Study of Mitral stenosis in resting and exercised heart using ABAQUS™

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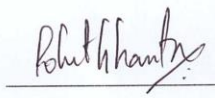

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Approval Sheet

This thesis entitled "**Study of Mitral stenosis in resting and exercised heart using ABAQUS™**"by **Ghanta Rohit** is approved for the degree of Master of Technology from IIT Hyderabad.

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Dedicated to

My parents and friends.

Abstract

Cardiovascular diseases (CVDs) are the leading cause of mortality in India contributing nearly 25% to total mortality. Computational models of the heart are a new tool that can be used to conduct research on such diseases, and test the efficacy of medical devices used in their treatment. Computational models take lesser time to deliver the results, suffer lesser restrictions on the number of samples, and more importantly reduce the testing of medical devices on animals. In this study, we used Living Heart Human Model (LHHM) (v2.0 beta) developed on ABAQUS™, a computational model which consists of both electrical and mechanical models of the adult male human heart, to study the effects of mitral stenosis on heart function; mitral stenosis is a major cause of mortality in India.. We first validated the LHHM model by simulating healthy adult male human heart function. We then evaluated its efficacy for severe mitral stenosis in a randomly selected patient, and found that LHHM predictions matched clinical observations. We proceeded to obtain LHHM predictions for 8 patients with varying degrees of mitral stenosis: comparison with clinical data showed a qualitative and quantitative match for pulmonary capillary pressure but only qualitative match for pulmonary arterial pressure. Simulations were also performed for heart function in mitral stenosis during exercise, but LHHM predictions matched neither quantitatively, nor qualitatively, with data indicating further improvement of the model.

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1.Introduction

1.1 Anatomy of Human Cardiovascular System

Cardiovascular system or circulatory system is an important organ system of the human body. It consists of the heart, blood and the blood vessels. The circulation of blood through the blood vessels is achieved by the pumping of heart; blood delivers oxygen and nutrients to every cell in the body and removes carbon dioxide and waste products produced by those cells. A hierarchy of blood vessels - namely arteries, arterioles, capillaries, venules and veins- facilitates the circulation of blood from the heart to the cells in the body, and back to the heart again. Arteries carry oxygen rich blood from the heart to the cells in the body and veins carry the oxygen depleted blood from those cells back to the heart.

The human heart is a muscular 4-chambered hollow organ which pumps around 5 liters of blood in a minute [Hall, 2015]. These four chambers are split based on their location and function in the heart. The right side of the heart consists of the Right Atrium and the Right Ventricle which are separated by the Tricuspid valve. Similarly the left side consists of the Left Atrium and the Left Ventricle which are separated by the Mitral valve. The oxygen poor blood from the body is carried via the superior vena cava to the Right atrium and travels through the Right ventricle, from where it is pumped to the lungs for oxygenation. On the other hand the oxygenated blood is transported from the lungs into the Left atrium, and then into the Left ventricle which, in turn, pumps this blood to the body to support cell metabolism.

1.2 Cardiac Cycle

Cardiac cycle refers to the sequence of electrical & mechanical events that repeat with every heartbeat, and which are responsible for the pumping action of heart. A single cardiac cycle can be divided into two phases- Diastole & Systole. Both these terms are used in context of the

ventricular function. Diastole refers to the time period when the ventricles are relaxed. During this phase the atrioventricular (Tricuspid and Mitral) valves open and blood passively flows from the atria into the ventricles. At the end of diastole, both atria contract, which pushes an additional amount of blood into the ventricles. Systole, which follows Diastole, refers to the time during which the ventricles contract. The atrioventricular (Tricuspid and Mitral) valves close preventing the back flow of blood into the atria. Nearly simultaneously, the aortic & pulmonary valves open to allow ejection of blood from the ventricles into the aorta and the pulmonary artery. The frequency of the cardiac cycle is expressed in beats per minute. Typically for a normal heart, time period for each cardiac cycle is of 0.8sec corresponding to a heart rate (pulse) of 72 beats per minute [Jose and Collison, 1970].

1.3 Cardiovascular Diseases

Cardiovascular diseases (CVDs) account for nearly 25% of the deaths per year in India [Prabhakaran et al., 2005]. However, this percentage could be higher because of lack of data from the rural parts and the consequently smaller sample for which data was collected.

In India, Ischemic heart disease (IHD) & stroke occur more frequently than other types of CVDs. The ratio of IHD to stroke is also higher than the global average. Together IHD & stroke are responsible for 21% of deaths in India, and the survey also shows that one-tenth of the years of life are lost due to these diseases. The years of life lost due to CVD also increased by 59% from 1990 to 2000 [Prabhakaran et al., 2005].

Though a lot of investment is done for the research of prevention & control strategies of CVDs, the limitations of the results outweigh the positive findings. With the increasing number of cases for CVDs, there is a need for better surveillance & treatment facilities. These have a high potential of making impact in controlling these diseases.

There is also a need to improve the knowledge base about the causes of diseases in order to tackle the increasing CVD epidemic.

1.3.1 Heart Valve Diseases

The most common type of CVDs are heart valve diseases which are those due to the blockage of heart valves: this leads to the hindrance of blood flow to the heart chambers and reduces the pumping capacity. Narrowing of the mitral or tricuspid valves leads to reduced blood flow to the

ventricles which in turn reduces the cardiac output. Leakage of valves is also another major cause of heart valve diseases: in these pathologies there is a backflow of blood which strains the heart to pump harder to maintain the cardiac output. Chest pains, difficulty in catching breaths, and weakness are symptoms of heart valve diseases. Repairing or replacement of heart valves is a dominant mode of the treatment for these type of diseases.

The mitral valve regulates the blood flow between the left atrium and the left ventricle. Damage to the mitral valve is initially asymptotic but it has negative long term effects which lead to the decreased cardiac output. In this study, we focus on cardiac output (and simulation of the same) in the presence of varying levels of blockage of the mitral valve (referred to as mitral stenosis). In the next section, we detail the features and consequences of this pathology.

1.3.2 Mitral Stenosis (MS)

Mitral stenosis (MS) is defined as the narrowing of the mitral valve orifice which ensures the blood flow between left atrium and left ventricle. Due to the blocked valve there is a pressure and volume buildup in the left atrium, which holds the oxygenated blood from the lungs, leading to filling of the lungs with backflow of fluid causing the patient to feel tired or short of breath. The mechanical consequences of MS cannot be expressed by a single hemodynamic measurement, but data suggests that the left atrium is changed significantly. This change in left atrium triggers the changes in electrical signals which regulate the heartbeat, causing atrial fibrillation. The atrial fibrillation leads to enlargement of left atrium which was initially occurring in small amount. MS is generally triggered by rheumatic fever and can be treated by either repairing or replacing the mitral valve.

1.3.3 Mitral Regurgitation (MR)

Mitral Regurgitation (MR) is the leakage of blood from the left ventricle to left atrium through the mitral valve during systole. This has severe effects on the left atrium which gets enlarged due to the pressure and volume buildup, and this in turn causes atrial fibrillation which reduces the heart's efficiency to pump blood normally. It can also affect the pulmonary veins leading to pulmonary hypertension. Treatment is required even for mild MR for which the mitral valve is repaired or replaced.

1.4 Computational Simulations of Heart Physiology

Computational simulations are increasingly being used to understand normal human physiological functions, etiology of diseased states, surgical implementation and also the design and evaluation

of artificial implants. The advantage of having devices designed and tested on a computational model reduces the animal experimentation for the functional evaluation of the prototypes [Chandran, 2010]. In the case of the (adult/pediatric) human heart, a versatile computational model of the heart should be able to provide the simulated results for normal function, different pathologies and also of heart function during implementation of devices such as pacemakers, left-ventricular assist devices (LVADs), etc. Computational models of heart that are available in the market or in development for academic use include the Living Heart Human Model (LHHM) – an initiative by Dassault Systemes. We currently have a license for the LHHM (v 2.0 beta) - and we will briefly describe its features below. The advantages and drawbacks associated with this choice instead of other models available in the literature is discussed in the Literature Survey (Section 2)

1.5 Living Heart Human Model

Living Heart Human Model (LHHM) developed by Dassault Systemes is a Multiphysics model of the 4 chambered normal human heart in an adult male: it was developed as part of the Living Heart Project of Dassault Systèmes [Baillargeon et. al, 2014]. Testing of heart in a non-invasive way is made much more convenient by using this model. It reduces the risk involved in directly handling the heart and performing experiments invasively.

LHHM works on a Finite Element model embedded with governing equations and parameters for the rhythmic simulation of excitation and contraction. The electrical potential and mechanical deformation across the heart are analyzed and can be visualized throughout the cardiac cycle either for the normal heart or for various pathological states. The constitutive equations and parameters used for the various structures are obtained from publications in reputed journals. For visual analysis of the results on the simulator, two forms of model are developed: solid model and fluid model. Solid model illustrates the deformations and contours whereas the fluid model consists of blood flow model where the flow dynamics can be analyzed [Baillargeon et al., 2014].

Two individual models namely ELEC and MECH models are created in the LHHM. ELEC model contains fiber meshes which analyze changes in electrical field. MECH model contains cavities and valves for understanding the mechanical deformations of the heart. For interaction between electrical and mechanical fields to be studied, the coupling is assumed to be unidirectional. The changes in electrical field potential induces the changes in mechanical field. So, the ELEC model

is run first to obtain the changes in electric field then the MECH model is run for simulating a complete cardiac cycle. The predicted results from these models combined agrees well with clinical data for certain parameters of the human adult cardiac cycle.

Further, the parameters and properties of either of these models can be changed for a given condition of heart, and the simulations can be run which then provides the results to be analyzed for research purposes.

In this study, we evaluate the efficacy of the LHHM (v 2.0 beta) in simulating heart function in the mitral stenosis case, and in predicting the pressure-volume behavior observed during exercise in the mitral stenosis case by comparing it with clinical data for the same. The plan of study first involves the validation of the LHHM (v 2.0 beta) predictions for heart function in the normal physiological state and during exercise. We then compare predictions of the LHHM model for mitral stenosis cases in both the normal physiological state and the exercised states.

2.Literature Survey

2.1 Computational Models of Heart and Valve Function

Heart is a most vital and complex organ in the human body. The functioning of the human heart is precisely controlled by the interplay of electrical and mechanical fields. The 4-chambers and 4-valves, have a synchronized rhythm to regulate filling and ejection of blood. Many computational models have been developed to study the function of the heart. However, many of these models show either electrical responses or mechanical responses alone [Eriksson et al., 2013; Gonzales et al., 2013; Hurtado et al., 2014].

LHHM on the other hand is an integrative electro-mechanical model in which the interplay of electrical and mechanical responses can be observed simultaneously. Other computational models of the heart include those for pediatric VADs by JF Antaki et al. [Wearden, P.D., 2006, Johnson Jr, C.A., 2011] and Physiome project by International Union of Physiological Sciences (IUPS) [Hunter, P., 2002.].

Valve dynamics is a sub-topic of interest in computational studies of the heart. To understand valve dynamics, many numerical & experimental studies have been carried out. Experimental studies are done using echo-cardiography, Doppler testing etc. Later, with the availability of computers, the studies shifted progressively for understanding the physics in detail. Initial computational studies concentrated on artificial heart valves because of their simple geometry and their motion, and the flow between aortic and mitral valve in peak systole phase. Later, the focus shifted to study the valve leaflet & it's interaction with blood. Modelling of valve dynamics were be done by making some simplifications like: a) not considering elasticity - contraction of valve cusps, and b) assuming only pressure difference & shear stress drive the blood through valves. [Korakianitis and Shi, 2006] have modelled valve dynamics considering the pressure, flow, tissue fraction, and vortex effects of blood. This model was used to study pathological cases of mitral stenosis & aortic regurgitation. The results coincided with the data from cardiovascular textbooks. This model was also able to show the influence of various effects which were not easily obtained through clinical observation.

[Haj-Ali et.al. 2008] have highlighted the need for computer models which can analyze non-linear geometry coupled with materials in formulation of elements. A prosthetic valve made of polymeric material is tested by both experiments and by using finite element model on ABAQUS. Fluid-Structure Interaction modelling was not considered in this model which cannot tell about the local concentration areas but it can resolve the overall deformation.

2.2 Effects of Mitral Stenosis (MS)

Mitral stenosis, the blockage of the mitral valve, develops over a period and creates a constant pressure overload in left atrium which leads to its swelling. This in turn causes disturbed left atrium functioning due to atrial fibrillation. The atrial kick, which is present at the start of diastole, is lost due to this improper left atrium function thereby causing improper left ventricle filling. This leads to reduced cardiac output leading to heart failure.

In a study of group of people having pure MS, effect of MS on left atrium was studied in detail. A broad group representing patients from an early stage of MS to patients from advanced stages was studied in [Probst et al., 1973].

The mechanical consequences of MS cannot be expressed by a single hemodynamic measurement, but data suggests that the left atrium is changed significantly. This change in left atrium triggers the changes in electrical signals which regulate the heartbeat, causing atrial fibrillation. Once this happens, the atrial fibrillation leads to further enlargement of left atrium which initially occurred in small amount.

The relationship between severity of MS & changes in left atrium is also influenced by the age factor. [Horwitz, L.D., 1973] suggested that young people were less prone to atrial fibrillation, even though their left atrium is significantly enlarged. People of older age (above 48 years) having established atrial fibrillation experience significant distortion to their left atrium structure. There is disruption in normal shape & loss of muscle mass, which are presumably the consequences of chronic atrial fibrillation, at an advanced stage where the atrial enlargement is high. This suggests that age (rather than severity of MS alone) is an important factor for the development of atrial fibrillation.

Less cardiac output in MS is not always attributed to the mechanical obstruction of the mitral valve: few researchers believe the reduced cardiac output is due to some sort of ventricular

dysfunction [Heller and Carleton, 1970; Grant, 1953; Feigenbaum et al., 1966]. Many studies have been done to understand the causes but only a few have come up with adequate reasoning. In one study, patients with MS are observed by selective LV cardiography, & the results suggested that the posterobasal area (outer surface of LV) had some distortion causing rigidity in that area [Heller and Carleton, 1970].

The volumes of the left ventricle were obtained by cardiography with patients having MS. It was observed that there was slight increase in end diastolic volume & end systolic volume, which led to a decrease in stroke volume thereby reducing the cardiac output. It was also hypothesized that- in MS the thickening of valve leaflets & fibrosis of chordae tendineae convert the valve into a rigid cylinder [Grant, 1953], thereby impairing its movement and leading to dysfunction of the wall of left ventricle. It is also observed that there are abnormal rises in the diastolic pressure for a given increase in the diastolic volume suggesting reduced left ventricle compliance [Feigenbaum et al., 1966], but it is observed that this effect does not significantly reduce the cardiac output.

2.3 Effect of exercise on heart function

Testing of valvular heart pathologies during exercise has limited significance in terms of diagnosis but these tests are helpful in identifying cardiovascular dysfunction and how it progresses. Exercise provokes interactions of metabolic, neurologic, and hemodynamic responses. Its capacity is normally determined by the availability of oxygen required for metabolism of cardiac and muscle movements. Increase in cardiac output and also increased tissue extraction of oxygen from blood are primary mechanisms meeting the oxygen requirements during exercise [Rosing et al., 1974].

There are number of adaptive mechanisms which can meet the oxygen demands during exercise. Age, sex, and physiological conditioning of the individual have effect on these mechanisms which in turn influence the exercise capacity. After age of thirty, cardiac output, pulse rate, oxygen consumption, and stroke volume, all decrease eventually. Women have smaller hearts and blood capacity, and are also generally less physically conditioned compared to men. These suggest lower maximal cardiac output, oxygen consumption, and exercise capacity compared to men. Improved physiological conditioning contributes towards more efficient distribution of cardiac output to the exercising muscles and changes the autonomic tone in the nervous system which significantly

improve the cardiac output and stroke volume meeting the oxygen demand of the exercising muscles.

3.Problem Formulation

The Living Human Heart Model (LHHM), when run with different parameters gives results for heart function which match the textbook values. The model is extensively being tested for various treatment modalities by research groups around the world. We propose to study the LHHM for a cardiovascular pathology which is common in India, namely Mitral Stenosis. In order to obtain predictions for various pathological states using the LHHM, parameters like heartbeat rate, valve areas, material properties, etc. are to be changed to correspond with those of the pathology.
We first validate the LHHM model by obtaining predictions for function of a healthy adult male heart under resting condition and exercise condition. We then run the model for severe and moderate cases of MS under resting conditions. After comparing these results with clinical data, we simulate the effect of exercise on heart function in the case of moderate and severe types of mitral stenosis and compare with clinical data where available. Where clinical data is not available, we summarize the predictions and put them up for comparison.

3.1 Simulation of Normal Heart

To validate the model predictions for normal heart, we used LHHM (v2.0 beta, coarse mesh) with the default parameters for 5 cardiac cycles. The ELEC model is simulated first, then followed by the MECH model. The simulations were run using Parallel architecture on a 12core 3.47GHz workstation (Make: FUJITSU R-670 Celsius, Year 2012): they took 58hours to complete, and the output database is created with the results. These results are discussed in the next chapter.

3.2 Simulation of Mitral Stenosis under resting conditions

Mitral stenosis is classified into 3 types based on the extent of blockage of the mitral valve area (MVA) as follows: mild (MVA < 4cm^2), moderate (MVA < 2cm^2), and severe (MVA < 1cm^2). To understand this pathology, we studied the severe type of mitral stenosis on LHHM.

The parameter associated with mitral stenosis was the ‘Effective exchange area’ between Left atrium and Left Ventricle. The value for the normal exchange area is 5.2±0.9 cm^2 [Poutanen,

et al., 2013], but the parameter value in LHHM is 10.39 cm^2 (see Fig 3.1). This has been explained by the LHHM development team as part of necessary parameter tuning in order to reproduce overall normal behavior for the normal case (PV loops, cardiac output, etc.).

In order to use LHHM for our study we used a scaling factor as given below in all our cases of mitral stenosis.

$$\text{Scaling factor} = \frac{Exchange\ area\ in\ LHHM}{Normal\ MV\ area}$$

$$\text{Scaling factor} = \frac{10.39}{5.2} = \mathbf{2.0}$$

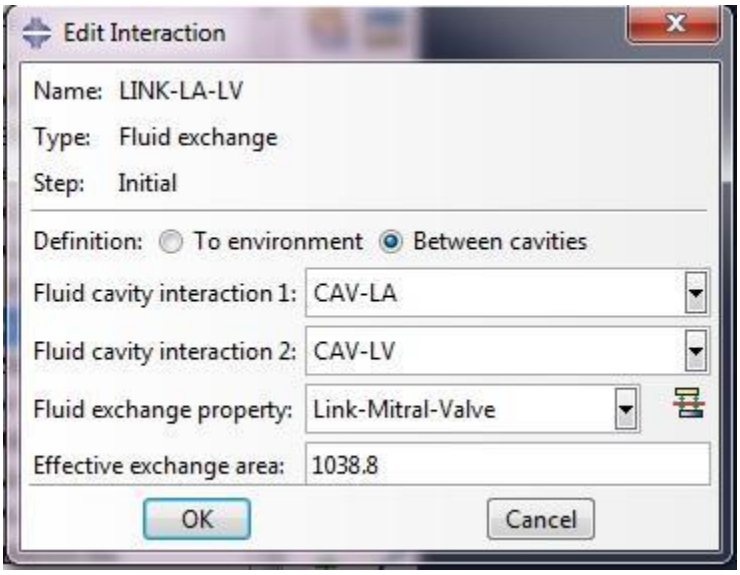

Figure 3.1 Effective exchange area (MV area) - Normal Heart

We simulated the severe mitral stenosis case with mitral valve area of 1cm^2 (normal value). We changed the 'Effective exchange area' parameter to 2cm^2 using the scaling factor as shown below (Fig 3.2) and run the ELEC model followed by the MECH model. The simulations for all MS cases took 69 hours to complete on the same hardware for normal simulation as given in Section 3.1.

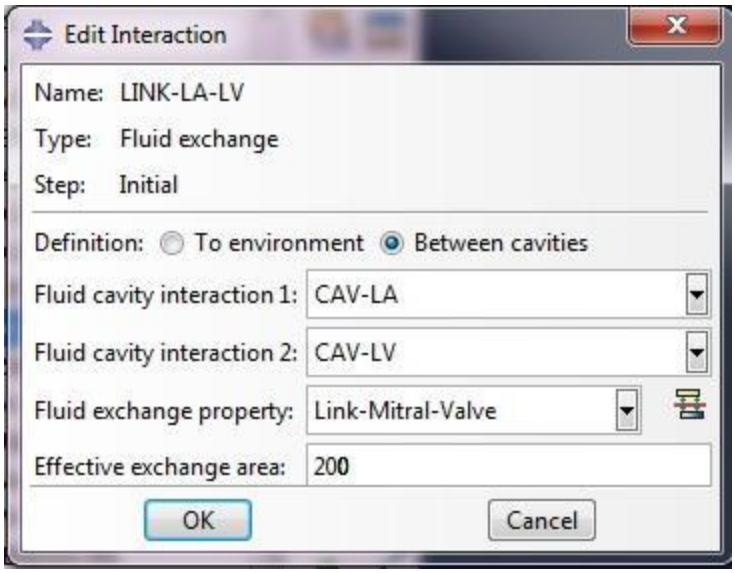

Figure 3.2 Effective Exchange area (MV area) - Severe MS

4.Results

4.1 Validation: Heart Function in Healthy Heart (Resting)

The results generated from the simulations are analyzed and reported below: we observed that many of them lie within the normal ranges [Edward Lifesciences, 2009]. The Pressure-Volume (PV) loop of Left Ventricle of Normal heart (Resting) is generated from the output database (Fig 4.1), and it shows the end-systolic and end-diastolic points and the stroke volume.

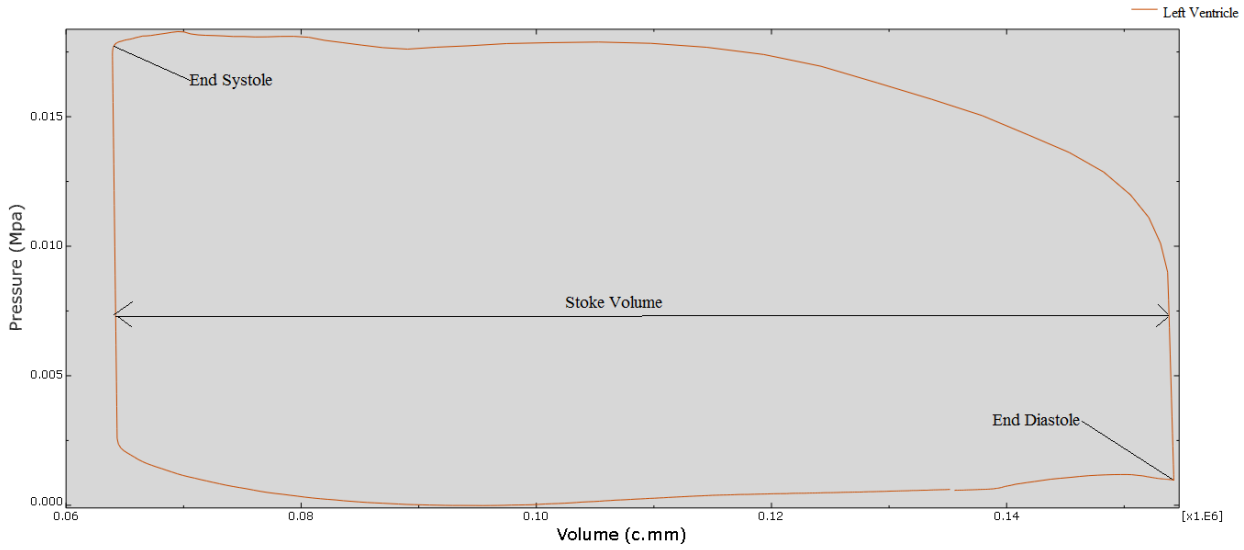

Figure 4.1 - PV Loop for Left Ventricle of Normal Heart (Resting) after 5th cardiac cycle as simulated on LHHM (v 2.0 beta)

These results show good agreement with those presented in the literature [Phibbs B., 2007, Goers et al., 2008]. Comparison of the simulated results for various cardiac parameters with clinical data for the normal ranges is given in table 4.1.

Output	**Model Result (LHHM v2.0 Beta)**	**Clinical Data ([Edward Lifesciences, 2009])**
Left Ventricle (LV) Ejection Fraction	56%	>50%
Right Ventricle (RV) Ejection Fraction	49%	40-60%
Max LV Pressure	136.3 mmHg	100-140 mmHg
Min LV Pressure	6.8 mmHg	3-12 mmHg
Max RV Pressure	29.8 mmHg	15-30 mmHg
Min RV Pressure	0.2 mmHg	2-8 mmHg
Left Atrium Pressure Range	1.8-6.5 mmHg	2-6 mmHg
Right Atrium Pressure Range	8.7-24.5 mmHg	4-12 mmHg

Table 4.1 Results from LHHM (v 2.0 beta) for Normal Heart in resting conditions

4.2 Prediction: Heart Function in Severe Mitral Stenosis case (Resting)

Normal mitral valve area is 5.2±0.9 cm^2 [Poutanen et al., 2013] as already noted. When the mitral valve area reduces below $2cm^2$, (moderate type of MS), the valve causes hindrance to the flow of blood in the left ventricle [Gorlin and Gorlin, 1951; Dexter, 1952]. This in turn causes a pressure gradient (or pressure difference) to build across left atrium & left ventricle. This pressure gradient

delays the diastolic filling time thereby reducing the stroke volume. To counter this effect, heart rate is increased to maintain the cardiac output. When the heart rate goes above a certain point, the filling time is insufficient to fill the ventricle completely, thereby increasing the pressure in left atrium, leading to pulmonary congestion.

When the mitral valve gets stenosed further up to $1cm^2$ (severe type of MS), the pressure gradient across the mitral valve builds up to 20mm Hg: this leads to an increase in Left atrium pressure to 25mm Hg so as to maintain a normal 5mm Hg left ventricle pressure for normal cardiac output [Klabunde R., 2011]. This elevation in left atrium pressure is transmitted to the pulmonary vasculature & causes pulmonary hypertension.

When the mitral valve area is set to $1cm^2$ in the LHHM model, we therefore expect that the simulations should predict:

a) Left atrial pressure to be around 25mmHg, and

b) There should be increase in the pressure difference between Left atrium and Left ventricle pressures so as to maintain the normal cardiac output.

The results showed that this is indeed the case, and they are reported below.

Figure 4.2 reports the variation of Left atrial pressure and Left ventricle pressure with time for 5 cardiac cycles for Normal heart under resting conditions as obtained from the output database of the simulations using LHHM (v 2.0 beta), whereas Figure 4.3 reports the same pressures for the heart with Severe type of mitral stenosis (MVA = $1cm^2$) .

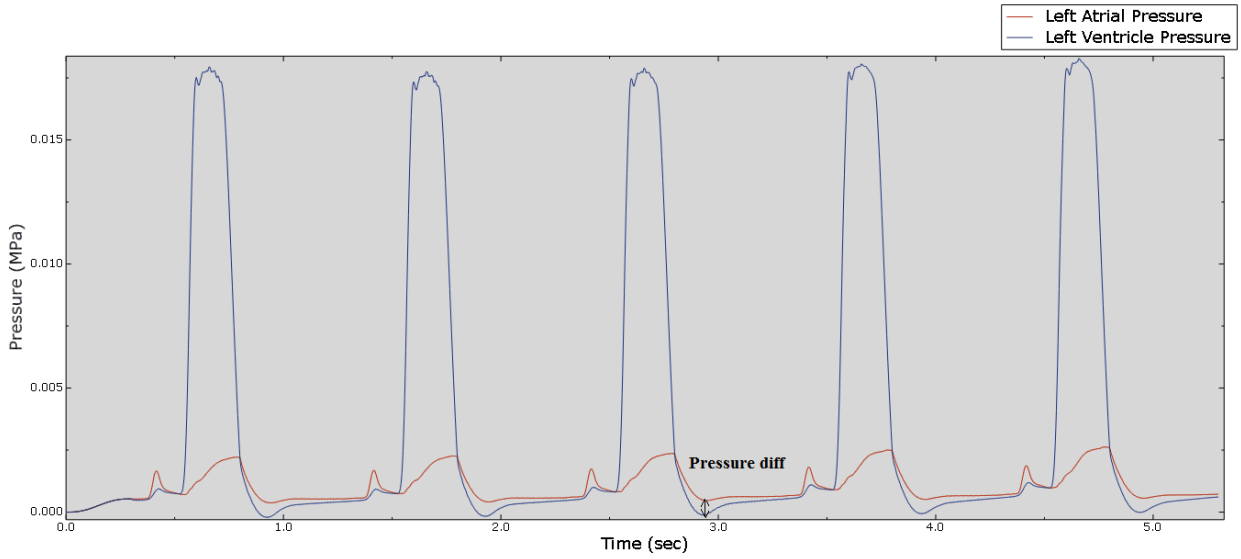

Figure 4.2 Left Atrial and Left Ventricle Pressure for Normal heart in resting conditions as predicted by LHHM (v2.0 beta)

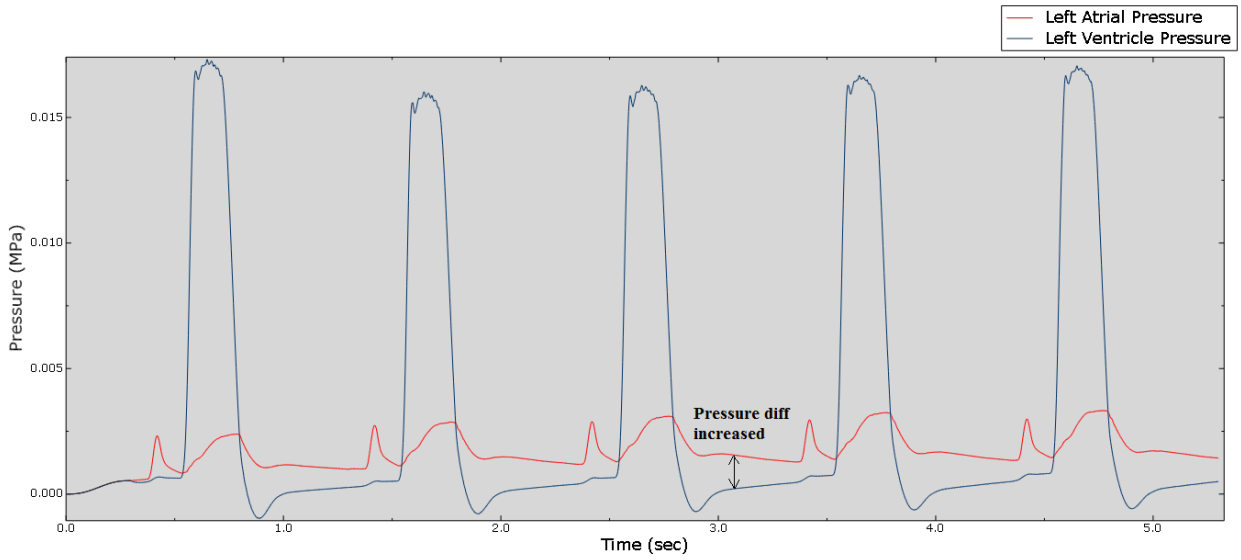

Figure 4.3 Left Atrial and Left Ventricle Pressure for heart with severe type of MS as predicted by LHHM (v2.0 beta)

We can see from Fig 4.2 and Fig 4.3, that there is an increase in the pressure difference between Left atrium and Left Ventricle in Mitral Stenosis, and this confirms clinical hypothesis (b).

The Left atrial pressure data from output database for the normal case and severe MS case are extracted and plotted in MS-Excel by changing the units from MPa to mmHg. The figure (Fig 4.4) below shows these plots.

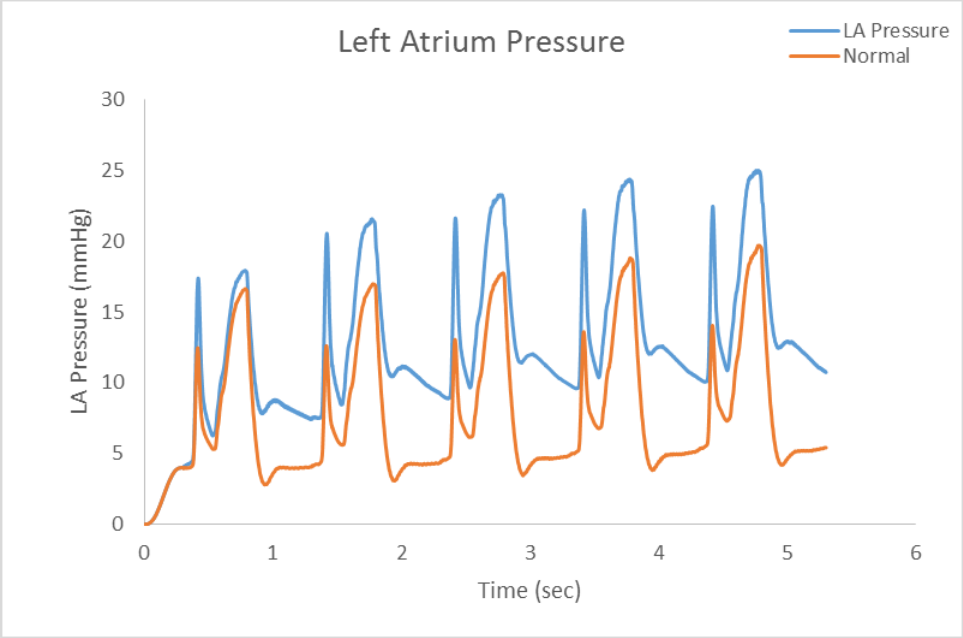

Figure 4.4 Left atrial Pressure in Normal Heart and severe MS as predicted by LHHM (v2.0 beta)

Here we note that the Left atrial pressure in the severe MS case shows that Left atrial pressures reaches up to 25mm Hg after the 5^{th} cardiac cycle.

This confirms clinical hypothesis (a) from [Klabunde R., 2011]

4.3 Prediction: Heart Function in Mitral Stenosis (Resting): Multiple cases ([Gorlin et.al, 1951])

[Gorlin et.al, 1951] observed that the symptoms of mitral stenosis are mainly attributable to pulmonary congestion (congestion in the lungs). Pulmonary congestion is caused by circulatory changes which result from the narrowing of the mitral valve. Eight patients were chosen for observing these circulatory changes in the pulmonary region both at rest and after exercise. The data for the average pulmonary arterial pressure (tapped at the base of pulmonary artery at the exit

of right ventricle) and average pulmonary capillary pressure (tapped at the entrance of left atrium near outlet of pulmonary vein) was reported for all the patients both at rest and during exercise.

In our study, we obtained the LHHM predictions for pulmonary arterial pressure and pulmonary capillary pressure at rest for all the eight patients. The mitral valve areas and the pulse rate were changed for each patient. The simulations were run for 5 cardiac cycles and the pressure data was recorded: the average of this data is calculated and reported for each patient. The comparison of the average pulmonary arterial pressure and pulmonary capillary pressure results from [Gorlin et.al 1951] (referred as Gorlin et al. in table), and LHHM (v2.0 beta) are tabulated below in Table 4.2.

Patient I.D.	**MV Area (cm^2)**	**Pulse rate (bpm)**	**Pulmonary Arterial Pressure**		**Pulmonary Capillary Pressure**	
			Gorlin et.al. (mmHg)	**LHHM (v2.0 beta) (mmHg)**	**Gorlin et.al. (mmHg)**	**LHHM (v2.0 beta) (mmHg)**
JD	2.5	100	25	15.5	19	19.3
JF	1.6	72	32	18.6	21	17.4
LT	0.9	70	45	20.6	24	19.4
MB	0.8	96	23	17.6	17	21.5
ES	0.7	80	48	19.3	26	21
RW	0.6	70	46	20.8	34	21.9
MM	0.4	56	55	24.5	22	23.8
Average			39.1	19.5	23.3	20.6
SD			12.4	2.8	5.6	2.1

Table 2 Comparison of Pulmonary arterial and pulmonary capillary pressure in heart function with mitral stenosis at rest: Model (LHHM (v2.0 beta)) vs Data ([Gorlin et. al. 1951])

Fig 4.5 and Fig 4.6 are the plots showing comparison of the pulmonary arterial pressure and pulmonary capillary pressure [Gorlin et.al, 1951] and LHHM (v2.0 beta), respectively. Fig 4.5 shows that the model simulations are able to capture only the qualitative trend of data for pulmonary arterial pressure versus mitral valve area, and not the quantitative aspect. However, the model performs much better and captures both quantitative and qualitative trend of data for pulmonary capillary pressure (Fig. 4.6). This may be attributed to the fact that pulmonary capillary pressure is measured much closer from the mitral valve than pulmonary arterial pressure, and hence the error due to the modelling shows up to a lesser extent.

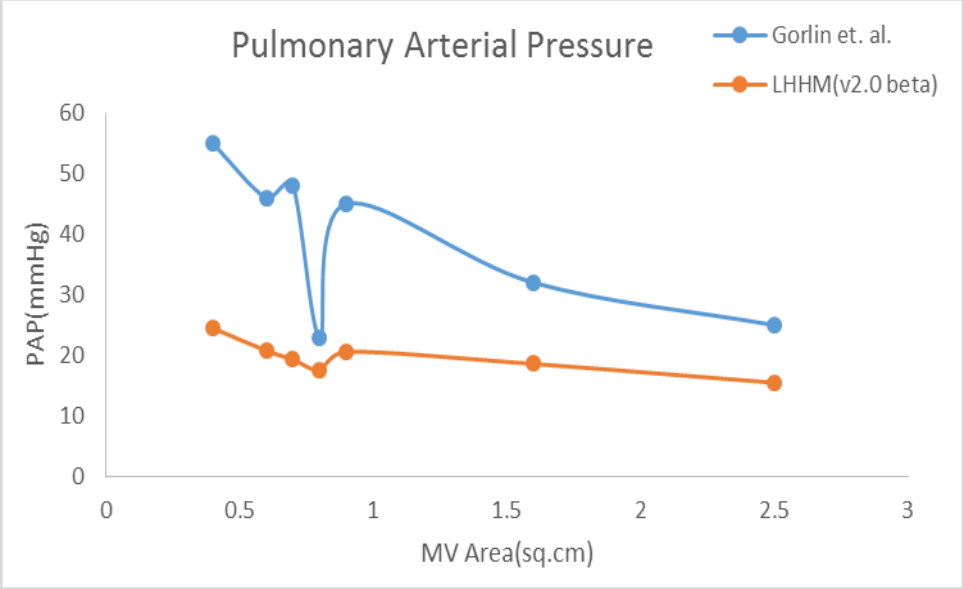

Figure 4.5 Pulmonary arterial Pressure for Heart function in Mitral Stenosis cases (Resting): Model (LHHM (v2.0 beta) vs Data ([Gorlin et al., 1951])

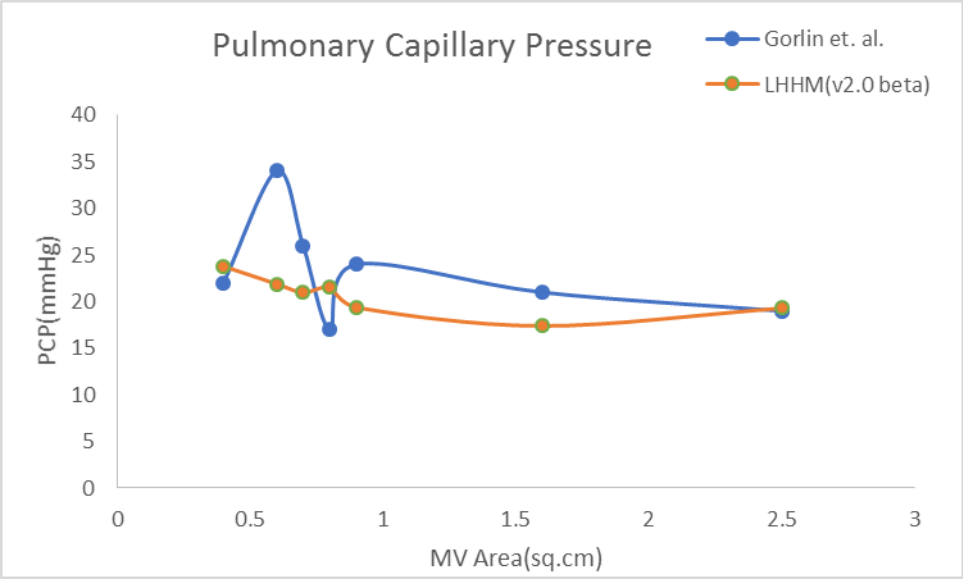

Figure 4.6 Pulmonary capillary Pressure for Heart function in Mitral Stenosis cases (Resting): Model (LHHM (v2.0 beta) vs Data ([Gorlin et al., 1951])

4.4 Prediction: Heart Function in Mitral Stenosis (Exercise)

[Gorlin et.al, 1951] further studied the effects of mitral stenosis during exercise. Observation of circulatory changes after exercise for the above eight patients was done and reported. Based on their observations they came up with a conclusion, that the pulmonary capillary pressure rose along with the increase in mitral valvular blood flow and, pulmonary arterial pressure rose due to the rise in pulmonary capillary pressure along with increase in blood velocity flow in some cases. Pulmonary arteriolar resistance which is the difference between pulmonary arterial pressure and pulmonary capillary pressure over cardiac output showed no consistent change on exercise. The average values are identical both at rest and after exercise.

In our study, we have simulated the data for one patient (J.F.) with mitral valve area of 1.6cm^2 and pulse rate of 72 bpm at rest and 108 bpm during exercise. The simulations were run for 5 cardiac cycles in both cases and the average values for the pulmonary arterial pressure, pulmonary capillary pressure and difference between both the pulmonary pressures is collected and reported. We expect that LHHM should predict the following:

a. Pulmonary arterial pressure (PAP) and pulmonary capillary pressure (PCP) should rise during exercise than the value at rest.

b. Difference between pulmonary arterial pressure and pulmonary capillary pressure should not significantly change during exercise than at rest.

Patient II	**Cardiac Output (Lpm)**		**Mean PA pressure (mmHg)**		**Mean PC pressure (mmHg)**		**Mean gradient (PA-PC) (mmHg)**	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
Gorlin et.al.	6.5	9.4	32	58	21	46	11	12
LHHM	5.25	6.48	19.08	16.12	17.9	24.34	1.18	-8.22

Table 3 Comparison of Pulmonary data in heart function with mitral stenosis during exercise: Model (LHHM (v2.0 beta)) vs Data ([Gorlin et. al. 1951])

Table 3 shows that LHHM was not able to confirm the above predictions because:

a. Pulmonary arterial pressure didn't rise during exercise and,

b. Difference between pulmonary arterial pressure and pulmonary capillary pressure changed significantly during exercise

We can hence conclude that the usage of LHHM (v2.0 beta) for mitral stenosis study is limited only to resting conditions and not during exercise. Further, predictions of LHHM (v2.0 beta) are better at locations close to the mitral valve than for locations farther away.

5.Conclusions

With increasing mortality due to cardiovascular diseases, there is a need to control and minimize this by understanding and implementing new treatment techniques on heart. Studying heart on a computational model (LHHM v2.0 beta) has given us a greater advantage over the traditional method in that an engineering study is able to offer insights which may be of use to clinical practitioners.

We studied heart function for common cardiovascular pathology in India: Mitral Stenosis (MS). Initially, we evaluated the efficacy of LHHM v2.0 beta for a healthy heart under resting conditions and validated the results with data from [Edward Lifesciences, 2009] (see Sec 4.1). We then predicted the heart function for a severe mitral stenosis case from [Klabunde R., 2011] and noted that results from LHHM matched clinical hypotheses namely: a) that the pressure difference between Left atrium and Left Ventricle will increase for MS case, and b) Left atrium pressure will rise upto 25mmHg (see Sec 4.2). With this confirmation, we then simulated the MS cases from multiple patients reported in [Gorlin et.al, 1951]. We observed that LHHM (v2.0 beta) show good match with data under resting conditions:- Pulmonary arterial pressure was following the trend as predicted and the average values for pulmonary capillary pressure were nearly same for both the model (LHHM) and the data ([Gorlin et.al, 1951]) (see Sec 4.3). However, further testing of LHHM where we simulated the clinical data for one patient from [Gorlin et.al, 1951] *after exercise* showed that the predictions made were not consistent with the model (LHHM). Pulmonary arterial pressure didn't rise during exercise and the pulmonary arteriolar resistance value was not similar to that during rest (see Sec 4.4).

We conclude from our tests that LHHM v2.0 beta can be used for studying mitral stenosis under resting states; further model improvement is needed before it can be used for the exercised state, and we record this as scope for future work below.

5.1 Future Work

We have recorded a limitation of LHHM (v2.0 beta), that it was not able to capture exercise data for mitral stenosis cases, we can improve the model in such a way that it can used for exercised

conditions as well. Towards this end, we can include pulmonary constraints in the model as it can increase the accuracy of the model given that the function of heart extends to the pulmonary region.

Further studies, along similar lines to the one in this thesis, could compare LHHM predictions with clinical data for other pathologies like Mitral Regurgitation, Aortic Stenosis, Myocardial Infarction (Heart Attack), etc, and new treatment techniques can also be tested for those pathologies.

6.References

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