Hemodynamics of Mitral Stenosis

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Abstract
Hemodynamic is the intravascular pressure and flow that circulate blood throughout the body. In both the venous and arterial compartments, variations in pressure and flow will necessarily affect each other. Flow and pressure within and between the arterial and venous compartments are influenced by hemodynamic on a beat-to-beat basis. Hemodynamic values that are treated in one compartment are dependent on the state of the other compartments. There are several curved proximal isovelocity surface areas as the streamlines of flow approach the stenotic orifice. A stenotic valve's spatial flow velocity profile depends on its anatomy, inlet geometry, and degree of flow acceleration. A patient with Mitral Stenosis (MS) experiences a pressure gradient from the left atrium to the left ventricle that propels the flow abruptly across the stenotic orifice. An arc-shaped flow profile is created, and the atroventricular valve will therefore have a hemi elliptical velocity profile. At the level of narrowed stenotic orifices, high-velocity jets form in laminar flow when it reaches the vena contracta, the narrowest cross-sectional area downstream from the anatomic orifice, the flow profile in cross-section is relatively flat at the jet's origin and remains flat until the jet reaches the anatomic orifice. Distally from the stenotic region, the blood flow becomes disorganized with multiple velocities and directions. Stenotic mitral valves exhibit thickened leaflets with a reduced excursion. In this review, we will discuss the challenges and changes which occur in hemodynamic of MS.

Keywords: Hemodynamics; Mitral stenosis; Transmittal pressure gradients; Mitral valve area; Echocardiogram

Introduction
Histories of hemodynamic date back hundreds of years. William Harvey (1578–1657) developed a quantitative technique that led him in 1628 to conclude that blood continues to circulate. A relationship was established between arterial pulse propagation speed and the elastic properties of arteries by Thomas Young (1773–1829). In one of his
articles, Otto Frank (1865-1944) describes the mechanical interaction with the elasticity of the aorta and major arteries when blood is ejected from the left ventricle during systole. Observations and analyses of the time-dependent motion of blood in an elastic artery driven by fluctuating pressure gradients began in the 1950s with the work of John R. Womersley (1907-1958) and Donald A. McDonald (1917-1973)\cite{1,2,3}. Hemodynamic is the intravascular pressure and flow that circulate blood throughout the body. In both the venous and arterial compartments, variations in pressure and flow will necessarily affect each other. Flow and pressure within and between the arterial and venous compartments are both influenced by hemodynamic on a beat-to-beat basis. Hemodynamic values that are treated in one compartment are dependent on the state of the other compartments. MS throws a lot of changes in hemodynamics and clinical challenge. In this review, we will discuss the challenges and changes which occur in hemodynamic of MS\cite{4,5}.

**Mitral Stenosis**

Stenotic mitral valves exhibit thickened leaflets with a reduced excursion. This thickening, calcification, and shortening can extend into the sub valvular apparatus in MS to involve the sub valvular apparatus. It is possible for an elderly individual to develop stenosis without much impairment of the mitral valve tip motion because of a very narrowed, calcified mitral annulus with extension into the mitral valve leaflets' bases. MS can also be caused by congenital parachute mitral valves, in which the leaflets attach to a single papillary muscle\cite{6,7,8}. Figure 1 depicts the causes and consequences of MS.

**Figure 1:** A Causes of MS (Rheumatic endocarditis, thrombi, calcification, etc); B Consequences of MS (Decrease cardiac output, Heart failure, atrial emboli, etc); C Echo of normal Vs patients with MS.

There are more cases of rheumatic MS in women (80% of the cases) than in men. Rheumatic MS can present clinically in a variety of ways, with patients from areas where a high disease prevalence is seen presenting young (teenagers to 30 years) with a fusion of commissural valves but flexible noncalcified valve leaflets. Conversely, in regions with low disease prevalence, the presentation of rheumatic fever occurs more frequently in older patients (aged 50 to 70 years) with calcified fibrotic leaflets in addition to the fusion of the commissures and sub valvular involvement [9-10].

Following are the etiology behind MS [11]:

1. Rheumatic valvular disease: A most common cause of MS
2. Congenital deformities: infancy or early childhood.
4. Pseudo-MS - anatomically normal. The barrier of transvalvular flow is triggered by an extrinsic structure such as a cardiac tumor.
5. Dense mitral annular calcification (MAC) - with expansion into the mitral valve leaflets and limitation in leaflet motion.

**Stages of MS**

MS stages are characterized by symptoms, anatomy and hemodynamic of the valve, and the consequences of valve obstruction on the left atrium (LA) and pulmonary circulation (Figure 2). There is anatomic evidence that rheumatic valve disease is the primary cause of MS. Symptom severity and the degree to which interventions will improve symptoms are considered criteria for defining "severe" MS [12].

![Figure 2: Stages of Mitral stenosis](image-url)
Therefore, a mitral valve area of $\leq 1.5 \text{ cm}^2$ under normal heart conditions corresponds to a transmittal gradient between $>5 \text{ mm Hg}$ to $10 \text{ mm Hg}$. Meanwhile, the mean pressure gradient is highly dependent on the transvalvular flow rate, the diastolic filling period, and the heart rate$^{[6-13]}$.

**Hemodynamics of MS**

Hemodynamic factors that affect heart valves include the valve itself, as well as those upstream and downstream of the valve. A stenotic orifice has several curved surfaces with proximal isovelocity surfaces as they approach the streamlines of flow. The post-jet disturbance occurs adjacent to and distal to the laminar jet of MS$^{[14]}$. The level of flow acceleration and valve anatomy influences the velocity profile proximal to stenotic valves. Flow passively from the large inlet chamber (the left atrium) abruptly across the stenotic orifice in patients with MS is enabled by the left atrium to left ventricle pressure gradient$^{[15]}$. Hemodynamic is characterized by the formation of a laminar jet at the level of the narrowed stenotic orifice. At the point of origin of the jet, the flow profile is relatively flat and remains flat until the jet reaches the vena contracta, which has the narrowest cross-section behind the anatomic orifice. Beyond the stenotic region, blood flow becomes disorganized, with multiple blood flow directions and velocities. According to stenosis severity, the spread of this disturbance downstream depends on the distance it propagates$^{[16-18]}$.

![Figure 3: Hemodynamics of MS](image)

The factors affecting the hemodynamics of MS are cardiac output, stroke volume, venous return, and inotropy or contractility (Table 1).

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Haemodynamic Assessment of MS

The evaluation of MS depends on the extent of the pressure gradient and on the calculation of the valve area.

### Table 1: Factors affecting hemodynamic of MS\(^{[19-23]}\)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (CO)</td>
<td>Hemodynamic studies focus mainly on CO. Blood is pumped into the aorta by the heart each minute, represented by the CO. Cardiac Output (CO) = Stroke volume (SV) (\times) Heart rate (HR)</td>
</tr>
<tr>
<td>Stroke volume (SV)</td>
<td>The amount of blood pumped by the left ventricle in one cardiac cycle is known as stroke volume (SV). Stroke Volume (SV) = end diastolic volume (EDV) – End systolic volume (ESV)</td>
</tr>
<tr>
<td>Venous return (VR)</td>
<td>Normal, VR should be equal CO. By increasing sympathetic activity</td>
</tr>
<tr>
<td>Inotropy or contractility</td>
<td>It is an amount of the amplitude of myocardial contractions.</td>
</tr>
</tbody>
</table>

Transmittal pressure gradients

In MS, the blood flow from the left atrium to the left ventricle is constrained, causing in a pressure gradient between the two chambers during diastole. The most accurate way to determine the mitral valve gradient is to record both left atrial and left ventricular pressures using a transseptal technique with retrograde catheterization of the left ventricle. Most cardiac catheterization facilities assess the transmittal gradient with simultaneous pulmonary artery wedge pressure and left ventricular pressure for practical reasons. Though the left atrial pressure is measured indirectly by the mean pulmonary artery wedge pressure; as a result, the mean pulmonary artery wedge pressure/left ventricular pressure gradient often miscalculates the exact severity of MS. The transmittal pressure gradient can be measured non-invasively in clinical practice through evaluating transmittal flow velocity with CW doppler echocardiography and by means of Bernoulli equation:

\[
\Delta P = 4v^2
\]

\(\Delta P = \text{mean diastolic pressure gradient among the left atrium and left ventricle (mmHg)}, \ v \text{ velocity.}\)
This enables highly reliable, accurate, and repeatable calculations of the peak pressure gradient (from peak velocity) and mean pressure gradient (representing the average of numerous instantaneous pressure gradients)\[14\text{--}24\]. Peak velocity, which is affected by left atrial compliance, left ventricular diastolic function, and loading conditions, determines the peak gradient. As a result, in patients with MS, the mean gradient is the most important haemodynamic measure. The mean gradient, however, does not only depend on mitral valve area but also on factors that affect transmittal flow rate, for instance, heart rate, cardiopulmonary output, and mitral regurgitation. All these aspects must be considered, and the heart rate at which pressure gradients are measured should be always reported\[25\text{--}26\].

1. **Mitral valve area by Gorlin formula:**

The Gorlin formula is used to calculate the area of the mitral valve in the cardiac catheterization laboratory.

\[
\text{MVA} = \frac{\text{SV}}{\text{DFP}} + (C \times 44.3 \times [\sqrt{\Delta P}])
\]

Where MVA= mitral valve area SV= stroke volume (mL/beat), DFP= diastolic filling period (sec/beat, since the antegrade flow across the mitral valve occurs only in diastole), ΔP= mean diastolic pressure gradient among the left atrium and left ventricle (mmHg), and 44.3 is equal to the square root of twice the gravity acceleration factor (980 cm/sec/sec). The Gorlin formula, in its simplest form, connects the transvalvular pressure gradient and the stroke volume, adding an empirical constant (C= 0.85) to account for orifice contraction and energy failure to better compare with actual valve regions found during autopsy or surgery. A patient in sinus rhythm with normal left ventricular function and no concomitant valve abnormalities can benefit most from the Gorlin formula. These considerations are crucial in recognizing that calculated valve areas have evident limitations in the diagnosis of valvular stenosis\[27,28\].

2. **Mitral valve area by echocardiography**

Mitral valve area can be calculated by echocardiography by following approaches

   a. **Direct imaging (planimetry)**

Using two-dimensional (2D) echocardiography in the parasternal short-axis view and finding the smallest orifice at the leaflet tips in mid-diastole, the area of the mitral valve orifice can be directly measured. This method is essentially loaded agnostic, and it has been demonstrated to have the best connection with anatomical valve area in explanted valves. It is the standard measurement of the mitral valve area. However, 2D echocardiography may not be able to reliably measure mitral valve area in individuals with severely deformed and/or thicker mitral valves, especially the following commissurotomy. Because it offers guidance to align the picture in the plane of the smallest orifice at the
leaflet tips, three-dimensional (3D) echocardiogram is more exact and reproducible for measuring the mitral valve area\textsuperscript{[29-31]}.

\textit{b. Pressure half-time}

Blood flow from the left atrium to the left ventricle is significantly influenced when the mitral valve orifice area diminishes, and the time required for blood to flow from the left atrium to the left ventricle increases. As a result, the length of time necessary for the pressure gradient across the mitral valve to fall during diastole decreases as the valve area decreases. The time interval in milliseconds between the peak of the doppler-estimated transmittal pressure gradient and one-half of the peak pressure gradient (pressure $T_{1/2}$) is a measure of the rate of decline of the mitral valve gradient. The $T_{1/2}$ approach can be used even in patients with severely deformed and/or thicker mitral valves, as well as late after commissurotomy, because it calculates the functional mitral valve area (Table 2) \textsuperscript{[32-33]}.

\textbf{Table 2: Echocardiographic parameters used to quantify MS severity\textsuperscript{[32,33,36]}}

<table>
<thead>
<tr>
<th>Method</th>
<th>Strength</th>
<th>Formula</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernoulli equation</td>
<td>Simple</td>
<td>$\Delta P=4v^2$</td>
<td>Affected by heart rate and flow conditions</td>
</tr>
<tr>
<td>Planimetry</td>
<td>Relatively flow-independent. Reference method</td>
<td>-</td>
<td>Difficult to measure the smallest area. Distorted/thickened valve post PBMV</td>
</tr>
<tr>
<td>$T_{1/2}$</td>
<td>Functional MVA. Feasible in distorted mitral valves</td>
<td>$MVA=\frac{220}{T_{1/2}}$</td>
<td>Aortic regurgitation, Severe MR, High LVEDP immediately post PBMV</td>
</tr>
<tr>
<td>PISA</td>
<td>Relatively flow-independent.</td>
<td>$MVA=2r^2x(\text{angle } \alpha/180) x (V/\text{Vmax})$</td>
<td>Technically challenging, Angle correction. Not recommended for routine use</td>
</tr>
<tr>
<td>Continuity equation</td>
<td>Relatively flow-independent. Transmitral flow = aortic stroke volume</td>
<td>$MVA=\frac{SV}{VTI}$</td>
<td>LVOT measurements. Atrial fibrillation. Mitral regurgitation Aortic regurgitation</td>
</tr>
<tr>
<td>Bernoulli equation</td>
<td>Simple</td>
<td>$\Delta P=4v^2$</td>
<td>Arbitrary estimation of right atrial pressure</td>
</tr>
</tbody>
</table>

c. \textit{Proximal isovelocity surface area}

The proximal isovelocity surface area (PISA) method is grounded on the continuity principle. It believes that hemispheric isovelocity shells arise when blood flow converges on a flat opening. By analysing the PISA of the flow
convergence on the atrial side, the mitral valve area can be approximated using the concept of conservation of mass\textsuperscript{34}. As the colour flow scale baseline is moved upward by this method, a lower colour aliasing velocity is achieved by applying flow convergence analysis proximal to the stenotic orifice. The diastolic flow rate is estimated using a hemispheric shape for the proximal isovelocity surface. A mitral valve area is calculated by:

\[
MVA = 2\pi r^2 \times \left( \frac{\alpha}{180} \right) \times \frac{V_{alias}}{V_{max}}
\]

MVA: mitral valve area, Valas: Velocity aliasing; Vmax: Velocity maximum.

Despite these theoretical advantages, unlike valvular regurgitation, the PISA approach for assessing MS severity is rarely employed in regular practice\textsuperscript{35}.

d. **Continuity equation**

When the transmittal flow is equal to the aortic stroke volume, and there is no major regurgitation or shunts, the continuity equation can be used to estimate the mitral valve area by:

\[
MVA = \frac{SV}{VTI}
\]

MVA= mitral valve area, SV= stroke volume, VTI: Velocity time integral.

The area of the mitral valve measured using the continuity equation approach correlates with the area measured by catheterization\textsuperscript{36-37}.

3. **Real-Time 3D method (RT3D)**

RT3D color doppler echocardiogram can accurately estimate MVA in degenerative MS patients when a high-quality image can be obtained. When compared to 2D planimetry, RT3D may provide a more accurate estimate of MVA by finding the plane with the narrowest MV area\textsuperscript{38}.

a. **Transoesophageal echocardiography (TEE)**

TEE is another way of evaluating MV morphology and MS severity. It is possible to estimate MVA accurately by using RT3D and TEE. Moreover, TEE may be used to guide percutaneous MV interventions\textsuperscript{39}.

b. **Cardiac computed tomography (CCT)**

Moreover, TEE may be used to guide percutaneous MV interventions. Due to calcium's high X-ray attenuation
properties, this technique offers superior spatial resolution and can detect calcification more accurately. Preprocedural CCT assists in surgical planning by allowing a detailed view of the MV annulus, the extent of calcification, and its relationship to neighboring structures\[^{40}\].

c. **Radiation-induced MS**

The MV is frequently exposed to ionizing radiation in survivors of thoracic cancer. In radiation-induced MS, the MV and aortomitral curtain become severely calcified and thickened. In patients with prior radiation, thickened aortomitral curtains during cardiothoracic surgery are associated with a higher mortality rate. In contrast to MAC, radiation-induced MS generally impacts the anterior mitral annulus\[^{38,41}\].

d. **Congenital MS**

An early diagnosis of congenital MS is usually made in the early stages of life. A variety of congenital MV abnormalities are included in this group. To prevent permanent changes in pulmonary vascularity, as well as to improve mortalities and morbidities, early surgical interventions are usually necessary for the successful treatment of this type of MS\[^{42}\].

**Assessment of hemodynamic consequences of MS:**

1. **Left atrium (LA) and Left ventricle (LV)**

The left atrium (LA) enlargement and structural remodeling of the left ventricle is directly related to the severity and chronicity of MS. As measured by Doppler echocardiography, increased LA size may lead to atrial fibrillation (AF), resulting in reduced flow velocities and blood stasis within the LA and left atrial appendage (LAA). A reduction in LA flow also reduces systolic pulmonary vein flow, which increases thrombus risk.

In patients with MS, the left ventricle (LV) is usually normal in size, and diastolic filling is typically prolonged and reduced. MS leads to a normal-sized left ventricle (LV) and reduced diastolic filling. The transmittal gradient is prolonged and increased. AF causes an increase in heart rate and a reduction in diastolic filling time. Transmittal gradients are further increased. In AF, loss of LA contraction may also lead to a reduction in forwarding stroke volume. As a result of both mechanisms, the LA pressure increases significantly\[^{43}\].

2. **Pulmonary arterial hypertension**

Pulmonary artery hypertension (PAH) may develop with the progression of the disease. In advanced stages of PAH, right ventricular dilation, hypertrophy, and eventually right heart failure can occur. MS is associated with various hemodynamic complications based on the degree of PAH. All patients with significant MS should be serially evaluated for pulmonary pressure. An annulus diameter of 40 mm or more appears to be a predictor for severe tricuspid regurgitation following MV surgery. It should also be assessed when considering surgery\[^{44}\].
Stress Testing
Additional information about the MV and pulmonary pressure gradients during a stress test can be obtained by using dobutamine or physical exercise. An important consideration is when evaluating asymptomatic patients or patients whose symptoms and MS severity do not correlate, as well as when evaluating women with MS who are considering pregnancy[45,46].

Hemodynamic For Structural Interventions For MS
The pressure waves in the left atrium (LA) depend on the pulmonary vein blood flowing into the LA from the lungs, the valve outflow into the left ventricular (LV), and the left ventricular back pressure or flow, which produces resistance to LA outflow. The stiffness of the chamber also affects pressure waves in the LA (and any other chamber). A low-compliance LA has a steeper P-V curve, implying that a minor change in flow can result in a large change in pressure, whereas a compliant or easily expandable LA chamber has a flatter P-V curve. MS influences LA stiffness as well as the anatomic valve-related structures[47,48].

Transvalvular mitral hemodynamics and clinical presentations
Increased LA pressure causes exertional dyspnea in people with MS because it raises pulmonary venous and capillary pressures. The pressure gradient is quadrupled when the velocity is doubled. Aggravating conditions for MS contain tachycardia, pregnancy, hyperthyroidism, anemia, infection, and atrial fibrillation. All these disorders have one thing in common: a faster heart rate coupled with a shorter diastolic filling time[49-51].

MS hemodynamic in balloon valvuloplasty
As discussed above, the stenotic mitral valve area (MVA) can be assessed by numerous ways. According to the echocardiographic data, patients may be suitable for balloon valvuloplasty to open a stenotic valve and allow sufficient cardiac output and defend against pulmonary hypertension. It is recommended to utilize direct LA pressure from a transseptal approach rather than the pulmonary capillary wedge pressure. When pulmonary capillary wedge pressure is modest and normal, it can be used as a first-line screening technique for substantial mitral valve gradients[52-54].

Percutaneous mitral balloon valvuloplasty (PBMV) hemodynamic
MS can be treated with percutaneous balloon valvuloplasty as a desired choice of treatment if subvalvular disease, calcification, thickening, and mobility of the valve leaflets is moderate or less (by means of Wilkin’s score<11) [55]. The severity of mitral valve regurgitation is modest, and in the left atrium, there is no thrombus. PBMV causes a
gradient decrease of 50% or more, and a valve area increases to 1.5 cm². When the mitral valve anatomy is ideal, its area will typically increase by 1.8 cm² or more. In a study, the PBMV results in low Wilkins scores with reduction of the mitral gradient after single balloon inflation. The hemodynamics of this study indicate a competent valve; in fact, no mitral regurgitation was identified by echocardiography.[56-58].

For PBMV, the standard stepwise Inoue balloon (Toray) procedure requires deciding a maximum balloon size based on the patient's height; inflations normally begin with a balloon size several millimetres smaller. Hemodynamic are checked after each inflation to see if the gradient has decreased or if any new mitral regurgitation has developed. This is accomplished by the use of a mix of echocardiography and hemodynamic techniques. A drop in gradient of at least 50%, as well as a one-grade increase in mitral insufficiency, should alert the operators to come to a standstill.[59,60].

A comprehensive physical examination, including chest x-ray, electrocardiogram (ECG), and detailed 2D and 3D echocardiography, should be performed before PBMV.[61] If there is a discrepancy between the clinical presentation and the graphic evidence of stenosis severity, exercise hemodynamic investigations may be required before PBMV. During PBMV, operators should pay close attention to the pressure gradient decrease to provide an acceptable result with a reduced gradient, but a competent valve.[62,63] Figure 4 depicts the intervention of MS[64].

Figure 4: Mitral stenosis intervention
The strength of recommendation 1: strong; 2a moderate; 2b: weak; based on the likelihood and magnitude of benefits as a function of risk.

AF: atrial fibrillation; CVC: comprehensive valve centre; MR: mitral regurgitation; MS: mitral stenosis; MV: mitral valve; MVA: mitral valve area; PASP: pulmonary artery systolic pressure; PMBC: percutaneous mitral balloon commissurotomy.

Conclusion

Concepts of hemodynamic, and their basis in understanding fluid and solid mechanics, will remain important, as they provide the necessary framework for understanding cellular functions in terms of the integrated structural and functional properties of the circulatory system. There is a considerable amount of understanding of hemodynamic physical and mechanical aspects. A basic understanding of LA function is necessary for the treatment of mitral valve disease. While traditional echocardiographic evaluation can guide transcatheater mitral valve interventions, intraprocedural changes in anatomy, geometry, and hemodynamic states complicate purely non-invasive assessments and necessitate continuously. MS is an incredibly complex pathology with complex hemodynamics, which will undoubtedly result in improved patient outcomes through more research. It is possible for patients to misinterpret or even ignore any limiting symptoms due to the gradual and slow progression of their physical disability. The cardiac catheterization remains the most important means of assessing the extent of mitral valve obstruction. In MS, the left ventricle (LV) is usually normal in size, but the diastolic filling is usually prolonged and reduced. MS results in a normal LV and reduced diastolic filling. As the disease progresses, pulmonary artery hypertension may develop. In addition, it is important to consider asymptomatic patients and patients whose symptoms are not correlated with the severity of their MS, as well as pregnant women with MS.

Future research will likely focus largely on the interaction between hemodynamic and cellular mechanisms. There are many ways in which this interaction takes place, including the role of hemodynamic forces during vasculogenic, angiogenesis, and vascular remodeling, the potential contribution of pressure and wall shear stress to local regulation of blood flow, and more. In addition to the effects of wall shear stress on atherosclerotic lesions, there are many examples of the interaction between arterial hemodynamic and cardiac function and remodeling, the acute control of blood pressure, and the role of vascular responses in hypertension.

Ethical Approval: N/A
Conflict of Interest: Nil
Financial Disclosure: None
References: