



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Floppy Valve Syndrome

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ABSTRACT

Mitral valve prolapse is a valvular heart disease which results from the systolic movement of abnormally thickened mitral valve leaflets into left atrium during left ventricular systole. MVP refers to expansion of area of mitral valve leaflets with elongated chordae tendineae or rupture of chordae and mitral annular dilation. Rupture of chordae may be associated with heritable syndromes of connective tissue disorders. It usually inherited either through the autosomal dominant gene or chromosome X, which is less common compared to the former. MVP may lead to either progressive MVR or stimulate autonomic nervous system or neurohumoral activation. The former is termed as MVP and later is termed as “Floppy valve syndrome”. Symptoms of FVS include palpitations, dyspnea, chest pain, and neuropsychiatry symptom. Complications of FMV include infective endocarditis, Thromboembolic complications, systolic arterial hypertension, cardiac arrhythmias or cardiac death. Initially pharmacological agents are used as first line therapy. When severe mitral regurgitation is present in asymptomatic patient with FMV/MVP surgical intervention such as valve repair or valve replacement is recommended.

Keywords: Mitral valve, FMV.

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Received 01 October 2018, Accepted 17 November 2018

Please cite this article as: Siddhartha L *et al.*, Floppy Valve Syndrome . American Journal of PharmTech Research 2018.

INTRODUCTION

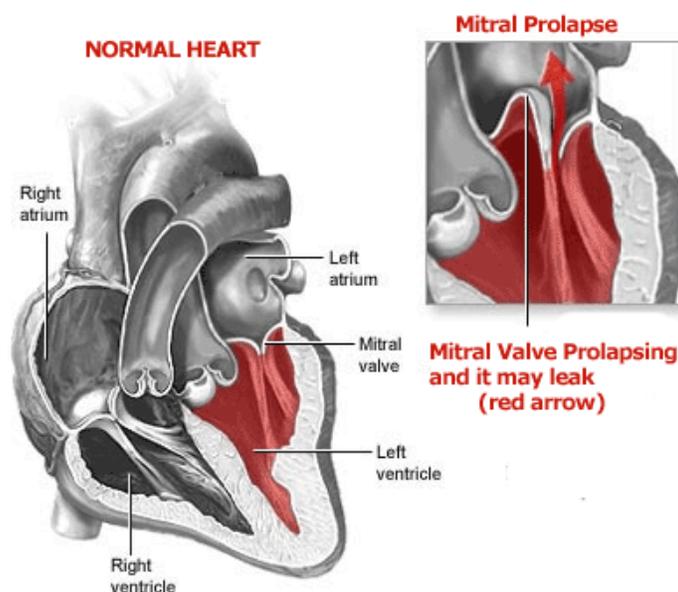
“MITRAL VALVE SYNDROME” [MVP] is also known as, “Floppy mitral valve syndrome”, “Click murmur syndrome”, “Billowing mitral leaflet” or “Barlow syndrome”. MVP is a valvular heart disease results from the systolic movement of portion(s) or segments of mitral valve leaflets into left atrium during left ventricular systole. The term FMV(Floppy mitral valve) comes from surgical and pathologic studies and refers to expansion of area of mitral valve leaflets with elongated chordae tendineae, chordae tendineae rupture and often mitral annular dilation.

Inheritance:

It is transmitted by two forms of inheritance:

Autosomal dominant inheritance, which is the most common type. At present 3 gene loci have been reported.

Chromosome X, which is rarely seen.



Classification:

- FMV/MVP occurs in heterogeneous group of patients with wide spectrum of mitral valve involvement and hemodynamic abnormalities from mild to severe. Mitral valves with diffuse thickening are referred to as “Barlow’s valve”, while patients with regional thickening of mitral valve are referred to as a “Fibroelastic deficiency valve”. Two types of symptoms can be defined in FMV/MVP patients.

Classification of FMV/MVP	
FMV/MVP/MVR	FMV/MVP syndrome
<ul style="list-style-type: none"> • Common mitral valve abnormality with a spectrum of structural changes, mild to severe <p>The basis for:</p> <ul style="list-style-type: none"> • Systolic click; mid-late systolic murmur • Mild or progressive mitral valve dysfunction • Progressive MVR, atrial fibrillation, congestive heart failure • Infective endocarditis • Embolic phenomena • Characterized by long natural history • May be heritable or associated with heritable disorders of connective tissue • Conduction system involvement possibly leading to arrhythmias and conduction defects 	<ul style="list-style-type: none"> • Patients with FMV/MVP • Symptoms complex: palpitations, fatigue, exercise intolerance, dyspnea, chest pain, postural phenomena, syncope-presyncope, neuropsychiatric symptoms • Neuroendocrine or autonomic dysfunction may provide explanation for symptoms including: high catecholamine regulation abnormality, β-adrenergic receptor abnormality, hyperresponsive to adrenergic stimulation, parasympathetic abnormality, baroreflex modulation abnormality, renin-aldosterone regulation abnormality, decreased intravascular volume with upright posture, atrial natriuretic factor secretion abnormality • FMV/MVP – a possible marker for autonomic dysfunction

Based on these symptoms it is classified into FMV/MVP/MVR and FMV/MVP syndrome. In one group of patients, symptoms, physical findings and natural history are directly related to progressive mitral regurgitation and its complications through their effects on left ventricular structure and function, and pulmonary circulation. In the other group of patients, symptoms cannot be explained by degree of MVR alone, activation of the autonomic nervous system or neuroendocrine dysfunction has been implicated for explanation of the symptoms in this group of patients. This group is referred to as the “FMV/MVR SYNDROME”.

- Based on leaflet thickness, type of connection to the mitral annulus, and concavity. Subtypes can be described as classic and non classic, symmetric and asymmetric, flail and non flail.

Classic and nonclassic:

Prolapse occurs when mitral valve leaflets are displaced more than 2mm above the mitral annulus high points. The condition can be further divided into classic and non classic subtypes: based on the thickness of mitral valve leaflets: upto 5mm is considered non classic; while beyond 5 mm is considered classic MVP.

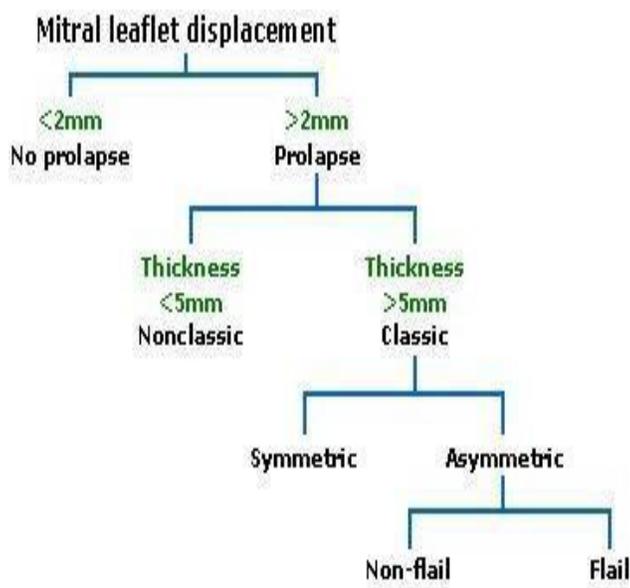
Symmetric and asymmetric:

Classical prolapse may be subdivided into symmetric and asymmetric; referring to point at leaflet tips join the mitral annulus. In symmetric coaptation, leaflet tips meet at a common point on the annulus. Asymmetric coaptation is marked by one leaflet displaced toward the atrium with respect

to the other. Patients with asymmetric prolapse are susceptible to severe deterioration of mitral valve, with possible rupture of chordae tendineae and the development of a flail leaflet.

Flail and non- flail:

Asymmetric prolapse is further subdivided into flail and non flail. Flail prolapse occurs when a leaflet tip turns outward, becoming concave toward the left atrium, causing the deterioration of the mitral valve. The severity of flail leaflet varies, ranging from tip eversion to chordal rupture. Dissociation of leaflet and chordae tendineae provides for unrestricted motion of the leaflet. Thus, patients with flail leaflets have higher prevalence of mitral regurgitation than those with the non-flail subtype.

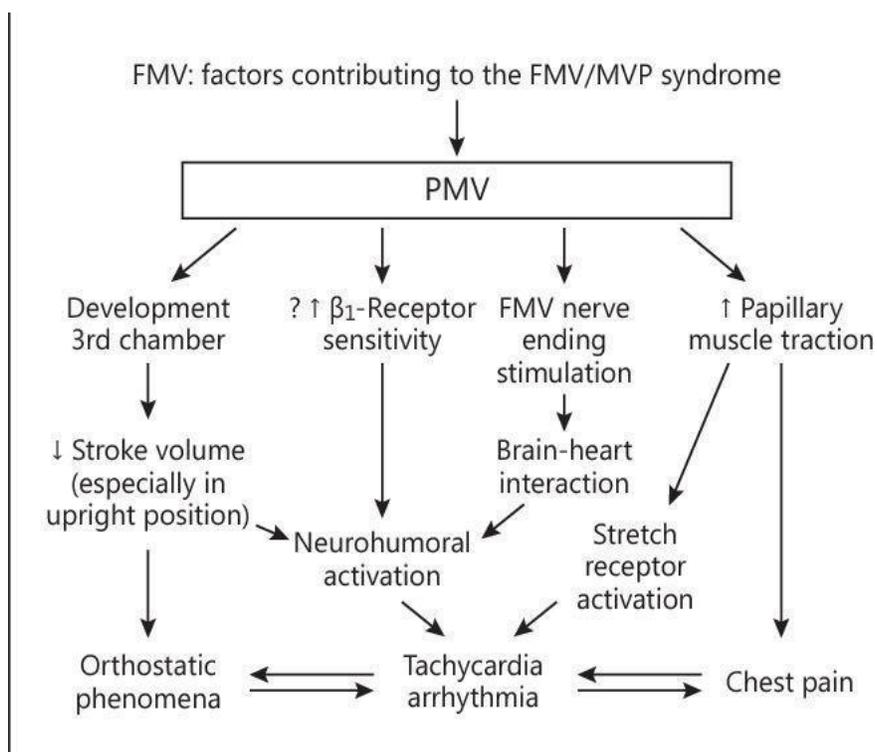


Signs and symptoms:

Most individuals with MVP have no symptoms and do not require treatment or close monitoring. However, some individuals can be symptomatic and most common symptoms in these patients include:

- Murmur: When the posterior leaflet prolapses, the murmur may radiate anteriorly along the left sternal border; when the anterior leaflet prolapses, the murmur may radiate to axilla and to spine.
- Orthostatic phenomena (orthostatic tachycardia, hypotension and arrhythmias)
- Syncope or Presyncope
- Fatigue/ exercise intolerance
- Palpitations
- Chest pain
- Dyspnea, Hyperventilation
- Migraine (one sided headache, accompanied with nausea)

- Dizziness
- Panic attacks
- Anxiety
- Lightheadedness.
- Balance problems, vertigo
- Insomnia, sleep disturbances
- Difficulty in concentrating
- Cold sweats
- Numbness or tingling in fingers or toes.



Risk factors:

- MVP occurs at equal rates in men and women. However, for the reasons not clear, men are with MVP are at higher risk of complications (such as infectious endocarditis, sudden cardiac death, heart attack, stroke or severe mitral regurgitation) than women.
- Certain connective tissues disorders also increase the risk of MVP such as:
 1. Ehlers -Danlos syndrome
 2. Osteogenesis imperfecta
 3. dominant cutis laxa
 4. Pseudoxanthoma elasticum

5. X-linked valvular dystrophy

6. Marfan syndrome.

- Another risk factor of MVP is hypertrophic cardiomyopathy, which may cause the mitral valve leaflets to elongate or thicken. Scoliosis, some type of muscular dystrophy, polycystic kidney disease, and Grave's disease also increase the risk of MVP.

- Other risk factors include:

1. Family history of floppy valve syndrome

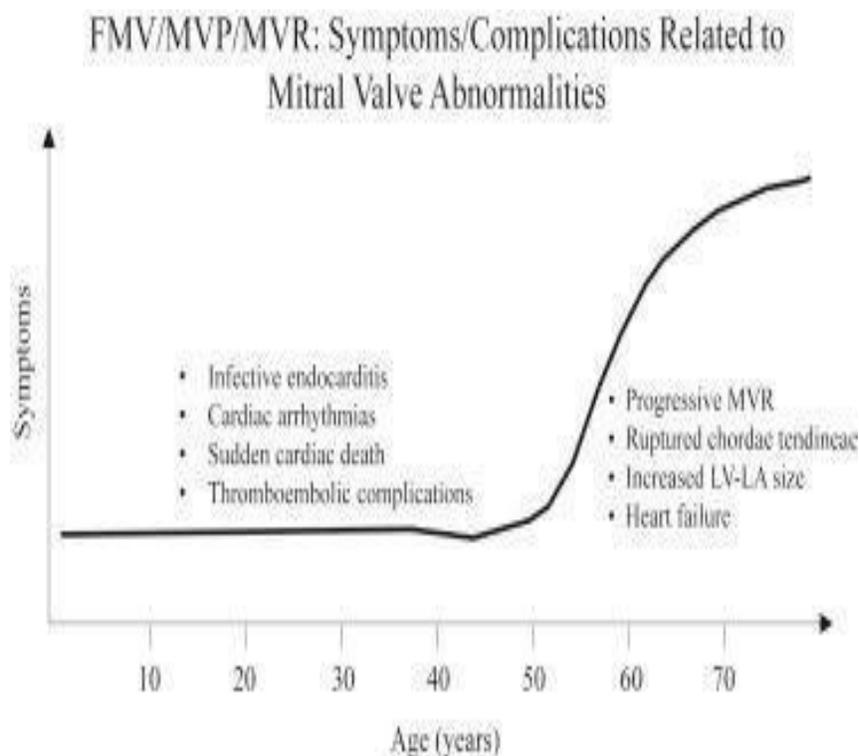
2. Hypotension(low blood pressure)

3. Low body weight

4. Thin chest diameter

5. Chest wall deformities

6. A history of rheumatic fever



Complications:

- Mitral valve regurgitation
- Arrhythmias
- Infective endocarditis
- Sudden cardiac death
- Cerebrovascular ischemic events

- Thromboembolism

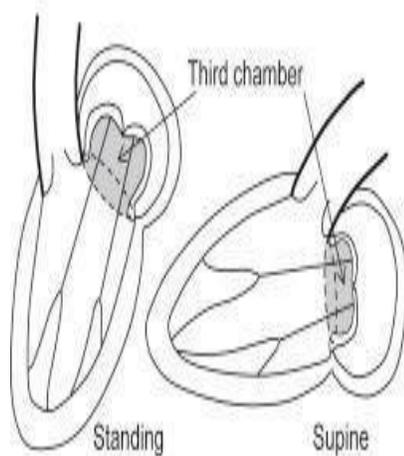
Diagnosis:

The FMV should be the basis for the diagnosis of MVP. Auscultatory findings and imaging characteristics are directly related to pathology and function of mitral valve apparatus.

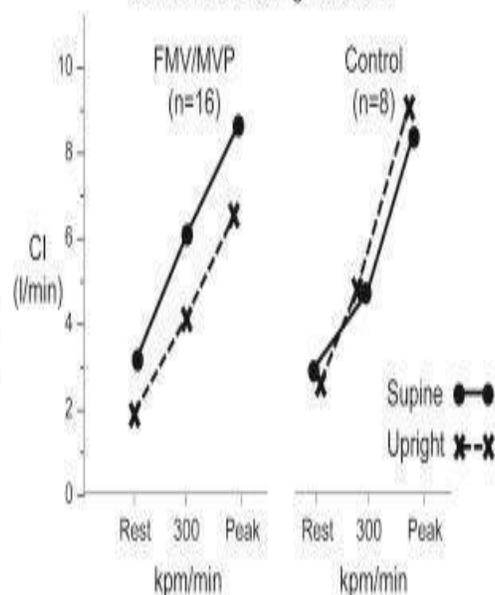
1. Physical examination
2. Electrocardiogram and Chest X ray
3. Echocardiography and Doppler echocardiography
4. Cardiac magnetic resonance imaging
5. Cardiac catheterization
6. Surgical inception
7. Post mortem examination

Pathogenesis:

Prolapse of the FMV is the situation in which a redundant mitral valve leaflet(s) prolapses into left atrium during left ventricular systole. As the result, a dynamics events are set in motion. The prolapsing FMV becomes a space occupying lesion into left atrium, which results in the development of third chamber with the border of mitral valve annulus and prolapsing mitral valve leaflets. Thus, during the ventricular systole the left heart consists of three chambers: left ventricle, left atrium and third chamber. Physiologically, the third chamber acts like a ventricular aneurysm since the blood within the space of this chamber do not contribute to effective stroke volume. FMV/MVP syndrome patients consistently exhibited a smaller ventricular end diastolic volume and cardiac output in the upright position compared to supine, and this difference was maintained throughout the exercise period.

FMV/MVP Syndrome: Orthostatic Phenomena (3rd Chamber)

Cardiac index (CI) in the Supine and Upright Posture, at Rest and During Exercise



- The prolapsing mitral valve results in traction of papillary muscles. Papillary muscle traction may result in left ventricular contraction and relaxation abnormalities and stretch receptors. Stretch receptors activation may result in membrane depolarization and cardiac arrhythmias.
- The human mitral valve has distinct patterns of invention. Mechanical stimuli caused by abnormal coaptation of FMV/MVP may cause an abnormal autonomic nerve feedback between central nervous system and mitral valve. Patients with FMV/MVP syndrome with normal left ventricular size and function, and normal left atrial size without significant mitral regurgitation and heart failure had higher 24 hour urinary epinephrine and norepinephrine excretion compared to normal controls. In addition, the frequency of premature ventricular beats detected in these patients by ambulatory monitoring paralleled urine catecholamine excretion. Catecholamines and premature ventricular beats decreased significantly during the night; the supine position may also have contributed to decrease in catecholamines. An increase in the adrenergic tone can be associated with shortening of left ventricular systole. Increased adrenergic tone in the patients with FMV/MVP syndrome prompted a study to determine the response of adrenergic stimulation

TREATMENT:

- **MEDICATIONS:**

1. **Beta blockers:** Beta blockers such as atenolol(Tenormin), metoprolol (Lopressor) and propranolol(Inderal) are drugs which helps in reducing chest pain, abnormal heart rhythms, anxiety attacks and palpitations. These act by increasing the size of left ventricle, thereby

reducing the degree of prolapse.

2. **Diuretics:** Diuretics such as furosemide (lasix), torsemide (Demadex), hydrochlorothiazide (Microzide) are prescribed in order to drain fluid from lungs.
3. **Heart rhythm medications:** Antiarrhythmic medications such as flecainide (Tambocor), amiodarone (Cordarone, Pacerone) and propafenone (Rythmol, Rythmol SR). Antiarrhythmics help to control heart rhythm by normalizing electrical signals in heart tissue.
4. **Aspirin:** Aspirin is recommended for:
 - Patients with history of recurrent cerebral transient ischemic attack.
 - Patients younger than 65 years with atrial fibrillation and no history of hypertension, mitral regurgitation, or congestive heart failure.
 - Post stroke patients with contraindications to warfarin.
 - Patients in normal sinus rhythm with echocardiographic evidence of high risk mitral valve prolapse.
5. **Prescription anticoagulants (Blood thinners):** These medications include: warfarin (Coumadin), heparin, dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Savaysa)- prevent blood from clotting. Warfarin therapy is indicated for:
 - Patients older than 65 years with atrial fibrillation and with hypertension, mitral regurgitation, or congestive heart failure.
 - Post stroke patients
 - Patients with recurrent cerebral transient ischemic attack despite aspirin therapy.

Table 5. Endocarditis Prophylactic Regimens for Dental, Oral, Respiratory Tract, and Esophageal Procedures

Standard prophylaxis:

Amoxicillin 2.0 g orally 1 h before procedure

For patients on NPO status:

Ampicillin 2.0 gm g IM or IV 30 min before procedure

For patients allergic to penicillin: any one of the following:

Clindamycin 600 mg orally 1 h before procedure

Cefadroxil 2.0 g orally 1 h before procedure

Cefalexin 2.0 g orally 1 h before procedure

Azithromycin 500 mg orally 1 h before procedure

Clarithromycin 500 mg orally 1 h before procedure

For patients on NPO status and allergic to penicillin: either of the following:

Clindamycin 600 mg IV 30 min before procedure

Cefazolin 1 g IM or IV 30 min before procedure

IM = intramuscularly; IV = intravenously; NPO = nothing by mouth.

Data from Dajani *et al.*³¹

6. A serious complication of mitral valve prolapse is endocarditis (valve leakage or valve infection) therefore the individuals with MVP usually are prescribed with antibiotics prior to any procedure that can introduce bacteria into the Bloodstream. Examples of procedures include routine dental work, minor surgery and procedure that can traumatize the body tissues such as colonoscopy or gynecologic or urologic examinations. Recommendations for preventive measures of bacterial endocarditis and stroke include:

- **Surgery:** Usually doctors do not suggest surgery in case of FVS. Surgery is only option case of severe mitral valve regurgitation as is can eventually lead to other cardiac complications. If doctor suggests a surgery, the doctor may suggest for repairing or replacing the mitral valve.

VALVE REPAIR: Mitral valve repair is as surgery that preserves your own vsk vwe. For most people with mitral valve prolapse, this is preferred surgical treatment to correct the condition.

VALVE REPLACEMENT: Surgeon may perform a valve replacement if valve repair isn't possible. In valve repair replacement surgery, the damaged mitral valve is replaced in surgery, the damaged mitral valve is replaced by an artificial (prosthetic)valve. Artificial valves are mechanical or tissue valves.

Alternative treatment:

The good news is that there is a whole array of “natural” therapies for people with mitral valve prolapse, which can help alleviate the multiple symptoms. They range from behavioral therapies to diet modifications and nutritional supplements.

COGNITIVE THERAPY:

This is the basic ground for the holistic approach to MVP. It's important for everyone with this condition to seek out a sympathetic or holistic physician who can clearly explain the variety of possible symptoms, confirm that they are not imaginings or hypochondriasis and provide a program of treatment. If you understand clearly what is happening, you can learn ways to block the feedback loops that can lead to panic attacks or hyperventilation, and break the cycle.

EXERCISE: Exercise is one of best therapies we have for deconditioning learned sensitivities and relieving neurologic symptoms.

DIET: Proper diet is essential to stabilization of MVP symptoms. Avoidance of stimulants, sugar and artificial flavoring agents like MSG and NutraSweet are mandatory. Complex carbohydrates may be combined with protein to avoid precipitous rises and falls of blood sugar. Moderate salt intake is usually encouraged to stimulate adrenal function.

NUTRITIONAL THERAPY: There are several key nutrients that can affect the underlying causes of mitral valve prolapse symptoms.

L-carnitine is an amino acid that act as a shuttle for fat that is required for cellular metabolism. It can be used as a cellular equalizer and also acts to strengthen the heart. Dosage: 500-1000 mg two-three times daily. Acetyl-L-carnitine is related nutrient that may be more bio available. Dosage : 120 mg three times Daily.

Coenzyme Q10 appears to improve disturbed bio energetic function at the molecular level. Coenzyme Q10 enhances the pumping action of heart, output of blood, speed of heart muscle contraction and general cardiac efficiency. Dosage: 60-120 mg/day.

B Vitamins reduce high levels of lactic acid in the blood that are associated with anxiety and panic attack. B vitamins niacin and thiamin can help reduce them. Dosage: vitamin B1(thiamine) 100 mg/day; vitamin B3(niacin) 50 mg/day.

Vitamin B6 (pyridoxine) can favor the production of higher levels of the neurotransmitter serotonin in the brain, which are relaxing and sedating. Dosage: 50mg/day.

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