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# Editorial

**Pr S. ABIR KHALIL**
Professor of Cardiology
Past president of the Moroccan Society of Cardiology

Morocco has made remarkable progress in many areas opening up to the our African continent and diversifying its activities by opening up to the world under the leadership of His Majesty King Mohammed VI, may God assist him.

The Moroccan Society of Cardiology is certainly part of this dynamic, with a highly successful innovative annual congress bringing together leading experts from Africa, the Middle East, Europe and the United States.

The choice of English as the official language of the congress has enabled optimal exchange and interaction between all participants.
There's no doubt that this appropriate choice can only be perpetuated. So a big thank you to the organizers thanks also to the MSC scientific journal's director.
This issue of the MSC scientific journal dedicated to valvular pathologies includes features didactic, well-documented articles. Although rheumatic etiologies are on the decline, they continue to represent a serious problem in developing countries, while degenerative etiologies have emerged with the ageing population. This scientific review provides an excellent update .

Thus mitral dIsease is the most common valve abnormality in rheumatic heart disease . Echocardiography remains the key to imaging and secondary mitral regurgitation the most undertreated form of mitral regurgitation:
The authors point out that in Aortic regurgitation, isolated or associated with other valvulopathies diagnosis and treatment have benefited from major advances; Surgical techniques have evoved but aortic repair require experieced centers
Pulmonary regurgitation has long been neglected among cardiac valve diseases, but its clinical significance is increasingly recognized.

Tricuspid regurgitation is associated with significant morbidity and mortality, attributed to the late presentation of the disease, poor use of surgical solutions range of transcatheter therapies has emerged, showing promising Management of tricuspid regurgitation.

These items review all the advances made in this regurgitant valve diseases, highlighting the etiology, diagnostic modalities, management strategies, and long-term prognostic with insights derived from recent research and advancements in cardiac imaging and therapeutic measures.

# Unraveling aortic regurgitation: from diagnosis to treatment

Z.Agoumy, H.El Assili, S. El Mhadi, N.Bentama, L.Bakamel, Z.Fassi Fehri, H.Bachri, B. ElHajjaj ,K.Berrag, N.Bendagha, A.Soufiani, S.Moughil
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**Résumé**

L'insuffisance aortique est une maladie valvulaire complexe et multifactorielle. Pour comprendre les diverses causes et mécanismes conduisant à la régurgitation aortique, il est essentiel d'avoir une compréhension approfondie de la structure valvulaire aortique et de la racine aortique. L'imagerie multimodale est utilisée pour évaluer et classer la gravité de la fuite aortique, ainsi que ses conséquences sur le ventricule gauche (VG) en termes de dimensions et de fonction systolique, en tenant compte des avantages et des limites de chaque technique. L'échocardiographie 2 dimensions demeure la modalité d'imagerie de première intention pour le diagnostic. L'apparition des symptômes représente un tournant dans l'évolution de la maladie avec un pronostic sombre, et une indication claire pour la chirurgie valvulaire. D'autres indications chirurgicales sont retenues chez les patients asymptomatiques tenant compte de la dilatation de la racine aortique, la présence d'une dysfonction VG ou d'un certain degré de dilatation du VG. Les techniques chirurgicales ont nettement évolué, et les ambitions de réparation aortique exigent des centres expérimentés.

**Mots clés :**

insuffisance aortique, valvulopathie, valve aortique, imagerie multimodale, aorte

**Summary**

Aortic regurgitation (AR) is a complex and multifactorial valvular disease. To understand the diverse causes and mechanisms leading to AR, a comprehensive grasp of the aortic valve and the aortic root's structure is essential. An integrated multimodality imaging is used for assessing and grading AR severity, as well as the consequences on the LV in terms of dimensions and function, taking into account the strengths and limitations of each technique. Two-dimensional Echocardiography remains the first-in line imaging modality for diagnosis. The onset of symptoms represents a turning point in the evolution with poor prognosis and denotes a strong indication for intervention. Surgery is also indicated when the aortic root is dilated, or when there is a certain degree of LV dilatation or dysfunction. Surgical techniques have evolved, and ambitions of aortic repair require experienced centers.

**Keywords :**

aortic regurgitation, valvular disease, aortic valve, multimodality imaging, aorta

## Introduction

Aortic regurgitation (AR) or insufficiency is defined as the presence of retrograde blood flow through the aortic valve across the LV during the diastole. It is the third most common valvular pathology in the general population (1). It may be caused by a variety of either congenital or acquired etiologies preventing complete coaptation of the aortic valve leaflets. It can also be divided into primary or organic AR (leaflets disease) and secondary AR (by distortion/dilatation of the ascending aorta). Severe AR is associated with significant Morbi-mortality. Even in asymptomatic patients, mortality can reach up to 19% within 6.6 years of diagnosis (2). This can explain the actual thresholds for surgery in asymptomatic patients in the

## 2. Epidemiology

AR represents 5.3% of all valvular heart diseases as reported by the 2019 Euro heart survey. Etiology in Europe is mainly dominated by dystrophic and congenital causes; whereas rheumatism is more frequent in Northern Africa (3). This pathology mostly concerns young male adults with a median age of 58 years. The prevalence and severity increase with age and AR is frequently underdiagnosed (4). When treated conservatively, AR has high mortality (34% mortality at 10 years, with a progression of 4.7% a year). It is even higher when the patient is symptomatic, with an increase to 9.4% a year (5).

## 3. Physiopathology: AR is not just "another volume overload etiology"

AR leads to both LV volume and pressure overload. Patients with mild AR are not exposed to significant regurgitant volume and are generally asymptomatic. At a chronic stage of severe AR, the LV end diastolic volume (LVEDV) leads to a compensatory increase of LV wall stress, thus LV remodeling. The LV undergoes detrimental structural changes, that eventually leads later on to LV dysfunction. At this stage, the patient is symptomatic. Also, the magnitude of AR reflects both the severity and chronicity.

An interesting physio-pathological notion is that AR differs greatly from mitral regurgitation (MR), as the two leaks diverge in "the driving pressure" of regurgitation. Discordant "afterload" conditions may be the most critical factor underlying differences in LV morphology and systolic function. In AR, the LV faces higher afterload, ejecting a large stroke volume through a relatively unexpanded aortic valve orifice into the high-pressure systemic circulation. In contrast, in severe MR, lower LV afterload results from regurgitation into the low resistance left atrium and obviates the "afterload mismatch" manifested in AR, thus resulting in smaller LV end-systolic diameter (LVESD) for an equivalent level of leak. These disparate responses in LV dilatation and diastolic wall stress could explain the differences in intervention cut-offs between AR and MR (6).

## 4. The functional unit of the aortic valve

The aortic valve consists of complex structures surrounding the aortic orifice along the outflow tract of the left ventricle (LVOT). Typically, the valve has three leaflets with a semi-lunar shape. The cusps are inserted into a fibrous connective tissue sleeve, which is attached to the aorta above (the valsalva sinuses and the sino-tubular junction). Below, the cusps are attached to the myocardium of the LVOT and to the anterior mitral leaflet (creating a virtual basal ring), below the anatomic ventricular-aortic junction, assuring the anatomic integrity of the "functional unit" of the aortic valve (figure 1).

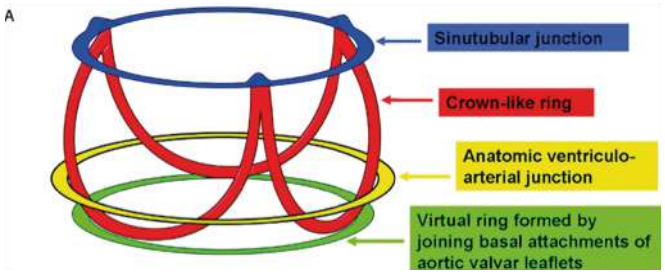


Figure 1:
Schematic drawing that describes the anatomic arrangement of the aortic valve leaflets supported in crown-loke fashion.
(Courtesy of Professor Robert Anderson)

Consequently, the true anatomic aortic annulus is not actually in a form of a ring projected at the most basal leaflet insertion, but a crown-like 3D structure. Notably, the dimensions of the aortic annulus and root are subject to inner pressure and undergo dynamic fluctuations throughout the cardiac cycle.
Hence, AR results from the disruption of any component of the "functional unit" of the aortic root. Causes include those involving the cusps (calcific degeneration = senile leaflet, congenitally bicuspid valve, infective endocarditis, rheumatic disease, myxomatous degeneration) and those that encompass the aortic root leading to distortion of the leaflets (aortic dissection, aortitis, connective tissue disorders such as Marfan syndrome).

## 5. Mechanisms

The most common classification used for AR is the one proposed by the Belgian team of Al Khoury (7), which follows the same principle as Carpentier for mitral regurgitation, integrating data from the valve and the root (normal cusps but insufficient coaptation due to the dilatation of the aortic root, cusp prolapse, and retraction wit) (figure 2).
In the type I mechanism, the jet is central, whereas in the type II and III, the jet is eccentric (8). Identifying the mechanism of AR is an important step, as it can suggest certain etiologies (for example bicuspid valve in case of prolapse, restriction in case of degenerative valve). Also, this functional evaluation can guide surgeons in term of valve repair. In some cases, AR may be caused by two different mechanisms. In Marfan's disease, both the valve and the aortic root are affected leading to composite organic and functional regurgitant valve.

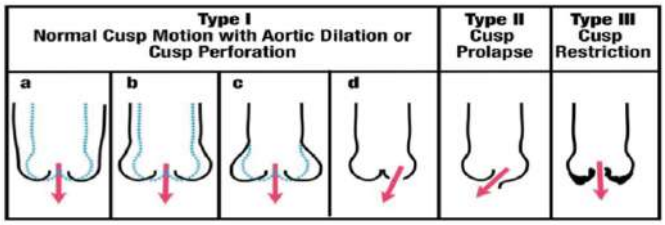


Figure 2:
Suggested classification of AR morphology, depicting the various mechanisms of AR (8).
Type Ia: sinotubular junction enlargement of the ascending aorta
Type Ib: dilatation of the sinuses of valsavla and sinotubular junction
Type Ic: dilatation of the ventriculoarterial junction (annulus)
Type Id: aortic cusp perforation

## 6. Multimodality imaging (9)

### 1) Transthoracic echocardiography (TTE)

Two-dimensional TTE is the first-line imaging modality in valvular regurgitation. In patients with AR, careful aortic valve analysis is mandatory. Different information should be included in the echocardiography report about the etiology, the lesion process, and the type of dysfunction. Therefore, the report should contain a meticulous description of the pathological cusp (redundancy, restriction, cusp height, mobility, thickness and integrity), commissures variations (fusion, splaying, attachment site and alignment) as well as the

root morphology (annular size, sinus and sino-tubular junction dimension and ascending aorta dimensions in the parasternal long-axis views). The likelihood of valve repair should also be discussed in case of pure AR.
The echocardiographic evaluation should follow an integrative and comprehensive approach using multiple parameters to assess AR severity.
The analysis should also expand to evaluating the consequences of AR on LV size and function. In acute AR, the LV is not classically enlarged, while in the chronic situation (moderate to severe), LV dilatation occurs progressively. A careful measurement of the cavities is recommended as the thresholds for surgery in asymptomatic patients in current ESC guidelines include LVEF and LV end-systolic diameter. Additional strain imaging may be helpful in identifying subclinical LV dysfunction when the GLS <-19% (10).

**o Echocardiographic tools to assess AR severity**
AR assessment according to the 2021 ESC guidelines for the management of valvular heart disease considers the use of qualitative, semi-quantitative and quantitative parameters (11).

**• Qualitative parameters**
The first steps in evaluating valvular regurgitation starts with a detailed anatomic description of the valve morphology. In favor of severe AR: abnormal or large coaptation defect, and the presence of a flail valve is specific for severe chronic AR. This diastolic fluttering of the anterior mitral leaflet is produced by the regurgitant jet.
The addition of the color doppler gives a first visual assessment of AR, but is not recommended for quantification. The regurgitant jet can be visualized from multiple views, and the color jet area and length are correlated to the degree of AR.
In general, the apical view is most sensitive for detection, but the zoomed parasternal long- and short-axis views are mandatory to visualize the three components of the color jet: proximal flow convergence, vena contracta (VC) and jet width (figure 3). Of note, central jets are suggestive of rheumatic disease, whereas eccentric jets are often associated with aortic prolapse or perforation.

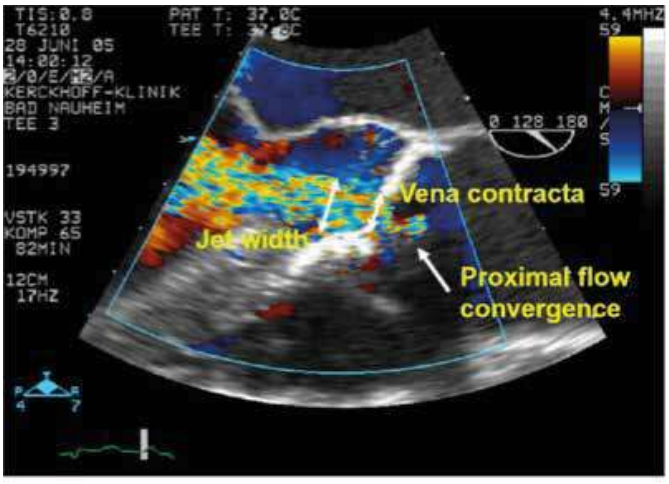


Figure 3 :
Depiction of the three components of a color flow regurgitant jet of AR: jet width, vena contracta, and proximal flow convergence (12).

The use of pulse wave Doppler at the upper descending aorta of the aortic isthmus in suprasternal view shows diastolic flow reversal. It can also be seen in the abdominal aorta. The Doppler filter should be decreased to its lowest setting allowing eventual detection of low velocities (<10cm/s). The more severe the regurgitation is, the more the duration and the velocity of this reversal flow increases. The cut-off value for severe AR is 20cm/s.

**• Semi-quantitative approach**
The VC is the narrowest portion of the jet that occurs at or immediately downstream from the regurgitant orifice. It is quick and easy to obtain, and can be used for eccentric jets as well as extreme regurgitation. Also, it is relatively independent of hemodynamic factors. However, it is not valid in case of multiple jets, calcifications, irregular or elliptic orifice (bicuspid valve).
It is considered severe when it exceeds 6mm, but needs confirmation by a more quantitative method when feasible. This cut-off is smaller than in mitral regurgitation (MR) because of the longer duration of diastolic AR compared to systolic MR.
Another parameter is the Pressure-half-time (PHT), derived from the continuous-wave Doppler signal of the AR jet. It requires a good Doppler beam alignment. It represents the pressure equilibration rate between the aorta and the LV. In parallel with AR severity, the PHT decreases throughout the diastole with a steeper deceleration slope. A PHT <200 msec is in favor of severe AR, while a value >500msec suggests mild AR. This parameter remains limited as it is affected by LV and aortic compliance.

**• Quantitative approach**
The proximal isovelocity surface area (PISA) is the quantitative method of choice. It starts with imaging of the flow convergence zone obtained by the parasternal long-axis or upper right parasternal views. The radius of the PISA is measured at diastole using the first aliasing, obtained from the apical three- or five chamber or parasternal long-axis or upper parasternal views. Then, R Vol (regurgitant volume) and EROA (effective regurgitant orifice area) are obtained using standard formulas.
The PISA method has also certain limitations. Actually, the flow convergence is difficult to obtain when there is an interposition of valve tissue, making it difficult to correctly identify the flow convergence zone. Also, a non-planar or confined flow convergence invalidates the hemispheric assumption of the PISA method, causing a potential under or over estimating of AR severity.
When the evidence from the different parameters is congruent, it is easy to grade AR severity. Conversely, when parameters are discordant in any way, the Doppler volumetric method can be useful as an alternative approach. It relies on the equation stating that the total stroke volume is derived from the LVOT stroke volume. Therefore, in the absence of MR, the regurgitant flow equals the aortic flow minus the mitral flow. It is significant for severe AR when it exceeds 50%. Nevertheless, this approach is time consuming and has been left out of the 2021 ESC guidelines.

2) 3D echocardiography
When facing patients with complex valve lesions, three-dimensional echocardiography can provide additional information giving more accurate quantification of hemodynamic consequences of the regurgitation on cardiac chambers.

**3) TOE**
Transesophageal echocardiography (TOE) is advocated in case of suboptimal acoustic window, allowing for better visualization of the mid-distal ascending aorta and the aortic arch.

**4) Cardiac magnetic resonance (CMR)**
CMR serves as an additional diagnostic tool for assessing severity and quantification of LV remodeling. It gives precise measurement of the Regurgitant volume (RV) and regurgitant fraction (RF). The latter is calculated by dividing the RV by the LV stroke volume. The cut off value for severe AR is the same for TTE (50%). The RF is crucial as it is an independent predictor of outcomes in patients with AR (13). Actually, a RF >33% has been shown to predict the likelihood of requiring surgery within 9 years (14).

## 7. Management of AR and future perspectives

Some entities like infective endocarditis and aortic dissection may require urgent surgery. Medical management is limited and consists in stabilizing patients temporarily.
In presence of symptoms, surgery is recommended regardless of the LV function. In asymptomatic patients, timing of surgery is dictated by other parameters such as dilatation of the aorta and LV dimensions.
In presence of significant enlargement of the ascending aorta, ESC guidelines recommend surgery irrespective of AR stage. The class 1 recommendation threshold for Marfan disease equals 50mm and higher. Between 45 and 50mm, surgery should be considered in presence of additional risk factors* (Family or personal history of aortic dissection, severe AR or MR, desire for pregnancy, uncontrolled systemic arterial hypertension and/or aortic size increase >3mm/year) or patients with a TGFBR1 or TFFBR2 mutation.
Valve-sparing aortic replacement is recommended in young patients with aortic root dilatation (class 1 recommendation). Different techniques have been described (figure 4).
Aortic surgery should also be considered when the maximal ascending aortic diameter is ⩾55 mm in all patients or is ⩾50 mm in the presence of bicuspid valve (with additional risk factors*) or coarctation.

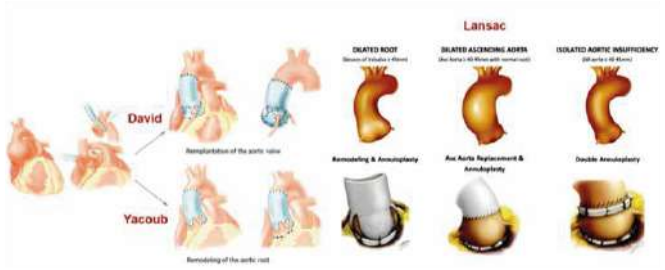


Figure 4 :
Valve-sparing aortic replacement techniques

Furthermore, while symptomatic severe AR is a clear indication for surgery, the LVEF and LV dilatation cut-offs indicating surgery for asymptomatic patients vary between European and American guidelines (11,15,16).
Actually, the AHA/ACC and ESC agree on the LVESD threshold of >50mm or LVESD >25mm/m2 body surface area (in patients with small body size). It may be considered with a LVESD >20 mm/m2 BSA (especially in patients with small body size) or resting LVEF 55%, if surgery is at low risk. This recommendation follows the study of Yang et al in 2019, who objected that LVESD was the only chamber criteria associated with all-cause death.
However, while ESC recommends surgery when the LVEF <55%, the AHA/ACC guidelines pushes the threshold to <55% when another cause cannot explain the LVSD.
There are two surgical options for the aortic valve: either AV replacement (using bioprosthesis or mechanical valve prosthesis), or AV repair. AVR has been shown to improve long-term survival in patients with severe AR and normal LVEF (18). Promising long-term surgical outcomes of AVR in patients with important isolated aortic regurgitation within severe left ventricular dysfunction have been objected by literature (19), and personal results in our center are even more encouraging (20).
The choice of the technique depends on the center expertise. AV repair in an alternative for valve replacement in selected patients. Due to technical challenges, it is restrained to selected specialist centers with high expertise. Emerging transcatheter therapies may offer alternative for high-risk surgery candidates, but are still not validated due to the lack of studies.

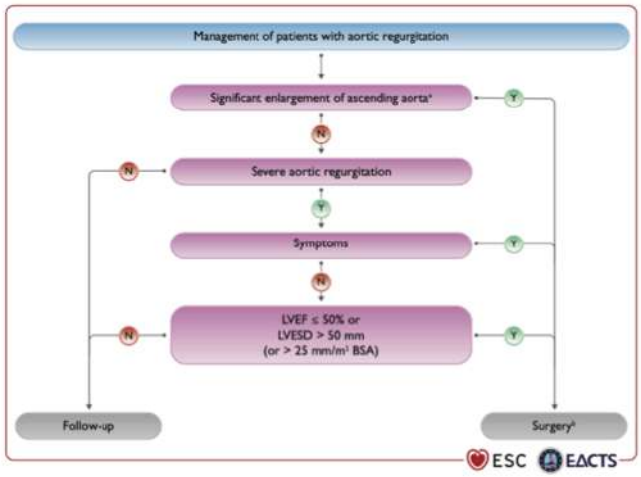


Figure 5 :
Management of patients with aortic regurgitation according to the 2021 ESC guidelines for the management of valvular heart disease

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# Pulmonary Regurgitation: The Forgotten Entity

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**Résumé**

L'insuffisance pulmonaire (IP) a longtemps été négligée parmi les maladies valvulaires cardiaques, mais sa signification clinique est de plus en plus reconnue. Cette revue complète explore l'étiologie, les modalités diagnostiques, les stratégies de prise en charge, et les implications pronostiques à long terme de l'IP. Grâce à des informations récentes issues de la recherche et aux progrès dans l'imagerie cardiaque, nous examinons les diverses causes de la RP, allant des anomalies congénitales aux affections acquises. En mettant en lumière cette condition souvent négligée, cet article vise à sensibiliser et à guider la prise de décision clinique efficace concernant l'IP.

**Mots clés :**

Insuffisance pulmonaire (IP), Maladie valvulaire cardiaque (MVC), Cardiopathie Congénitale, Tétralogie de Fallot.

**Summary**

Pulmonary regurgitation (PR) has historically been overshadowed in the realm of valvular heart diseases, yet its clinical significance is increasingly recognized. This comprehensive review explores the etiology, diagnostic modalities, management strategies, and long-term prognostic implications of PR. With insights derived from recent research and advancements in cardiac imaging, we delve into the diverse causes of PR, ranging from congenital anomalies to acquired conditions. By shedding light on this often-neglected condition, this article aims to enhance awareness and guide effective clinical decision-making regarding PR.

**Keywords :**

Pulmonary regurgitation (PR), Valvular heart disease (VHD), Congenital heart disease (CHD), Tetralogy of Fallot.

## Introduction

Pulmonary regurgitation (PR), characterized by the backward flow of blood from the pulmonary artery into the right ventricle during diastole, has historically received less attention compared to other valvular heart diseases. However, recent advances in cardiac imaging and a growing understanding of its clinical significance have highlighted the importance of PR in cardiovascular medicine.

Pulmonary regurgitation (PR) is common after surgical or percutaneous relief of pulmonary stenosis and following repair of tetralogy of Fallot. PR is usually well tolerated in childhood. However, recent long-term studies have demonstrated that PR leads to progressive right ventricular (RV) dilatation and, with time, to RV dysfunction, exercise intolerance, ventricular tachycardia, and sudden cardiac death (SCD) 1-2. Furthermore, recent advances in non-invasive imaging, and in particular wider availability of cardiovascular magnetic resonance (CMR), have improved the assessment of PR and RV function in these patients.

This article comprehensively explores the various facets of PR to bridge the knowledge gap surrounding this condition.

## AETIOLOGY OF PR :

PR can arise from various causes, both congenital and acquired. Congenital etiologies often involve structural abnormalities such as pulmonary valve stenosis, tetralogy of Fallot, or Ebstein's anomaly. The intricate interplay of genetic and environmental factors contributes to the development of congenital PR. An in-depth examination of the genetic basis of congenital PR is ongoing, with emerging insights into potential therapeutic targets.

### Tetralogy of Fallot

PR is extremely common in patients after repair of tetralogy of Fallot. While most of these patients carry an excellent prognosis,3-4 there is a late morbidity and mortality related largely to RV dysfunction, PR in these patients is shown to relate to the use of a transannular patch—more liberally performed in an earlier surgical era to reconstruct the RV outflow tract (RVOT). Furthermore, transannular patching and/or aggressive infundibulectomy predispose to RVOT aneurysms or akinetic regions. The latter, combined with chronic PR, have an adverse effect on RV function and overall prognosis.5

As a result, routine and generous transannular patch type of repair has now been abandoned and limited RVOT patching with preservation of pulmonary valve function have become key therapeutic goals during primary repair of tetralogy in infancy

**Pulmonary stenosis :**
Balloon valvuloplasty has become the treatment of choice for patients with valvular pulmonary stenosis. Surgical valvotomy—widely employed in the 1960s and the 1970s— is now reserved for patients with supra- or sub-valvular stenosis. Variable degrees of PR are seen in more than 70% of patients after either a surgical or transcatheter intervention,6-7 although PR appears to be less frequent following balloon valvuloplasty.mIn the Second Natural History Study of Congenital Heart Defects, 87% of the surgically operated patients had PR on echocardiography, being more than moderate in 28%.8 A number of these patients now return requiring pulmonary valve replacement (PVR).

**Absent pulmonary valve syndrome :**
Absent pulmonary valve syndrome is a rare manifestation comprising faulty development and dysplasia or complete absence of pulmonary valve cusps leading to PR. It is commonly associated with tetralogy of Fallot although occasionally it is seen in isolation. Its management and prognosis are often determined by the degree of pulmonary arterial dilatation, which can be excessive in some patients causing external bronchial compression.

- In contrast, acquired PR may result from infective endocarditis, rheumatic heart disease, or iatrogenic causes such as prior cardiac surgeries. Understanding the underlying etiology is crucial for tailoring appropriate treatment strategies. Rheumatic heart disease remains a significant contributor to acquired PR in certain regions, highlighting the continued importance of preventive measures and access to healthcare.

**Pathophysiology of PR**

Table 1 Pathophysiology of chronic PR

| | |
|---|---|
| Substrate | Post-repair of tetralogy of Fallot |
| | Post-valvotomy for pulmonary stenosis (balloon or surgical) |
| | Absent pulmonary valve syndrome (rare) |
| | Isolated congenital PR (rare) |
| Co-variable/s | Peripheral pulmonary artery stenosis (−) |
| | Pulmonary hypertension (−) |
| | RVOT aneurysm/akinesia (−) |
| | RV restrictive diastolic physiology (+ in the older patient) |
| Clinical progression | RV dilatation (there is usually a long compensatory phase while RV systolic function is maintained) |
| | QRS prolongation (associated with increased risk of sustained ventricular tachycardia and SCD) |
| | Onset of tricuspid regurgitation |
| | RV systolic dysfunction |
| | Overt symptoms ensue |

(−/+) indicates negative or positive effect on PR and/or RV function.

Bouzas, B., Kilner, P. J., & Gatzoulis, M. A. (2005). Pulmonary regurgitation: not a benign lesion. European Heart Journal, 26(5), 433–439.

**Diagnosis :**

Accurate diagnosis of PR relies on a combination of clinical evaluation, imaging modalities, and hemodynamic assessment. Echocardiography remains the cornerstone for diagnosing and assessing the severity of PR. Recent advancements in three-dimensional echocardiography, cardiac magnetic resonance imaging (MRI), and computed tomography (CT) have improved our ability to visualize the pulmonary valve and assess regurgitation severity. Additionally, Doppler echocardiography provides valuable information on regurgitant flow velocity and volume.
**ECG** Most patients are in sinus rhythm although atrial arrhythmia can be present. In patients with isolated PR the presence of QRS prolongation, with rSr morphology in the right pre-cordial leads, reflects volume overload of the RV. Right bundle branch block is extremely common in patients who underwent tetralogy repair via a right ventriculotomy and may mask RV hypertrophy. QRS duration in these patients increases with time, reflecting progressive RV enlargement and potentially RV dysfunction. As discussed above, QRS duration and QRS change have prognostic implications for malignant arrhythmia and SCD in these patients.2-9
**Chest X-ray** Patients with severe PR characteristically have dilatation of the pulmonary trunk and central pulmonary arteries. There is also RV enlargement, evident as filling of the retrosternal space on lateral projections.
**Echocardiography**

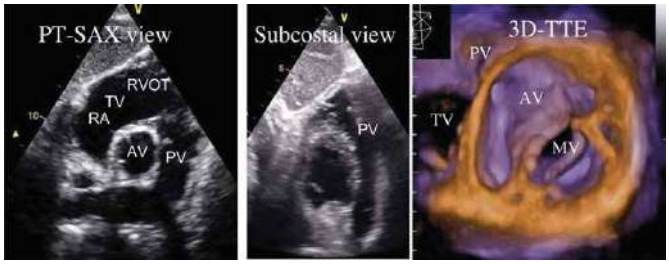


Figure 3 :
Two- and three-dimensional echo recordings of the pulmonic valve.
PT-SAX, parasternal short-axis view.(10)

**Colour ftow Doppler**
Detection of PR relies almost exclusively on colour flow imaging. PR is diagnosed by documenting a diastolic jet in the RV outflow tract directed towards the RV. Pathological PR is distinguished from physiological PR by a longer duration of flow (holodiastolic) and a wider jet as the regurgitant jet crosses the pulmonic valve.11 Functional PR jets are usually very small, central, and spindle- shaped. In severe PR, where equalization of diastolic pulmonary artery and RV pressures occurs early in diastole, the colour jet area can be brief and inaccurate (dependency on the driving pressure)12 The assessment of PR severity is usually estimated by the diameter of the jet at its origin.13 The maximum colour jet diameter (width) is measured in diastole immediately below

the pulmonic valve (at the junction of the RV outflow tract and pul- monary annulus) in the parasternal short-axis view or from the subcostal view. Although this measurement suffers from a high inter-observer variability, a jet width that occupies .65% of the RV outflow tract width measured in the same frame is in favour of severe PR.

**Vena contracta width**

Although the vena contracta width is probably a more accurate method than the jet width to evaluate PR severity by colour Doppler, it lacks validation studies (Figures 4 and 5). As for other regurgitations, the same limitations are applicable. The shape of the vena contracta is complex in most cases. The 3D vena contracta is correlated with the 2D vena contracta but pro- vides more quantitative assessment of PR.45 The EROA values of ,20, 21 – 115, and .115 mm2 have been proposed to serve as cut-offs for PR grade mild, moderate, and severe. By multiplying

the 3D vena contracta with the spectral Doppler-derived velocity integral of the PR jet, the R Vol can be obtained. The regurgitant volume values of ,15, 15 – 115, and .115 mL have also been pro- posed to serve as cut-offs for PR grade mild, moderate, and severe. These values require further validation since they are coming from a single study. Values are relatively high and could reflect some technical drawbacks.

**The ftow convergence method**

In some patients, the flow convergence zone can be assessed (Figure 5). However, no studies have examined the clinical accu- racy of this method in quantifying the severity of PR.

**Pulsed Doppler**

Theoretically, PW Doppler assessment of the forward and the reverse flows at the pulmonary annulus and in the pulmonary artery can been used to calculate R Vol and regurgitant fraction.

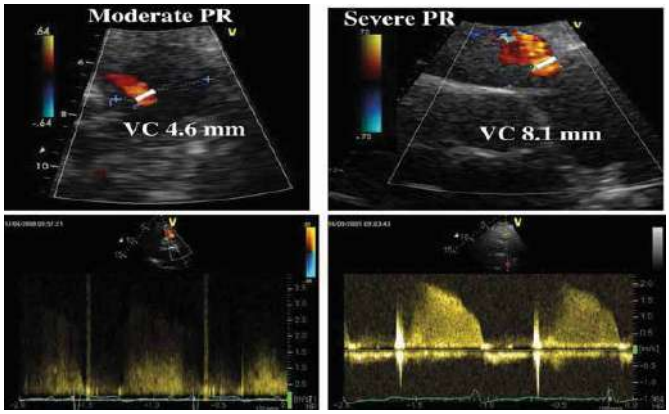


Figure 4 :
Assessment of pulmonary regurgitation (PR) severity by using colour flow imaging. (Top) Measurement of the vena contracta width in two patients with PR (left: moderate, right: severe). (Bottom) Continuous-wave Doppler recordings.

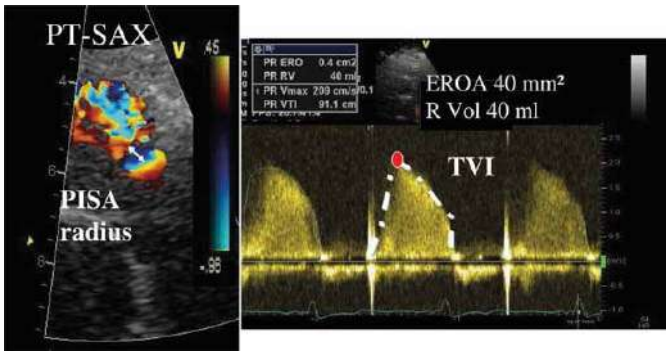


Figure 5 :
Assessment of pulmonary regurgitation by the proximal isovelocity surface area (PISA) method. PT-SAX, parasternal short-axis view; EROA, effective regurgitant orifice area; R Vol, regurgitant volume.

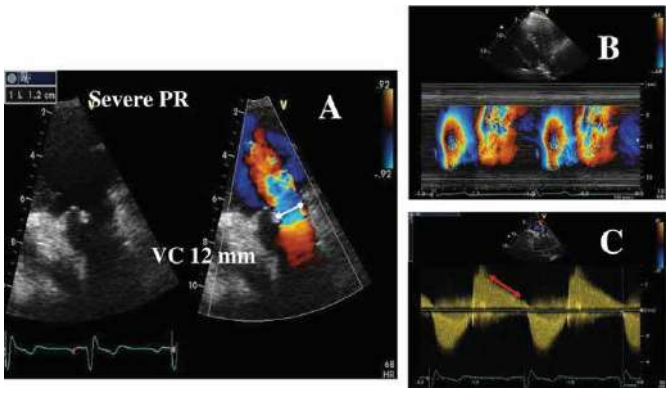


Figure 6 :
Example of a patient with a severe pulmonary regurgitation (PR). (A) Complete lack of valve coaptation (left) and measurement of the vena contracta width (VC) (right); (B) colour-coded M-mode depicting the time dependency of flow signal during the heart cycle; (C ) con- tinuous Doppler recording of PR showing a rapid flow deceleration during the diastole (red arrow) and increased systolic flow velocity (not related to concomitant pulmonary stenosis).

**Table 4** Grading the severity of PR

| Parameters | Mild | Moderate | Severe |
|---|---|---|---|
| Qualitative | | | |
| Pulmonic valve morphology | Normal | Normal/ abnormal | Abnormal |
| Colour flow PR jet width[a] | Small, usually <10 mm in length with a narrow origin | Intermediate | Large, with a wide origin; may be brief in duration |
| CW signal of PR jet[b] | Faint/slow deceleration | Dense/variable | Dense/steep deceleration, early termination of diastolic flow |
| Pulmonic vs. Aortic flow by PW | Normal or slightly increased | Intermediate | Greatly increased |
| Semi-quantitative | | | |
| VC width (mm) | Not defined | Not defined | Not defined |
| Quantitative | | | |
| EROA ($mm^2$) | Not defined | Not defined | Not defined |
| R Vol (mL) | Not defined | Not defined | Not defined |
| +RV size[c] | | | |

PR, pulmonic regurgitation; CW, continuous wave; EROA, effective regurgitant orifice area; PW, pulse wave; RV, right ventricle; R Vol, regurgitant volume; VC, vena contracta.
[a]At a Nyquist limit of 50–60 cm/s.
[b]Steep deceleration is not specific for severe PR.
[c]Unless for other reasons, the RV size is usually normal in patients with mild PR. In acute severe PR, the RV size is often normal. Accepted cut-off values for non-significant RV enlargement (measurements obtained from the apical four-chamber view): Mid RV dimension ≤33 mm, RV end-diastolic area ≤28 $cm^2$, RV end-systolic area ≤16 $cm^2$, RV fractional area change >32%, maximal.

The pulmonary annulus should be measured carefully during early ejection (2 – 3 frames after the R wave on the ECG), just below the valve. This technique is subject to errors in measurement and is not well validated.14

**Continuous-wave Doppler**

There is no clinically accepted method of quantifying PR using CW Doppler. The density of the CW signal provides a qualitative measure of regurgitation.15 In mild PR, there is a slow deceleration of the jet velocity. A rapid deceleration rate with termination of flow in mid to late diastole is not specific but compatible with severe regurgitation.

**Consequences of pulmonary regurgitation**

Evaluation of the size and function of the RV in the absence of pulmonary hypertension provides indirect clues to the severity of PR.16

**Table 5 Echocardiographic parameters used to quantify PR severity: recordings, advantages, and limitations**

| Parameters | Recordings | Usefulness/Advantages | Limitations |
|---|---|---|---|
| Pulmonic valve morphology | • Visual assessment<br>• Multiple views | • Flail valve is specific for significant PR | • Other abnormalities are non-specific of significant PR |
| Colour flow PR jet | • Optimize colour gain/scale<br>• Evaluate in parasternal short-axis view | • Ease of use<br>• Evaluates the spatial orientation of PR jet<br>• Good screening test for mild vs. severe PR | • Influenced by technical and haemodynamic factors |
| VC width | • Parasternal short-axis view<br>• Optimize colour gain/scale and identify the three components of the regurgitant jet<br>• Reduce the colour sector size and imaging depth to maximize frame rate<br>• Expand the selected zone (zoom) and find the best frame for measurement<br>• Measure the smallest VC | • Possible if the pulmonic valve is well visualized<br>• Relatively independent of haemodynamic and instrumentation factors<br>• Not affected by other valve leak<br>• Normally good as for the other valves | • Difficult to perform in the majority of patients<br>• Lacks published data |
| PISA method | • Parasternal short-axis view<br>• Optimize colour flow imaging of PR and zoom the selected region<br>• Decrease the Nyquist limit (colour flow zero baseline)<br>• Measure the PISA radius at mid-systole using the first aliasing and along the direction of the ultrasound beam<br>• Measure PR peak velocity and TVI (CW)<br>• Calculate flow rate, EROA, R Vol | • Quantitative<br>• Normally good as for the other valves | • Difficult to perform in the majority of patients<br>• Lacks published data |
| CW PR jet profile | • Parasternal short-axis view | • Simple, easily available | • Qualitative, complementary finding |
| RV size | • Use preferably the RV dimension from the apical four-chamber view | • Dilatation sensitive for chronic significant PR<br>• Normal size almost excludes significant chronic PR | • Dilatation observed in other conditions (non-specific)<br>• May be normal in acute severe PR |

CW, continuous-wave; RV, right ventricle; MR, mitral regurgitation; VC, vena contracta

Patrizio Lancellotti(Chair)1*, Christophe Tribouilloy 2, Andreas Hagendorff 3, Luis Moura 4, Bogdan A. Popescu 5, Eustachio Agricola 6, Jean-Luc Monin 7, Luc A. Pierard 1, Luigi Badano 8, and Jose L. Zamorano 9 on behalf of the European Association of Echocardiography European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation (native valve disease)

Evidence of RV dilatation is however not specific for severe PR. Nevertheless, its absence suggests milder degree of PR. As for TR, the RV function is classically evaluated by the RV ejection fraction. The utility of the new indices deriving from tissue Doppler imaging has not been extensively examined in the context of PR unrelated to congenital heart disease. In the tetralogy of Fallot, the severity of PR has a negative influence on RV functional parameters and there is significant relation between RV functions and exercise capacity. In this disease, the myocardial acceleration during the isovolumic contraction is a new emerging index of RV function. The assessment of RV function in the setting of congenital heart disease is not the scope of this document.

**Role of exercise echocardiography**

Latent RV dysfunction and impaired functional response to stress can be unmasked by exercise echocardiography. Except in the setting of congenital heart disease, the value of exercise testing in patients with PR has not been examined.48

**Integrating indices of severity**

Echocardiographic assessment of PR includes integration of data from 2D/3D imaging of the pulmonary valve and RV as well as Doppler measures of regurgitant severity (Table 4). In the absence of extensive data on quantitation of PR, the experts rec- ommend to assess the PR severity by using the different approaches available and to corroborate each other. Advantages and limitations of the various echo Doppler parameters used in assessing PR severity are detailed in Table 5.

**Key point**

Grading of PR severity remains difficult since standards for quantification of PR are less robust than for AR. The vena contracta is probably the most accurate approach. If poss- ible the PISA method could provide quantitative evaluation of PR. In all cases, the experts recommend cor- roborating the results of these methods with the other available parameters.

In complex cases, cardiac catheterization may be required to obtain hemodynamic data and assess the feasibility of intervention. Non-invasive imaging techniques like cardiac CT and CMR continue to evolve, enhancing our ability to diagnose and monitor PR and became nowadays essentials before treatment of PR, all potential candidates for PPVI underwent a complete CMR protocol for the evaluation of the PV, RVOT and PA anatomy, quantification of PR and biventricular volumes, and assessment of coronary anatomy .17

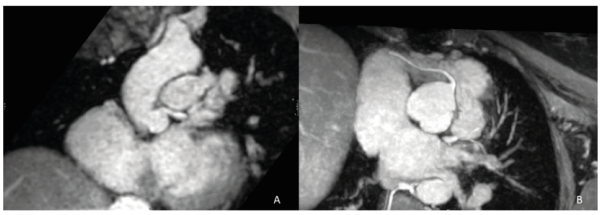

Figure 7 :
Examples of an unfavorable coronary anatomy for PPVI. Extreme proximity of the left main coronary artery to the RVOT (<1 mm) has contraindicated percutaneous pulmonary intervention (A). (B) shows an acute take-off angle (<90°) of the proximal right coronary artery which is an issue for successful PPVI.

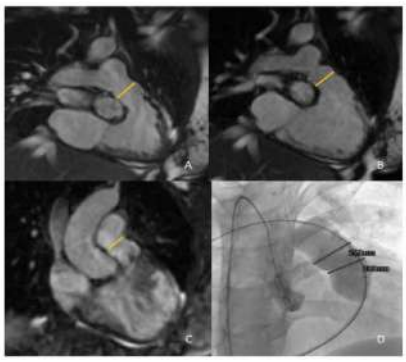

Figure 8 :
Measurement of the RVOT by CMR for PPVI feasibility and valve sizing: 2D cine views at end-systole and end-diastole ((A) and (B), respectively), and 3D whole heart imaging sequences (C). Final check of CMR data with invasive angiography (D).

## Management / Follow up

### Medical

Diuretics have a role for patients presenting with symptoms of right heart failure, although identification of residual lesions and elective intervention prior to clinical decompensation is clearly desirable. Recent evidence suggests that patients with tetralogy of Fallot have both neurohormonal activation and impaired cardiac autonomic nervous activity.18,19 Neurohormonal antagonism, therefore, with ACE-inhibitors and/or beta-blockers, and other interventions such as physical conditioning (known to modulate the autonomic nervous system) may convey symptomatic benefits, improve prognostication, and delay the need for re-operation. Clearly, prospective controlled studies in this area are needed.

### Surgical

PVR for PR is usually required in about 15% of patients with repaired tetralogy.18 This is a low-risk intervention with a peri-operative mortality of 1–4%35 and excellent mid-term survival (10-year survival of 86–95%).19-20 Young adults undergoing PVR are likely to require further surgery as prostheses have a limited lifespan. Optimal timing of pulmonary valve implantation is, therefore, crucial for preserving RV function (not too late) and avoiding the need for early subsequent pulmonary valve implantation (not too early).
Peri-operative Ongoing research is focused on developing less invasive interventions, such as percutaneous pulmonary valve replacement, which can improve outcomes and reduce the need for open-heart surgery. Long-term follow-up is critical to assess the durability of interventions and monitor the progression of PR.
Risk is higher in patients with established RV dysfunction at the time of pulmonary valve implantation.20 While such patients should still be considered for PVR (with the exception of the occasional patient with advanced left ventricular dysfunction) as they will benefit from a competent pulmonary valve, they usually require longer post-operative intensive care. The rate of freedom from further valve replacement is 81% at 5 years, 58% at 10 years, and 41% at 15 years.21 However, these data refer to a mixture of children and adults. The lifespan of pulmonary valve prostheses in adult patients is known to be longer, ranging between 15 and 30 years. With regard to the type of valve prosthesis employed, bioprosthetic valves (homograft or porcine), have a lower complication rate compared with mechanical prostheses, and thus have established themselves as the valves of choice for PVR.22,23 Patients with severe RV dilatation and large akinetic or aneurysmal region in the RVOT should be considered for additional pulmonary infundibuloplasty, shown to improve RV performance by reducing RV volumes and restoring RV geometry.24 In such patients, employing a stented tissue valve as opposed to a freestanding human homograft is advisable, as it may secure a longer lifespan for the bioprosthesis. Indications for surgery Therapeutic goals of PVR should be improved functional class and quality of life, maintenance of ri ght (and left) ventricular function, risk modification of arrhythmia and SCD and overall improved prognostication. In general, patients should be considered for PVR when both moderate-to-severe or severe PR, and progressive RV dilatation are present, irrespective of the presence of overt symptoms (such as shortness of breath, clinical arrhythmia etc).21,25 Delaying surgery in such patients risks irreversible RV dysfunction. A combination of clinical signs (new onset tricuspid regurgitation murmur) with an enlarging cardiothoracic ratio, further QRS prolongation, echocardiographic RV dilatation, and/or increasing RV end-systolic volumes (exceeding normal CMR values) constitute reasons for elective PVR.

### Outcome after PVR

Most patients (even those who consider themselves asymptomatic) improve their functional class after PVR. There are conflicting reports, however, regarding recovery of RV function following PVR. When timely PVR is performed there is, almost universally, reduction of RV size and improvement of RV ejection fraction.21,25 In contrast, when PVR is performed late, RV recovery is incomplete.45 We submit that to preserve RV function, PVR in adults should be considered before RV dysfunction and overt symptoms of RV failure ensue.42 Although PVR per se reduces RV size and stabilizes QRS duration, thus reducing the risk of arrhythmia and SCD,37 additional concomitant ablative procedures, and particularly implantation of an intra-cardiac defibrillator, should be considered for patients at risk of sustained ventricular tachycardia, and SCD.21 Prospective data in this area are clearly required.
Long-term studies are essential to assess the impact of different treatment strategies on patient outcomes and quality of life. The management of PR requires a multidisciplinary approach, involving cardiologists, cardiac surgeons, and imaging specialists, to provide the best possible care.

### Percutaneous implantation of a pulmonary valve

Percutaneous pulmonary valve implantation (PPVI) has emerged in recent decades and has shown earlier treatment promise in PR compared to surgery before irreversible RV failure occurs [26]. PPVI can help to avoid the complications related to cardiopulmonary bypasses and sternotomies and has a favorable reduction in hospital stay and patient recovery time when compared to surgical PVR. Recent studies have demonstrated encouraging long-term results of PPVI in terms of infective endocarditis, the need for reintervention and overall survival [27]

### Recommended follow-up

As for other valvular regurgitation, the follow-up of patients with PR depends on the aetiology and the severity of PR, the size and function of the RV, and the associated diseases. Although infor- mation is limited, careful follow-up should be organized in patients with moderate-to-severe PR. 10

## Conclusion :

Pulmonary regurgitation, often overlooked in the past, deserves recognition as a significant entity in cardiovascular medicine. This comprehensive article has provided an in-depth exploration of the epidemiology, etiologies, diagnostic strategies, management options, and prognosis associated with PR. A thorough understanding of PR is crucial for healthcare providers to offer optimal care to affected individuals, ultimately improving their quality of life and long-term outcomes.

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# Rheumatic mitral regurgitation: Hope for a better journey of care

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**Résumé**

L'insuffisance mitrale rhumatismale représente l'atteinte valvulaire la plus fréquente du rhumatisme articulaire aigu. C'est donc l'une des pathologies les plus fréquemment rencontrées, qu'il s'agisse d'une indication primaire d'échocardiographie ou d'une découverte fortuite lors de l'examen d'autres maladies cardiovasculaires. Cependant, elle reste encore sous-diagnostiquée et insuffisamment traitée chez un grand nombre de patients. Etant une maladie des pays en voie de développement, l'insuffisance mitrale rhumatismale est l'une des maladies les plus négligées, et par conséquent, les progrès thérapeutiques restent limités depuis la dernière décennie.

**Mots clés :**

Rhumatisme articulaire aigu – L'insuffisance mitrale rhumatismale - Réparation valvulaire

**Summary**

Rheumatic mitral regurgitation is the most common valve abnormality in rheumatic heart disease, yet, still underdiagnosed and undertreated in a substantial number of patients. It is, therefore, one of the most common pathologies encountered by echocardiographers as both a primary indication for echocardiography and a secondary finding when investigating other cardiovascular diseases. However, being a disease of poverty, rheumatic mitral regurgitation is one of the most neglected diseases. Subsequently, there has been limited fundamental medical advances in this field for over the past decade.

**Keywords :**

Rheumatic heart disease – Rheumatic mitral regurgitation – Valve repair

## Introduction

Rheumatic heart disease (RHD) remains a serious global health problem, with an estimation of over 15 million cases worldwide (1). It is the leading cause of mitral valve (MV) disease in the developing world with a peak age of 25 to 35 years (2), resulting in mitral regurgitation (MR) in the early stages, and stenosis in later stages (3). Echocardiography is the key technique for the diagnosis of rheumatic MR (RMR) based on World Heart Federation echocardiographic criteria, the evaluation of the severity, and determination of the appropriate timing of intervention (4). Surgical MV repair and the advent of transcatheter MV technologies hold promise to treat RMR despite the complexity of the rheumatic MV, avoiding the mortality and morbidity associated with open heart surgery. However, most patients are seen at an advanced stage of the disease, where the use of these techniques remains limited.

### Pathophysiology :

RHD is a long-term sequela of acute rheumatic fever (ARF) (5), caused by an abnormal immune response to group A streptococcal infections, usually during childhood and adolescence (5).

Valvular involvement can manifest several years after the initial onset of ARF, affecting typically left-sided valves, with greater affinity and consequence for the mitral valve.
Progressive fibrosis can occur, resulting in rigidity and thickening of the leaflets as well as sub-valvular apparatus with chordal shortening, accompanied by varying degrees of calcification (3).


Figure 1:
(A) Atrial and (B) ventricular sides of mitral valves showing thick leaflets with retraction. (C) Mitral valve showing calcification.

The anterior leaflet assumes "dog-leg" or "hockey-stick" morphology, and the posterior leaflet is restricted most commonly having a Carpentier type 3a abnormality, resulting in malcoaptation of valve cusps. Immobility of the posterior leaflet is the hallmark of RMR which differentiates it from non-rheumatic mitral regurgitation on echocardiography.

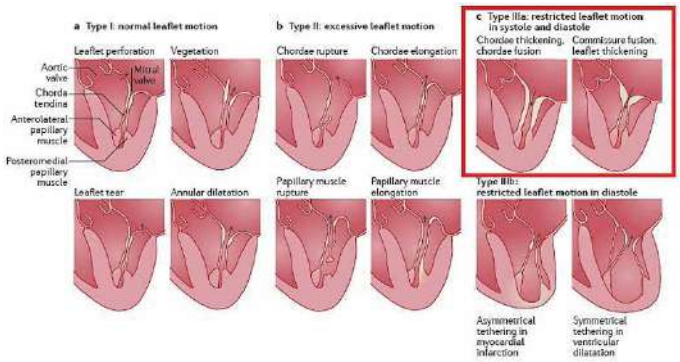



Figure 2 :
Carpentier classification of mitral valve regurgitation

**How is RMR diagnosed ?**

Echocardiography is the gold standard for the diagnosis of RMR. According to the World Heart Federation echocardiographic criteria released in 2012, diagnosis of RMR requires the presence of a pathologic MR and at least two morphological features of a rheumatic MV (4) :

**Pathological MR (all four criteria) :**

- Seen in at least two views
- Jet length ≥2 cm in at least one view
- Peak velocity ≥3 m/s for one complete envelope
- Pansystolic jet in at least one envelope

**Morphological features of a rheumatic MV :**

- Anterior mitral valve thickening ≥ 3 mm
- Chordal thickening
- Restricted leaflet motion
- Excessive leaflet tip motion during systole

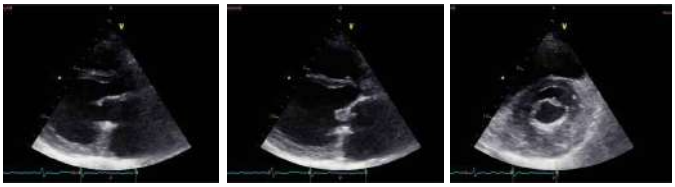


Figure 3:
TTE images from our department showing morphological features of RMR (A) Restricted posterior leaflet (B) Thickening of MV with malcoaptation of valve cusps (C) Thickening of the MV

**How to evaluate RMR ?**

2D transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) in the case of non diagnostic TTE, play a key role in the assessment of the severity of RMR and the hemodynamic effects on the cardiac chambers.

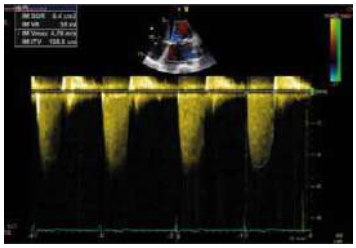
3D echocardiography (3DE) is particularly useful for investigating the regurgitant orifice or guiding surgical planning or interventional mitral procedures. Combined with color doppler, 3DE provides an accurate and reliable measurement of RMR severity and has been demonstrated to correlate well with cardiac magnetic resonance imaging (6).

Cardiac magnetic resonance (CMR) appears to be a better investigation than echocardiography for accurate assessment of MR severity, ventricular volumes and systolic function (7,8), however, no outcome studies are yet available that can be used to incorporate these measurements into clinical decision-making. Clinically, CMR should help to differentiate severe from non-severe MR in patients whose echocardiographic evaluation is not conclusive, particularly if contemplating surgery (8).

Exercise testing can be useful to unmask the objective occurrence of symptoms in asymptomatic patients and evaluate changes in mitral regurgitant volume and pulmonary pressures during peak exercise particularly in patients with discordant symptoms and regurgitation grade at rest (9). Moreover, in patients with advanced disease, stress testing might provide additional information on ventricular contractile (10).

**What is the severity of RMR ?**

The hemodynamic aspects of RMR follow the same principles of American Society of Echocardiography and the European Association recommendations on non-rheumatic mitral regurgitation (11,12).



| | MR severity* | | | |
|---|---|---|---|---|
| | Mild | Moderate | | Severe |
| Qualitative Doppler | | | | |
| Color flow jet area[9] | **Small, central, narrow, often brief** | Variable | | Large central jet (>50% of LA) or eccentric wall-impinging jet of variable size |
| Flow convergence[10] | **Not visible, transient or small** | Intermediate in size and duration | | **Large throughout systole** |
| CWD jet | Faint/partial/parabolic | Dense but partial or parabolic | | Holosystolic/dense/**triangular** |
| Semiquantitative | | | | |
| VCW (cm) | <0.3 | Intermediate | | ≥0.7 (>0.8 for biplane)[9] |
| Pulmonary vein flow[9] | **Systolic dominance** (may be blunted in LV dysfunction or AF) | Normal or systolic blunting[9] | | Minimal to no systolic flow/ **systolic flow reversal** |
| Mitral inflow[**] | **A-wave dominant** | Variable | | E-wave dominant (>1.2 m/sec) |
| Quantitative[11,12] | | | | |
| EROA, 2D PISA (cm$^2$) | <0.20 | 0.20-0.29 | 0.30-0.39 | ≥0.40 (may be lower in secondary MR with elliptical ROA) |
| RVol (mL) | <30 | 30-44 | 45-59[11] | ≥ 60 (may be lower in low flow conditions) |
| RF (%) | < 30 | 30-39 | 40-49 | ≥50 |

Figure 4 :
severity of MR based on 2D echocardiography

Additional findings of severe MR include left atrial enlargement, pulmonary hypertension, and left ventricular systolic dysfunction.

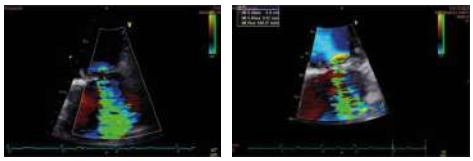


Figure 5:
TTE images from our department showing a severe RMR with Large central jet

**What is the hemodynamic consequences ?**

Once the diagnosis of RMR is made and its severity clarified, left ventricle (LV) and left atrial dimensions, LV systolic function and pulmonary artery pressures must be carefully evaluated.

Current recommendations for timing of intervention are based on these parameters evaluated by 2D echocardiography. Global longitudinal strain may become useful in evaluating earlier myocardial dysfunction in MR, although cut-off values are not uniform (13). Right heart catheterization is systematically used to confirm pulmonary hypertension diagnosed by echocardiography when this is the only criterion to refer the patient for surgery.

**Management :**

Indications for intervention are similar to those of non-rheumatic MR (14).

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Surgery is recommended in symptomatic patients who are operable and not high risk.[293–296] | I | B |
| Surgery is recommended in asymptomatic patients with LV dysfunction (LVESD ≥40 mm and/or LVEF ≤60%).[277,286,292] | I | B |
| Surgery should be considered in asymptomatic patients with preserved LV function (LVESD <40 mm and LVEF >60%) and AF secondary to mitral regurgitation or pulmonary hypertension[c] (SPAP at rest >50 mmHg).[285,289] | IIa | B |
| Surgical mitral valve repair should be considered in low-risk asymptomatic patients with LVEF >60%, LVESD <40 mm[d] and significant LA dilatation (volume index ≥60 mL/m$^2$ or diameter ≥55 mm) when performed in a Heart Valve Centre and a durable repair is likely.[285,288] | IIa | B |

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**Percutaneous interventions**

RMR is unlikely to be amenable to the transcatheter techniques used for non-rheumatic disease because of the presence of valve thickening, variable degrees of commissural fusion and subvalvular disease.

Transcatheter repair with the MitraClip system is now an established therapeutic option for non-rheumatic MR with anatomically suitable mitral valve (15,16). Anatomical exclusion criteria have included RMR because it is typically associated with mitral stenosis (MS). However, a recent case report demonstrated the possibility of RMR being treated with the MitraClip system in appropriately selected patients (17). Significant MS has to be excluded and the Heart team should carefully consider if the benefits of MR reduction is felt to significantly outweigh the risk of MS.

Percutaneous valve implantation holds promise, however, its application in young rheumatic patients appears less probable in the foreseeable future, due to the complexity of the MV apparatus, the noncircular saddle-shaped annulus and the excessive calcification to allow for secure device anchoring (18).

**Surgery**

Valve repair, if feasible, is preferred over valve replacement since repair avoids the risk of long-term anticoagulation associated with mechanical valves and the long-term risk of deterioration of a bioprosthesis (14).

Although traditional dogma holds that MV repair is very difficult in RMR and is associated with a high failure rate, because of valve deformity and mixed lesions, experienced operators have reported success for repair in up of 75% of cases of RMR (19–21). Additionally, data on comparative outcomes for MV repair versus replacement suggests that mortality rates with surgical MV repair are generally similar to or lower than those with MV replacement, but reoperation was more common after MV repair (22,23). Therfore, in RHD-endemic regions, the most important considerations may be the risk of needing reoperation given limited resources and the surgical team having more expertise in valve replacement than repair.

Mitral valve replacement is often required but there are important clinical considerations. Bioprosthetic valves tend to degenerate faster in younger than in old patients and outcomes with mechanical valve replacement are often adversely influenced by poorly managed postoperative anticoagulation. Thus, surgical decision-making for advanced RMR must take into account the individual, the geographic location, and the educational level of the patient, amongst other factors

**Medical management**

Medical management of moderate to severe RMR includes diuretic agents (loop diuretic agents and spironolactone) and afterload reduction with vasodilator therapy, most often angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. However, there is no evidence showing long-term benefits in terms of reduction of progression of valve regurgitation or need for surgery (24), and they do not have a recommendation from the American College of Cardiology (ACC) and American Heart Association (AHA) (16). In patients with overt heart failure, medical treatment as per current heart failure guidelines applies (25).

## Conclusion :

RMR remains a neglected cardiovascular disease which causes significant morbidity and mortality in low- and middle-income countries. In many rheumatic heart disease-endemic countries there is little or no access to life-saving heart valve surgery. Therefore, the main strategies for control of RHD is prevention, early recognition and intervention based on a tailored heart team approach due to the complexity of the disease.

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# Secondary Mitral Regurgitation : from acute to chronic conditions

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**Résumé**

L'insuffisance mitrale secondaire (IMS) survient en l'absence de maladie organique de la valve mitrale et résulte essentiellement d'une maladie du ventricule gauche, ou dans certains cas d'une maladie et dilatation auriculaire. C'est la forme d'insuffisance mitrale la plus courante et la moins traitée. L'IMS se développe chez environ 50 % des patients après un infarctus du myocarde (IM), accompagne l'insuffisance cardiaque (IC) chez environ un tiers jusqu'à 50 % des patients et est associé à un pronostic plus sombre, contribuant à la détérioration clinique, et à la progression du syndrome.
L'IMS est classé selon l'étiologie ; comme ischémique/non ischémique ou selon la présentation comme aiguë/ chronique, et selon la classification de Carpentier selon la morphologie et le mouvement des feuillets.
L'échocardiographie reste la principale modalité d'imagerie pour le diagnostic du l'IMS ; évaluation de la sévérité et le choix thérapeutique. L'IMS aigu, avec des signes d'œdème pulmonaire ou de choc cardiogénique, nécessite une action immédiate pour améliorer l'hémodynamique jusqu'à la réalisation d'une intervention définitive. La GDMT est la stratégie de traitement initiale du SMR chronique visant à traiter les symptômes de l'IC. Une sélection minutieuse des patients avec l'approche Heart Team jouera un rôle essentiel après l'évaluation individuelle du patient afin de sélectionner les meilleurs candidats pour un traitement particulier.

**Mots clés :**

Insuffisance mitrale secondaire, Valve mitrale, Insuffisance mitrale ischémique, Échocardiographie, Insuffisance cardiaque, Mitral clip.

**Summary**

Secondary mitral regurgitation (SMR) occurs in the absence of organic mitral valve disease and is essentially a result of left ventricle disease, or in rarer cases atrial disease and dilatation. It's the most common and undertreated form of mitral regurgitation. SMR is developed in about 50% of patients after myocardial infarction (MI), accompanies heart failure (HF) in about one-third up to 50% of patients and associated with poorer prognosis, contributing in clinical deterioration, progression of syndrome, and adverse outcomes.
SMR is classified according to etiology as ischemic / non-ischemic or according to presentation as acute /chronic, and by Carpentier classification describing leaflet morphology and motion.
Echocardiography remains the primary imaging modality for the diagnosis of SMR, assessing severity and orienting therapeutic management. Acute SMR, with evidence of pulmonary edema or cardiogenic shock, requires immediate action to improve hemodynamics until the emergent definitive intervention. Guideline-directed medical therapy (GDMT) is the initial treatment strategy, for chronic SMR with HF aimed at treating the HF symptoms. Careful patient selection with the Heart Team approach will play a critical role after individual evaluation of the patient in order to select the best candidates for a particular treatment.

**Keywords :**

Secondary mitral regurgitation, Mitral valve, Ischemic mitral regurgitation, Echocardiography, Heart failure, Mitral clip.

## Introduction

In contrast to primary mitral regurgitation, functional or secondary mitral regurgitation (SMR) occurs in the absence of organic MV disease and is essentially a result of LV disease due to ischemic vs. non ischemic etiologies, or in rarer cases atrial disease and dilatation (1).
Echocardiography is the gold standard imaging modality of assessing the mitral valve and determining the therapeutic approach by elaborating the underlying mechanism primary vs. secondary, assessing the severity, and choosing the best therapeutic option.

Management of this disease might be challenging, it starts with good evaluation in order to select the best candidates for a particular treatment, avoiding futility. It depends in many factors including the severity, hemodynamic consequences, valve anatomy, underlying etiology, patient comorbidities, and the experience of the heart team (2).

### Clinical and prognostic importance of SMR

Mitral regurgitation (MR) is the most common valve disease worldwide; this prevalence is expected to increase substantially over the next few decades as the population ages (3). SMR is the most common and undertreated form of MR (4).

Prior studies have shown that prevalence of chronic SMR is high and accompanies heart failure (HF) in about one-third up to 50% of patients and associated with poorer prognosis, contributing in clinical deterioration, progression of syndrome, and adverse outcomes (5) (6). Concerning ischemic mitral regurgitation (IMR) studies showed that SMR is developed in about 50% of patients after myocardial infarction (MI) (7) , with higher mortality rates ranging from 15–40% at 1 year after MI (8) (9).

Severe chronic SMR reported to be independently associated with a twofold increase in death and rehospitalization over a mean 3-year follow-up (9) .Acute IMR emerge at the early stage of MI, with the severity ranging from mild to severe valve disease. The incidence of severe form has been significantly decreasing after the advent of primary percutaneous coronary intervention, these patients have a poor long-term prognosis even after surgical correction (10) , a study done by Bursi et al. (11) reported that up to 50% of patients with acute MI had evidence of MR within 30 days after the ischemic event, almost 40% of patients had mild MR and 12% had either moderate or severe MR (11), ischemic papillary muscle rupture is a rare mechanical complication , It affects 0.07–0.26% of patients following MI,with an In- hospital mortality rate approaching 80% without and between 19% and 53% with surgical correction (12) .

Therefore, there has been much interest and effort to develop optimized methods for quantifying and classifying the severity of SMR, as well as developing effective therapeutic interventions to improve outcomes in patients with significant acute and chronic SMR.

## Pathophysiology of SMR

The mitral apparatus is a complex structure including the anterior and posterior mitral leaflets, mitral valve annulus, chordae tendineae, papillary muscles, the left atrium, and because of its potential effect on mitral valve function, the left ventricle (Figure:1).

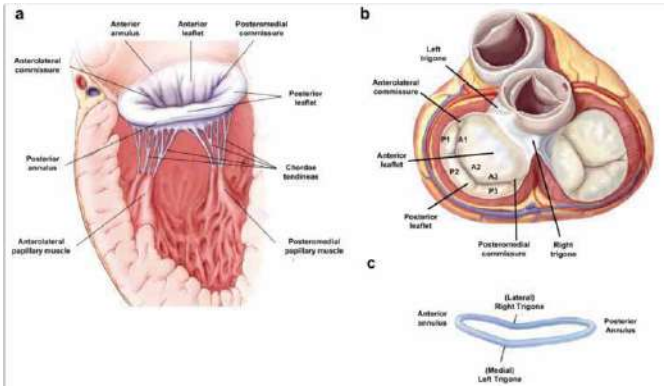


Figure 1:
Mitral valve anatomy in (a) long axis view and (b) short axis view.
(c) Schematic diagram showing the saddle-shape mitral annulus.
From Secondary Mitral Regurgitation: Cardiac Remodeling, Diagnosis, and Management DOI:10.1016/j.shj.2022.100129

SMR indicates a disease of the ventricle or atrium , it is classified according to etiology as ischemic / non-ischemic or according to presentation as acute /chronic , where the pathophysiology is quite different .This condition occurs as a result of morphological and functional changes to the MV, LV and/or LA , explaining its dynamic nature . These changes which impairs leaflet coaptation are due to complex relationship of LV or LA dilatation/dysfunction, abnormal valvular/subvalvular apparatus geometry, displacement /dysfunction of one or both PM, this complex relationship between these various factors explains the main mechanisms (Figure :2) of developing acute and chronic SMR which is further classified according to leaflet motion by Carpentier (13) .

## Ischemic causes of MR (IMR)

IMR is the most frequent etiology of regurgitation in SMR. According to clinical setting and installation it can be divided in two different entities:

## Acute IMR

Several pathogenic mechanisms and dynamics may lead to ischemic mitral regurgitation (MR) after an acute myocardial infarction (MI). These mechanisms include papillary muscle ischemia and changes in left ventricular (LV) geometry and function (14) . Ischemia to Papillary muscle may result in its dysfunction as well as partial/complete rupture in extreme cases , although papillary muscle rupture is considered by many authors as a primary valve disease (15) , here we integrated it as a secondary mitral regurgitation because of its pathophysiology and etiology resemblance to other forms of acute ischemic MR , this results in leaflet tethering or in rarer cases flail leaflet ,this rapid condition may cause hemodynamic instability due to acute mitral regurgitation, with subsequent pulmonary edema or cardiogenic shock, eventually resulting with poor short-term outcomes, the asymmetrical tethering with eccentric jet is occasionally associated with unilateral pulmonary edema (16).the posteromedial papillary muscle (PMPM) is more sensible to ischemia because it's blood supply which is limited to a single coronary artery, the posterior descending artery originating either from right coronary artery or from the LCx in left dominant Anterolateral papillary muscle (ALPM) receives blood supply from two major coronary branches, left anterior descending and left circumflex artery (LCx) (14).

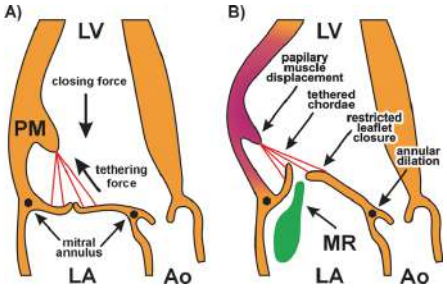


Figure 2 :
Mechanism of secondary mitral regurgitation.
(A) Balance of closing and tethering forces.
(B) Disrupted balance of closing and tethering forces due to LV remodeling. LA: left atrium; LV: left ventricle; PM: papillary muscle MR: mitral regurgitation .
from Cardiac Dyssynchrony as a Pathophysiologic Factor of Functional Mitral Regurgitation: Role of Cardiac Resynchronization Therapy byBarbara Brzezińska

### Chronic IMR

LV remodeling after MI results in PM displacement causing systolic tenting of the MV and this can occur even with normal left ventricular ejection fraction (LVEF) as ventricular remodeling with regional wall motion abnormalities can cause MV tethering and reduced closing forces leading to regurgitation (17).Type IIIb Carpentier which is systolic restricting of the leaflet is most common form of chronic IMR, Asymmetric mitral leaflets tethering is commonly seen with inferolateral MI and remodeling, alongside with kinesis or dyskinesia at the base of the LV causing a MR jet that is posterior directed , Symmetric pattern with larger tenting areas and a MR jet that is centrally directed is seen in greater LV eccentric remodeling due to large anterior or multiple infarcts and bi-leaflet apical tethering (18) . In addition, reduced closing forces can cause reduction in synchronicity between the two PMs, alter systolic annular contraction and decrease LV contractility which leads to a self-perpetuating physiology where resultant MR leads to further ventricular dilatation, leading to further PM displacement, annular enlargement and further regurgitation (18).

### Non ischemic causes of chronic SMR

Non-ischemic causes of SMR as in idiopathic dilated cardiomyopathy are characterized by global LV dysfunction and dilatation with increased sphericity and a centrally located regurgitant jet. Typically, non-ischemic SMR is characterized by LV dilatation, loss of mitral annulus contraction, mitral annular dilatation, and inadequate leaflet length (Carpentier type I), with resultant MV mal-coaptation (19).

### SMR of atrial origin

LA enlargement, with or without atrial fibrillation has recently been recognized as an important cause of SMR. It results in mitral annular dilatation and reduced leaflet coaptation causing MR even without LV systolic dysfunction. Both AF and heart failure with preserved ejection fraction (HFpEF) appear to be associated with its evolution (20).

## Clinical presentation

Patients with SMR have heterogeneous clinical presentation; In severe MR secondary to acute MI, patients are severely symptomatic, pulmonary edema, hypotension, and frank cardiogenic shock may develop, the physical examination will reflect the respiratory distress and evidence of poor systemic perfusion, such as tachycardia, cool extremities, and diaphoresis. However, the cardiac examination may not be always helpful because acute in acute MR systolic murmur is often difficult to hear or may be absent (21), while In chronic SMR the symptoms are related to LV dysfunction and patients often present with HF symptoms, but many are asymptomatic with MR detected incidentally on physical examination when holosystolic murmur is noticed, or in echocardiography (21) .
Initial evaluation of patients with SMR should include: History and physical examination to define functional, hemodynamics, volume status, and HF severity.

### Imaging evaluation of SMR
### Echocardiography

Transthoracic echocardiography (TTE) is the first-line imaging technique for the assessment of MR. Nevertheless, when further diagnostic refinement is needed or therapeutic procedure is considered; Trans esophageal echocardiography (TEE) plays an essential role to further characterize the severity of MR and provides essential morphological data to evaluate the reparability. The diagnostic accuracy of TEE may be further increased using 3-dimensional (3D) imaging, which improves the visualization of MV anatomy and morphology (22), this evaluation must be careful as it defines the best therapeutic approach, by answering the main three questions:

### When to think of SMR?

As we mentioned earlier in pathophysiology , the evaluation in SMR should be global ,this involves determination of the morphology features of the mitral apparatus (leaflets, annulus, subvalvular apparatus, and supporting myocardium) as well as their motion (Carpentier) classification , left atrium , left ventricle (Figure:3) .When both morphology and motion are combined, it is usually straightforward to determine the mechanism of MR is it primary, secondary, or mixed .Beside the normal valve morphology , the common findings In SMR are LV abnormalities ; either by global LV dilatation and dysfunction or by focal wall motion abnormalities with preserved global LV function (i.e., inferobasal akinesis or dyskinesis) which in turn causes systolic tethering of the leaflets into the LV (Figure :4) , This restrictive motion is more frequent in patients with previous inferolateral infarction , and results in the anterior leaflet coapting with the body of the posterior leaflet rather than the tip , creating mechanism of pseudo-prolapse that directs the jet in the direction of the lesion, in this case posteriorly (asymmetric pattern) and responsible for the famous « seagull sign » appearance of the valve (Figure :5) (23) . Reduced closing force on the leaflets, and global dilation are associated with more symmetric pattern of tethering and annular dilatation leading to central jet, this centrally directed jet is found as well in LA dilatation (24).

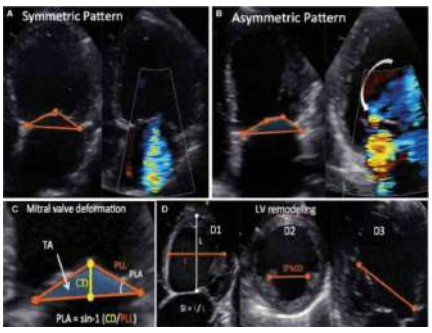


Figure 3 :
Assessment of mitral valvular deformation and global and regional left ventricular remodeling in patients with secondary mitral regurgitation. A, Symmetrical tenting pattern. B, Asymmetrical tenting pattern C, Measurements of the tenting area (TA), coaptation distance (CD), and posterolateral angle (PLA). D, Measurements of the sphericity index (D1), interpapillary muscle distance (IPMD; D2), and apical displacement of the posteromedial, papillary muscle (D3). PLL indicates posterior leaflet length; and SI, sphericity index.
From Lancellotti P et al. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2013 et 14(7):611–44

## Is it severe mitral regurgitation?

Over time Changes in guidelines have been done based on new data from randomized clinical trials (RCTs) or large registry studies supporting new recommendations or the up- or downgrading of existing recommendations. The currently published 2021 European Society of Cardiology (ESC)/ European Association of Cardio-Thoracic Surgery (EACTS) guidelines introduced several important new recommendations on SMR evaluation and management (25). Due to its dynamic nature, guidelines recommend an integrated approach to severity grading using qualitative and quantitative methods, of which effective regurgitant orifice area (EROA), regurgitant volume (RVol) and regurgitant fraction (RF) are the most established. The echocardiographic criteria to define severe SMR do not differ from those used in PMR (Table :1) .However, it should be acknowledged that when quantifying EROA and regurgitant volume in SMR, lower thresholds may be applied to define severe SMR , an EROA ≥30 mm2 by 2D proximal isovelocity surface area (PISA) likely corresponds to severe SMR (25) other measurements should always be done include right ventricular dimensions and function, concomitant tricuspid regurgitation, and pulmonary artery pressures in acute setting the presence of a flail leaflet, a ruptured papillary muscle or a large coaptation defect indicates severe MR (15)

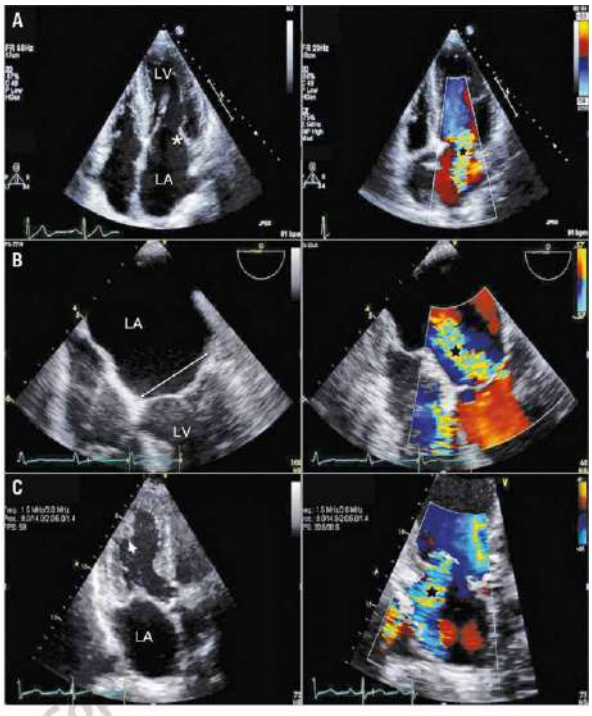


Figure 4 :
Echocardiographic mechanisms of secondary mitral regurgitation (MR) A) restricted motion of the posterior mitral leaflet (asterisk), and colour Doppler flow (right) in the same view demonstrating significant jet of MR (black star). B) Mitral annular dilatation (double-headed arrow) secondary to severe left atrial dilatation, and colour Doppler flow (right) in the same view demonstrating significant jet of MR (black star). C) apical tethering of mitral leaflets secondary to apical displacement of the posteromedial papillary muscle (arrowhead), and colour Doppler flow (right) in the same view demonstrating significant jet of MR (black star). LA: left atrium; LV: left ventricle .
from Long-Term Mortality in Patients with Severe Secondary Mitral Regurgitation and Normal Left Ventricular Ejection Fraction: Interventional Perspective by amr barakat

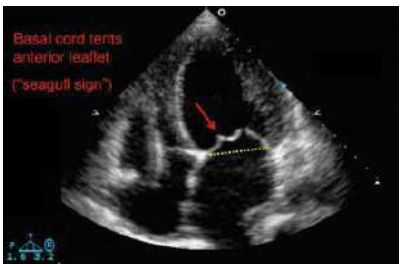


Figure 5 :
Apical 4 chamber view showing, Basal cord tents, Anterior and posterior leaflets, ("seagull sign"), with increased tenting area.
from Surgical Management of Ischemic Mitral Regurgitation by Mitesh V Badiwala

Table 1: Severe mitral regurgitation criteria based on 2D echocardiography. 2D = two-dimensional; ESD = end systolic diameter; EROA = effective regurgitant orifice area; LA = left atrium; PMR = primary mitral regurgitation; SMR = secondary mitral regurgitation; PISA = proximal isovelocity surface area; TVI = time-velocity integral.
From ESC 2021 guidelines

| Qualitative | Secondary mitral regurgitation |
|---|---|
| Mitral valve morphology | Normal leaflets but with severe tenting, poor leaflet coaptation |
| Colour flow jet area | Large central jet (>50% of LA) or eccentric wall impinging jet of variable size |
| Flow convergence | Large throughout systole |
| Continuous wave Doppler jet | Holosystolic/dense/triangular |
| Semiquantitative | |
| *Vena contracta* width (mm) | ≥7 (≥8 mm for biplane) |
| Pulmonary vein flow | Systolic flow reversal |
| Mitral inflow | E-wave dominant (>1.2 m/s) |
| TVI mitral/TVI aortic | >1.4 |
| Quantitative | |
| EROA (2D PISA, $mm^2$) | ≥40 $mm^2$ (may be ≥30 $mm^2$ if elliptical regurgitant orifice area) |
| Regurgitant volume (mL/beat) | ≥60 mL (may be ≥45 mL if low flow conditions) |
| Regurgitant fraction (%) | ≥50% |
| Structural | |
| Left ventricle | Dilated |
| Left atrium | Dilated |

## Is it eligible for percutaneous repair?

Preprocedural echocardiography may optimize patient selection for MitraClip therapy, by determining echocardiographic characteristics, including the presence of bicommissural MR, severe annular dilatation, and propionate MR which are predictive of suboptimal residual MR following TEER (26) .

## Cardiac magnetic resonance imaging (CMR)

MR can be quantified by CMR and it is used to predict outcomes in patients undergoing surgical MV intervention for IMR .also it provide superior assessment of the subvalvular mitral apparatus and tissue characterization of the myocardium, which can be an essential component of understanding the etiology of the underlying cardiomyopathy (27).

**Cardiac computed tomography (CT)**

Cardiac CT can also be used in evaluating MR and by providing accurate volumetric measures of chamber dimensions, and assessment of the MV and mitral annular geometry. It has an important role for pre-procedural planning for percutaneous MV replacement interventions to predict the risk of left ventricular outflow tract (LVOT) obstruction, which has been associated with increased procedural mortality (28).

**Other exploration tests**

• Electrocardiogram (to demonstrate baseline rhythm , repolarization abnormalities , and QRS duration)
• Laboratory measurements (haemoglobin, renal function, and natriuretic peptides …)
• Invasive or non-invasive coronary angiography

**Therapeutic considerations of acute and chronic SMR**

Management of patients with SMR presents a significant challenge and requires careful clinical and imaging assessment, addressing the anatomical and functional features of the mitral valve and left ventricle, and relevant comorbidities. It is better be done by the Heart Team after individual evaluation of the patient in order to select the best candidates for a particular treatment, here we discuss the most validated approaches in acute and chronic SMR conditions.

**Acute condition**
**Pharmacotherapies and Mechanical Circulatory Support**

Acute SMR, with evidence of pulmonary edema or cardiogenic shock, requires immediate action to improve hemodynamics until the emergent definitive intervention. Vasodilators, including sodium nitroprusside, are most frequently used and are beneficial in reducing afterload, but it may worsen hypotension, necessitating the use of vasopressors and or mechanical circulatory support (MCS). Vasopressors such as dopamine and dobutamine improves ventricular contractility, reduce systolic volumes and decrease regurgitant volumes, but their use may also lower blood pressure (29). levosimendan is also considered an effective in this clinical context. And reduced acute left ventricular deterioration (30) .However, pharmacotherapy in these patients presents a significant challenge as alterations in preload or inotropy may in fact worsen MR or pulmonary congestion.
In cases of acute cardiogenic shock, MCS has been described as a bridge to surgery. Intra-aortic balloon pump (IABP), the Impella device, Extra Corporeal Membrane Oxygenation (ECMO), aid in the stabilization, however, prompt surgical intervention remains the gold standard of care (31).

**Surgical Management**

Acute severe IMR is poorly tolerated, a surgical approach is necessary to prevent biventricular failure leading to multiorgan dysfunction. In a retrospective study analyzing the postoperative outcomes of emergent surgical intervention for acute MR by Lorusso et al, the overall 30-day mortality was 22.5% (32).

The timing of surgery is typically determined by the haemodynamic condition of the patient; with a reported median time to intervention (combined valvular and coronary artery bypass grafting) of 7 days (33) other studies suggest that an early intervention strategy was recommended to improve 30-day mortality rates (34).
Patients with severe acute IMR due to PM rupture require rapid mitral valve surgery, and the majority undergoing MV replacement. While mortality rates in patients undergoing surgical intervention for acute IMR remain high (35), there have been reports of mortality rates of 80% in the absence of intervention (36).
Mitral valve repair in the setting of acute IMR remains a challenging valve surgery; the most widely accepted technique for MV repair is ring annuloplasty. Sultan et al. (33)described successful mitral valve repair in 30% of patients.

**Percutaneous Management**

While surgical intervention is the gold standard of care for acute IMR , There are emerging data to support the use of Transcatheter MitraClip implantation in the setting of significant symptomatic MR with high surgical risk . A study of 44 patients with acute IMR who underwent Transcatheter MitraClip implantation after a median of 18 days after MI , 86.6% of patients had the MitraClip successfully implanted, with good haemodynamic improvement (37) , The 30-day survival was 90.9% and 81.8% at 6 months , While these data suggest that it is safe and feasible to treat IMR with MitraClip in these patients, further studies are warranted before definitive conclusions regarding its use in this high-risk clinical context.

**Chronic SMR**

Chronic SMR therapeutic options should be tailored accordingly the goal of secondary MR therapy is to alleviate symptoms, improve functional status, and reduce morbidity and mortality. To achieve this, one needs to address reversible causes of LV dysfunction and underlying heart failure as well as the MR. Pharmacological, surgical, device, and transcatheter treatment options (and criteria for their optimal use) are constantly evolving (Figure :6), (Figure :7).

**Medical therapy**

Optimal guideline directed medical therapy (GDMT) should be the first-line treatment for patients with chronic SMR, it is aimed at optimizing LV remodeling and management of heart failure(HF) .it should include replacement of ACEI or ARB with sacubitril/valsartan, sodium-glucose co-transporter 2 inhibitors and/or ivabradine, whenever indicated (25) .

**CRT**

cardiac resynchronization therapy (CRT) is a class I recommendation for patients in sinus rhythm with NYHA functional class II to IV symptoms on GDMT with LVEF ≤35%, left bundle branch block and QRS ≥150 ms . It has shown to be effective in treatment of MR. a study done by van Bommel et al., showed that CRT in these patients had significant reduction in MR measured by vena contracta width, EROA, tenting area, left atrial volume and jet area with superior survival after CRT (38)

**Coronary revascularization**

Although the merits of surgical revascularization in HF have been well investigated, there are only limited data demonstrating a lower incidence of cardiovascular adverse events compared with medical therapy in patients with SMR, following isolated CABG, MR may improve in about 50% of patients (39).

**Surgery**

Surgery options include MV replacement vs. MV repair by annuloplasty which aims to downsize the annulus diameter to its native geometry. The optimal surgical approach remains controversial. While MV repair is the preferred technique because it is associated with lower perioperative risk , recurrent MR is frequent outcome resulting in more HF symptoms and admissions.

Valve replacement should be considered in patients with echocardiographic risk factors for residual or recurrent mitral regurgitation as described by Lancellotti (40) ,which includes coaptation distance ≥1 cm ,tenting area .2.5–3 cm2 ,local LV remodelling with Interpapillary muscle distance >20 mm , global LV remodelling with EDD >65 mm, ESD >51 mm (ESV >140 mL) , and sphericity index >0 .7 , so the surgical approach has to be individually tailored to the patient.

Isolated surgery of severe SMR carries significant operative mortality, has high rates of recurrent mitral regurgitation, and lacks a proven survival benefit (41). Only patients undergoing coronary artery bypass grafting (CABG), or other indication of cardiac surgery with associated severe SMR have a strong indication to MV surgery (in particular patients with LVEF > 30%), In other cases, although severe SMR is associated to a worse prognosis, there is no conclusive evidence that surgery improves survival. Thus, indications for isolated surgery in SMR are particularly restrictive (25).

Moreover, in patients with moderate SMR who are scheduled to undergo CABG, indication for MV surgery remains controversial. The addition of mitral-valve repair did not significantly improve survival or reduce overall adverse events or readmissions and was associated to increased rate of perioperative complications (25).

In patients with atrial SMR, LVEF is usually normal, LV dilatation less pronounced and mitral annular dilatation represents the main mechanism of mitral regurgitation. This subgroup may be more effectively treated by ring annuloplasty often associated with ablation of AF but evidence is still limited (25) . Finally, patients with end-stage LV and/or RV failure and no option for revascularization may be better served by cardiac transplantation or LV assist device implantation. Valve intervention is generally not an option when LVEF is <15% (25) .

**Percutaneous therapy**

Percutaneous edge-to-edge repair for SMR is a low-risk option that may fulfill a major unmet need. Recently, two major (COAPT) and the MITRA-FR trials done to evaluate percutaneous repair with the MitraClip Device by assessing the survival benefit in patients with severe functional regurgitation have demonstrated conflicting results and have resulted in much debate and controversy, Therefore, TEER should be considered in selected patients with severe SMR fulfilling the COAPT inclusion criteria (25) . Despite reduced efficacy of this technique in reducing MR compared with surgery (42) , it can improve symptoms, functional capacity, and quality of life (43). Edge-to-edge MV repair with the MitraClip system is the most widely used device [33] with more than 70,000 procedures already performed worldwide (44).

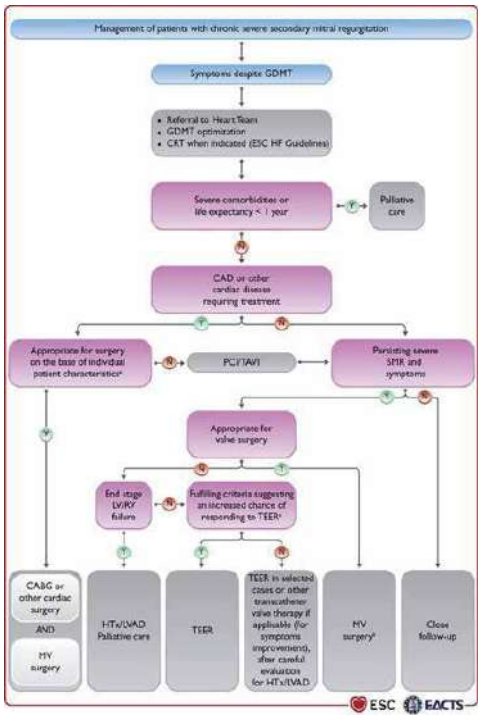


Figure 6 :
Management of patients with chronic severe secondary mitral regurgitation. CAD = coronary artery disease; CABG = coronary artery bypass grafting; CRT = cardiac resynchronization therapy; ESC = European Society of Cardiology; GDMT = guideline-directed medical therapy; HF = heart failure; HTx = heart transplantation; LVAD = left ventricular assist devices; LV = left ventricle/left ventricular; LVEF = left ventricular ejection fraction; MV = mitral valve; PCI = percutaneous coronary intervention; RV = right ventricle/right ventricular; SMR = secondary mitral regurgitation; TAVI = transcatheter aortic valve implantation; TEER: transcatheter edge-to-edge repair. aLVEF, predicted surgical risk, amount of myocardial viability, coronary anatomy/target vessels, type of concomitant procedure needed, TEER eligibility, likelihood of durable surgical repair, need of surgical mitral replacement, local expertise. bParticularly when concomitant tricuspid valve surgery is needed. cCOAPT criteria (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation).

**Decision Making and Importance of a Multidisciplinary Heart Team Approach**

Managing care for patients with complex cardiovascular disease has changed substantially over the last decade. Patients are older, have more complex cardiovascular disease, and have a greater number of comorbidities. The decision between treatment of MR (catheter-based or surgical), ventricular assist devices, heart transplantation, and continued conservative therapy should be made by the Heart Team after careful individual evaluation of the patient in order to select the best candidates for a particular treatment.

| Recommendations | Class[b] | Level[c] |
|---|---|---|
| Valve surgery/intervention is recommended only in patients with severe SMR who remain symptomatic despite GDMT (including CRT if indicated) and has to be decided by a structured collaborative Heart Team.[247,323,336,337] | I | B |
| **Patients with concomitant coronary artery or other cardiac disease requiring treatment** | | |
| Valve surgery is recommended in patients undergoing CABG or other cardiac surgery.[329,330,333] | I | B |
| In symptomatic patients, who are judged not appropriate for surgery by the Heart Team on the basis of their individual characteristics,[d] PCI (and/or TAVI) possibly followed by TEER (in case of persisting severe SMR) should be considered. | IIa | C |
| **Patients without concomitant coronary artery or other cardiac disease requiring treatment** | | |
| TEER should be considered in selected symptomatic patients, not eligible for surgery and fulfilling criteria suggesting an increased chance of responding to the treatment.[337,338,356,357] [e] | IIa | B |
| Valve surgery may be considered in symptomatic patients judged appropriate for surgery by the Heart Team. | IIb | C |
| In high-risk symptomatic patients not eligible for surgery and not fulfilling the criteria suggesting an increased chance of responding to TEER, the Heart Team may consider in selected cases a TEER procedure or other transcatheter valve therapy if applicable, after careful evaluation for ventricular assist device or heart transplant.[f] | IIb | C |

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Figure 7 :
Recommendations on indications for mitral valve intervention in chronic severe secondary mitral regurgitation , 2D = two-dimensional; CABG; coronary artery bypass grafting; CRT = cardiac resynchronization therapy; EROA = effective regurgitation orifice area; GDMT = guideline-directed medical therapy; LVEF = left ventricular ejection fraction; SMR = secondary mitral regurgitation; PCI = percutaneous coronary intervention; SMR = secondary mitral regurgitation; TAVI = transcatheter aortic valve implantation; TEER: transcatheter edge-to-edge repair.

## Conclusion

Although recent significant progress in understanding mechanisms, diagnosis and treatment of SMR has been made, this condition is still strongly associated with poor prognosis regardless of underlying etiology. Earlier revascularization in patients presented with acute MI is being key in the prevention of permanent and severe forms of MR. Echocardiography is the first-line imaging technique for the assessment of MR, however advanced imaging modalities are being increasingly utilized for improving assessment of degree of MR, as well as to delineate the etiology and the underlying cardiomyopathy. Acute severe SMR requires immediate action to improve hemodynamics until the emergent definitive intervention. GDMT is the initial treatment strategy in chronic SMR associated with HF. Other therapeutic options must be considered when appropriate include CRT, revascularization, mitral valve surgery and percutaneous interventions. Careful patient selection with the Heart Team approach will play a critical role after individual evaluation of the patient in order to select the best candidates for a particular treatment.

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# Tricuspid regurgitation: All new!

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**Résumé**

L'insuffisance tricuspide est une valvulopathie fréquente, associée à une morbi-mortalité importante, attribuée à la présentation tardive de la maladie, au faible recours aux solutions chirurgicales et à la mauvaise compréhension du processus pathologique. L'évaluation de la gravité de l'insuffisance tricuspide est une tâche difficile, et bien que l'échocardiographie soit l'examen de choix, l'imagerie par résonance magnétique cardiaque et par tomodensitométrie peuvent jouer un rôle important en tant que modalités d'imagerie complémentaires. Cependant, il n'existe pas de stratégie de prise en charge optimale actuellement, le traitement médical se limite aux diurétiques et la chirurgie de la valve tricuspide est rarement pratiquée et associée à des risques élevés. Par conséquent, une gamme de thérapies transcathéter est apparue, affichant des résultats initiaux prometteurs mais rencontrant plusieurs défis.

**Mots clés :**

Insuffisance tricuspide , Échocardiographie , Chirurgie, Thérapie transcathéter

**Summary**

Tricuspid regurgitation (TR) is a common valvular pathology and is associated with significant morbidity and mortality, attributed to the late presentation of the disease, the low use of surgical solutions and the misunderstanding of the disease process. Assessing the severity of tricuspid regurgitation is a challenging task, and although echocardiography is the test of choice, Cardiac magnetic resonance imaging and computed tomography angiography may play significant roles as adjunctive imaging modalities, However, there is no currently defined optimal management strategy; medical therapy is limited to diuretics, and tricuspid valve surgery is rarely performed and associated with high risks. Consequently, a range of transcatheter therapies has emerged, displaying promising initial outcomes but encountering several challenges.

**Keywords :**

Tricuspid regurgitation (TR), Trans-thoracic echocardiography (TTE), Surgery, Transcatheter therapy

## Introduction

Tricuspid regurgitation is frequently diagnosed in the general population, it has been regarded for years to be a surrogate of LV and RV dysfunction and pulmonary hypertension. Recently, the attention has turned to the clinical and prognostic implications of severe TR. While the most functional TR's cause found is attributable to left-sided heart pathology, organic etiologies of TR (such as rheumatic valvular heart disease) are less frequent.

### Anatomy and physiology :

The tricuspid valve (TV), has some features, it is situated at the highest point among the four cardiac valves, holds the distinction of being the largest and it normally maintains a regular orifice area ranging from 7 to 9 $cm^2$. Because of its significant dimensions and the minor pressure gradient between the right atrium (RA) and the right ventricle (RV), the maximum velocities during tricuspid valve diastole usually stay below 1 m/s. correspondingly, the average gradients remain below 2 mm Hg (1).

The TV is made up of four elements: the leaflets, the papillary muscles, the chordal attachments, and the annulus (with attached atrium and ventricle) (2,3,4). Due to the relationship between the leaflets on the one hand and the chordae and papillary muscle on the other hand, the tricuspid valve plays a major role not only in ensuring the closure of the tricuspid valve during systole but also in its potential connection to the size and in functioning of the right ventricle (RV).

**• TRICUSPID VALVE LEAFLETS :**

The TV consists of 3 leaflets (typically thinner than those of the mitral valve) made of different size, anatomical variations are not rare, 2 (bicuspid) or more than 3 leaflets may exist as anatomic variants in healthy subjects (1,5). These leaflets are called the septal, anterior, and posterior leaflets, respectively.

- The anterior leaflet is the most mobile, commonly the largest and the longest in the radial direction, with the larger area.
- The posterior leaflet may have several scallops and is the shortest circumferentially. It may not be clearly individualized from the anterior leaflet in approximately 10% of patients.
- The septal leaflet is the shortest in the radial direction with the slightest movement. It is linked to the tricuspid annulus directly above the interventricular septum (7), with many third-order chordae that may be related directly to the septum (1,2,3); it is inserted into the septum 10 mm apically to the septal insertion of the anterior mitral leaflet (i.e., apically displaced) (6).

The coaptation of the TV normally takes place at the level of the annulus or just below it, with a coaptation length of 5 to 10 mm (8).

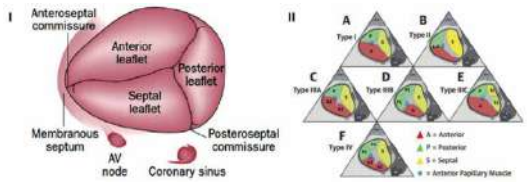



Figure 1:
(I) Anatomy of the normal tricuspid valve showing orientation of the leaflets and surrounding structures
(II) Classification of anatomic varieties of the tricuspid leaflets (3,5)

**• TRICUSPID VALVE TENSOR APPARATUS (papillary muscles and chordae) :**

The chordae support the tricuspid-valve leaflets and are connected to a major anterior papillary muscle along the lateral wall of the midright ventricle, besides one or more smaller posterior papillary muscles (9).

The anterior papillary muscle affords chordae to the anterior and posterior, while the posterior papillary muscles provide chordae to the posterior leaflet (or leaflets) and the posterior segment of the septal leaflet. The tricuspid valve is also characterized by unique chordal attachments born from small septal papillary muscles or from the septum directly, supporting thus the anterior segment of the septal leaflet and the adjacent segments of the anterior or posterior leaflet (8,10).

As a consequence of the intricate chordal arcades and their attachment sites, the tricuspid valve changes proportionally to the free wall's function and position of the right ventricle, as well as the interventricular septum (9).

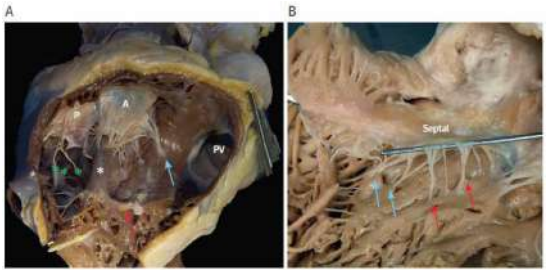



Figure 2 :
(A) Typical papillary muscle distribution for the tricuspid valve. The anterior papillary muscle is typically the largest (white asterisk), which provides chordal support for the A and P leaflets. The moderator band (orange arrows) may join this papillary muscle. The posterior papillary muscle is often bifid or trifid (green asterisks) and lends chordal support to the posterior and septal leaflets. The septal papillary muscle is variable (blue arrow). (B) Septal leaflet chordal attachments to the septal papillary muscle are shown (blue arrows) and directly from the septal myocardium (orange arrows).

**• TRICUSPID VALVE ANNULUS :**

The normal annulus has a saddle-shaped form with 2 different segments, a C-shaped segment which is larger and corresponds to the free wall of the RA and the RV, and a relatively straight segment which is shorter, refers to the septal leaflet and the ventricular septum. Moreover, it is a dynamic structure, expanding during early diastole and atrial systole to accommodate large flow volumes under low pressure.

Normal tricuspid annular circumferences and areas in healthy subjects are estimated at 12 +/- 1 cm and 11+/- 2 $cm^2$ in healthy subjects, respectively, as objectified by 3D echocardiography (5,3,12)

Healthy subjects have a nonplanar and non–single-plane structure of the TA with homogeneous contraction (6). The tricuspid annulus dilates to the lateral and posterior free wall and takes a shape which is more planar and spherical in secondary TR (9). Dilation of the septal segment is restricted because of its anatomic relation with the fibrous skeleton of the heart (10).

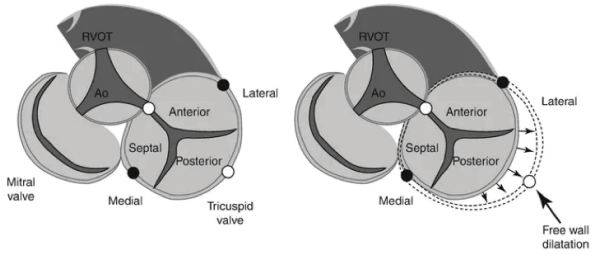



Figure 3 :
tricuspid annulus configuration seen from the right atrium in normal situation and after dilation (6)

**• ADJACENT ANATOMY :**

Adjacent to the annulus, the right coronary artery and the atrioventricular node keep a significant anatomical importance in surgical or transcatheter interventions. The right coronary artery is situated within the atrioventricular groove, running almost all along the extension of the anterior and posterior annulus. As it becomes tighter to less than 3 mm inferiorly, there is a possible risk of injury when devices that anchor in the annulus seem to be used. Furthermore, the atrioventricular node and the bundle of His cross the septal leaflet attachment approximately 3 to 5 mm from the anteroseptal commissure. Atrioventricular blocks can occur as a result of injuries to the node (13,14,15).

The noncoronary sinus of Valsalva is close to the commissure between the anterior and septal leaflets. Transcatheter devices using anchor in this particular region can lead to aortic perforation (13).

The superior and inferior vena cavae are other considerable structures related to the TV anatomy when it comes to transcatheter intervention for TV. They stand for the ultimate access for the transcatheter approaches to the TV and may represent, in some situations, a landing zone or the site of the implanted device (16).

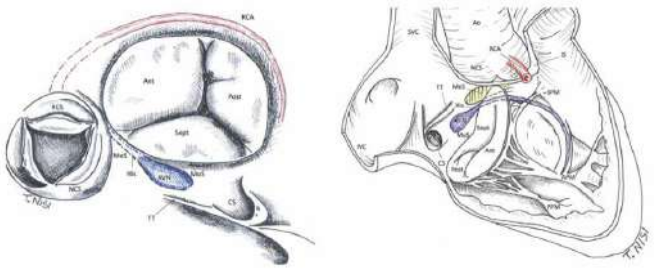


Figure 4 :
Schematic representation of the RA, tricuspid valve and RV. Ant, anterior leaflet; Ao, aorta; APM, anterior papillary muscles; AVN, AV node; CS, coronary sinus ostium; His, bundle of His; IS, infundibular septum; IVC, inferior vena cava; MeS, septum membranosum; MuS, muscular portion of the AV septum; NCS, noncoronary sinus of the aorta; Post, posterior leaflet; PPM, posterior papillary muscle; Sept, septal leaflet; SPM, septal papillary muscle; SVC, superior vena cava; TT, tendon of Todaro (9).

## Clinical presentation :

In mild-to-moderate isolated TR, symptoms are not commonly observed. But in advanced right heart failure's cases, there are several signs and symptoms of chronic right heart failure that may appear in patients, including systemic fluid retention, causing peripheral edema, ascites, and anasarca; decreased cardiac reserve, resulting in dyspnea, and poor functional capacity;

The signs and symptoms of reduced cardiac output and left heart failure may be intricate and therefore a delayed diagnosis of tricuspid regurgitation. Although many signs of severe tricuspid regurgitation may be responsive to diuretics in the beginning, the cardiac output when becoming decreased associated to the accompanying neurohormonal alterations can lead to rise to liver disease (known as the cardiohepatic syndrome) and kidney disease (recognized as the cardiorenal syndrome). The cardiohepatic syndrome majors the risk of bleeding in patients with tricuspid regurgitation and represents by its own a strong independent predictor of death or hospitalization for heart failure within 1 year (18)

In physical examination, a holosystolic murmur typical of TR is usually found, it is high pitched loudest in the fourth intercostal space in the parasternal region. The murmur is often increased during inspiration and decreased in intensity and duration not only in the standing position but during a Valsalva maneuver as well. When present, echocardiographic assessment is required. (19,20)

Atrial arrhythmias (particularly, atrial fibrillation) are frequent in patients with tricuspid regurgitation and appears in both incident and progressive valvular disease. (20) Atrial fibrillation on the one hand, left plus right atrial dilatation, annular dilatation, as well as atrioventricular valvular regurgitation on the other hand, have been associated, (21) furthermore rhythm control and a reduction in tricuspid regurgitation are associated. (22,23)

## Epidemiology :

Tricuspid regurgitation (TR) is often found incidentally on routine echocardiography when performed in patients suffering from left-sided heart disease. As a mild degree is generally considered as a benign physiological entity, moderate and severe TR are associated with worse outcome.

In terms of prevalence, as it is the case with other valvular heart diseases, the tricuspid regurgitation's prevalence is proportionally related to age (24-20). Clinically significant valvular disease is diagnosed more frequently in men than it is in women, (26), nevertheless the overall prevalence of clinically significant is about four times higher in women (27). The basis for these differences is still unknown, but the higher female prevalence of heart failure with a preserved ejection fraction (28) and atrial fibrillation (29) seem to be a good reason partly. It has been also shown that female sex is an independent predictor of tricuspid regurgitation's severity and progression. (24,29,30)

In addition to older age, female sex, and atrial fibrillation, there are other clinical predictors of severe and progressive tricuspid regurgitation including elevated pulmonary artery systolic pressure and increased left atrial size, suggesting thus that not only pre- but also postcapillary pulmonary hypertension as well participate to this process (32).

It had been clearly shown by the latest and the largest evaluation including 33305 patients, that the presence of any degree of TR is collaborated with adverse clinical outcome. At least moderate TR is an independent factor associated with augmented mortality (figure 5) (34).

Because of lack of Morrocan valvulopathy registry, Ethiopia, another developing country on the same continent, has a register collecting 3287 cases along 22years from 2000 to 2022, showing that the Tricuspid regurgitation's prevalence is 4.1%, without any difference between genders, moreover the moderate to severe form accounted for 60% of TR, with 1.22% of cases (>) with rheumatic etiology coming after 2.3% cases of predominant congenital etiology (35).

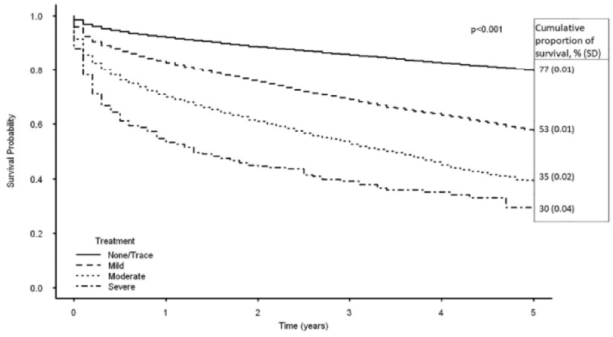
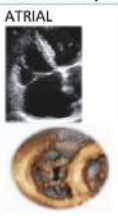
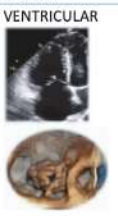



Figure 5 :
Curve showing the relationship between the importance of TR and the observed mortality rate (20)

## Causes and classification :

The current classification scheme has not just replaced the old tricuspid regurgitation's subdivision considering primary and secondary (nonleaflet) disorders, but has also allowed to reflect a clear understanding of different TR's mechanisms (36,38) and their associated outcomes. (38,39)
While the atrial and ventricular secondary regurgitation are the subdivision of the secondary tricuspid regurgitation, we distinct TR associated with a lead from a cardiac implantable electronic device, which is separated from primary etiologies (Table 1)

Table 1: Classification of tricuspid regurgitation (35).

| | FUNCTIONAL/SECONDARY | | CIED-RELATED | ORGANIC / PRIMARY | |
|---|---|---|---|---|---|
| | ATRIAL  | VENTRICULAR  |  |  | |
| **Parameter** | **Atrial FTR** | **Ventricular FTR** | **CIED-Related** | **Primary TR** | |
| | | | | **Prolapse(I)** | **RHD (IIA)** |
| **Leaflet Tethering** | - | +++ | ++ | - | - |
| **Leaflet Restriction** | - | Systole | Systole/ Diastole | - | Diastole |
| **RA/TA Dilatation** | +++ | ++ | +/- | ++ | ++ |
| **RV Dilatation** | +/- | +++ | +/- | +/- | +/- |
| **RV Dysfunction** | +/- | +++ | +/- | +/- | +/- |

### 1. Primary tricuspid regurgitation :

Primary tricuspid regurgitation is the result of intrinsic valve disease, which can be following an abnormality of any of the components of the TV apparatus (tricuspid leaflets, chordae, papillary muscles, or annulus), because of congenital or acquired etiologies (Table 2). Ebstein's disease is the most common congenital cause of the TR and it is marked by an apical displacement of the leaflets originating directly from RV's wall without individualised chordae (40). The Acquired etiologies of primary TR are represented by rheumatic disease, endocarditis, tumors (such as carcinoid disease), iatrogenic injury (such as RV endomyocardial biopsy, transvenous pacing, or defibrillator leads), drug-induced leaflet damage (such as anorectic drugs, dopamine agonists, and ergot alkaloids) (41), systemic diseases (such as lupus erythematosus and sarcoidosis), radiation as well as trauma (42).

Table 2 : etiologies of primary tricuspid regurgitation (35)

| Classification | Etiologies |
|---|---|
| **Degenerative Disease** | • Prolapse<br>• Flail |
| **Congenital** | • Ebstein's Anomaly<br>• Leaflets clefts |
| **Acquired** | • Rheumatic disease (usually with left-side disease)<br>• Infective endocarditis<br>• Endomyocardial fibrosis<br>• Carcinoid disease, serotonin active drugs<br>• Traumatic (blunt chest injury, laceration)<br>• Iatrogenic<br>  ○ Right ventricular biopsy<br>  ○ Drugs (e.g. exposure to fenfuramine-phentermine, or methsergide)<br>  ○ Radiation therapy of the mediastinum |

### 2. Secondary tricuspid regurgitation :

Although the intrinsic structure of the leaflets may appear normal in patients with secondary tricuspid regurgitation, there can still be abnormalities concerning right atrium, tricuspid annulus, or right ventricle that result in leaflet malcoaptation.
Functional TR (FTR) mechanisms are not the same in atrial FTR and ventricular FTR regardless of similar ERO (valve lesion) with specific valvular-ventricular complex alterations. Atrial FTR principal valvular mechanism is depletion of annular coverage reserve, normally insured by tricuspid leaflets owing to scarred annular enlargement, however valvular tenting plays no or minimal role. Ventricular FTR main mechanism is valvular tethering with tenting on top of the annular level, decreasing coaptation, nevertheless annular enlargement remains modest (figure 6). (54)

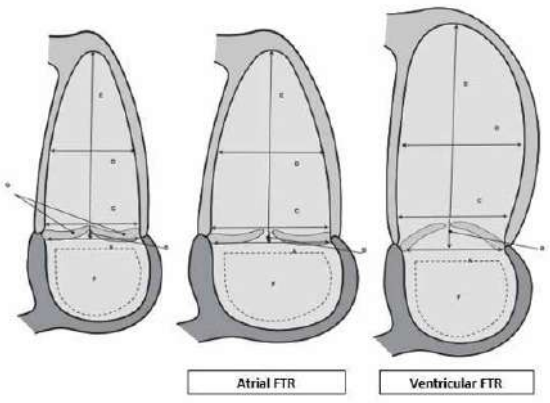



Figure 6 :
Diagram of atrial and ventricular RT mechanisms (50)

- Atrial secondary TR which is a diagnosis of exclusion, can't just be defined by the missed abnormality of any leaflet, left ventricular (LV) dysfunction (ejection fraction <60%), left-sided valve disease, pulmonary hypertension (pulmonary artery systolic pressure >50mmHg) or CIED, but also backed up by the clinical history of the patient with evidence of longstanding or permanent atrial fibrillation (55).
- Ventricular secondary TR is predominantly seen in the context of elevated pulmonary artery pressures appearing as a result of precapillary or postcapillary pulmonary hypertension. It may also be due to right ventricular remodeling, caused by primary cardiomyopathies with right ventricular involvement, as right ventricular ischemia, infarction or arrhythmias. (21) additionally, left ventricular dilation, dysfunction, or concomitant left-side valvular disease may be observed, participating to septal abnormalities that may affect septal leaflet tethering and coaptation.

The new classification of TR separating the atrial from the ventricular form of secondary TR regains its interest in prognostic and treatment implications. (60,61,62) Atrial secondary TR has a fast progression of severity and poor outcome, and secondary RV dilation and/or dysfunction frequently appears in advanced stages.

Table 3 : etiologies of secondary tricuspid regurgitation (35)

| Classification | Etiologies |
|---|---|
| **Ventricular secondary TR** | • Left heart diseases (left ventricular dysfunction or left heart valve diseases) resulting in pulmonary hypertension<br>• Primary pulmonary hypertension<br>• Secondary pulmonary hypertension (e.g. Chronic lung disease, pulmonary thromboembolism, left-to-right shunt)<br>• Right ventricular dysfunction from any cause (e.g. myocardial diseases, ischemic heart disease, chronic right ventricular pacing) |
| **Atrial secondary TR** | • Atrial fibrilation<br>• Heart failure with preserved ejection fraction |

### 3. Tricuspid Regurgitation Associated with an Implantable Electronic Device:

Patients with permanent pacemakers who have TR may be approximately estimated at 25-29% (64). But, the pathophysiological relation between the presence of the device leads on the one hand and either the onset of significant TR or the worsening of a pre-existing disease on the other hand is a relatively recent clinical challenge.

Considering the classification of CIED-induced TR as its own category, primary and secondary disease may be the subdivision of patients with TR and a CIED. Primary CIED-induced TR can be defined as a rise of TR severity of more than 2 grades during follow-up after CIED implantation in patients with documented interference of the device lead with the TV apparatus.

Echocardiography as well as postmortem examinations of hearts with CIED, have objectified that the device leads can interfere with the TV apparatus in different ways; Impinging upon a leaflet, sticking to a leaflet, interfering with the s ubvalvular apparatus, perforating or lacerating a leaflet, avulsion of a leaflet which may be seen during lead extraction, and transection of papillary muscles, or chordae tendinea. (65)

Secondary CIED-induced TR is the result of the remodeling of the TV coming after the RV dilatation due to pacing or heart failure. Among the secondary CIED-induced TR's predictors, permanent atrial fibrillation and previous open-heart surgery, (68) in addition to as a pre-existing RV dilation (69) have been reported.

## Diagnosis :

In order to identify the cause, morphologic characteristics, and severity of tricuspid regurgitation, Echocardiography represents the main imaging technique, nevertheless cardiac magnetic resonance imaging (MRI) and cardiac CT still have expanding roles, in a particular way for patients for whom transcatheter therapies are envisaged. (figure 7) (37)

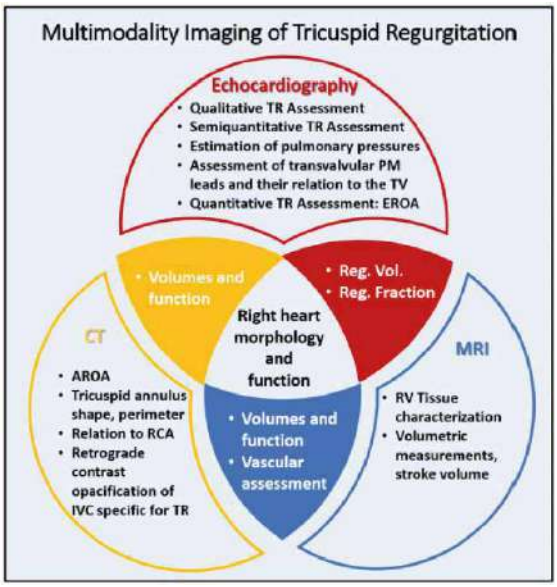



Figure 7 :
The complementarity of different imaging methods in assessing the severity of tricuspid regurgitation (60)

### 1. Echocardiographic methods:

While Echocardiography remains the gold standard for evaluating the TR's severity and mechanism, transthoracic echocardiography (TTE) is used for the initial diagnosis (75,76); somehow transoesophageal echocardiography may be a must in some cases including poor-quality TTE, endocarditis, as well as pacemaker lead infection. Moreover, 3D echocardiography provides the visualization of all leaflets at the same time. (77)

Qualitative, semiquantitative and quantitative methods should be the basis to grade severity according to the guidelines (78,79,3,81)

Since TR changes accordingly to both pre-load and afterload, respirophasic and loading conditions variabilities will introduce significant changes in TR severity. It is required that the patient has to be in a euvolaemic state, with measurements performed along quiet respirations, and 5–10 beats averaged when the rhythm is not regular.

**• Qualitative methods :**

Assessment of tricuspid valve morphology, color flow TR jet and continuous wave Doppler spectral signal in addition to leaflet mobility are the qualitative parameters. A motion's excess of one of the leaflets may refer to a traumatic chorda rupture, however when it is the case of redundant tissue, it may also point to the presence of myxomatous valve disease. Given that a combination of thickened and limited motion of the leaflets may be due to carcinoid syndrome or rheumatic disease, the presence of mobile masses attached to the leaflet surface may refer to tricuspid valve endocarditis, as noticed in intravenous drug use.
In functional TR, the progression of dilatation of the tricuspid valve annulus and RV is associated with severe tethering and restrictive motion of morphologically normal leaflets. Exact leaflet identification by 2D echocardiography mostly indicates different imaging windows (parasternal, apical and subcostal) and remains difficult, since simultaneous visualisation of all three tricuspid leaflets is not possible in an only single plane. While the RV and tricuspid valve are placed anteriorly in the chest, three-dimensional (3D) echocardiography allows better identification of the three leaflets than 2D echocardiography because of a biplane view or an en face view from the atrial or ventricular side provided by 3D echocardiography.
In lead-induced TR, 3D echocardiography has not just permit indentifying the position where impingement of a leaflet appears but also be using it for further safe positioning of the RV pacing lead (82).
In terms of Qualitative Doppler parameters, there are the colour flow jet characteristics (area and eccentricity), flow convergence zone, as well as continuous wave Doppler jet density. The size of the TR colour jet by colour Doppler echocardiography on a one hand and the right atrial area assessed with colour Doppler echocardiography on the other hand are related to a high ratio which may refer to severe TR's existence. But, in case of eccentric regurgitant jets, colour Doppler may severely underestimate the severity of TR (Coanda effect) and consequently should not be used solely for TR severity's estimation. The presence of a dense, triangular signal with early systolic peaking on continuous wave Doppler recordings points to a severe TR. Yet, in massive TR, the peak velocity of the regurgitant jet may be conversely low as a result of chronically elevated right atrial filling pressures.
It should thus be highlighted that colour flow imaging should only diagnose the presence of TR and a more quantitative approach is indicated when more than a small central TR jet is found. (83,84,85)

**• Semi-quantitative methods :**

The assessment of vena contracta width, proximal isovelocity surface area (PISA) radius as well as tricuspid valve inflow and hepatic vein flow permit deriving semi-quantitative parameters. The vena contracta width is measured in the middle systole at the tightest part of the jet in the apical four-chamber view, reflecting thus the highest regurgitant velocity. A severe TR is defined by a vena contracta width >7 mm;

But a complex jet shape can be seen because of the variable num of leaflets and commisures, therefore any assessment depending on a single linear measurement might not describe precisely the complex jet. Typically, the VC is measured from the apical 4-chamber view. Somehow, this septo-lateral dimension is commonly the minor dimension of an elliptical orifice. The use of the average VC from the parasternal inflow view and the apical 4-chamber view using a cut-off of 9mm to discriminate moderate from severe have been required by some authors. (86, 59)
When adapting the Aliasing velocity to ±30 cm/sec, the PISA method can be used in the four-chamber view by measuring the distance from the vena contracta to the first convergence velocity in mid systole, with a PISA radius >9 mm suggestive of severe TR.
Other semi-quantitative parameters are taken from pulsed-wave Doppler recordings, with a peak velocity of the early diastolic tricuspid inflow (E-velocity) ≥1 m/sec and a systolic reversal of the hepatic vein flow representative a severe TR.

**• Quantitative methods :**

Quantitative measurements of TR severity refer to the effective regurgitant orifice area (EROA), regurgitant volume (RegVol), and regurgitant fraction (RegFr). These measurements may permit physicians to adjust finer risk stratification (86, 59) and afford supplementary information for interventions. (88)

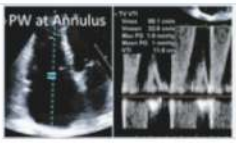
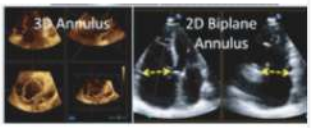
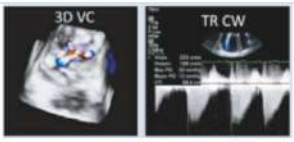
**PISA method :**

The main quantitative method required is the proximal isovelocity surface area (PISA). In order to calculate it, color Doppler baseline is positioned in the direction of the regurgitant flow, the aliasing velocity (VAlias) and PISA radius (r) can be useful in calculating flow ($2r^2$ VAlias). The division of the PISA flow by the peak TR velocity (VTR) quantifies EROA. Additionally, RegVol is calculated by multiplying the TR velocity time integral (TRVTI) by EROA.
It has been demonstrated that cut-offs of an EROA ≥40 mm2 or an RVol ≥45 mL carry prognostic importance in patients with isolated TR (59)
When these measurements are singly used, they will not permit the RegFr's calculation since the total stroke volume is not measured. But when 3DE RV stroke volume used, RegFr can not only be measured but has also prognostic importance. (89)

**3D colour Doppler quantification :**

Different studies have objectified the feasibility of 3D colour Doppler planimetry of the VC area (VCA) by both TTE73 and TOE. (59) Studies indicate the quantitative cut-offs for severe TR are: 3D-VCA 0.60–0.61 cm2, (85, 86) Doppler-EROA 0.65 cm2, and PISA-EROA 0.34 cm2. (89) The 3D-VCA method is correlated with quantitative Doppler method ($r = 0.92$; $P < 0.0001$).

Table 4 : Quantitative methods for echocardiographic assessment of the tricuspid regurgitation

| Quantitation method | Measurments required | Example | Calculation |
|---|---|---|---|
| **PISA** | 1. PISA radius (r)<br>2. PISA aliasing velocity (v) (approximatively 28 cm/s)<br>3. TR peak velocity ($V_0$)<br>4. TR peak velocity time integral ($TR_{VTI}$) |  | - $Q = 2\pi r^2 v$<br>- $ROA = Q/V_0$<br>- Reg Vol = ROA * $TR_{VTI}$ |
| **Quantitive Doppler** | 1. TV velocity time itegral ($TV_{VTI}$)<br>• PW Doppler sample volume at the annulus<br>1. Diastolic TV $_{annulus}$ Area<br>• 3D annular area OR<br>• Biplane annular area |  <br>  | - Diastolic Stroke Volume = TV $_{annulus}$ Area * $TV_{VTI}$<br>- Reg Vol = Diastolic Stroke volume – Forward Stroke Volume<br>- ROA = Reg Vol + $TR_{VTI}$<br>Note : Forward stroke volume may be either the left ventricular or right ventricular stroke volume |
| **3D Color Doppler** | 1. 3D Color Doppler planimetred vena contracta area (VC,....)<br>2. TR velocity time integral ($TR_{VTI}$) |  | - $ROA = Vc_{area}$<br>- Reg Vol = $VC_{area}$ * $TR_{VTI}$ |

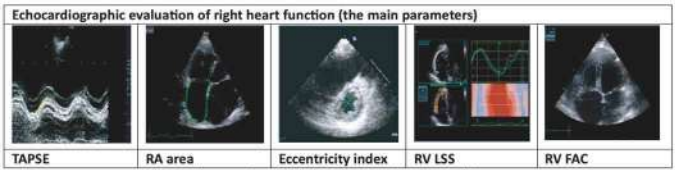
Abbreviations: PISA=proximal isovelocity surface area, TR= Tricuspid regurgitation, Q= Flow, ROA= regurgitant orifice area, TV= tricuspid valve, PW= pulsed wave, 3D= three dimensional, Reg Vol= regurgitant volume, VC= vena contracta

**• Right heart evaluation :**

Every echocardiographic assessment for TR severity should include the evaluation of haemodynamic impact's parameters, which are right atrial, RV dimensions, function and pressures. The apical four-chamber view does not just allow the assessment of right atrial short-axis and long-axis dimensions, but also the measurement of the right atrial area by tracing the endocardial border at end-systole. The estimation of the right atrial pressure is possible by measuring the inferior vena cava dimensions and respiratory variation in the subcostal view.
The pulmonary arterial systolic pressure can be derived from the peak TR velocity on continuous wave Doppler recordings, reflecting the afterload of the RV due to using the modified Bernoulli equation.
Because of its complex crescent-shaped geometry, assessment of RV dimensions and function by 2D echocardiography represents a real challenge (76). Although they are load-dependent and measure only a singular segment of a complex 3D structure, myocardial velocities and tricuspid annular plane systolic excursion (TAPSE) (<17 mm is regarded as abnormal) are the most frequently used markers of RV function. Fractional area change represents the percentage of change in RV area between end-diastole and end-systole ; a value <35% is considered abnormal. Less angle and load dependent, RV myocardial longitudinal strain by 2D speckle tracking echocardiography is quantified as the percentage of systolic shortening of the RV free wall from base to apex measured in the RV-focused apical four-chamber view. Reference values for global RV strain corrected for sex have been suggested; an RV global longitudinal strain (GLS) of the free wall ≥ 20% is probably abnormal (91).

Tricuspid annular dilation estimated by transthoracic echocardiography may be a better predictor of severe late TR after mitral valve surgery (35, 36); dilation is represented by transthoracic echocardiography as a diastolic diameter >40 mm or >21 mm/m2 (92) in the 4-chamber apical view (36)
Transthoracic echocardiographic measurements of tricuspid valve tethering distance >0.76 cm (93) or tethering area >1.63 cm2 (76) belong to post-operative relapsing TR's predictors as well as annular dimensions.

Table 5 : main parameters of right heart function echocardiographic assessment




**• Grading of TR severity :**

In order to determine efficacy of new transcatheter procedures for these patients, a new grading scheme had been recently suggested, extending the severity scale for TR to “massive” and “torrential” (Table 6)

Table 6 : Current grades and cut-offs suggested for tricuspid regurgitation, based on (semi) quantitative parameters.

| Parameters | Mild | Moderate | Significant/ Moderate-severe | Severe | Massive | Torrential |
|---|---|---|---|---|---|---|
| Vena contracta width | <3mm | 3–6.9 mm | 6-6.9mm | 7-13mm | 14-20mm | ≥21mm |
| EROA | 20 $mm^2$ | 20-39 $mm^2$ | 20-29 $mm^2$ | 40-59 $mm^2$ | 60-79 $mm^2$ | ≥ 80 $mm^2$ |
| Regurgitant Volume | <30 ml | 30-40 ml | 30-44 ml | 45-59 ml | 60-74 ml | ≥75 ml |
| Regurgitant fraction 30 Echo (MRI) | <25% (30%) | 25-44% (30-49%) | | 45% (50%) | | |
| 30 vena contracta | | | | 75-94 $mm^2$ | 95-114 $mm^2$ | ≥115 $mm^2$ |

**2. Cardiac magnetic resonance assessment :**

CMR is characterized by a high spatial resolution and excellent endocardial border delineation. One advantage is that three different methods were qualified to calculate the reference stroke volume reliably (phase contrast imaging from the pulmonic valve or aortic valve, and volumetric LV stroke volume) (94)
In order to quantify regurgitant volume when isolated regurgitation (i.e., when no other regurgitant lesions or intracardiac shunts are detected) is existent, the difference between right ventricular stroke volume (RVSV, ml) and forward flow (Qs or Qp, ml); and/or the difference between RVSV and left ventricular stroke volume (LVSV, ml) can be used (95).
Late gadolinium enhancement and more currently T1 mapping in addition to extracellular volume quantitation can afford information about myocardial impairment and fibrotic remodeling.
CMR has some limitations including the presence of arrhythmias and transvalvular pacemaker leads often found in patients with TR (95).

**3. Computed tomography :**

Due to the arrival of percutaneous tricuspid treatment techniques, measurement of the tricuspid annular area is useful for percutaneous valve replacement or annuloplasty sizing as well as evaluation of the intervention's results. Furthermore, annular dimensions affect clinical outcomes (96) and could be probably related to transcatheter procedural success.
To measure the tricuspid annular area with CTA, different methods can be used including multiplanar reconstruction and cubic spline interpolation. a tricuspid annulus area of more than 14 to 15 cm2 is linked to severe functional TR.
It is possible to measure the AROA by CTA which may also be used as a further grading device of TR severity in patients with discordant echocardiographic resulats. To do so, multiplanar reconstruction is performed and the contours of the AROA are afterwards traced on the reconstructed short axis by depositing points or nodes linked by cubic spline interpolation (97).

**4. Right heart catheterization :**

Invasive assessment of the hemodynamic profile has shown to be strongly informative. In addition, it may help identifying patients profiting most from transcatheter therapies according to several studies (98; 99).

Pre-capillary profiles are generally associated with less survival and poor outcomes compared to other profiles, and patients with a PCWP >16mmHg may need more intensive monitoring after TTVR due to the higher rates of death, cardiac readmission and TR recurrence.

## Therapy :

**• Medical therapy:**
Tricuspid regurgitation's medical therapy is nowadays restricted to diuretics and the treatment of underlying causes when it is the case of secondary tricuspid regurgitation (37, 55, 62, 101).
Diuretics are useful in the existence of right heart failure by counterbalancing the activation of the renin-angiotensin-aldosterone system associated with hepatic congestion.
Medical treatment of secondary tricuspid regurgitation doesn't only demand a comprehensive evaluation of the type and severity of pulmonary hypertension but also the assessment of left ventricular function as well as the consideration of rhythm control for atrial fibrillation. (102, 91)
Recent European guidelines give a class I recommendation for right heart catheterization in patients with severe tricuspid regurgitation in the presence or the absence of left heart disease, before surgical or catheterbased valve interventions are performed, because of the poor prognosis for patients with tricuspid regurgitation and precapillary pulmonary hypertension. (102)

**• Surgical therapy:**
Tricuspid regurgitation surgery is mostly indicated at the time of the left heart surgery. It doesn't only instigate reverse remodelling of the RV but also ameliorate functional status when annular dilatation exists, even if the tricuspid regurgitation is not severe. (91, 104)
Surgery is suggested in symptomatic patients with severe primary tricuspid regurgitation. In selected asymptomatic or mildly symptomatic operable patients, with RV dilatation or declining RV function is objectified, an intervention should also be envisaged.
When comparing the surgical correction of isolated secondary tricuspid regurgitation with medical treatment; the benefit is not completely obvious (428), besides the non-negligeable risk of periprocedural mortality and morbidity of the procedure especially when patients are late. (105, 106)
Annuloplasty with prosthetic rings should be prioritized to valve replacement whenever it is possible, (91, 106, 107) nevertheless valve replacement should only be suggested when the tricuspid valve leaflets are tethered and the annulus severely dilated. But In presence of a cardiac implantable electronic device lead, the choice of the technique should be adjusted to both patient's condition and surgeon's experience. (108)
TRI-SCORE is a dedicated risk score model based on eight easy to ascertain parameters to evaluate the risk of isolated tricuspid valve surgery, ranged from 0 to 12 points, A risk score < 3 could define a low surgical risk, a score of 4–5 refer to an intermediate risk, and a score >6 point at a high surgical risk (109).

**• Transcatheter therapy :**

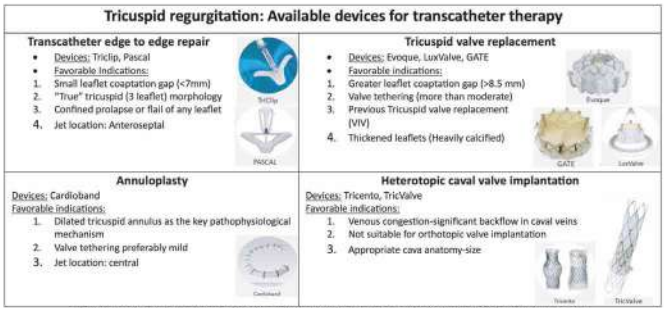
The transcatheter procedures can largely be divided into four groups including edge-to-edge repair (TEER), TV replacement, tricuspid annuloplasty and palliative tricuspid therapy. These strategies are being pursued as lower-risk interventions in higher risk patients with tricuspid regurgitation (Table 7) (110).

Tricuspid transcatheter edge-to-edge repair (TEER) has been the most widely evaluated intervention for severe isolated tricuspid regurgitation. (113)

The TRILUMINATE trial was the latest to be published which has objectified that tricuspid TEER by the TriClip was safe, the severity of the TR was decreased to moderate or less at 1 year in the majority of patients who underwent the procedure, and it was associated to a further boost in quality-of-life scores; compared with medical therapy for patients suffering from severe, symptomatic, isolated tricuspid regurgitation with an intermediate or greater surgical risk; (101)

The bRIGHT registry, considered as a real-world cohort of patients with symptomatic TR. demonstrated low rates of MAE and mortality through 30 days with significant TR reduction, and significant clinical improvements in KCCQ score and NYHA functional class following the TTEER procedure (102).

Table 7: current four techniques for the transcatheter management of tricuspid regurgitation. Each technique, based on anatomical considerations, has some




| Recommendations on primary tricuspid regurgitation | | |
|---|---|---|
| Surgery is recommended in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery. | I | C |
| Surgery is recommended in symptomatic patients with isolated severe primary tricuspid regurgitation without severe RV dysfunction. | I | C |
| Surgery should be considered in patients with moderate primary tricuspid regurgitation undergoing left-sided valve surgery. | IIa | C |
| Surgery should be considered in asymptomatic or mildly symptomatic patients with isolated severe primary tricuspid regurgitation and RV dilatation who are appropriate for surgery. | IIa | C |

Figure 8 :
ESC guidelines for management of primary tricuspid regurgitation (62)

| Recommendations on secondary tricuspid regurgitation | | |
|---|---|---|
| Surgery is recommended in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.[423–427] | I | B |
| Surgery should be considered in patients with mild or moderate secondary tricuspid regurgitation with a dilated annulus (≥40 mm or >21 mm/m$^2$ by 2D echocardiography) undergoing left-sided valve surgery.[423,425–427] | IIa | B |
| Surgery should be considered in patients with severe secondary tricuspid regurgitation (with or without previous left-sided surgery) who are symptomatic or have RV dilatation, in the absence of severe RV or LV dysfunction and severe pulmonary vascular disease/hypertension.[418,433 a] | IIa | B |
| Transcatheter treatment of symptomatic secondary severe tricuspid regurgitation may be considered in inoperable patients at a Heart Valve Centre with expertise in the treatment of tricuspid valve disease.[f] | IIb | C |

Figure 9 :
ESC guidelines for management of secondary tricuspid regurgitation (62)

--> To summarize the different treatment options based on the recently published data and guidelines, all patients with severe or moderate to severe TR, under optimum medical therapy, who are operable or nonhigh surgical risk must proceed with surgery (repair or replacement). Conversely, other cases, transcutaneous approach should be the main indicated in highly dedicated heart valve centers, except those who are in end stage RHF with precapillary PH and high PVR (115)

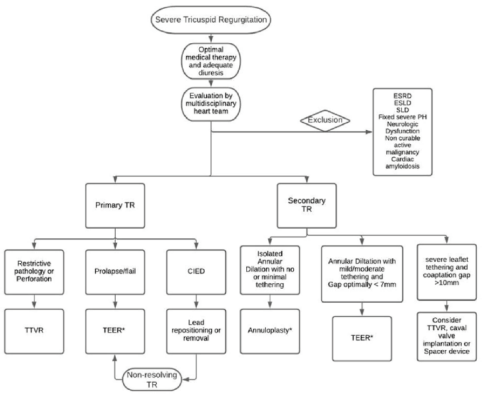



Figure 10 :
Proposed algorithm to guide transcatheter tricuspid valve intervention device selection. CIED, cardiovascular implantable electronic device; ESLD (end-stage liverg disease); ESRD (end-stage renal disease); PH (pulmonary hypertension); SLD (severe lung disease); TEER (transcatheter edge to edge repair); TTVR (transcatheter tricuspid valve replacement) (113).

## Conclusion :

Interest in TR has quickly enlarged in the setting of poor clinical results associated with the disease and the restricted indications and options for treatment. Nowadays, severe TR should be managed at the time of surgery for left-sided valve disease, or if symptomatic isolated TR before the onset of right ventricular dysfunction. But ongoing trials will evaluate the utility of earlier intervention. Given the high surgical risk for isolated TV surgery, novel transcatheter approaches (both repair and replacement) are currently being investigated, and delivering satisfactory outcomes.

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# GUIDE FOR AUTHORS

The moroccan journal of cardiology is the official press of the Moroccan Society of Cardiology. It appears quarterly and publishes original French and English scientific works.
The moroccan journal of cardiology ensures the publication of original articles, trials meta-analyses clinical reviews and case reports. It allows to communicate the results of studies and enhance the development of scientific research in the cardiovascular fields.

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## Manuscript preparation and submission principles

The test of the articles on studies follows the structure « IMRD » divided into four sections : Introduction, Methods, Results and Discussion. The format of usable text files is MS World.
Manuscripts should be submitted excusively in electronic format on the website on the Moroccan Society of Cardiology at this address :smcmaroc.org

**Title page :**

The title page contains :
- The title of the article (in franch and in english), with a subtitle if necessary
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The maximum length of the texts (including references) must be as follows :
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- Case reports : 4 pages
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The submitted text should be clear and easily understandable, Precise and concise. The languae should be simple and correct. Abbreviations should be explained when they first appear in the text and then used consistently and invariably.

**Abbraviations and symbols :**
Only a limited number of standard abbreviations may be used. Avoid using them in the title of the manuscripts. Abbraviations must be explained when they first appears in the text. Units of measurement must conform to the international nomenclatures.

**Figures and tables :**
Iconographic documents (fugures and tables) must be called up in the text and conform to the following recommendations :
- Captions for illustrations should be presented on a separate page using the arabic numerals corresponding to the illustrations (Figure 1)
- The tables are numbers in Roman numerals, in order of appearance in the text (Table I)
- The figures must be presented on a separate sheet, and provided in separate files at the rate of one file per figure ; they are all accompanied by a legend. Explanations or other notes necessary for understanding are provided below each table.
- If a figure has already been published, acknowledge the original source and submit written permission from the copyright holder to reproduce the figure.
- Abbreviations should be avoided. If the figure or table contains abbreviations, they must be explained in the legend.
- Drus should be listed by their international non proprietary names (INN). Trade names should be iven in brackets after the INN. Symbols, figures and text in figures should be clear and of sufficient size to ensure that each element is perfectly legible. The publication of illustration in color is recommended.

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References to articles in a journal must include the named of the first six authors with first name initials (followed by « and al. » from the 7th author), the full title of the article in the original language, the name of the journal according to the Index Medicus abbreviations, the year, the volume number, pages (first and last).

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La revue marocaine de cardiologie, est l'organe de presse officiel de la société marocaine de cardiologie à but non lucratif, d'apparition trimestrielle, qui publie en langue française et anglaise des travaux scientifiques originaux.
La revue marocaine de cardiologie assure la création d'un espace de publication d'articles originaux, essai clinique méta-analyse de mises au point et de cas cliniques. Elle permet de communiquer les résultats d'études menées et d'assurer le développement de la recherche scientifique dans le domaine cardiovasculaire.
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Les manuscrits sont à soumettre exclusivement sous format électroniques sur le site de la société marocaine de cardiologie à l'adresse suivant : smcmaroc.org
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La page de titre contient :
- le titre de l'article (titre en français et en anglais), avec éventuellement un sous-titre,
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- Nombre de figures et de tableaux.
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La longueur maximale des textes (références comprises) doit être comme suit :
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- cas cliniques: 4 pages ;
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Les auteurs doivent veiller à ce que les textes soumis soient clairs et facilement compréhensibles, précis et concis.

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