Mild Rheumatic Mitral Regurgitation in the Presence of Dominant Stenotic Pliable Valve: An Echocardiographic Structural Valve Analysis in Patients Undergoing Balloon Valvuloplasty

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ABSTRACT:

Background: Understanding the mechanism and the main components involved in rheumatic mitral regurgitation (MR) associated with dominant pliable mitral stenosis (MS) may improve our ability to repair some mixed rheumatic mitral valve pathologies.

Objectives: To assess mitral valve structural components in pure mitral stenosis versus mitral stenosis associated with mild regurgitation

Methods: Using two-dimensional echocardiography, we performed mitral valve structural analysis in two groups of patients prior to balloon mitral valvuloplasty (BMV). The first group, consisting of 13 females and 2 males (mean age 39 ± 5 years), suffered from pure pliable mitral stenosis (PPMS), while the second group, with 22 females and 2 males (mean age 44 ± 5 years), had mixed mitral valve disease (MMVD) characterized by mild MR in the presence of dominant pliable MS. All echocardiographic measurements relating to the mechanism of MR were undertaken during the systolic phase.

Results: The mean Wilkins scores of the PPMS and MMVD groups were 7 ± 1 and 8 ± 1 respectively ($P = 0.004$). No significant differences were found between the MMVD group and the PPMS group regarding annular circumference (15.5 ± 1.4 cm vs. 15.4 ± 1.6 cm, $P = 0.84$), annular diameter (36 ± 4 mm vs. 38 ± 5 mm, $P = 0.18$), and chordae tendinae length directed to the anterior mitral leaflet (AML) (10 ± 2 mm vs. 11 ± 2 mm, $P = 0.137$). However, anterior vs. posterior mitral leaflet length during systole was significantly lower in the MMVD than in the PPMS group (2.2 ± 0.5 vs. 2.8 ± 0.4, $P = 0.02$), whereas the AML thickness at the co-aptation point was greater in the MMVD than in the PPMS group (7 ± 1 vs. 5 ± 1 mm, $P = 0.0004$).

Conclusions: In rheumatic valves, thickening and shortening of the AML are the main factors determining the appearance of mild MR in the presence of dominant pliable MS.

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KEY WORDS: rheumatic mixed valvular pathology, mitral regurgitation (MR), mitral stenosis (MS), mitral valvuloplasty, valve repair

Mixed rheumatic valvular disease is considered the most complex lesion treated by preservation therapeutic modalities [1]. This type of pathology, where different valvular structural components may undergo damage of variable intensity and severity [2], presents a therapeutic challenge for both cardiac surgeons and interventional cardiologists. Specifically in the context of percutaneous balloon valvular dilatation, where angiographic mitral regurgitation > 2/4 is considered an absolute contraindication for this procedure [3], the immediate result of this technique in the presence of mild to moderate mitral regurgitation is multifactorial, depending mainly on valve morphology [4]. Therefore, in order to plan and manage an optimal therapeutic approach in this group of patients characterized by mixed valvular pathology, the contribution of every structural element to this pathophysiology and its potential correction by any of the available therapeutic conservative modalities should be carefully evaluated.

The aim of our study was to focus on two groups of rheumatic patients who today can potentially be treated by either surgical or percutaneous conservative approaches: patients with pure pliable mitral stenosis and patients with mixed mitral valve disease characterized by pliable MS and mild mitral regurgitation. In view of the difference in valvular structure between these two groups and understanding the basic functional valve abnormalities may clarify the curative approach needed in other large variations of mixed rheumatic mitral valve pathologies.

PATIENTS AND METHODS

Sixty-four technically successful balloon mitral valvuloplasties were performed in our institute between January 2008 and December 2009. All procedures were undertaken using the trans-septal antegrade approach with the Inoue balloon catheter (Toray Industries Inc., Tokyo, Japan) and the step-wise

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MS = mitral stenosis

dilatation technique [5]. Balloon diameter was determined by the patient's height [6].

All medical files and pre-procedural trans-thoracic echocardiographic data were retrospectively evaluated regarding pliable MS associated with or without mild MR in order to divide the patients into two groups: the first comprising patients with PPMS and the second with MMVD. We excluded patients who had had previous surgery or balloon dilatation, patients with additional significant valvular pathology with either left ventricular dilatation or dysfunction, and patients who had concomitant coronary artery disease or persistent atrial fibrillation. We included only patients in whom all echoardiographic structural analysis had been completed.

Following this screening, the study group comprised 39 patients who fulfilled the criteria of clinically pliable MS with or without associated mild MR by TTE criteria, i.e., jet area ≤ 4 cm^2 and vena contracta < 3 mm [7]. Based on these criteria, 24 patients were diagnosed with MMVD and 15 patients with PPMS.

TTE EVALUATION

GENERAL ASSESSMENT

All TTE examinations were performed using Acuson-Sequoia-C 256 before, during and 24 hours after balloon valvular dilatation. Pre- and post-BMV mitral valve area (in cm^2) was determined by plannimetry. For pre-procedure TTE, the Wilkins' score [8] and posterior leaflet mobility were determined [9]. Post-procedure MVA, MR grade, including central or eccentric jet direction, were determined in both groups.

PRE-BMV MITRAL VALVE STRUCTURE ANALYSIS IN RELATION TO MILD MR

To explore structural differences between the two groups regarding pre-procedure MR, off-line analysis was performed using the Medcon measurement functions. Standard parasternal long and short axis views, including the modified views exploring the sub-valvular apparatus, were performed [10]. The following parameters were measured during end-systolic phase as determined by electrocardiographic signal:

- *Annular circumference (cm):* measured in the parasternal short axis view at commissural level along the epicardial borders
- *Annular diameter* **(mm):** measured in the apical four-chamber view between the hinges points of anterior and posterior mitral leaflets
- *Anterior and posterior mitral leaflet length* **(AML & PML) (cm):** measured in the parasternal long axis view from the

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MR = mitral regurgitation
PPMS = pure pliable mitral stenosis
MMVD = mixed mitral valve disease
TTE = trans-thoracic echocardiography
BMV = balloon mitral valvuloplasty
VA = mitral valve area

hinges point towards the co-aptation point of each leaflet respectively

- *AML thickness* **(mm):** measured in the parasternal long axis view at the co-aptation point (rough zone segment)
- *Chordae tendine length directed towards AML* **(mm)**: originating from both papillary muscles and inserted in the ventricular aspect of anterior leaflet at the rough zone – measured from both posterior and anterior papillary muscles by using the modified long axis view. The average chordae tendine length measured from the two papillary muscle systems was calculated.

STATISTICAL ANALYSIS

All continuous parameters are presented as mean ± standard deviation (SD) and were analyzed by the Student *t*-test. Categorical variables are expressed as a number of patients and percentages and are analyzed by Fisher's exact test. Differences were considered significant at $P \leq 0.05$.

RESULTS

Patients' baseline clinical characteristics are presented in Table 1. The patients with PPMS were younger than patients with MMVD: mean age 39 ± 5 vs. 44 ± 6 years respectively ($P = 0.01$). Most patients in both groups were women in New York Heart Association class III. No patients in the MMVD group were in NYHA class IV. None of the patients in either group showed calcific foci related to the mitral valve apparatus when examined by cardiac fluoroscopy.

Table 1. Patients' baseline clinical characteristics

	PPMS (n=15)	MMVD (n=24)	*P* value
Age (yrs)	39 ± 5	44 ± 6	0.01
Females (%)	13/15 (87)	22/24 (92)	0.6
NYHA class (%) II III IV	3 (20) 11 (73) 1 (7)	7 (29) 17 (71) None	0.43
Balloon/annulus diameter ratio	1.1 ± 0.1	1.0 ± 0.1	0.004

PPMS = pure pliable mitral stenosis, MMVD = mixed mitral valve disease,
NYHA = New York Heart Association classification

The TTE characteristics of both groups are presented in Table 2. The mean total Wilkins score of the PPMS group compared to the MMVD group was 7 ± 1 and 8 ± 1 respectively ($P = 0.004$). Based on this score, near normal anterior mitral leaflets were detected in 12/15 (80%) of PPMS patients vs. 4/24 (17%) in the MMVD group ($P = 0.003$). Thickened margins of the anterior leaflet were detected in 20/24 patients

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AML = anterior mitral leaflet
NYHA = New York Heart Association

Table 2. TTE characteristics

	PPMS (n=15)	MMVD (n=24)	*P* value
Wilkins score	7 ± 1	8 ± 1	0.004
Normal leaflet thickness ≤ 4 mm (%)	12/15 (80)	4/24 (17)	0.003
FPML (%)	13/15 (87)	21/24 (88)	NS
MVA (cm²) Pre-BMV Post-BMV	1.0 ± 0.2 1.6 ± 0.1	1.0 ± 0.1 1.5 ± 0.2	NS 0.08
MR pre-BMV Jet direction: central/eccentric	None	24 (100%) 4/20	
MR post-BMV Jet direction: central/eccentric	6/15 (40%) 0/6	22/24 (92%) 8/14	0.0008 0.04

FPML = frozen posterior mitral leaflet, MVA = mitral valve area,
BMV = balloon mitral valvuloplasty, MR = mitral regurgitation

Table 3. Pre-BMV mitral valve structural components in both groups

	PPMS (n=15)	MMVD (n=24)	*P* value
Annular circumference (cm)	15.4 ± 1.6	15.5 ± 1.4	0.84
Annular diameter (mm)	38 ± 5	36 ± 4	0.18
AMLL/PMLL (cm)	2.8 ± 0.4	2.2 ± 0.5	0.02
AMLT (mm)	5 ± 1	7 ± 1	0.0004
CTL (mm)	11 ± 2	10 ± 2	0.137

AMLL = anterior mitral leaflet length, PMLL = posterior mitral leaflet length,
AMLT = anterior mitral leaflet thickness, CTL = chordae tendinae length

(83%) in the MMVD group, but in only 3/15 (20%) in the PPMS group. No patient showed marked thickening of the entire leaflet, and no difference was found between the groups relating to the incidence of frozen posterior mitral leaflets.

Pre-BMV mitral valve structural analyses relating to the mechanism of MR are presented in Table 3. There was no difference between groups regarding MV annular circumference and diameter or chordae tendinae length directed to the anterior mitral leaflet. However, patients in the MMVD group exhibited a smaller AMLL/PMLL (anterior mitral leaflet length/posterior mitral leaflet length) ratio when compared with the PPMS group (2.2 ± 0.5 vs. 2.8 ± 0.4, *P* = 0.02). This indicates the presence of a relatively shorter length of AML in the MMVD group. The MMVD group demonstrated thickened AML edges compared to the PPMS group (7 ± 1 and 5 ± 1 mm respectively, *P* = 0.0004).

POST-BMV DATA

Non-optimal valve dilatation indicated by final MVA < 1.5 cm² was detected in 2/15 patients (13%) in the PPMS group and in 5/24 (21%) in the MMVD group (*P* = 0.34). Post-valvuloplasty, 6/15 of patients (40%) in the PPMS group demonstrated mild MR, whereas 2/24 (8%) in the MMVD group showed no MR post-procedure. No patient in the MMVD group demonstrated significant deterioration of

MR after valvular balloon dilatation. All the regurgitant jets that appeared after valve dilatation in the PPMS group were eccentric (opposite to the central jet).

DISCUSSION

Understanding the mechanism and pathophysiology of valve disorder is essential for determining the optimal therapeutic approach [11]. In the presence of mixed valvular pathology, i.e., stenosis and regurgitation, the dominant lesion should be determined and careful structural valve analysis performed before either a curative or palliative therapeutic approach.

According to the European guidelines on the management of valvular heart disease, mild rheumatic MR is not a contraindication for BMV [12]; however, assessing the mechanism of regurgitant pathology in the presence of MS is essential for extending our understanding of MR in the presence of other varieties of mixed valvular pathology. In their study of the spectrum of severe rheumatic mitral valve disease in developing countries, Marcus et al. [13] noted that mixed valvular pathology is present in a third of these patients. Pure regurgitation was the most common lesion in the first and second decades, whereas the relative prevalence of pure stenosis increased with age. Purely regurgitant valves had pliable unscarred leaflets (95%), dilated mitral annuli (95%), elongated chordae tendinae (92%) and anterior leaflet prolapse (81%). In contrast, pure stenotic valves had fused commissures (100%) and rigid leaflets (38%) but no evidence of prolapse. There was no anatomic description of mitral structural components regarding different varieties of regurgitation as a part of mixed pathology in that study.

Our data show that mild regurgitation associated with pliable stenotic mitral valve is characterized by a relatively shorter and thickened anterior mitral leaflet. Similar to other studies [4,14], our findings reemphasize the safety of BMV in patients with dominant pliable MS associated with mild MR. However, it should be remembered that these patients are older and have a relatively higher Wilkins score than the patients with isolated pure pliable MS.

During BMV the appearance of a new MR or the increase of a previously mild MR is quite frequent (30–50%), but fortunately the development of clinically significant MR is much rarer (4–12%). Generally, the anatomic substrate of severe MR is leaflet rupture and less frequently damage to the sub-valvular apparatus [15]; therefore, in our daily practice we avoid performing BMV in the presence of mild MR in patients with thick, rigid or calcific AML or in the presence of bilateral commissural calcification.

At present, short leaflets cannot be extended by percutaneous techniques. However, a surgical solution for this structural abnormality has been proposed by Chauvaud et al. [16] in which valve extension with glutaraldehyde-preserved autolo-

gous pericardium is performed during mitral valve repair.

In contrast to our patients, who are characterized by dominant stenotic lesion, in patients with predominant rheumatic MR the main steps in reconstructive surgery are ring annuloplasty and chordae shortening [17]. This indicates that in a different rheumatic setup, other valve components are involved in the regurgitant pathophysiology.

Our data also emphasize that BMV may act ambiguously in relation to MR: on the one hand, it may create MR in a manner similar to surgical commisurotomy. However, it may also abolish or decrease preexisting MR. Both phenomena indicate that commissural morphology and function may also play a role in the mechanism of rheumatic MR.

In conclusion, careful evaluation of mitral valve structural components together with awareness of the limitations of each therapeutic approach can improve our ability to repair rheumatic valves either percutaneously or surgically.

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The only sure thing about luck is that it will change

Wilson Mizner (1876-1933), American playwright