

Research Article: Basic and Applied Anatomy

## Anatomic characteristics of bileaflet mitral valve prolapse – Barlow disease – in patients undergoing mitral valve repair

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### Abstract

*Objective.* Barlow disease is a still challenging pathology for the surgeon. Aim of the present study is to report anatomic abnormalities of mitral valve in patients undergoing mitral valve repair.

*Methods.* Between January 1<sup>st</sup>, 2007, and December 31<sup>st</sup>, 2010, 85 consecutive patients (54 men and 31 women, mean age 59 ± 14 years - range: 28-85 years) with the features of a Barlow mitral valve disease underwent mitral repair. Forty seven percent of patients were in New York Heart Association functional class III or IV. Preoperative transesophageal echocardiography was compared with anatomical findings at the moment of surgery.

*Results.* Transthoracic echocardiography diagnosis of Barlow disease according to the criteria described by Carpentier was confirmed at anatomical inspection. Annular calcifications were found in 28 patients while 7 patients presented single or multiple clefts. A flail posterior mitral leaflet was detected in 32 subjects, while a flail anterior leaflet in 8. Elongation of chordae tendineae was demonstrated in 45 patients and chordal rupture in 31. All patients showed at trans esophageal echocardiography the typical features of Barlow disease. Seventy-seven (90.6%) patients had severe mitral valve regurgitation, in the remaining 9.4% it was moderate to severe. Transesophageal echocardiography failed to identify clefts in 2/7 and chordal rupture in 4/31.

*Conclusions.* bileaflet prolapse > 2 mm, billowing valve with excess tissue and thickened leaflets ≥ 3 mm, and severe annular dilatation, are characteristics of Barlow disease, however the identification of the associated and complex abnormalities of mitral valve is necessary to obtain optimal valve repair.

### Key words

Mitral valve, cardiac surgery, filamin.

### Background

Barlow disease is a relatively common cause of mitral regurgitation, secondary to bileaflet multisegment prolapse (Carpentier's type II dysfunction). The anatomic features of the disease include myxoid degeneration of all components of mitral valve apparatus, with excessive leaflets tissue involving all the scallops, severe annu-

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lar dilatation and multi-jet mitral regurgitation (Anyanwu and Adams, 2007). Aetiology of Barlow disease is at present unknown, however familial aggregation has been described. Recently Lardeaux et al (2011) in a French family have been able to identify three filamin A mutations, p.Gly288Arg and p.Val711Asp, and a 1,944-bp genomic deletion coding for exons 16 to 19. The recent finding of co-existence of Barlow's disease and axillary artery aneurysms in two brothers raises the possibility the disease to be part of a connective tissue disorder (Kasahara et al., 2012). Myxomatous degeneration of the extracellular matrix may depend on genetic and less often acquired conditions, with enhanced activity of matrix metallo proteases and cysteine endoproteases and local absence of tenomodulin (Guy and Hill, 2012) The disease is defined according to the criteria described by Carpentier (Carpentier et al., 1980; Carpentier, 1983) as a bileaflet prolapse > 2 mm, billowing valve with excess tissue and thickened leaflets  $\geq 3$  mm, and severe annular dilatation. Chordal elongation or rupture, annular and papillary muscle calcification may be present.

The goals of reconstructive surgery are preservation or restoration of normal leaflet motion, creation of a large surface of coaptation, and stabilization of the entire annulus with a remodelling annuloplasty (Savage et al., 2003; Adams et al., 2010). Support is restored by resection of prolapsing segments, chordal transfer, application of neochordae, or papillary muscle-repositioning. The sliding plasty technique may also be used to restore appropriate tension on mildly elongated chordae. Areas of leaflet and chordal calcification or fusion should be resected to restore mobility of the leaflet(s). Annular dilation is addressed by annular plication and annuloplasty (Carpentier et al., 1995). Aim of present investigation was to evaluate, in a single high-volume centre, the anatomical abnormalities of mitral valve apparatus observed at surgery in patients undergoing mitral valve repair and to compare them with transesophageal echocardiographic (TEE) findings.

## Materials and methods

Between January 1<sup>st</sup>, 2007, and December 31<sup>st</sup>, 2010, 85 consecutive patients (54 men and 31 women; mean age  $59 \pm 14$  years) presented at the authors' centre with features of Barlow Disease. All procedures were performed by a single surgeon. Barlow Disease was recognized by preoperative echocardiogram and confirmed at surgical inspection. Patients presenting features of fibroelastic deficiency and Marfan disease were excluded from the study.

### Preoperative examinations

Transthoracic echocardiography (TTE) and TEE were performed in all patients before surgery and the echocardiograms were reviewed by a senior cardiologist. TEE was also performed during surgical intervention in all cases.

### Surgery

Full sternotomy was performed in most cases (94.1%), whereas in 5 patients (5.9%) a minimally invasive approach through a smaller incision at the fourth right intercos-

tal space was possible. Mitral valve was accessed through a left atriotomy in the interatrial groove and the repair was performed according to the principles described by Carpentier et al ( 1995). Accurate inspection with assessment of abnormalities of mitral valve anatomy allowed the choice of the strategy for mitral valve repair.

### Statistical Analysis

Data are presented as mean  $\pm$  standard deviation for continuous variables, as number and percentage for categorical variables, and as median for non-parametric variables.

### Results

The clinical and echocardiographic characteristics of patients entered in the study are reported in Table 1 and 2. The main preoperative comorbidities were atrial fibrillation (31.8%) and hypertension (31.8%), Forty seven percent were in advanced New York Heart Association (NYHA) functional class (III or IV). TTE and TEE revealed dilated left atrium and dilated left ventricle with increased end-systolic and end-diastolic volumes. Mean left ventricular ejection fraction was 62%,. Seventy-seven (90.6%) patients had severe mitral valve regurgitation, in the others (9.4%) regurgitation was evaluated as moderate to severe.

At valve examination during surgery all patients showed bileaflet prolapse > 2 mm, billowing valve with excess tissue and thickened leaflets, and severe annular dila-

**Table 1** – Patients characteristics (n=85).

Number of Patient	85
Age (years) [range]	59 $\pm$ 14 [28-85]
Gender M/F	54/31
BSA (m2) [range]	1.84 $\pm$ 0.20 [1.35-2.38]
Clinical Parametres:	n (%)
NYHA Class	
I	27 (31.8)
II	18 (21.2)
III	30 (35.3)
IV	10 (11.7)
Atrial Fibrillation	27 (31.8)
Hypertension	27 (31.8)
Diabetes	1 (1.2)
COPD	2 (2.3)
Chronic Renal Disease	2 (2.3)

Abbreviations. M/F: Male/Female; BSA: Body Surface Area; NYHA: New York Heart Association; COPD: Chronic Obstructive Pulmonary Disease.

**Table 2** – Bidimensional echocardiographic features.

Echocardiographic Parametres	
EDD (mm)	58.02±6.14 [40-73]
ESD (mm)	34.81±6.88 [21-60]
ST (mm)	10.32±1.42 [7-14]
WT (mm)	10.04±1.27 [7-14]
EDV (ml)	152.40±43.91 [52-287]
ESV (ml)	55.84±19.54 [15-132]
EDVI (ml/m <sup>2</sup> )	82.30±19.36 [31-138]
ESVI (ml/m <sup>2</sup> )	30.26±9.36 [9-71]
LVEF (%)	62.32±7.11 [45-76]
LAD M-mode (mm)	47.95±6.47 [36-67]
LA Area (cm <sup>2</sup> )	28.50±7.46 [17-50]
PAP mean (mmHg)	37.08±15.88 [20-120]

Abbreviations. EDD: End-Diastolic Diameter; ESD: End-Systolic Diameter; ST: Septum Thickness; WT: Wall Thickness; EDV: End-Diastolic Volume; ESV: End-Systolic Volume; EDVI: End-Diastolic Volume Index; ESVI: End-Systolic Volume Index; LVEF: Left Ventricular Ejection Fraction; LAD: Left Atrium Diameter; LA: Left Atrium; PAP: Pulmonary Artery Pressure.

tation. In addition to these findings, which confirmed the diagnosis of Barlow disease, in 28 (33.0%) patients annular calcifications were found and 7 patients presented single or multiple clefts. A flail posterior mitral leaflet was detected in 32 (37%) subjects, while a flail anterior leaflet in 8 (9%). Elongation of chordae tendineae was demonstrated in 45 (53.0%) and chordal rupture in 31 (36.5%); the finding of papillary muscles elongation or calcification was rare (Figure 1).

All patients showed at TTE and TEE the typical features of Barlow disease (Figure 2). Seventy-seven (90.6%) patients had severe mitral valve regurgitation, in the remaining 9.4% it was moderate to severe. TEE failed to identify clefts in 2/7 and chordal rupture in 4/31.

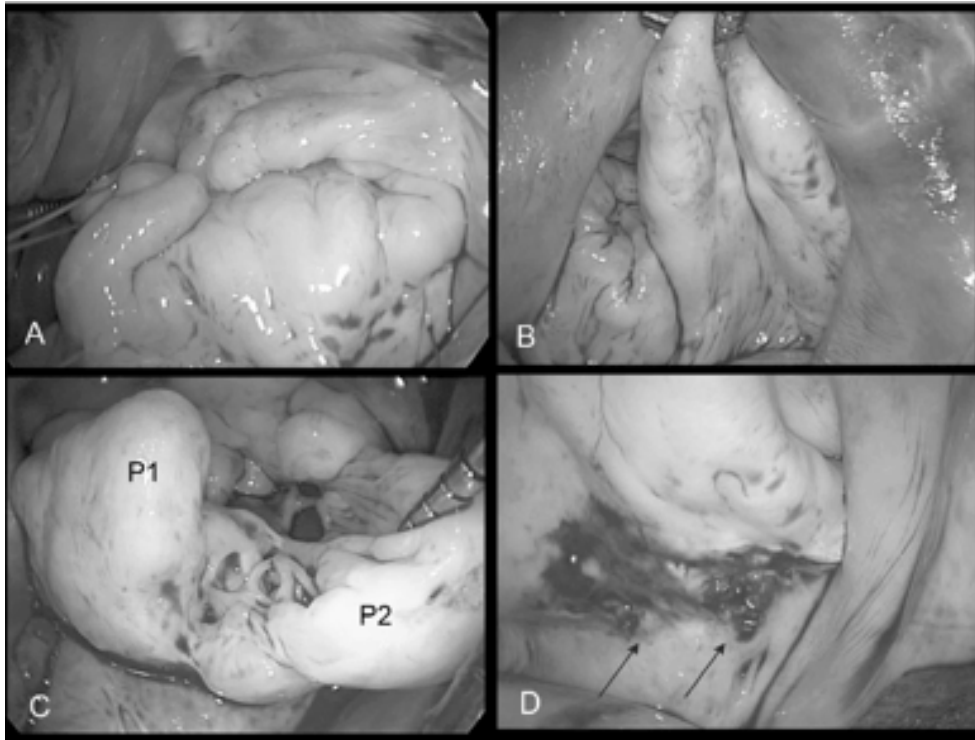
Mitral valve echocardiographic and inspective pathological characteristics are reported in Table 3.

The operative techniques adopted on the basis of anatomical evaluation are reported in Table 4.

## Discussion

In patients with bileaflet mitral valve prolapse, adequate preoperative evaluation of anatomic abnormalities through preoperative TEE and visual inspection at surgery allows to choice the more appropriate surgical strategy of mitral valve repair to obtain an optimal functional correction (Anyanwu and Adams, 2010).

Few studies have reported the anatomical abnormalities of mitral valve apparatus



**Figure 1** – Anatomical findings in Barlow disease (atrial views): A) Floppy mitral valve with bileaflet prolapse, thickened leaflets and dilated annulus, B ) Severe thickening of posterior leaflet with severe prolapse of the free edge c) anterior papillary muscle calcifications, fusion of chordae tendineae leading to decreased amplitude of P1-P2 junction. D) atrialization of left posterior leaflet, presence of “clefts” and thrombosis (arrows).

in Barlow disease and their relation with surgical strategy and clinical outcome. In particular the identification of further leaflets abnormalities, such as valve clefts, and of chordal integrity or elongation may suggest additional repair techniques to the surgeon, such as chordal transfer, application of neochordae, or use of sliding plasty technique that may improve surgical results and long term maintenance of valve competence (David et al., 2005; Adams et al., 2006a; Schaff et al., 2007).

In our study elongation of chordae tendineae and chordal rupture were found in more than 40% of patients. Leaflet clefts in 8% and annular calcification in 33%. Flail was more common for posterior leaflet. In the paper by Flameng et al. (2008) 83 patients with Barlow disease were examined. The incidence of leaflets clefts and chordal rupture were similar to that found in our patients. Elongation of chordae tendinae and mitral annulus calcification were less frequent than in our population. Mean age of patients was not significantly different ( 61 years in the study by Flameng et al in comparison to our patients).

The risk of late failure presents two phases: a peaking early risk phase in the first year followed by a slow-rising late phase with risk of undergoing reoperation

**Table 3** – Mitral Valve Analysis (n=85).

<b>Echocardiographic Findings</b>		
Mitral Valve Regurgitation n (%)		
Moderate-Severe	8 (9.4)	
Severe	77 (90.6)	
Vena Contracta (cm)	0.74±0.16 [0.3-1.1]	
EROA (cm <sup>2</sup> )	0.58±0.26 [0.25-1.6]	
Anulus AP (mm)	43.05±3.92 [33-55]	
<b>Surgical lesions: number (%)</b>	<b>Visual inspection</b>	<b>TEE</b>
Excess Tissue*	85 (100)	85 (100)
Bileaflet Prolapse*	85 (100)	85 (100)
Leaflet Thickening*	85 (100)	85 (100)
Anular Dilatation*	85 (100)	85 (100)
Anular Calcification	28 (33)	27 (31)
Chordae Elongation	45 (53)	45 (53)
Chordae Rupture	31 (36)	27 (31)
Multiple Clefts	7 (8)	5 (6)
Flail AML	8 (9)	8 (9)
Flail PML	32 (37)	32 (37)

Abbreviations. EROA: Effective Regurgitant Orifice Area; AP: Anterior-Posterior; PM: Papillary Muscle; AML: Anterior Mitral Leaflet; PML: Posterior Mitral Leaflet; TEE: Trans Esophageal Echocardiography.

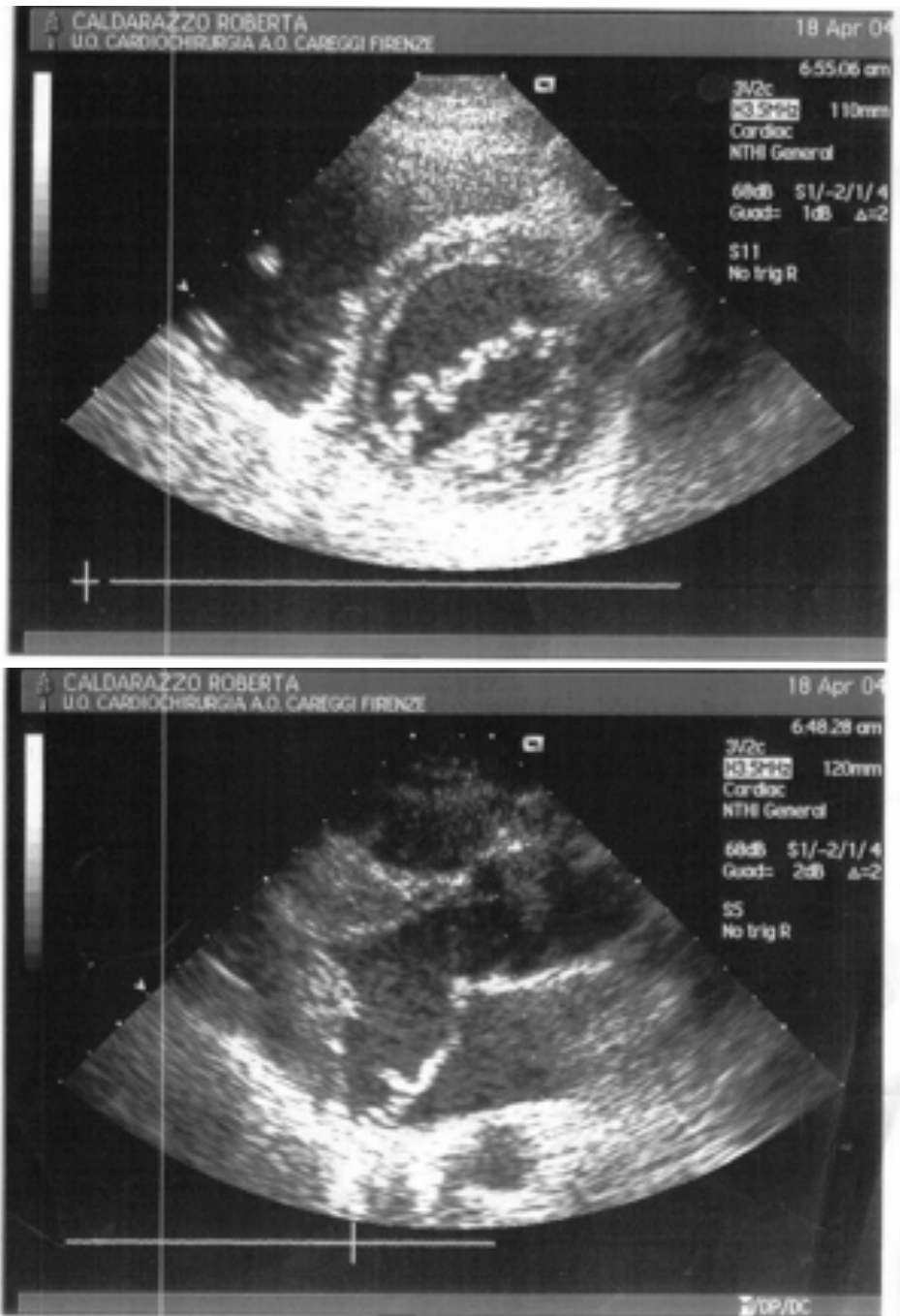
\* Fundamental criteria to define Barlow’s Disease at surgical inspection.

**Table 4** – Operative techniques.

<b>Type of Surgical Intervention:</b>	<b>number (%)</b>
PMLQR + Prosthetic ring	20 (23.5)
PMLQR + Prosthetic ring + Neochordae	13 (15.3)
PMLQR + Sliding PML + Prosthetic ring	20 (23.5)
PMLQR + Sliding PML + Prosthetic ring + Neochordae	23 (27.1)
Prosthetic ring + Neochordae	9 (10.6)

Abbreviations. PMLQR: Posterior Mitral Leaflet Quadrangular Resection; PML: Posterior Mitral Leaflet.

(Dumont et al., 2007). This may be due to the surgical technique or to valve-related factors, and is well recognized that the process of tissue degeneration, involving mainly the chordae, goes further after surgical correction, leading to recurrent regurgitation from chordal rupture or elongation; the implantation of artificial chordae is described to be associated to better outcomes, probably because they can prevent, at



**Figure 2** – Barlow disease at 2-D echocardiography A) short axis showing thickened and redundant mitral leaflets, B ) long axis demonstrates severe bileaflet prolapse with thickened chordae tendineae.

some extent, the disease to progress; we used artificial chordae in more than a half of cases, and this proportion is increasing in our more recent experience.

Repair of the mitral valve is currently the best surgical treatment for complex degenerative mitral valve disease and should be pursued even in the most advanced forms of Barlow disease. Careful selection of patients, accurate description of anatomical abnormalities leading to optimization of surgical techniques including use of large size annuloplasty rings (Adams et al., 2006b) and of artificial chordae, along with surgical expertise in mitral valve repair, are the main determinants to reduce the risk of recurrent mitral regurgitation and to ensure a better outcome.

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