Functional Mitral Regurgitation in the Critically Ill

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Introduction

Functional mitral regurgitation is the consequence of left ventricular systolic dysfunction in the presence of an anatomically normal mitral valve. Systolic left ventricular failure is often the cause of congestive heart failure, which is a frequent reason for admission to the intensive care unit (ICU). The most frequent cause of left ventricular dysfunction is ischemic heart disease. Both the ventricle and the mitral valve apparatus are involved in the pathogenesis of functional mitral regurgitation. The mitral valve is a complex apparatus, composed of the mitral valve leaflets, the chordae tendineae, papillary muscles, and the related regional area of the ventricular wall (**Fig. 1**). Malfunction of one or more components of this apparatus engenders improper functioning of the mitral valve.

Pathological mitral regurgitation, although heterogeneous in etiology, is a common corollary of ischemic cardiomyopathy, with great impact on mortality and morbidity, and its prevalence increases with age. Other causes of mitral regurgitation are related to myxomatous degeneration, endocarditis, and rheumatic disease [1]. The clinical outcome of this disease in the critically ill is scantily defined. The frequency of mitral regurgitation within society is difficult to estimate, but its causes are easier

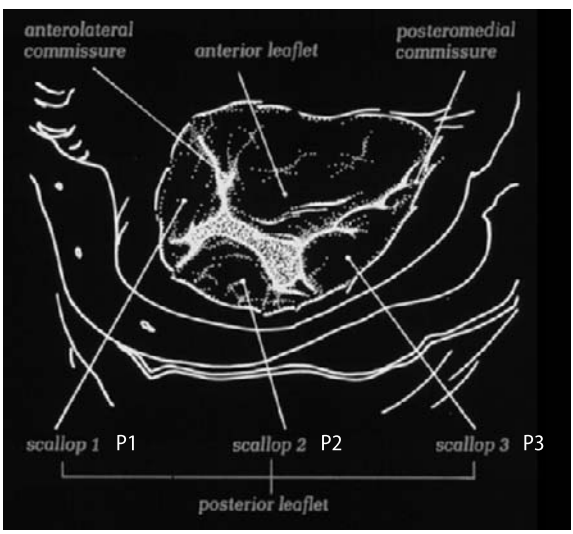

Fig. 1. The anatomy of the normal mitral valve. The different segments as used by cardiac surgeons, have been indicated.

to assess. Ischemic heart disease is the most frequent cause of death with great impact on quality of life for survivors. Ischemic mitral regurgitation doubles late mortality [2, 3]. Optimal care must include estimation of ventricular contractile reserve with respect to estimation of function and prognosis [4]. Furthermore, high-risk subgroups must be defined. To improve outcomes, these high-risk patients, even with asymptomatic mitral regurgitation, may benefit from surgical treatment [5]. The presence of mitral regurgitation after myocardial infarction should thus be taken into account in post-myocardial infarction risk stratification [6].

In this chapter, we will summarize the pathophysiological mechanisms, the diagnostic features, and the subsequent therapeutic management of functional mitral regurgitation.

Definition

Functional mitral regurgitation is the insufficiency occurring as a consequence of left ventricular dysfunction. The valve leaflets are completely normal and the regurgitant jet is straight into the left atrium, underlining the absence of any pathologic feature of the valve leaflets. Characteristic to functional mitral regurgitation is the abnormal and increased tension on the leaflets (tethering force), in conjunction with a sometimes severely (although potentially intermittent) decreased left ventricular function. **Table 1** summarizes the different causes of acute mitral regurgitation.

Mitral regurgitation is not always pathological. In a transesophageal echocardiographic (TEE) study, mitral regurgitation was shown to be present in 36 % of healthy volunteers [7]. Pathological mitral regurgitation flows are characterized by broad (> 10 mm) regurgitant jets with a long duration (> 30 ms) (**Fig. 2**). Further-

Table 1. Causes of acute mitral regurgitation in the critically ill.

Leaflet disorders
Myxomatous degeneration with acute deterioration of function
Rheumatic valve disease
Infective endocarditis
Trauma: penetrating or iatrogenic
Annular disorders
Dilation, concomitant with LV dilatation
Calcification
Chordae tendineae
Rupture (ischemic heart disease, calcification, trauma)
Lengthening
Retraction: rheumatic valve disease
Papillary muscles
Displacement, secondary to left ventricular remodeling
Infarction
Trauma
Regional wall motion abnormalities: Ischemic heart disease
Invading disorders
Infiltrative disorders: Amyloidosis, sarcoidosis
Tumors: atrial myxoma

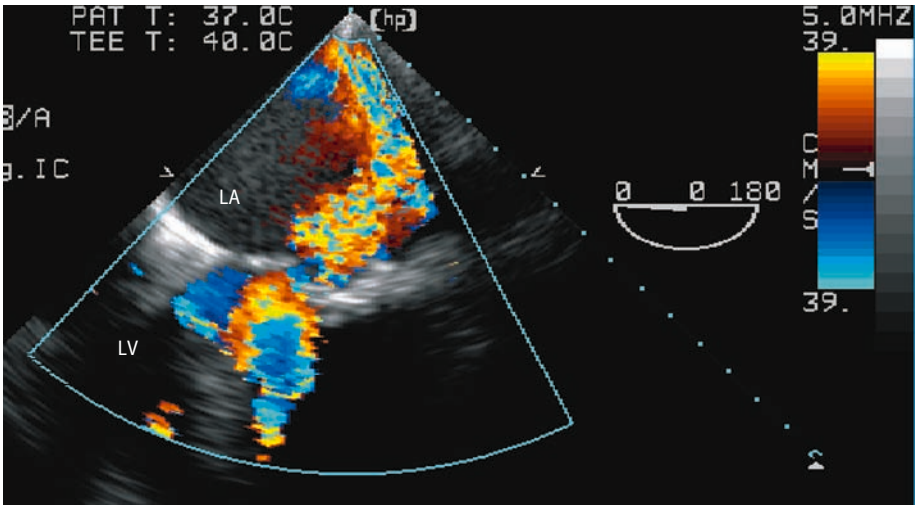

Fig. 2. Color Doppler evaluation is the mainstay for grading the severity of mitral regurgitation. Both the width and the length of the regurgitant jet in the left atrium (LA) should be assessed. LV: left ventricle

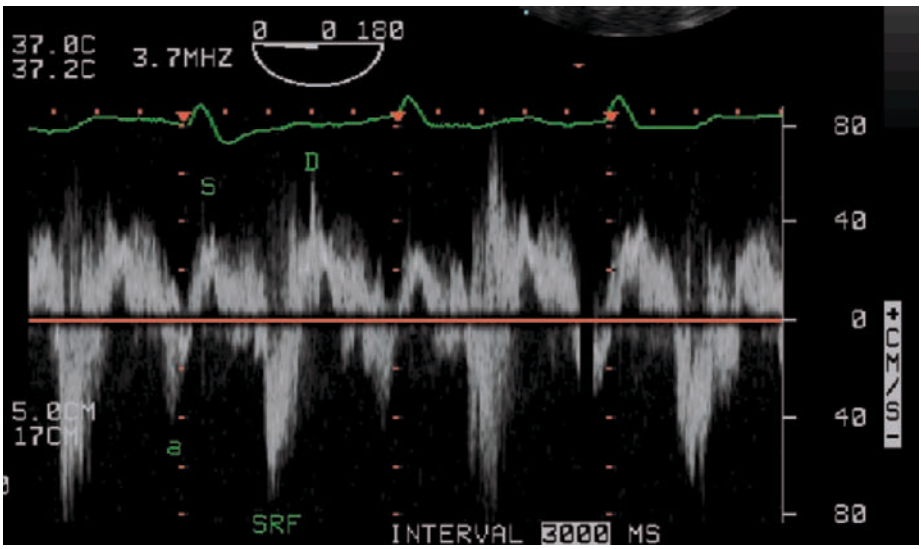

Fig. 3. Characteristic pattern of a pulmonary venous Doppler signal, with a large systolic reverse flow wave (SRF) and an enlarged reverse atrial contraction wave (a).

more, a characteristic pattern in the pulmonary veins is obtained with pulsed wave Doppler: the regurgitant flow is so high that it is deviated towards the right and/or left pulmonary veins (**Fig. 3**), inducing a backward directed increased atrial contraction flow wave due to the high residual volume in the left atrium, a blunted systolic forward flow wave, mainly due to a major systolic reverse flow wave, and finally a delayed filling of the left atrium with an increased diastolic flow wave. Other diagnostic features will be discussed below.

Pathophysiology

Opening of the mitral valve depends completely on the pressure gradient created throughout diastole; filling of the left ventricle starts with the energy consuming left ventricular relaxation and concomitant descent of left ventricular pressure below left atrial pressure. Proper closure of the mitral valve depends on the balance between the closing force, generated by the contraction of the left ventricle, and the tethering forces, built up between the anterolateral and posteromedial papillary muscles and the mitral annulus. Coaptation time and length are two features of the closure of the mitral valve. Functional mitral regurgitation is characterized by an imbalance between the tethering forces, inducing tenting of the mitral valve, and the closing force of the left ventricle. Coaptation time will be reduced when tethering forces are inadequately opposed by, e.g., decreased systolic left ventricular function, inhibiting the leaflets from reaching their proper closing point in time, at the level of the annulus. Coaptation length is reduced by tethering of the papillary muscles and the annular dilatation. The pathophysiological triad of mitral regurgitation was originally described by Carpentier et al., identifying three distinct classes of mitral valve disease [8]. These are summarized in **Table 2**. Functional mitral regurgitation is the first class. In contrast to the other classes described by Carpentier et al., a completely normal mitral valve is found in functional mitral regurgitation.

At the level of the leaking mitral valve, the regurgitant blood volume depends on the afterload characteristics of the left ventricle. Increased afterload (arterial hypertension, aortic stenosis) will increase, and low blood pressure and shock will decrease the regurgitant volume. In addition, whenever the tethering forces decrease, e.g., with akinesia or dyskinesia of the zone of a papillary muscle, mitral regurgitation may decrease or vanish completely, even with diminished closing force of the left ventricle.

Analysis of the acute effects of mitral regurgitation in comparison with aortic regurgitation on the left ventricle show a lesser increase in left ventricular end-diastolic pressure and volume following acute mitral regurgitation. In comparison with acute aortic regurgitation, acute mitral regurgitation reduces intraventricular pressure and left ventricular radius more, decreasing left ventricular wall tension. Hence, the ratio of left ventricular end-systolic wall thickness to radius is lower with acute mitral regurgitation than with acute aortic regurgitation [9].

Functional mitral regurgitation is rather the consequence of dilation of the left ventricle, decreased closing force, and systolic mitral valve tenting and, hence,

Table 2. Different characteristics of the mitral valve apparatus with respect to the various types of mitral regurgitation, as described by Carpentier et al. [8].

type	leaflets	leaflet motion	coaptation annulus	annulus	papillary muscles
I	Normal	normal	below	dilation	perforation possible
II	Thickening possible	Increased (prolapse)	above		(chordal) rupture/elongation
IIIa	Thickening	Systole, diastole restricted	below	thickening	
IIIb	Thickening	Systole restricted	below	thickening	apical displacement

incomplete closure of the mitral leaflets [10]. Dilation of the left ventricle alone already induces incomplete closure of the leaflets and production of a systolic mitral regurgitation flow. Characteristically, this jet is directed towards the roof of the left atrium [11]. After a myocardial infarction, the left ventricle undergoes secondary remodeling, explaining why recurrent leakage of the mitral valve may occur after initial correction of the mitral leakage by mitral annuloplasty [12].

Whenever regional wall motion abnormalities (severe hypokinesia, akinesia or dyskinesia) are present in the region of the papillary muscles, displacement of the papillary muscles as a consequence of left ventricular remodeling may occur. Traction occurs on the leaflets, displacing the coaptation point apically, finally resulting in a tented mitral valve (**Table 2**). In contrast, leaflet movement above the level of the annulus is either the consequence of rupture of chordae at the tip of or in the middle of the leaflet, resulting in prolapse or bulging of the leaflet, respectively (**Table 2**).

Diagnosis

Echocardiographic evaluation of a mitral valve should include the following aspects:

1. assessment of closure of the leaflets at the annular level
2. appropriateness of the closure (coaptation)
3. completeness of the valvular apparatus (i.e., chordae tendineae, papillary muscles, regional function of the ventricular wall)
4. color Doppler of the mitral valve, including estimation of the effective regurgitant orifice, the width and length of the jet, Doppler flow assessment of both transmitral and pulmonary veins (left and right)
5. assessment of right ventricular function and pulmonary hypertension
6. exclusion of aortic regurgitation/stenosis.

It cannot be stressed sufficiently that in acute circumstances an echocardiographic investigation should start with a short axis view of the left and right ventricle [13, 14], providing direct insight into important features, such as global systolic function, including presence of dilatation, (static) preload, and presence of regional wall motion abnormalities. The importance of obtaining all this information by eye-balling one view is immense; both exclusion of the heart as a cause of shock in a newly admitted ICU patient, and immediate (although rough) diagnosis of ventricular failure may be addressed with one view [14].

Estimation of the severity of functional mitral regurgitation is summarized in **Table 3**. Assessment of closure of the leaflets should encompass the level of closure. Closure above the annular plane indicates billowing (fixed tips of the leaflets and thus, intact chordae tendineae at this level, although ruptured chordae or part of a papillary muscle attached in the middle of the leaflet), prolapse (ruptured chordae, connected to the tips of the leaflets), or both. Closure below the annular level suggests increased tethering forces of the chordae resulting in tenting of the mitral valve leaflets. All these features can be elegantly seen with 3D-echocardiography [15].

It is essential to assess left ventricular size and function. A left ventricular end-systolic diameter above 45 mm is an important sign of dilatation, resulting in inadequate coaptation of the leaflets, even hampering closure at the level of the mitral annulus. Patients with an effective regurgitant orifice of 40 mm^2 minimally, have been shown to be at higher risk of death and complications than those with a smaller effective regurgitant orifice [5]. In addition to simple eye-balling, left ven-

Table 3. Estimation of the severity of functional mitral regurgitation, characterized by a central regurgitant jet.

Technique	mild	severe
Color Doppler jet length	not to LA roof	to LA roof
Vena contracta width	< 0.3 cm	> 0.6 cm
Filling LA by color jet	< 20 %	> 40 %
Flow convergence	absent or minimal	large
Pulmonary venous Doppler	S > D	S < D
LV end-systolic diameter	< 45 mm	> 45 mm
EROA	< 0.2 cm^2	≥ 0.4 cm^2

D, diastolic flow wave velocity, obtained at the level of one of the entries of the pulmonary veins; EROA, effective regurgitant orifice area (cm^2); LA, left atrium; LV, left ventricle; S, systolic flow wave velocity, obtained at the level of one of the entries of the pulmonary veins.

tricular systolic function can now be assessed easily using myocardial Doppler imaging at the level of the mitral annulus [16]. Systolic tissue velocities below 8 cm/s suggest decreased left ventricular systolic function. Care should be taken to interpret these data in view of preload conditions, as the systolic tissue velocity at the mitral annulus is preload dependent [17].

Furthermore, the completeness of the mitral valvular apparatus and its function must be checked, including chordae, papillary muscles, and the function of the ventricular wall.

Echocardiographic estimation of the presence of increased pulmonary artery pressures is best obtained from a continuous wave Doppler signal across the tricuspid valve [18, 19].

Associated pathology may have considerable impact on prognosis and outcome determination. Decreased right ventricular systolic function in conjunction with functional mitral regurgitation was reported to have a mortality rate of 28 % [20]. Survivors had a prolonged stay in the hospital because of heart failure. In this respect, it is important to evaluate both left and right ventricular function and estimate right ventricular systolic pressure from a trans-tricuspid flow pattern [18]. Knowledge of pulmonary artery hypertension is important in view of optimal support of right ventricular function.

Finally, the difference between acute and chronic mitral regurgitation should be discussed (**Table 4**). In chronic mitral regurgitation, onset is most often insidious and gradual, with symptomatology (dyspnea) rather moderate. The left heart bears the stigmata of chronic disease: A dilated left atrium with decreased compliance, emptying into a dilated and sometimes hypertrophic left ventricle with decreased

Table 4. Differences between acute and chronic severe mitral regurgitation, with respect to functional mitral regurgitation.

Symptomatology	Acute	Chronic
Onset	Acute	Insidious, gradual
Clinical picture	Severely ill	Moderate dyspnea
Echo LV size	Normal	Dilation, LVH
Echo LV function	Hyperkinesia	Normal-reduced
Echo LA size/compliance	Normal/normal-reduced	Dilation/reduced
Etiology	AMI, trauma, ...	IHD, endocarditis, ...

AMI, acute myocardial infarction; IHD, ischemic heart disease; LA, left atrium; LVH, left ventricular hypertrophy.

function. In contrast, acute mitral regurgitation is often combined with a hyperkinetic left ventricle.

Therapeutic Management

Medical

Medical treatment alone is indicated whenever asymptomatic mitral regurgitation is present and the effective regurgitant orifice is $< 40\ mm^2$, as explained above. All measures valid for the support of heart failure should be included in the treatment of functional mitral regurgitation. In this respect, vasodilator therapy is the mainstay to unload the left ventricle and to reduce regurgitation into the left atrium as much as possible. In acute mitral regurgitation, nitroprusside, a mixed venous and arterial vasodilator, is the drug of choice. Endocarditis prophylaxis should be started concomitantly. Measures should be undertaken to also support right and left ventricular function and to reduce pulmonary hypertension.

Surgical

Surgery should be considered in symptomatic patients with important mitral regurgitation. Coronary artery bypass grafting (CABG) alone, without concomitant mitral annuloplasty appears to have little benefit on outcome [21], suggesting that preoperative evaluation to guide intraoperative therapy is warranted. Intraoperative TEE consistently underestimates preoperative findings [21–23]. Several therapeutic options have been introduced over the years. Mitral annuloplasty seems a logical approach, to compensate for the dilation of the left ventricle [8]. Introduction of an undersized annuloplasty ring leads to reduction of end-diastolic left ventricular volume, improvement of ejection fraction, and diminished regurgitant volumes [24]. Care should be taken of residual mitral regurgitation, which could be related to inadequate downsizing of the annular ring, resulting in inadequate coaptation. A new development results in improved coaptation due to a reduced anteroposterior dimension allowing the often tethered P2-P3 segments to coapt more appropriately. Three-dimensional echocardiography may help to improve the choice of the annular ring, in particular when considering imitating the saddle shape of the native mitral annulus [15]. Recurrent mitral regurgitation is often related to continued remodeling of the left ventricle.

More than the surgical procedure itself, it is important for intensivists to know when patients with acute mitral regurgitation should be scheduled for surgery. It is now general policy to present patients in cardiac failure class II (dyspnea on heavy exertion) with an end-systolic left ventricular diameter > 45 mm and an end-systolic volume of $> 50\ ml/m^2$ body surface area. Less symptomatic patients should be carefully followed even after discharge from the ICU.

Conclusion

Full understanding of the nature of functional mitral regurgitation should help in correctly detecting this disease with all its pitfalls and consequences in the critically ill. Diagnosis starts with awareness of its potential presence and a subsequent pathophysiological approach to the mechanisms of this mitral regurgitation. Assessment

should encompass all facets of Doppler-echocardiography, including Doppler, myocardial Doppler imaging, and 3D-echocardiography, if available, to assess left and right ventricular function, and the respective preloads and afterloads. All facets of the mitral valve apparatus should be examined in this respect. Only these measures, followed by appropriate management will improve survival of patients with functional mitral regurgitation.

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