Clinical Triggers in Mitral Regurgitation: The Case for Early Repair

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Hospital de Santa Cruz, Carnaxide, Portugal
Conflicts of Interest: None
Consequences of Mitral Regurgitation

- Normal EF in MR is >65%
- Early Stage: Contractile Dysfunction Is Reversible
- RV Dysfunction: impacts prognosis
- Sympathetic Activation

Circulation. 2013;127:1567-1568
Left ventricular dysfunction after mitral valve repair—the fallacy of “normal” preoperative myocardial function

- N=1705
- MR and preserved LV function (EF>60%) undergoing mitral valve repair.
- 1 in 5 patients developed early LV dysfunction (EF<50%).
- Only 1 in 3 patients with postoperative LV impairment experience recovery of EF to preoperative levels at 5 year

What Are We Talking About?

• No RCT

• Current “practice guidelines” are based on inferences drawn from comparison of **observational cohorts**

• **Degenerative** Mitral Regurgitation (MV Prolapse occurs in 2% population)
What Is The Etiology?

- Results Pertain to Degenerative MR With Type II MR
- Rheumatic Mitral Regurgitation Associated With Less Predictable Results After Repair
- TTE, TEE, 3D Echo Allow Diagnosis of Unfavorable Features for Repair
  - Thickened Leaflets
  - Restrictive Leaflet Motion
  - Commissural Fusion
  - Calcification

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Diagnosis of Unfavorable Features
# Quantification is Key

## Criteria for Defining Severe Mitral Regurgitation

### Integrative approach

- Left atrial size, LV size, EF, PAP
- Leaflet morphology/motion,
- Mitral filling pattern,
- Pulmonary venous flow patterns

<table>
<thead>
<tr>
<th>Qualitative</th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve morphology</td>
<td>Flail leaflet/ruptured papillary muscle/large coaptation defect</td>
</tr>
<tr>
<td>Colour flow regurgitant jet</td>
<td>Very large central jet or eccentric jet adhering, swirling, and reaching the posterior wall of the LA</td>
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<td>CW signal of regurgitant jet</td>
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<td>Other</td>
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<th>Semiquantitative</th>
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<tbody>
<tr>
<td>Vena contracta width (mm)</td>
<td>≥7 (&gt;8 for biplane)</td>
</tr>
<tr>
<td>Upstream vein flow</td>
<td>Systolic pulmonary vein flow reversal</td>
</tr>
<tr>
<td>Inflow</td>
<td>E-wave dominant ≥1.5 m/s</td>
</tr>
<tr>
<td>Other</td>
<td>TVI mitral/TVI aortic &gt;1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quantitative</th>
<th>Primary</th>
<th>Secondary h</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA (mm²)</td>
<td>≥40</td>
<td>≥20</td>
</tr>
<tr>
<td>Regurgitant volume (mL/beat)</td>
<td>≥60</td>
<td>≥30</td>
</tr>
<tr>
<td>+ enlargement of cardiac chambers/vessels</td>
<td>LV, LA</td>
<td></td>
</tr>
</tbody>
</table>
Predictors of Mitral Valve Repair

- **Simple Lesions** = High Probability of Repair
  - Posterior Leaflet Prolapse
  - Annular Dilatation

- **Complex Lesions** = Reparability Depending on Experience
  - Anterior Prolapse/Flail
  - Bileaflet Proplapse/Flail

- **Higher Risk Unsuccessful Repair**
  - Prolapse + Extensive Annular Calcification
  - Prolapse + Hypoplasia Opposite Leaflet
Early Surgery Versus Conventional Treatment for Asymptomatic Severe Mitral Regurgitation

N = 610 consecutive asymptomatic patients; prospective registry
207 propensity score–matched pairs

Figure 3
Comparison of Endpoints in a Propensity Score–Matched Cohort

Association Between Early Surgical Intervention vs Watchful Waiting and Outcomes for Mitral Regurgitation Due to Flail Mitral Valve Leaflets

- N=1021 Flail Leaflets
- Without Class I triggers
- 5-year reduction in mortality of 52.6%
- Heart failure risk was also lower with early surgery

Early surgery is reasonable if surgical risk is low and the likelihood of successful valve repair is high, which is often the case for patients with a flail leaflet.

However if the surgical risk is high or the probability of repair is low it remains uncertain whether early surgical intervention is appropriate in the asymptomatic patient with severe MR when LV size and systolic function are normal.
Is there an outcome penalty linked to guideline-based indications for valvular surgery? Early and long-term analysis of patients with organic mitral regurgitation

N= 1512 patients
Mitral prolapse in 89%, Valve repair in 88%

Triggers for class I (symptoms, EF <60%, end-systolic diameter >40 mm) were independently associated with doubling of long-term death/heart failure risk

Triggers for class II (atrial fibrillation, pulmonary hypertension) were associated with a 40% increase in risk.

Enriquez Sarano M et al; J Thorac Cardiovasc Surg 2015;150:50-8
Superior survival with surgery for early- versus late-stage heart disease: Cause and effect or methodologic quirk?

• Early Stages may represent more benign form of disease
• Early disease pts are super selected pts likely to do well after surgery
• Patients treated at an advanced phase of disease may have a more rapidly progressing form of disease and generally do worse.
• Lead time bias: not necessarily the early surgical intervention that resulted in the good long-term survival, but rather the expected survival for the stage of disease (regardless of early intervention).
• Valve repair linear failure rate of up to 1% to 5% per year, depending on the etiology.
• Patients who do not have early surgery may still undergo surgery before the disease progresses to an advanced stage.
• RCT required

Anyanwu AC; JThorac Cardiovasc Surg 2016;152:401-5
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>IIa</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve repair should be the preferred technique when the results are expected to be durable.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery is indicated in asymptomatic patients with LVEF &gt;30%.</td>
<td>121,131,132</td>
<td></td>
</tr>
<tr>
<td>Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD &gt;45 mm and/or LVEF ≤60%).</td>
<td>122,131</td>
<td></td>
</tr>
<tr>
<td>Surgery should be considered in asymptomatic patients with preserved LV function (LVESD &lt;45 mm and LVEF &gt;60%) and atrial fibrillation secondary to mitral regurgitation or pulmonary hypertension (systolic pulmonary pressure at rest &gt;50 mmHg).</td>
<td>123,124</td>
<td></td>
</tr>
</tbody>
</table>

Surgery should be considered in asymptomatic patients with preserved LVEF (>60%) and LVESD 40–44 mm when a durable repair is likely, surgical risk is low, the repair is performed in a heart valve centre and at least one of the following findings is present:
- flail leaflet or
- presence of significant LA dilatation (volume index ≥60 mL/m² BSA) in sinus rhythm.
Management of severe chronic primary mitral regurgitation

Symptoms

No

LVEF ≤60% or LVESD ≥45 mm

No

New onset of AF or SPAP >50 mmHg

No

High likelihood of durable repair, low surgical risk, and presence of risk factors

No

Follow-up

Yes

Yes

LVEF >30%

No

Refractory to medical therapy

No

Medical therapy

Yes

Durable valve repair is likely and low comorbidity

No

Extended HF treatment/ percutaneous edge-to-edge repair

Yes

Surgery (repair whenever possible)
Mitral valve 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 greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence (101,106-112).

Mitral valve surgery is reasonable for asymptomatic patients with chronic severe primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) with a progressive increase in LV size or decrease in ejection fraction (EF) on serial imaging studies (112-115). (Figure 2)

NEW: Patients with severe MR who reach an EF ≤60% or LVESD ≥40 have already developed LV systolic dysfunction, so operating before reaching these parameters, particularly with a progressive increase in LV size or decrease in EF on serial studies, is reasonable.
Decision-Making: Requirements

**Prophylactic Surgery**

- Highly predictable (>90%), durable repair (<5% residual mitral regurgitation) with very low operative mortality (<1%) and morbidity

**Watchful Waiting**

- Regular and thorough echocardiographic and clinical surveillance and prompt immediate surgical referral once indicated

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## Decision-Making: Prophylactic Surgery Degenerative MR

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
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<tbody>
<tr>
<td>Prevents LV Dysfunction</td>
<td>Small risk of operative mortality morbidity</td>
</tr>
<tr>
<td>Less Cardiac Events</td>
<td>Risk of unwanted replacement with risk of prosthesis related events</td>
</tr>
<tr>
<td>Possible Survival Benefit</td>
<td>Risk of recurrent mitral regurgitation and associated risk of cardiac events</td>
</tr>
</tbody>
</table>
## Decision-Making: Watchful Waiting Degenerative MR

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>50% will avoid surgery in the midterm</td>
<td>Risk of missing surgical indications and subsequent higher cardiac events</td>
</tr>
<tr>
<td></td>
<td>Risk of irreversible LV dysfunction</td>
</tr>
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<td></td>
<td>May compromise long-term survival</td>
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</table>
New Tools for Decision Making

Association of B-Type Natriuretic Peptide With Survival in Patients With Degenerative Mitral Regurgitation

Marie-Amick Clavel, DVM, PhD, Christophe Tribouilloy, MD, Jean-Louis Vanoverschelde, MD, Rodolfo Pizarro, MD, Rakesh M. Suri, MD, DPhi, Catherine Szymanski, MD, Shiam Lazam, MD, Pablo Oberti, MD, Laurens F. Tops, Victoria Delgado, Nina Ajmone Marsan, and Jeroen J. Bax

Importance of Exercise Capacity in Predicting Outcomes and Determining Optimal Timing of Surgery in Significant Primary Mitral Regurgitation

Peyman Najj, MD; Brian P. Griffin, MD; Tyler Barr; Fadi Asfahan, MD; A. Marc Gillinov, MD; Richard A. Grimm, MD; L. Leonardo Rodriguez, MD; Tomislav Mihaljevic, MD; William J. Stewart, MD; Milind Y. Desai, MD

Strain Echocardiography and Functional Capacity in Asymptomatic Primary Mitral Regurgitation With Preserved Ejection Fraction

Amgad Mentias, MD, Peyman Najj, MD, A. Marc Gillinov, MD, L. Leonardo Rodriguez, MD, Grant Reed, MD, Tomislav Mihaljevic, MD, Rakesh M. Suri, MD, DPhi, Joseph F. Sabik, MD, Lars G. Svensson, MD, PhD, Richard A. Grimm, DO, Brian P. Griffin, MD, Milind Y. Desai, MD
Importance of Exercise Capacity in Predicting Outcomes and Determining Optimal Timing of Surgery in Significant Primary Mitral Regurgitation

Naji PJ et al Am Heart Assoc. 2014;3:e001010 doi: 10.1161

N= 576
Grade ≥3 myxomatous MR
Treadmill Exercise Echo

<table>
<thead>
<tr>
<th>Age</th>
<th>1.07 (1.03 to 1.12)</th>
<th>&lt;0.01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of age- and gender-predicted METs achieved</td>
<td>0.82 (0.71 to 0.94)</td>
<td>0.005</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.94 (0.89 to 0.99)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meier survival curves of the entire study population separated on the basis of having achieved >100% of age- and gender-predicted metabolic equivalents (METs).

Figure 2. Kaplan-Meier survival curves of the subgroup that achieved >100% of age- and gender-predicted metabolic equivalents (METs), separated on the basis of whether or not surgery was delayed >1 year.
Variations in rates of mitral valve repair for degenerative disease among 46 heart centres in the UK

Anelechi C Anyanwu,1 Benjamin Bridgewater,2 David H Adams1

The lottery of mitral valve repair surgery

Treatment approach at the contributing hospitals (n=5,163)

Variations in rates of mitral valve repair for degenerative disease among 46 heart centres in the UK

Anyanwu A C et al. Heart 2010
Mitral valve repair rates correlate with surgeon and institutional experience

Damien J. LaPar, MD, MSc, ‡ Gorav Ailawadi, MD, ‡ James M. Isbell, MD, MSCI, ‡ Ivan K. Crosby, MD, ‡ John A. Kern, MD, ‡ Jeffrey B. Rich, MD, ‡ Alan M. Speir, MD, ‡ and Irving L. Kron, MD, ‡ Investigators for the Virginia Cardiac Surgery Quality Initiative

• 4194 patients
• Median=13 operations/y/surgeon
• MV repair rate was 60% (0-90%)
• Likelihood for MV repair correlated with an operative volume of 20 procedures/y
# Table 3  Example targets for surgical outcomes in repair of mitral valve prolapse

<table>
<thead>
<tr>
<th></th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>$&lt;1%^{25,29}$</td>
</tr>
<tr>
<td>Major complication</td>
<td>$&lt;2%^{29}$</td>
</tr>
<tr>
<td>Repair rate for when judged ‘likely’ repairable by an MDT</td>
<td>$&gt;90%$ (95% for P2 prolapse)</td>
</tr>
<tr>
<td>Significant residual mitral regurgitation</td>
<td>$\leq 5%$ at 5 years$^{25}$</td>
</tr>
<tr>
<td>Reoperation rate</td>
<td></td>
</tr>
<tr>
<td>Posterior leaflet repair</td>
<td>$&lt;1%$ per year$^{30}$</td>
</tr>
<tr>
<td>Anterior leaflet repair</td>
<td>$&lt;2%$ per year$^{30,31}$</td>
</tr>
</tbody>
</table>
The Case for Early Repair

- Young Low Risk Patients
- Degenerative Mitral Regurgitation
- Isolated mitral prolapse of P2
- Mortality reduction
- Left Ventricular Function Less Affected
- Success rates in mitral valve repairs > 95%
- New Prognostic Factors

Clinical Triggers in Mitral Regurgitation:
The Case for Early Repair

Take Home Messages (1)

• Once left ventricular contractility is impaired, outcomes after MV repair are poor, with persistent symptoms of ventricular dysfunction

• **Quantitative evaluation** of mitral regurgitation requires expertise and awareness of pitfalls

• **Assessment of Valve Reparability** is Key

• Repair rates are related with **volume** of mitral surgical procedures by institution and by surgeon

• **Decision making** depends on repair rates, mortality & morbidity rates

• Strategy must be individualized and supported by the *Heart Valve Team*
Take Home Messages

• Optimal timing of surgery in primary MR remains challenging
• No Randomized Trials
• Better tools to define the optimal time for surgery in degenerative MR are desirable
  • BNP, Exercice Echo and Longitudinal Strain
• Regular follow-up is crucial in patients who have not reached the currently recommended indications for surgery.
Clinical Triggers in Mitral Regurgitation:
The Case for Early Repair

Santa Cruz Hospital

Mucho Obrigado
Late Outcomes of Mitral Valve Repair for Mitral Regurgitation Due to Degenerative Disease

Tirone E. David, MD; Susan Armstrong, MSc; Brian W. McCrindle MD; Cedric Manlhiot, BSc

Development of symptoms or minimal reduction in left ventricular ejection fraction associated with increased risk of cardiac mortality

6% cumulative risk of reoperation on the mitral valve at 20 years but 1/3 developed recurrent moderate or severe mitral regurgitation.

Advancing age, isolated prolapse of the anterior leaflet, and advanced myxomatous degeneration of the mitral valve were associated with higher risk of recurrent mitral regurgitation

degree of myxomatous changes in the MV, lack of mitral annuloplasty, and duration of cardiopulmonary bypass were associated with increased risk of recurrent MR. At 20 years, the freedom from recurrent severe MR was 90.7%, and the freedom from moderate or severe MR was 69.2%.

Conclusions—MV repair for degenerative MR restored life span to normal except in patients with symptoms at rest and impaired left ventricular function. Advanced age and complex mitral valve pathologies increased the risk of late recurrent MR. (Circulation. 2013;127:1485-1492.)
Caveats

- Rheumatic MR, Advanced Barlow Disease: Repair Likelihood Lower
- Is There an Increased Risk if Timing According to Guidelines?
- There is No Zero Risk Surgery Even in Low Risk Patients
- Older Age and Co-Morbidities
- Studies Showing Mortality Reduction Are Observational
- Volume Outcome Relationship
Echocardiographic Assessment

• Assess Severity
• Assess Feasibility of Repair
• TOE is recommended, particularly in the presence of suboptimal image quality
• 3D echocardiography provides additional information for selecting the appropriate repair strategy
• Global longitudinal strain
Repetition and experience include not only repeating steps in operations but also repeating preoperative assessment and choosing the proper treatment strategy.

Rates of mitral repair vs replacement vary widely and are clearly related to overall volume of mitral valve surgical procedures by institution and by surgeon.
Discordance Between Echocardiography and MRI in the Assessment of Mitral Regurgitation Severity

A Prospective Multicenter Trial

Seth Uretsky, MD, Linda Gillam, MD, MPH, Roberto Lang, MD, Farooq A. Chaudhry, MD

• Agreement between MRI and echo estimates of MR severity was modest

Is Left Ventricular End-Systolic Dimension a Reliable Predictor of Postoperative Left Ventricular Dysfunction in Patients with Mitral Regurgitation Secondary to Mitral Valve Prolapse?

**Figure 1** Recommended method for measuring LV internal dimensions. These measurements should be performed in the parasternal long-axis view, perpendicular to the long axis of the left ventricle at the tips of the mitral valve leaflets. Ao, Aorta; D, Diameter; LA, Left Atrium; LV, Left Ventricle; RV, Right Ventricle.
### Estratificação de risco no doente assintomático: Parâmetros do ECO de ESFORÇO

#### Table 1. Exercise echocardiographic parameters useful for risk stratification

<table>
<thead>
<tr>
<th>Parameters</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary mitral regurgitation</td>
<td></td>
</tr>
<tr>
<td>Exercise-induced increase in ERO area</td>
<td>$&gt; +10, \text{mm}^2$</td>
</tr>
<tr>
<td>Exercise-induced increase in regurgitant volume</td>
<td>$&gt; +15, \text{ml}$</td>
</tr>
<tr>
<td>Exercise systolic pulmonary arterial pressure</td>
<td>$&gt;60, \text{mmHg}$</td>
</tr>
<tr>
<td>LV contractile reserve</td>
<td></td>
</tr>
<tr>
<td>Exercise-induced changes in LV ejection fraction</td>
<td>$&gt; +4%$</td>
</tr>
<tr>
<td>Exercise-induced changes in LV global long. strain</td>
<td>$&gt; +2%$</td>
</tr>
</tbody>
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ERO, effective regurgitant orifice; EROA, effective regurgitant orifice area; LV, left ventricular; long., longitudinal.
Estratificação de risco no doente assintomático: o ECO de ESFORÇO pode ser útil?

Capacidade Funcional e Avaliação de SINTOMAS
- Identificação de doentes que não reconhecem os sintomas
- Avaliação de doentes com sintomas equivocos

Função Ventricular / disfunção latente
- Reserva contráctil (Δ Fr.Ej.% e Δ Deformação Longitudinal Global)

Modificação da gravidade da regurgitação mitral
- Comportamento dinâmico da regurgitação mitral

Hipertensão pulmonar induzida pelo exercício

Objectivo: Optimizar o timing da correção cirúrgica
Prevenir a disfunção ventricular pós-operatória
Regurgitação Mitral Degenerativa Assintomática Importância da Reserva Contráctil do VE

115 d consec assintomáticos IM degenerativa mod e grave Sem dilatação /disfunção VE

ECO TT Basal e após esforço Av. Reserva contráctil EF% (≥4%) GLS (≥2%)

Magne J et al. European Heart Journal 2013
Regurgitação Mitral Degenerativa Assintomática Importância prognóstica do BNP

135 dias consecutivos (60±14 anos), assintomáticos IM degenerativa, moderada e grave Função ventricular preservada (EF≥60%, sem FA)

BNP e ECO TT

Follow-up - 23±19 meses

54 dias (40%) c/ eventos sintomas internam 10 dilat/disf 5 morte 1 ambos 20

Magne J et al. Heart 2012;98:584-591
Caso Clínico: Eco em Out/2013

LV Diameters

LA Volume

EF

RVSP

Stroke Volume
INCOR

- Cirurgias Valvares: Jan - Out /2017

- Valva Isolada: 442

- Valva Ao 182:
  - 1ª op. 125
  - 2ª Op. 25
  - TAVI 32 (19 trans ap; 13 trans fem)

- Valva Mi n°: 195 – sendo:
  - 1ª troca valvar : 75
  - 2ª troca valvar: 56
  - Plastia 42
  - Valve in valve 22
Reparação mitral
10/01/2014

Resssecção quadrangular P2

Implantação de 2 cordas goretex no MP posterior para P2

Implantação de anel C-E

Physio 36
Caso Clínico: ETE - IO pós
ETE após reparação da válvula mitral
Avaliação do resultado cirúrgico

➢ Altura de coaptação dos folhetos
➢ Regurgitação residual
➢ Estenose mitral
➢ Desenvolvimento de “SAM”
➢ Regurgitação aórtica
➢ Oclusão artéria circunflexa

ETE –IO pós procedimento pode detectar lesões residuais que justificam correção em 5-10% dos casos
Grading the Severity of Organic MR

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tr>
<td><strong>Qualitative</strong></td>
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<tr>
<td>MV morphology</td>
<td>Normal/abnormal</td>
<td>Normal/abnormal</td>
<td>Flail leaflet/Ruptured PMs large coaptation defect</td>
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<td>Colour flow MR jet</td>
<td>Small, central</td>
<td>Intermediate</td>
<td>Very large central jet / eccentric jet adhering, swirling, and reaching the posterior wall of the LA</td>
</tr>
<tr>
<td>Flow convergence zone</td>
<td>No or small</td>
<td>Intermediate</td>
<td>Large</td>
</tr>
<tr>
<td>CW signal of MR jet</td>
<td>Faint /Parabolic</td>
<td>Dense /Parabolic</td>
<td>Dense /Triangular</td>
</tr>
<tr>
<td><strong>Semi-quantitative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VC width (mm)</td>
<td>&lt;3</td>
<td>Intermediate</td>
<td>≥7 (&gt;8 for biplane)</td>
</tr>
<tr>
<td>Pulmonary vein flow</td>
<td>Systolic dominance</td>
<td>Systolic blunting</td>
<td>Systolic flow reversal</td>
</tr>
<tr>
<td>Mitral inflow</td>
<td>A wave dominant</td>
<td>Variable</td>
<td>E wave dominant (&gt;1.5 M/s)</td>
</tr>
<tr>
<td>TVI mit /TVI Ao</td>
<td>&lt;1</td>
<td>Intermediate</td>
<td>&gt;1.4</td>
</tr>
<tr>
<td><strong>Quantitative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EROA (mm2)</td>
<td>&lt;20</td>
<td>20-29; 30-39</td>
<td>≥40</td>
</tr>
<tr>
<td>R Vol (mL)</td>
<td>&lt;30</td>
<td>30-44; 45-49</td>
<td>≥60</td>
</tr>
</tbody>
</table>

+ LV and LA size and the systolic pulmonary pressure
