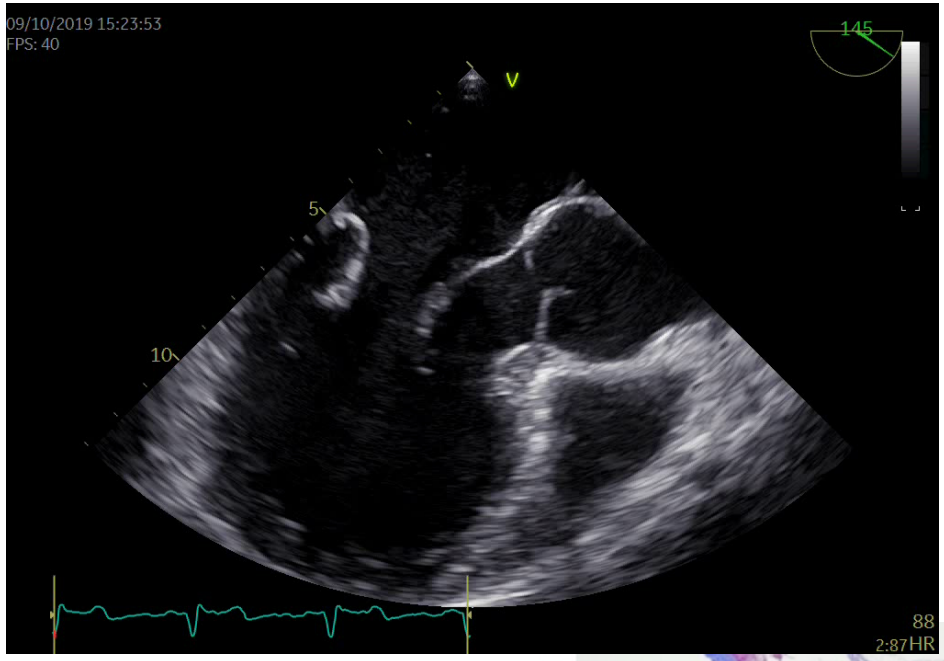
# Annular abnormalities

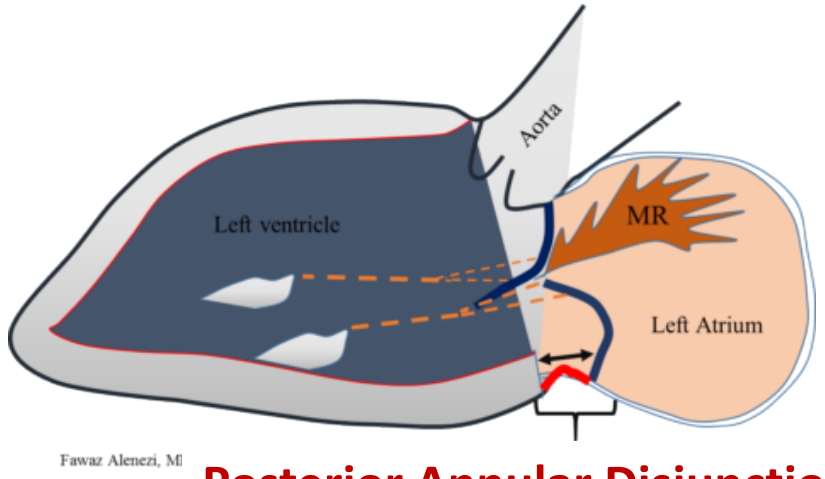



Posterior Annular “Curling”

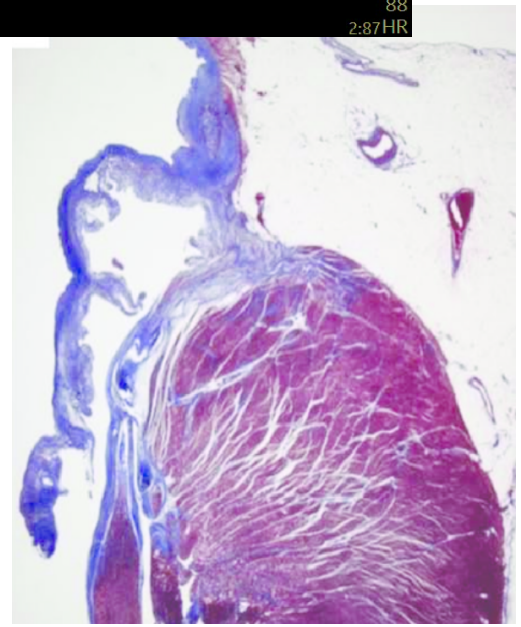



Annular Dilatation




Posterior Annular Disjunction



# Annular abnormalities

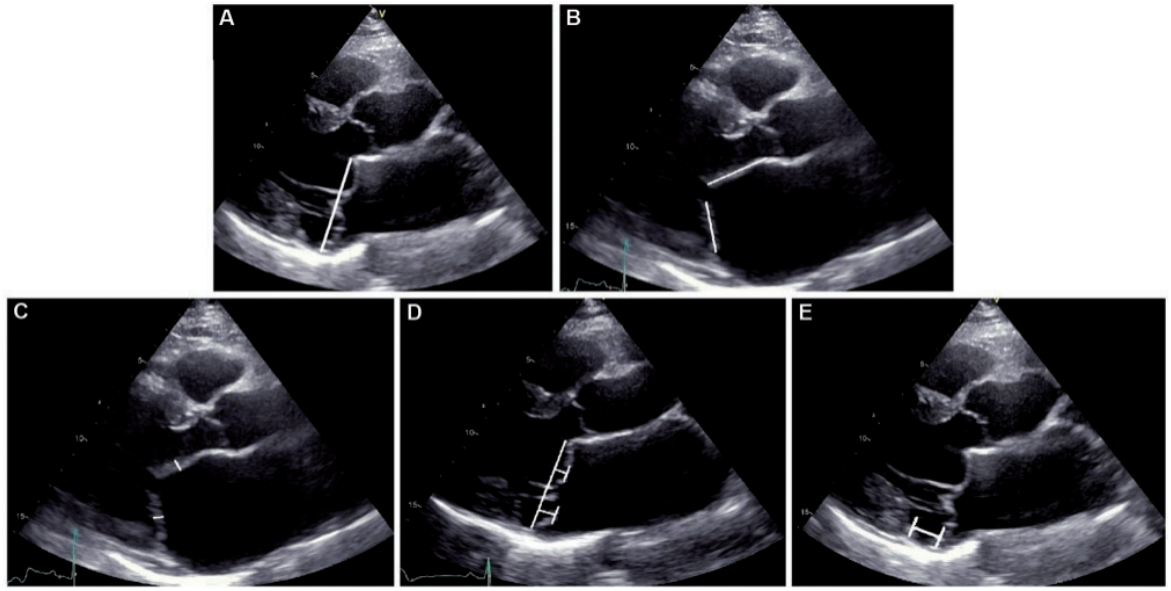
Interactive CardioVascular and Thoracic Surgery 32 (2021) 506–514
doi:10.1093/icvts/ivaa304 Advance Access publication 26 December 2020

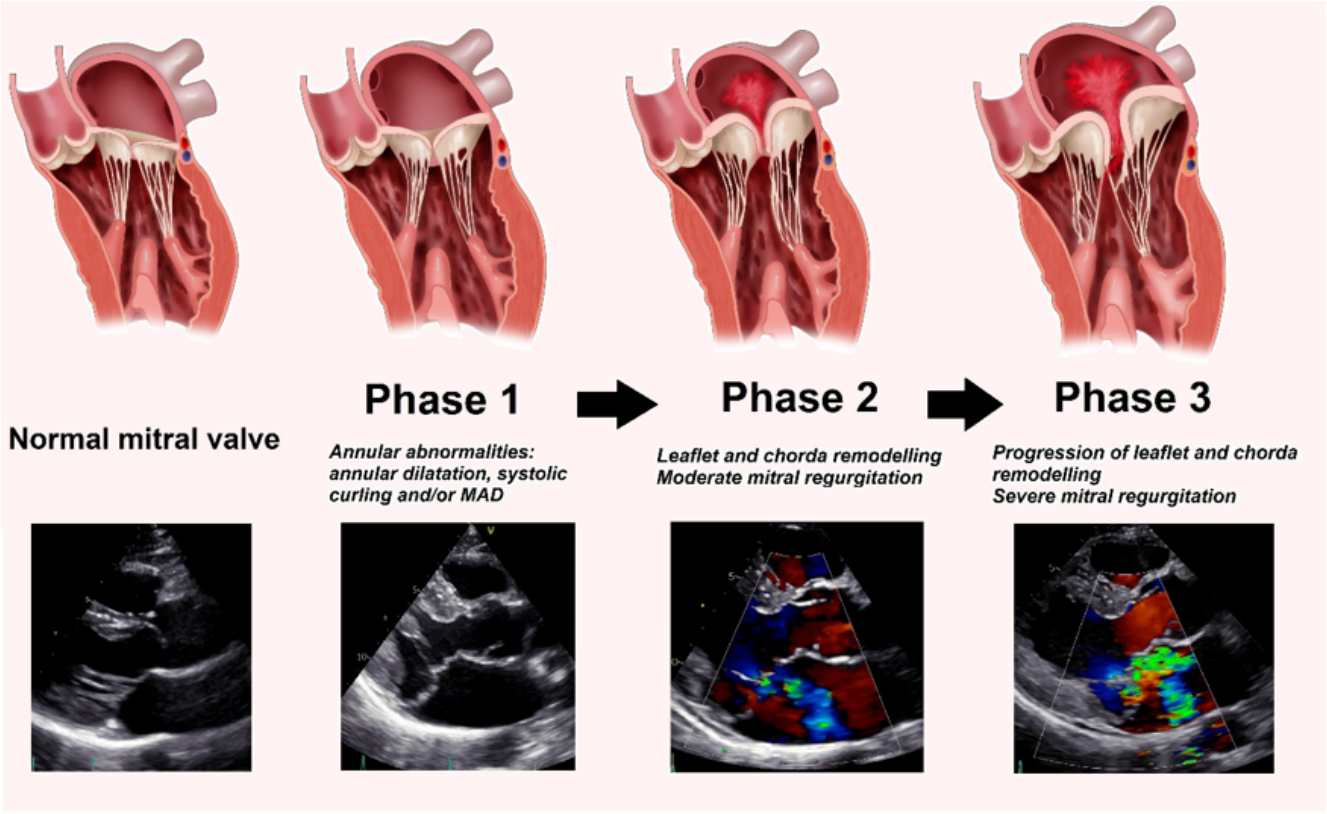
ORIGINAL ARTICLE

Cite this article as: Hiemstra YL, Tomsic A, Gripari P, van Wijngaarden AL, van der Pas SL, Palmen M *et al.* Evolution from mitral annular dysfunction to severe mitral regurgitation in Barlow's disease. Interact CardioVasc Thorac Surg 2021;32:506–14.

## Evolution from mitral annular dysfunction to severe mitral regurgitation in Barlow's disease

Yasmine L. Hiemstra [a], Anton Tomsic[b], Paola Gripari[c], Aniek L. van Wijngaarden[a], Stéphanie L. van der Pas[d,e], Meindert Palmen [b], Robert J.M. Klautz [b], Mauro Pepi[c], Jeroen J. Bax[a], Victoria Delgado [a] and Nina Ajmone Marsan[a,*]

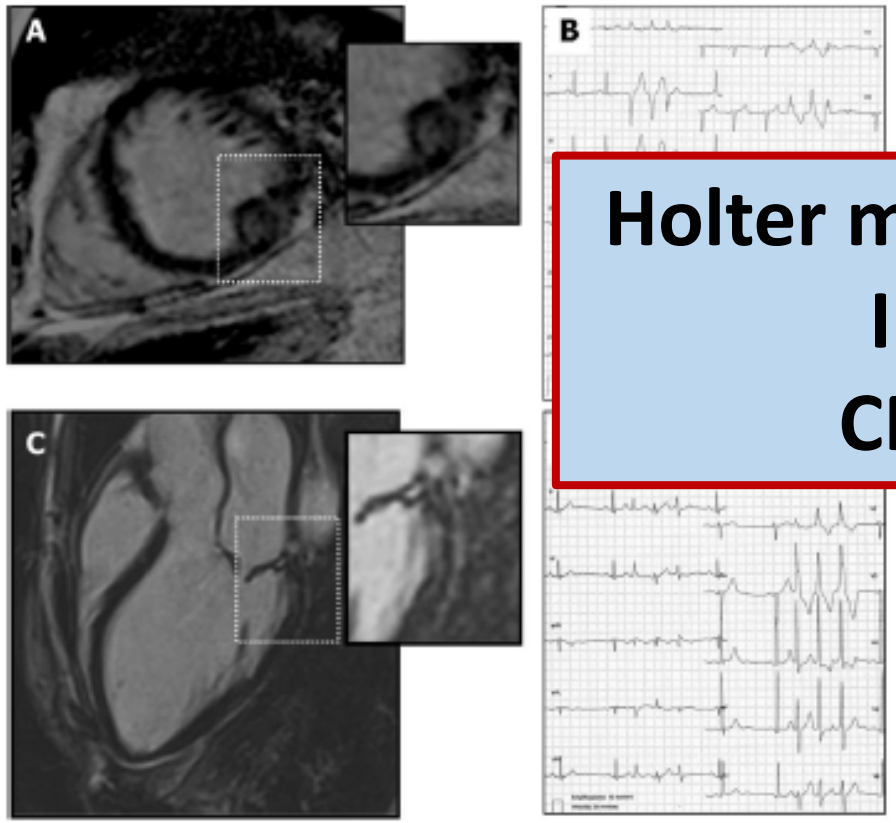


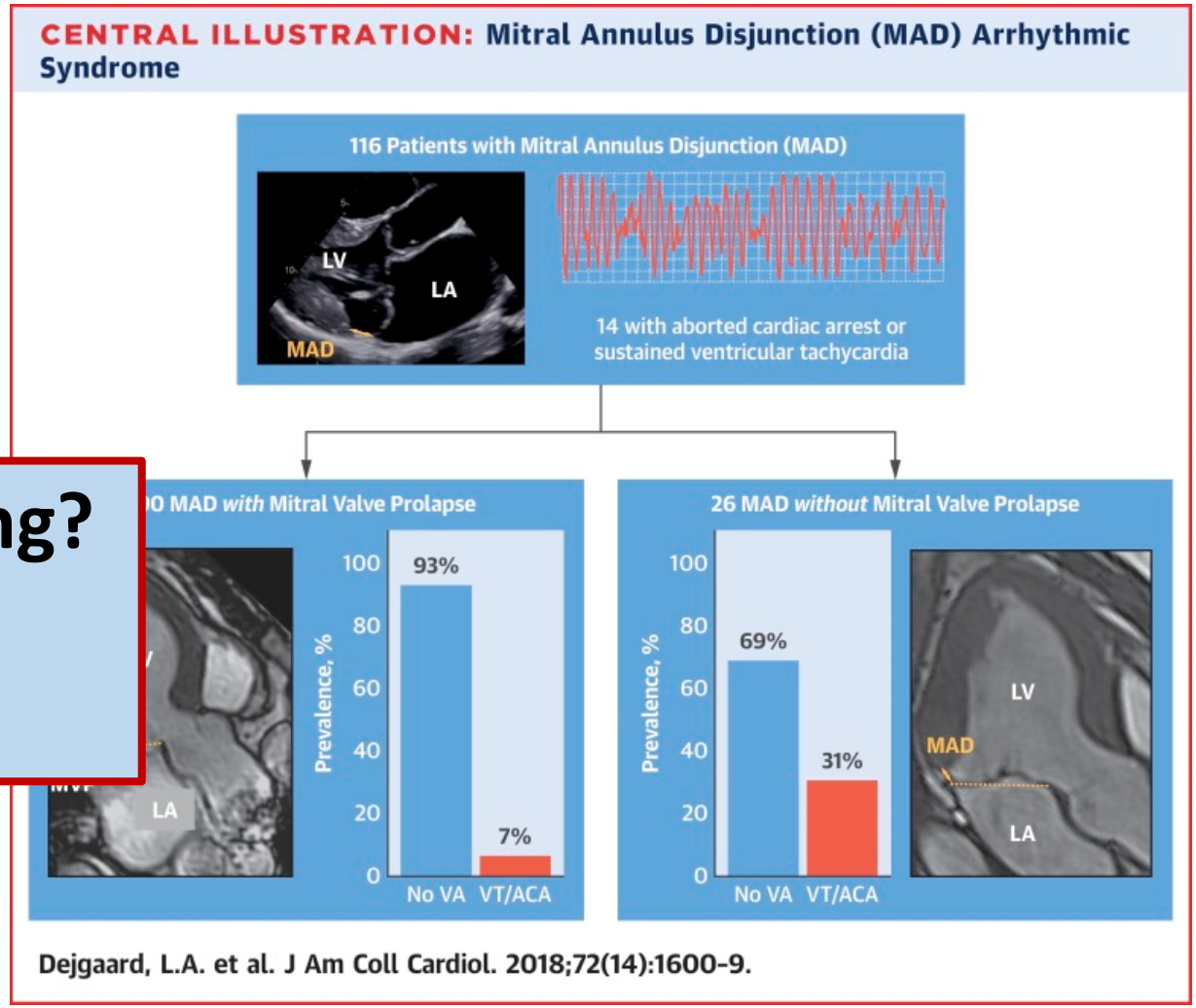

**Intrinsic annular abnormalities which need correction (annuloplasty) during surgery**

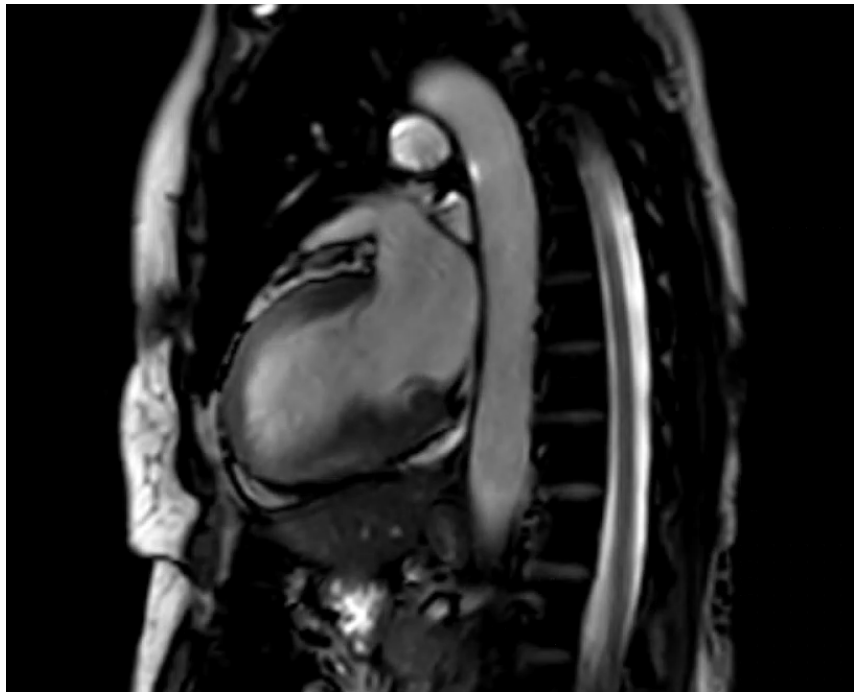
# Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death

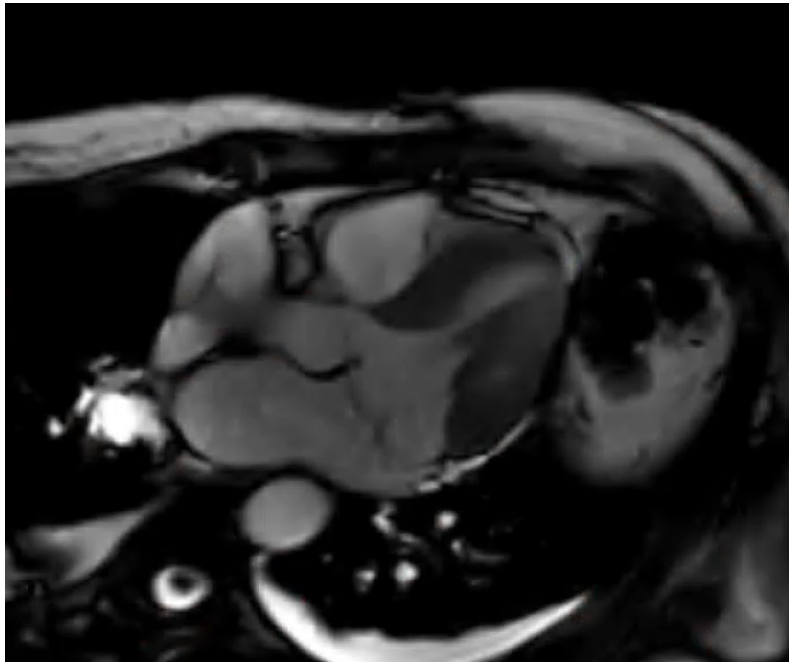
Cristina Basso, MD, PhD*; Martina Perazzolo Marra, MD, PhD*; Stefania Rizzo, MD, PhD; Manuel De Lazzari, MD; Benedetta Giorgi, MD; Alberto Cipriani, MD; Anna Chiara Frigo, MSc; Ilaria Rigato, MD, PhD; Federico Migliore, MD, PhD; Kalliopi Pilichou, PhD; Emanuele Bertaglia, MD; Luisa Cacciavillani, MD, PhD; Barbara Bauce, MD, PhD; Domenico Corrado, MD, PhD; Gaetano Thiene, MD; Sabino Iliceto, MD

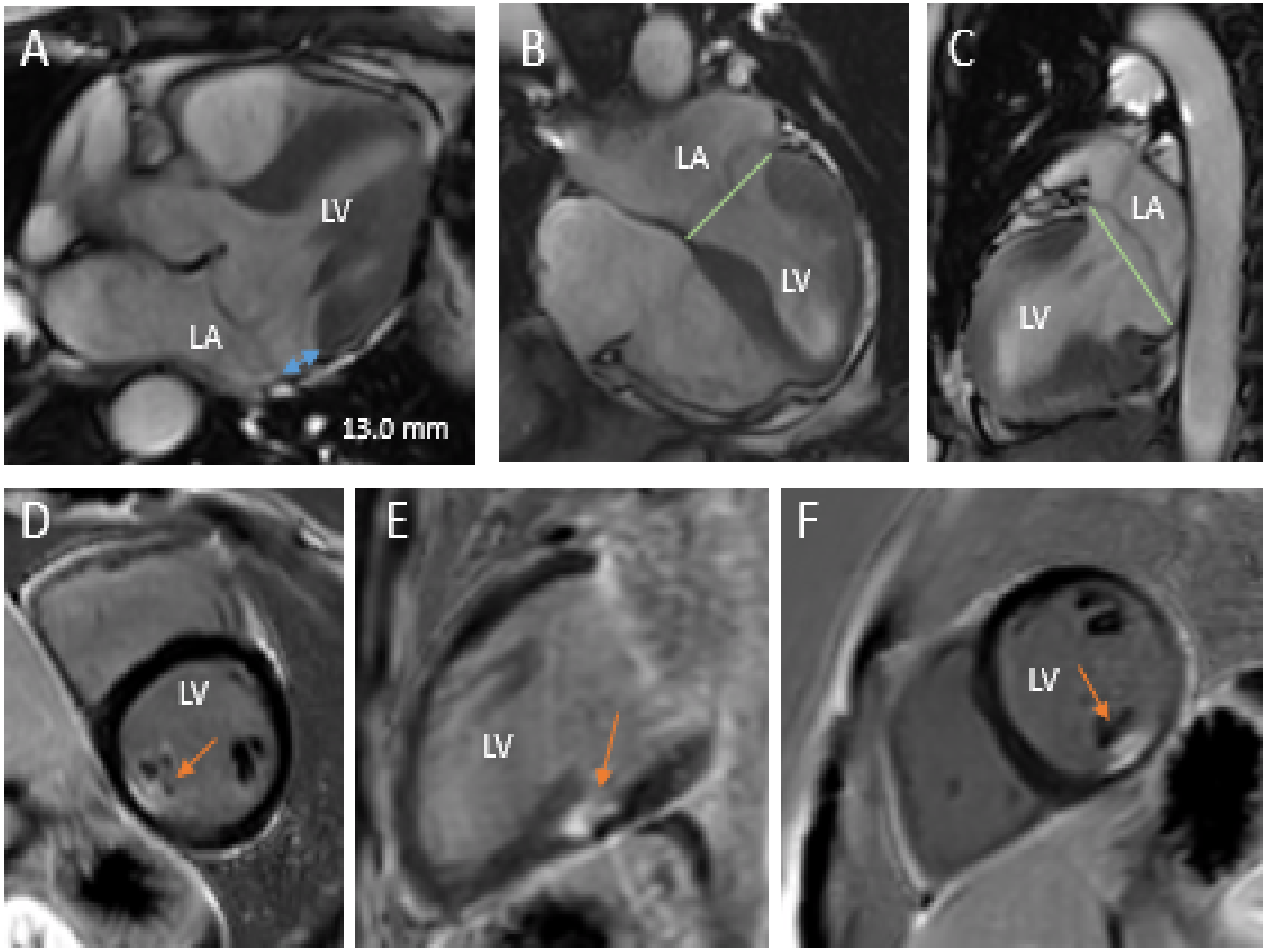



**Holter monitoring?**
**ILR?**
**CMR?**



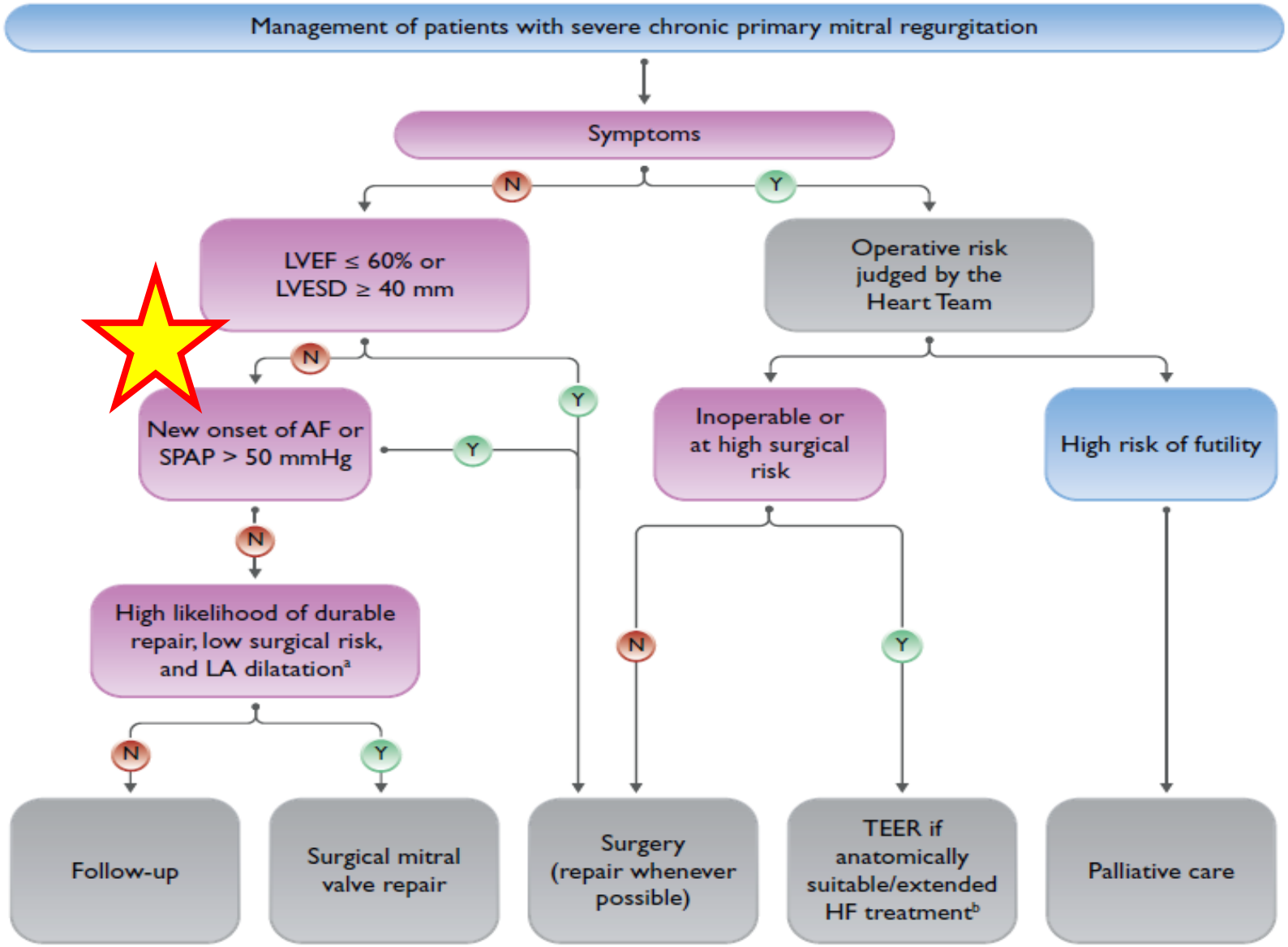





A
LV
LA
13.0 mm
B
LA
LV
C
LA
LV
D
LV
E
LV
F
LV

# Indication for surgery

**Secondary outcome determinants**




ESC/EACTS guidelilnes VHD 2021

# Indication for surgery: secondary outcome determinants

Circulation

ORIGINAL RESEARCH ARTICLE

## The MIDA-Q Mortality Risk Score: A Quantitative Prognostic Tool for the Mitral Valve Prolapse Spectrum

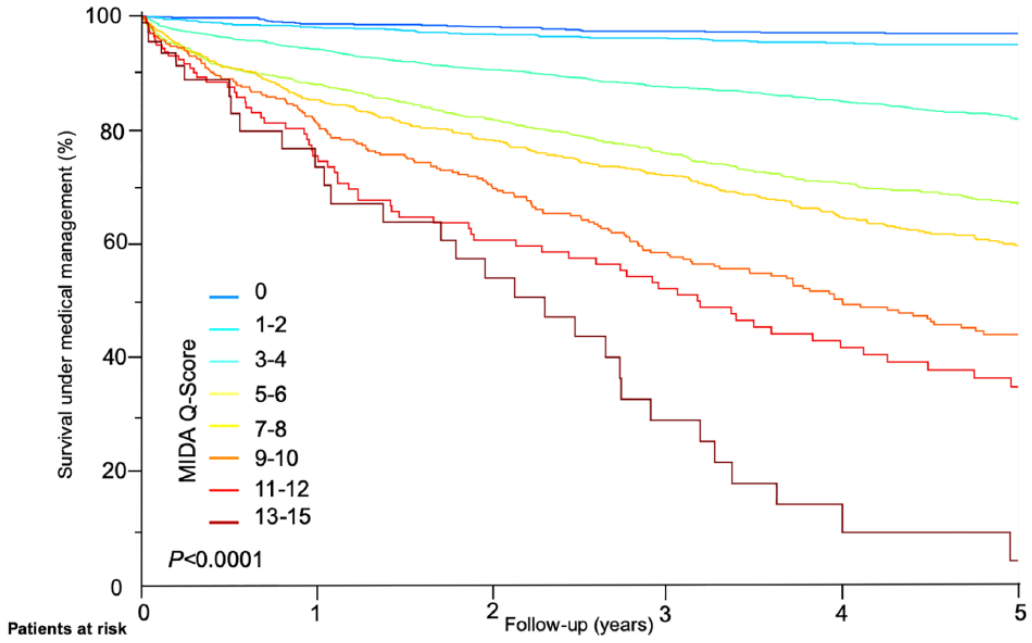
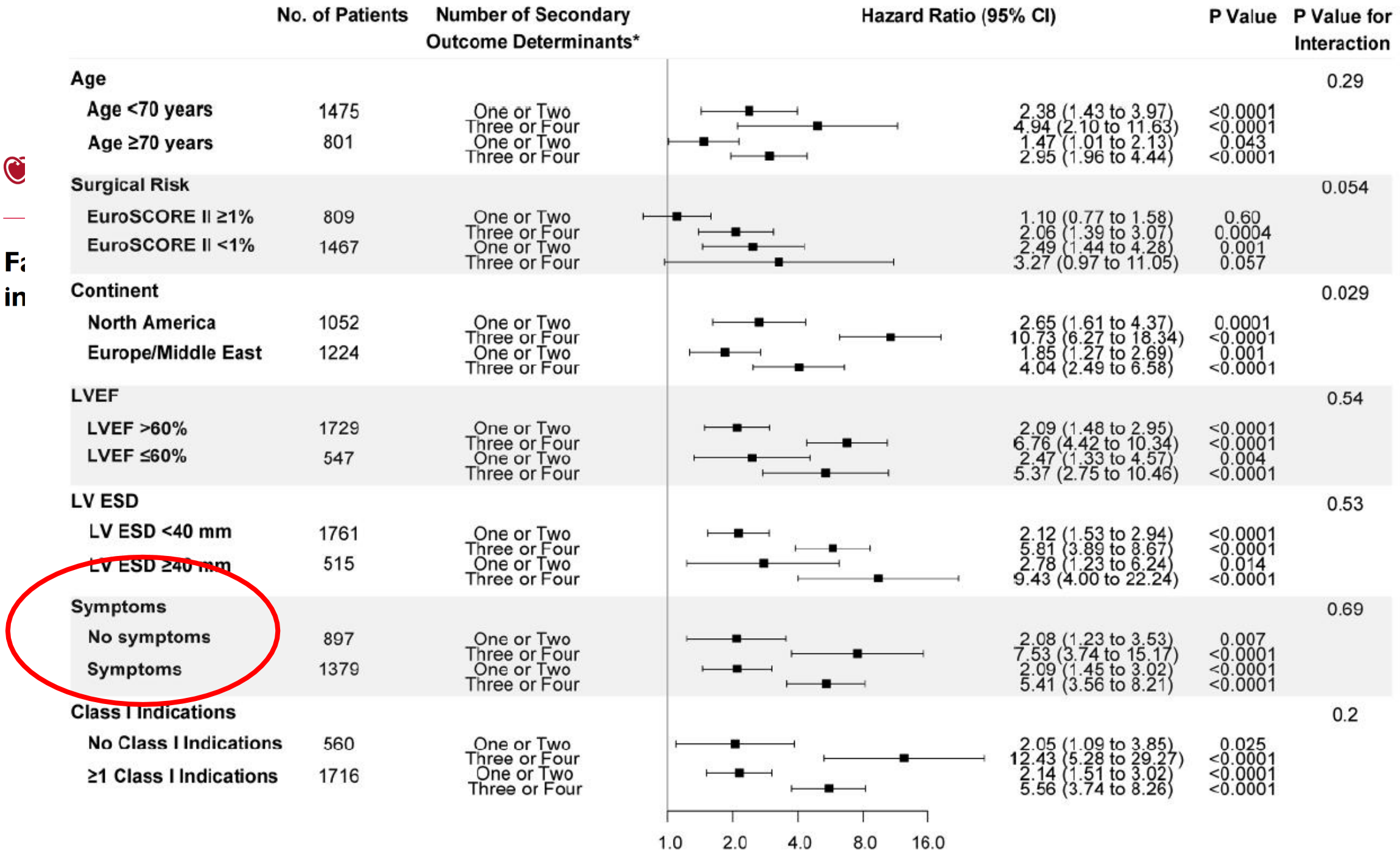



**Table 1. MIDA-Q Score Calculation**

| Characteristic | No. of points |
|---|---|
| Age ≥65 y | 3 |
| New York Heart Association ≥III | 3 |
| Atrial fibrillation | 1 |
| Left atrium volume index ≥60 mL/m² or left atrial diameter ≥55 mm | 1 |
| Systolic pulmonary artery pressure ≥50 mm Hg | 2 |
| Left ventricular end-systolic diameter ≥40 mm | 1 |
| Left ventricular ejection fraction <60% | 1 |
| Effective regurgitant orifice, mm² | |
| <20 | 0 |
| 20–40 | 1 |
| 40–60 | 2 |
| >60 | 3 |


No. of Patients
Number of Secondary Outcome Determinants*
Hazard Ratio (95% CI)
P Value
P Value for Interaction
Age
0.29
Age <70 years
1475
One or Two
2.38 (1.43 to 3.97)
<0.0001
Three or Four
4.94 (2.10 to 11.63)
<0.0001
Age ≥70 years
801
One or Two
1.47 (1.01 to 2.13)
0.043
Three or Four
2.95 (1.96 to 4.44)
<0.0001
Surgical Risk
0.054
EuroSCORE II ≥1%
809
One or Two
1.10 (0.77 to 1.58)
0.60
Three or Four
2.06 (1.39 to 3.07)
0.0004
EuroSCORE II <1%
1467
One or Two
2.49 (1.44 to 4.28)
0.001
Three or Four
3.27 (0.97 to 11.05)
0.057
Continent
0.029
North America
1052
One or Two
2.65 (1.61 to 4.37)
0.0001
Three or Four
10.73 (6.27 to 18.34)
<0.0001
Europe/Middle East
1224
One or Two
1.85 (1.27 to 2.69)
0.001
Three or Four
4.04 (2.49 to 6.58)
<0.0001
LVEF
0.54
LVEF >60%
1729
One or Two
2.09 (1.48 to 2.95)
<0.0001
Three or Four
6.76 (4.42 to 10.34)
<0.0001
LVEF ≤60%
547
One or Two
2.47 (1.33 to 4.57)
0.004
Three or Four
5.37 (2.75 to 10.46)
<0.0001
LV ESD
0.53
LV ESD <40 mm
1761
One or Two
2.12 (1.53 to 2.94)
<0.0001
Three or Four
5.81 (3.89 to 8.67)
<0.0001
LV ESD ≥40 mm
515
One or Two
2.78 (1.23 to 6.24)
0.014
Three or Four
9.43 (4.00 to 22.24)
<0.0001
Symptoms
0.69
No symptoms
897
One or Two
2.08 (1.23 to 3.53)
0.007
Three or Four
7.53 (3.74 to 15.17)
<0.0001
Symptoms
1379
One or Two
2.09 (1.45 to 3.02)
<0.0001
Three or Four
5.41 (3.56 to 8.21)
<0.0001
Class I Indications
0.2
No Class I Indications
560
One or Two
2.05 (1.09 to 3.85)
0.025
Three or Four
12.43 (5.28 to 29.27)
<0.0001
≥1 Class I Indications
1716
One or Two
2.14 (1.51 to 3.02)
<0.0001
Three or Four
5.56 (3.74 to 8.26)
<0.0001
1.0
2.0
4.0
8.0
16.0

# Indication for surgery: secondary outcome determinants

JACC: CARDIOVASCULAR IMAGING VOL. ■, NO. ■, 2022

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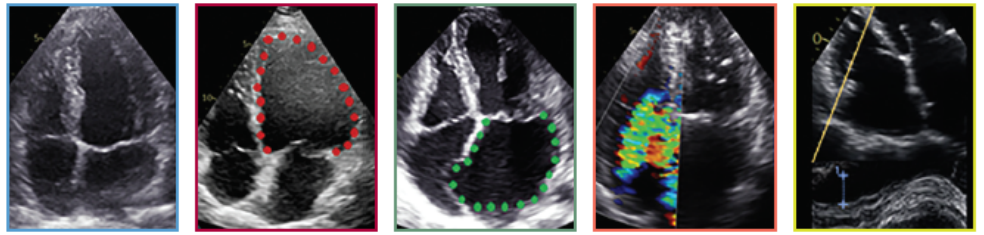
NEW RESEARCH PAPER

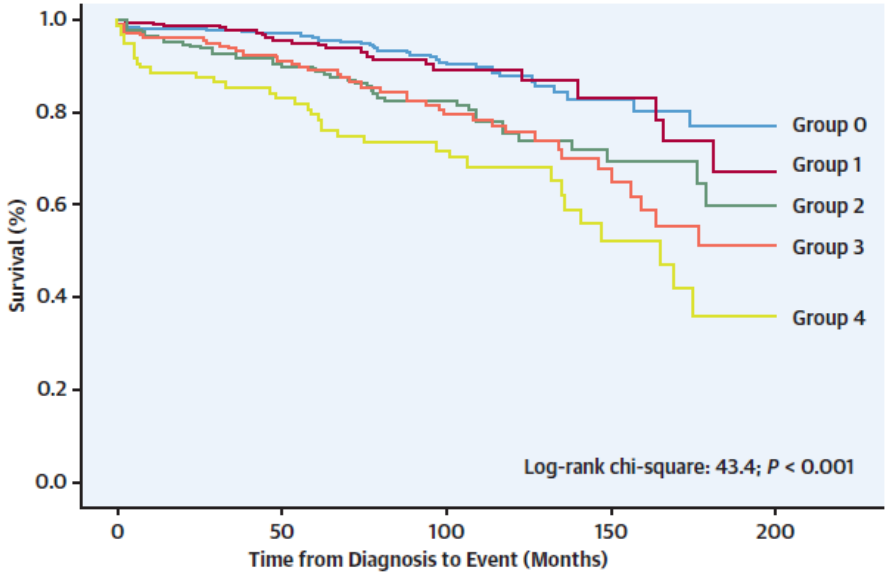
## Prognostic Impact of Extra–Mitral Valve Cardiac Involvement in Patients With Primary Mitral Regurgitation

**Classification of Primary Mitral Regurgitation Based on Extra-Mitral Valve Cardiac Involvement**



| Group 0 | Group 1 | Group 2 | Group 3 | Group 4 |
|---|---|---|---|---|
| No extra-mitral valve cardiac involvement | Left ventricular involvement | Left atrial involvement | Pulmonary vasculature or tricuspid involvement | Right ventricular involvement |
| N = 377 (34%) | N = 239 (22%) | N = 213 (19%) | N = 180 (16%) | N = 97 (9%) |

**Survival According to the Extent of Extra-Mitral Valve Cardiac Involvement**



# Indication for surgery: new tools!

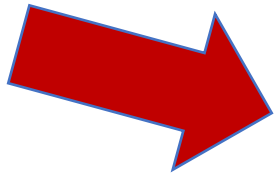
ESC European Society of Cardiology

European Heart Journal (2023) **44**, 28–40
https://doi.org/10.1093/eurheartj/ehac504

STATE OF THE ART REVIEW
*Valvular heart disease*

## Valvular heart disease: shifting the focus to the myocardium

**Nina Ajmone Marsan [1], Victoria Delgado [1,2], Dipan J. Shah[3], Patricia Pellikka[4], Jeroen J. Bax[1], Thomas Treibel[5], and João L. Cavalcante[6]**



| | Myocardial imaging biomarker | |
|---|---|---|
| | **Echocardiography** | **CMR** |
| **Primary mitral regurgitation** | | |
| Standard | • LVEDD<br>• LVEF<br>• LA diameter<br>• LA volume<br>• PAPs<br>• RV dimension and function (TAPSE, FAC) | • LVEDD<br>• LV volumes and EF<br>• LV hypertrophy/mass<br>• RV volumes and function |
| New | • LV GLS<br>• LV mechanical dispersion<br>• LA reservoir strain<br>• 3D LV volumes | • LGE (replacement fibrosis)<br>  • Extent<br>  • Location<br>• ECV (interstitial fibrosis)<br>• GLS |

# Indication for surgery: new tools!

JACC: CARDIOVASCULAR IMAGING VOL. 13, NO. 2, 2020

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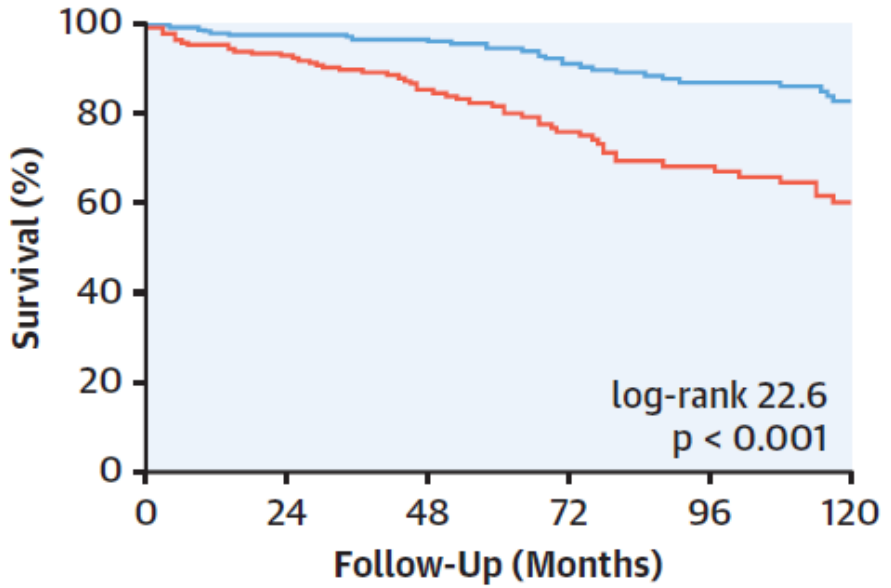
SPECIAL ISSUE: FOCUS ON LV STRAIN FOR PREDICTING HARD OUTCOMES

ORIGINAL RESEARCH

## Prognostic Value of Global Longitudinal Strain and Etiology After Surgery for Primary Mitral Regurgitation

Yasmine L. Hiemstra, MD,[a] Anton Tomsic, MD,[b] Suzanne E. van Wijngaarden, MD,[a] Meindert Palmen, MD, PhD,[b] Robert J.M. Klautz, MD, PhD,[b] Jeroen J. Bax, MD, PhD,[a] Victoria Delgado, MD, PhD,[a] Nina Ajmone Marsan, MD, PhD[a]




| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| LV GLS < -20.6% | 249 | 223 | 192 | 150 | 109 | 69 |
| LV GLS ≥ -20.6% | 229 | 182 | 124 | 89 | 59 | 37 |

LV-GLS < -20.6% LV-GLS ≥ -20.6%

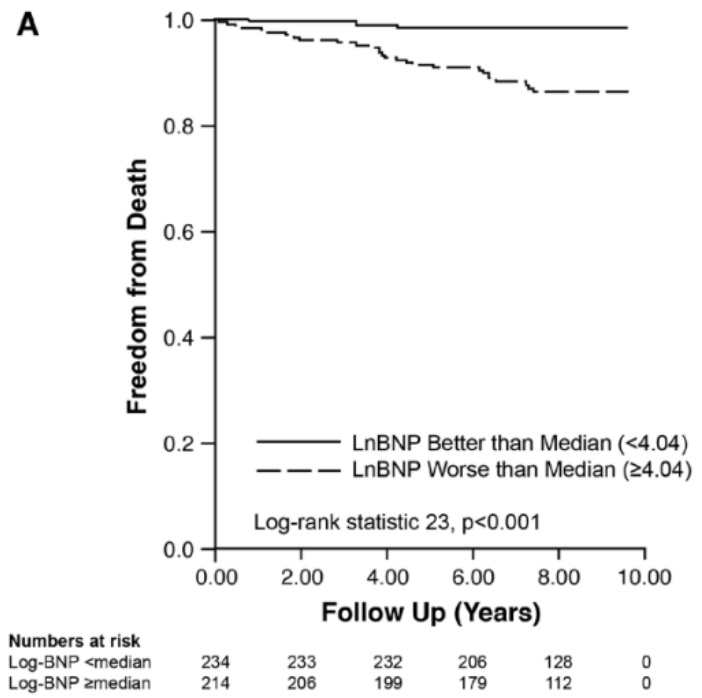
**Similar prognosis between Barlow and FED**

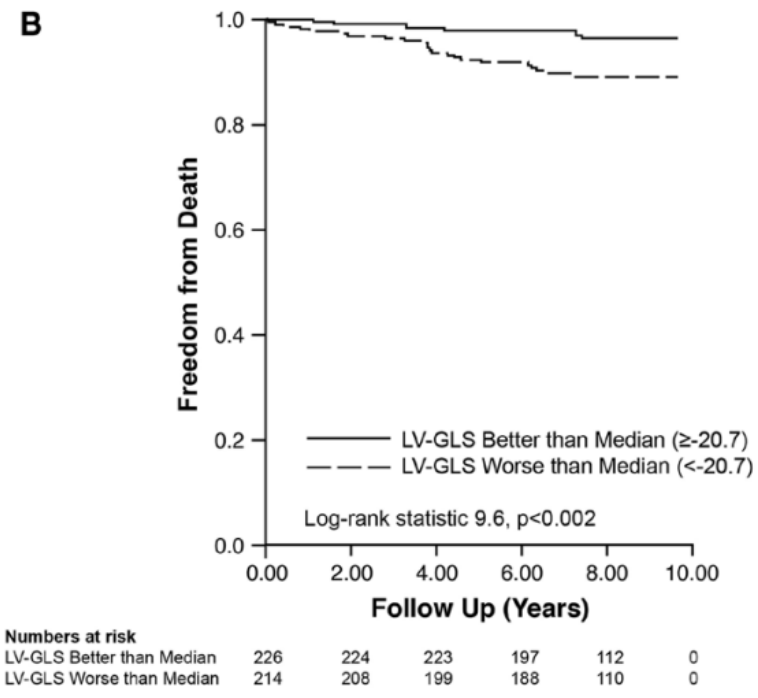
# Indication for surgery: new tools!

Valvular Heart Disease

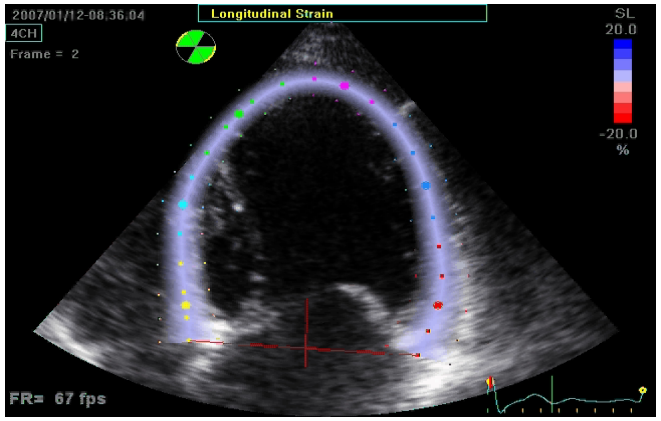
## Synergistic Utility of Brain Natriuretic Peptide and Left Ventricular Global Longitudinal Strain in Asymptomatic Patients With Significant Primary Mitral Regurgitation and Preserved Systolic Function Undergoing Mitral Valve Surgery

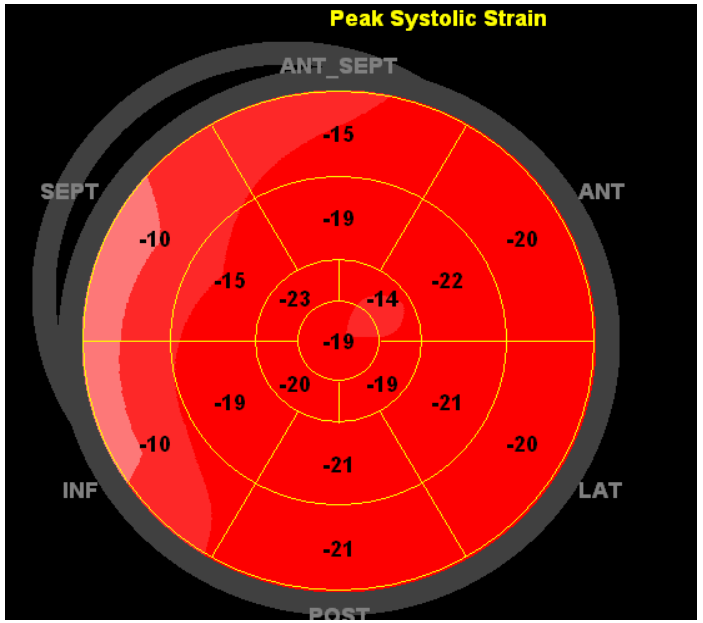
Alaa Alashi, MD; Amgad Mentias, MD; Krishna Patel, MD; A. Marc Gillinov, MD; Joseph F. Sabik, MD; Zoran B. Popović, MD, PhD; Tomislav Mihaljevic, MD; Rakesh M. Suri, MD, DPhil; L. Leonardo Rodriguez, MD; Lars G. Svensson, MD, Brian P. Griffin, MD; Milind Y. Desai, MD

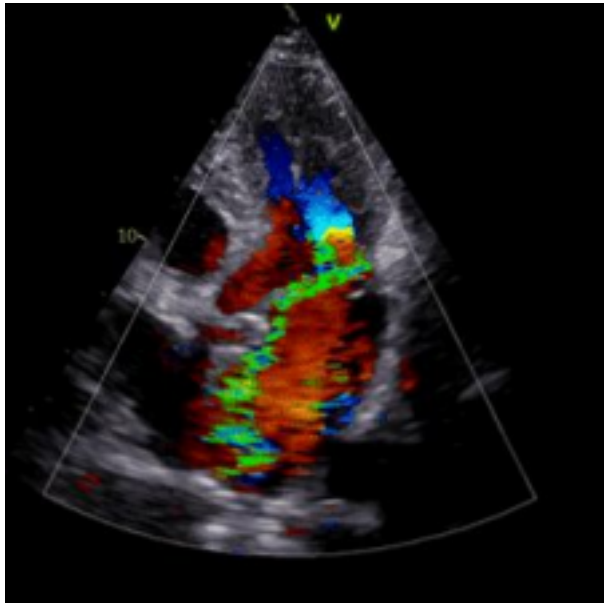


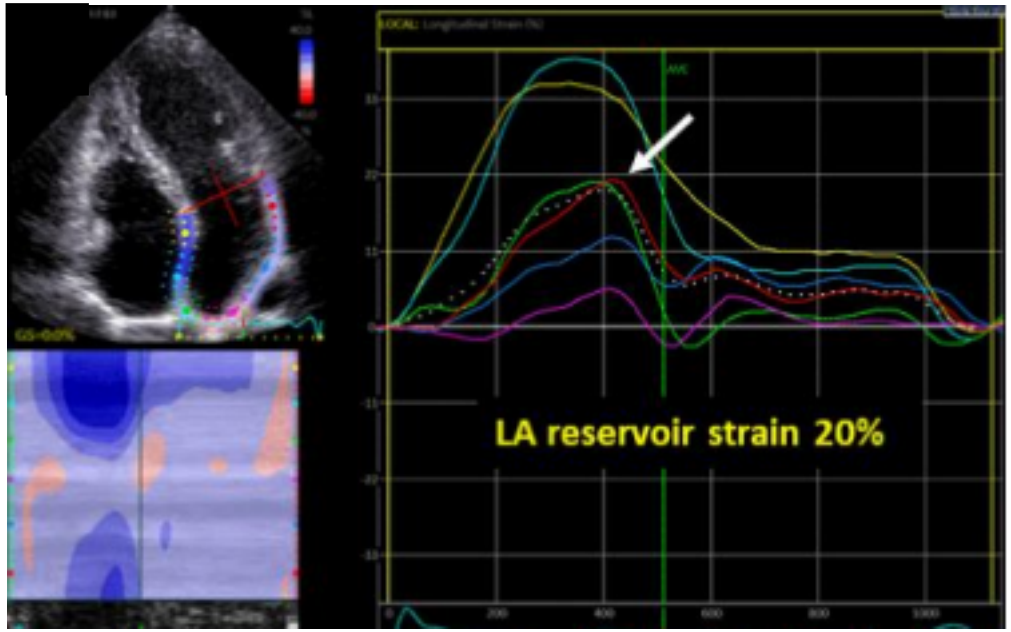
# Indication for surgery: new tools!



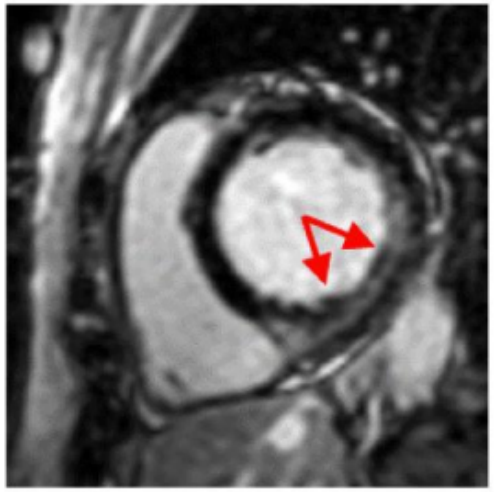

**Severe MR**
**GLS : -17.7%**



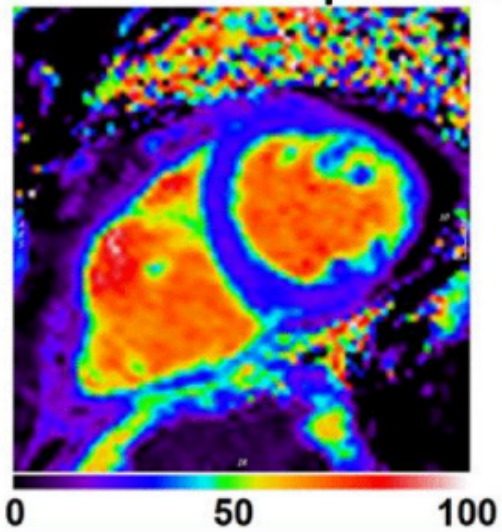
# Indication for surgery: new tools!

## Fibrosis in Primary MR

**LGE**



**ECV Map**




### Replacement Fibrosis

- More common in MVP than non-MVP
- Common located in segments adjacent to the posteromedial papillary muscle
- Growing evidence of association with arrhythmic risk

### Diffuse Interstitial Fibrosis

- Similar in both MVP and non-MVP
- Associated with severity of MR
- Emerging evidence of association with:
  - Exercise capacity
  - LV function
  - Need for mitral valve intervention


Edwards NC, Moody WE, Yuan M, Weale P, Neal D, Townend JN, *et al.* Quantification of left ventricular interstitial fibrosis in asymptomatic chronic primary degenerative mitral regurgitation. *Circ Cardiovasc Imaging* 2014;**7**:946–953.

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# Conclusions

- **Current management of patients with primary MR aim at optimizing long-term outcome by timely intervention and ensuring long-term results.**
- 
- **Prevention of irreversible damage of LV, LA, or pulmonary vasculature is crucial to reduce the risk of heart failure, arrhythmias, and death**

- **Accurate phenotyping and staging can help in this difficult assessment and decision-making**