# ROLE OF ISOMETRIC VERSUS DYNAMIC EXERCISE IN PRECIPITATING ARRHYTHMIAS IN MITRAL VALVE PROLAPSE SYNDROME

THESIS

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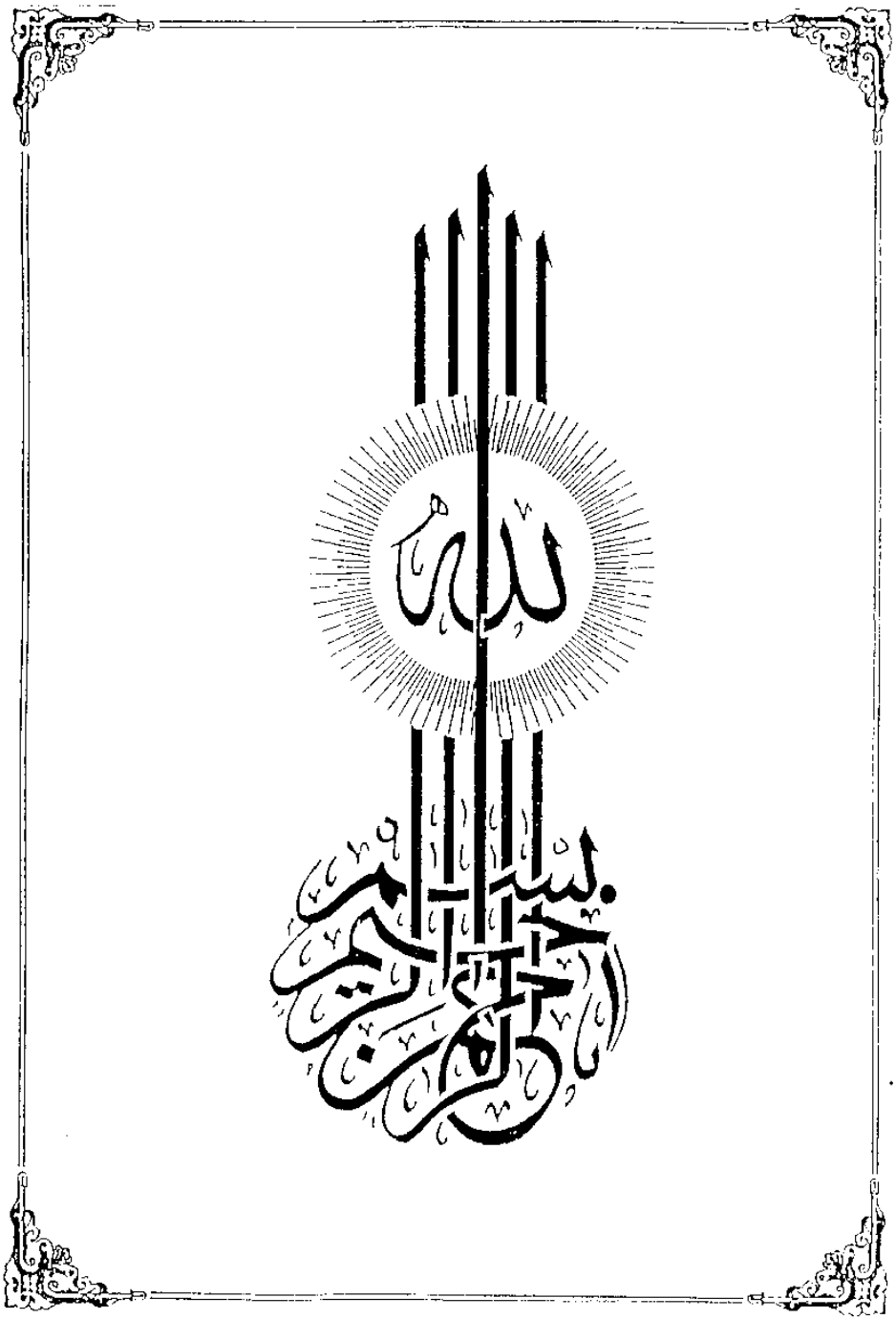

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# INTRODUCTION

In 1963, Barlow published an angiographic evidence that systolic clicks and late systolic murmurs are associated with prolapse of the posterior leaflet of the mitral valve (1). Since that first description, numerous reports have been published (2) and various terms have been applied to the disorder : floppy, billowing mitral valve, Barlow's syndrome or Reid - Barlow's syndrome, click - late systolic murmur syndrome, complex segmental cardiomyopathy .. etc. Mitral leaflet prolapse syndrome ( MLPS ) remains the commondenomenator and the sine qua non for the diagnosis (1).

This syndrome is a common but variable disorder resulting from diverse pathologic mechanisms of the mitral apparatus manifested by posterior displacement of one or both mitral leaflets across the atrioventricular groove into the left atrium during systole (2). There were four historical descriptions :

1. The initial extra cardiac or pericardial phase, lasted from 1913 ( Gallavardin ) to 1961. The mid systolic click associated with late systolic murmur was attributed to pleuropericardial adhesions (1).

2. The leaflet–chordal phase was introduced during the 1960S as an explanation of these acoustic phenomena (1).

3. Myocardial phase began in 1968 with Engle's observation of inferior wall contraction abnormalities seen in left ventricular cineangiograms (1).

4. The annular phase of investigations has centered chiefly on the role of intrinsic dilatation (1).

A wide spectrum of cardiac rhythm and conduction disorders occur in all patients with valvular heart diseases. Most notable in this regard is mitral leaflet prolapse, in which cardiac dysrhythmia is now recognised to be the complication of highest frequency (3). It is well known that exercise precipitates various ( and sometimes serious ) types of arrhythmias in MLPS which carry great hazards to the patients. Previous studies dealt with dynamic exercise-induced arrhythmias in this disorder. This study aims at dealing with isometric versus dynamic exercise-induced arrhythmias in MLPS, since different hemodynamic effects of the two types of exercise may affect the incidence, types and seriousness of the induced arrhythmias. This may give rise to detecting and understanding new aspects of that syndrome and aiding in the development of its management.

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# CHAPTER ONE

# MITRAL LEAFLET PROLAPSE SYNDROME

# CHAPTER ONE

## Mitral Leaflet Prolapse Syndrome ( MLPS )

Mitral leaflet prolapse syndrome ( MLPS ) is a descriptive term that can be applied to several cardiac physiologic and disease states (4). The characteristic lesion is prolapse of mitral valve leaflet (s) into the left atrium during systole (5).

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### I. Etiology

MLPS is usually reported as a primary lesion, in the form of myxomatous degeneration of the mitral valve leaflets (4). Its occurrence in Marfan's syndrome is well documented (6). But there is still no evidence that it is - as mentioned in some studies - a forme fruste of that syndrome (7). In one study on 85 patients with MLP, only one patient had a Marfanoid habitus (6). In fact, MLP is considered a specific sign in Barlow's syndrome (8), occurring in an autosomal dominant manner ( 9,10 ), with complete penetrance ( 26.8 % ) among first degree relatives, but may be also non familial (7).

Mitral leaflet prolapse syndrome ( MLPS ) is caused by diseases which involve one part or more of the mitral apparatus; left ventricular wall, papillary muscles, chordae, mitral annulus, leaflets, or atrial wall, such as the following :

1. Rheumatic mitral valve disease (4), that may lead to annular dysfunction during acute phase (11).

2. Spontaneous chordal rupture (4).

3. Papillary muscle dysfunction resulting from ischemic heart disease or dilated cardiomyopathy (4), or avulsion of a part of it during mitral valvotomy (12).

4. Ventricular contraction abnormalities resulting from any condition ( e.g. coronary artery disease ) (13).

5. Chest trauma involving the mitral valve apparatus (2).

6. In other cases, MLPS represents a dysfunction of the valve apparatus, i.e. prolapse of a normal valve, as occurs in the following conditions :

   - During ventricular premature beats, even in normal subjects ( 1,14 ).
   - Decreased blood volume (4).
   - Giving a potent vasodilator (4).
   - Hypercontractile states as in thyrotoxicosis (4).

- Hypertrophic cardiomyopathy (11), which leads to systolic prolapse of the posterior leaflet and anterior motion of the anterior leaflet of the mitral valve (4).

- ASD ostium secondum defect ( but there may be primary MLP in patients with ASD as well ) (4).

In the above conditions, the left ventricular volume is decreased, and a normal mitral valve may be disproportionately large compared with the ventricle during systole, which would permit it to prolapse.

MLP in the above cases is a secondary state (4).

It is well documented that primary MLP usually occurs in association with one or more of many disorders such as :

- Prolapse of other valve (s) ( 4,15 ).
- Thoracic skeletal abnormalities : pectus excavatum, pectus carinatum, scoliosis, rib deformity, and specially straight back syndrome (7). A study on 115 Chineses with MLPS showed that 31.3 % had straight back (7), while others found MLPS in 40 % of patients with thoracic skeletal abnormalities (16). According to various studies, it is likely that both MLP and the straight back syndrome are features of a more generalized disorder which is transmitted in an autosomal dominant manner. However, the familial occurrence of MLP doesnot depend on its association with the straight back syndrome (7).

- Secondum ASD ( 1,4 ) and other congenital heart diseases (4).
- Emphysema and pulmonary fibrosis (4).
- Autonomic nervous system disorders, such as beta adrenergic state (4).
- Atrioventricular bypass tracts (4).
- Systemic lupus erythematosis (1).
- Ischemic heart disease. It has been reported that both disorders lead to each other (11).
- Thyrotoxicosis : it has been reported that MLPS is found in high incidence in Graves' disease, but in normal incidence in toxic goitre (2). Four similarities between MLPS and Graves' disease are known (2) :

  1. The two conditions are dominant in females.
  2. Genetic factors are identified in both conditions.
  3. Graves' disease is associated with the major histocompatibility antigens, that are highly prevalent in MLP.
  4. Autoimmunity is a causative factor in Graves' disease, and has been also mentioned in the etiology of MLP.

Thus,there is a possibility of a common denomenator.

Other associated conditions were mentioned by Braunwald E (17).

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## II. Prevalence

The prevalence of the condition appears to be increasing, partly owing to increased clinical awareness and partly owing to increased use of echocardiography. Figures between 1 % - 21 % have been reported in otherwise normal population (2). In one study, it was discovered in 1,4 % of black south African school children, while others found it in 17,9 % of the same category, 4 % of presumably normal young males and 6 - 10 % of presumably normal young women studied by echo cardiography (18).

Prepubertal left ventricular volume, mass, and long axis are probably similar in both sexes, but the post pubertal growth pattern that normally results in a relatively smaller female body size appears to be accompanied by a relatively smaller left ventricular volume, mass, long axis, and perhaps annular circumference. This may give a partial explanation for the relative infrequency of prepubertal mitral leaflet prolapse, the striking predominance in the mature female, and the tendency for male incidence to increase by aging (1).

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## III. Pathology

The mechanism of mitral valve function is very complex and - as mentioned above - any condition which affects one or more of the six members of the mitral apparatus may lead to MLP. The primary disorder appears to be a degenerative condition of chordae and leaflets with resultant lengthening and attenuatien of chordae, and somewhat voluminous leaflets (11). Papillary muscle dysfunction from any cause - but most importantly occlusive CAD - will have the same functional effect. With chronic mitral valve disease, prolapse or partial prolapse probably relates more to fused, thickened and unequal chordae (19). However, the clinical spectrum of MLP ranges from normal mitral anatomy and function to severe distortion of leaflets and chordal anatomy with severe mitral regurgitation (18).

Main pathology of the disorder includes hook-like protrusion - or - generalized systolic ballooning of leaflet tissue into the left atrium, besides; redundancy may affect one, two , or the three scallops of the prolapsed leaflet. This abnormality affects mainly the posterior leaflet, less frequently both leaflets, but isolated anterior leaflet prolapse is rare (1). The cause of this abnormality was revealed histologically to be increased accumulation of the normally present acid mucopolysaccharides in the spongiosa of leaflets, which has led to the term : myxomatous degeneration (20). This does not mean that actual degeneration occurs in the valvular tissue (4). Abnormal periodicity in collagen fibres

was not observed, but small isolated areas of collagen destruction even within the fibrosa are very common even in otherwise normal hearts (21). Isolated fibrosis in and around the posterior papillary muscle has been described in an autopsy case (22). In the absence of an history of bacterial endocarditis, the valve cusps are not vascularised nor do they contain chronic inflammatory cells. Small areas of fibrin deposition occur on the surface (21). These histologic changes are not specific and may occur in mitral regurgitation of other origins (1). Non specific myxomatous changes in the mitral valve leaflet occur with aging, but are usually minor and not clinically significant. The incidence of extensive myxomatous changes that involve the mitral valve in older patients is low, and such changes are unlikely to be the result of aging alone (23). The result of these pathologic changes is that the leaflets become redundant, and in themselves may have considerable propensity to prolapse during systole (4). This fact was seen by the surgeons in all surgically excised prolapsed mitral valves (23).

The above changes are similar to those present in Marfan's syndrome (4). Other changes may include a limited area of damage in the papillary and adjacent muscle secondary to increased mechanical stress (24), enlarged mitral valve diameter (23), and mitral annular dilatation that may be moderate or marked. The annulus may also be calcified; a change that is , for all practical purposes, confined to Marfan's syndrome (1). Several radionuclide studies have documented the presence of perfusion defects at rest and following exercise in these patients in the absence of CAD (25).

## IV. Pathophyisology

1. Mechanisms of Production of Anatomically or Functionally Lengethened Chordae And Prolapse of The Posterior Leaflet :

- In primary MLP, the chordae are lengthened allowing the voluminous posterior leaflet to billow into the left atrium (11).

- In papillary muscle dysfunction, the chordae are functionally lengthened and there is prolapse of the posterior leaflet because of abnormal or no contraction of the papillary muscle and adjacent myocardium (11).

- Small left ventricular cavity ( as in HOCM ), leads to functionally enlarged chordae, and prolapse of the posterior leaflet due to asymmetrical myocardial hypertrophy (11).

- Anatomically and functionally unequal chordae lead to partial prolapse in chronic rheumatic mitral valve disease (11).

2. Left Ventricular Contraction Abnormalities :

The characteristic pathophysiological aspect of MLP is contraction abnormalities of the left ventricle as detected by