# EFFECT OF ORIENTATION OF PUMP ON THE PERFORMANCE PARAMETERS OF CHITRA LVAD

A Thesis

Submitted By

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# CERTIFICATE

This is to certify that the thesis titled **'Effect of Orientation on the Performance Parameters of Chitra LVAD'** being submitted by **Adarsh Narendra Madre** to SCTIMST Trivandrum, for the award of degree of **Master of Technology in Clinical Engineering** jointly offered by IIT Madras, CMC Vellore and SCTIMST Trivandrum, is a bonafide record of research work done by him under our supervision. The contents of this thesis in full or in parts have not been submitted to any other Institute or University for the award of any degree or diploma.

The research had been carried out at Sree Chitra Institute of Medical Sciences and Technology, Trivandrum.

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# Abstract

Congestive heart failure (CHF) is global healthcare problem due to its high fatality rate. The reliable methods for the End stage heart failure cases are mainly limited to the heart transplantation which is restricted by very limited number of available donor heart. However, transplantation cannot be the inherent solution as the demand of donors is very high and availability of a right donor is very scarce. As a result, the number of patients who actually receive heart transplantations is far less than that requiring the donor.

Due to these hurdles in the transplantation therapy, clinicians are forced to adopt alternative measures. One such promising measure is the employment of Mechanical Circulatory Devices. Mechanical Circulatory Devices particularly, Left Ventricular Assist Devices (LVADs) are the topic of discussion for they can be the best alternative to improve the failing left heart. As promising as they sound, there are numerous fields that need to be taken into consideration in developing a better Mechanical Circulatory System (MCS). The rotor of the device when implanted, undergoes continuous change in orientation thus it becomes a major concern for engineers to design the device in such a manner that the orientation has no or least effect on the performance parameters of the device.

The purpose of this study is to evaluate the effect of orientation of the Left Ventricular Assist Device (LVAD) that is under developmental stages in the institute. The study focuses on the major performance parameters of the pump such as pump inlet and outlet Pressure difference (ΔP), Flow, input and output powers and Overall efficiency that are studied by a set of experiments organized to be performed at three different orientations [-90 ˚, 0 ˚, +90 ˚] with vertical axis as the reference at 0 degree. The orientation studies of the LVAD were conducted using a pulse duplicator system, a mock circulatory loop that can mimic the left heart under numerous physiological and diseased conditions. The pump was studied at range of speed varying from 1600 – 2800 rpm for all three orientations.

The Orientation of the pump had minor effects on the pressure difference between inlet and outlet of the LVAD under certain conditions (highest for 0 degree). Also, the power required by the pump varies with the orientation slightly (least for 0 degree) thus a variation in overall efficiency is observed in the pump with respect to orientation. The Pulsatility Index (PI) was found to independent of the change in orientation with no significant effect on the pressure and flow hemodynamics of pump due to orientation.

# Keywords

Congestive Heart Failure, Mechanical Circulatory Devices, Primer Pump, Aorta, Ventricle, Atrium, Cardiac Output, Stroke volume, Valves, Pulse Pressure, Mean Arterial Pressure, Cardiac Contractility, Compliance, Systemic Vascular Resistance, Left Ventricular Assist Device, Impeller, Continuous Flow, Centrifugal Pump, magnetic levitation, Hydrodynamic Thrust, Pressure Head, Flow Rate, Hydraulic Efficiency, Pulsatility Index, SuperPump, Pulse Duplicator, Left heart Model.

# Table of Contents

# List of Figures

# List of Tables

# Abbreviations

| | |
|---|---|
| AoP | Aortic Pressure |
| AP | Atrial Pressure |
| BEP | Best Efficiency Point |
| Bpm | Beats per minute |
| BTR | Bridge to Recovery |
| BTT | Bridge to transplantation |
| BTC | Bridge to Candidacy |
| C | Compliance |
| CHF | Congestive Heart Failure |
| CO | Cardiac Output |
| DT | Destination Therapy |
| H | Head |
| HF | Heart Failure |
| HR | Heart Rate |
| LAP | Left Atrial Pressure |
| LHF | Left Heart Failure |
| LVP | Left Ventricular Pressure |
| MAP | Mean Arterial Pressure |
| MIH | Modified Index of hemolysis |
| NIH | Normalized Index of Hemolysis |
| P | Pressure |
| $P_h$ | Hydraulic Power |
| PAC | Pulmonary Arterial Compliance |
| PP | Pulse Pressure |
| $P_{dias}$ | Diastolic Pressure |
| $P_{sys}$ | Systolic Pressure |
| Q | Flow Rate |
| R | Resistance |
| SV | Stroke Volume |
| $\eta_h$ | Hydraulic Efficiency |
| $\rho$ | Fluid Density |
| $\mu$ | Fluid viscosity |
| $\Delta P$ | Pressure Difference |

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# Introduction | 1

Heart Failure or End stage Heart Failure is a major cardiovascular disease and is always in the headlines as a Global healthcare problem. It is one of the leading causes of mortality in world as well as in India. As stated by Global public health Burden of heart Failure, an estimated 64.3 million people around the world are suffering from various heart diseases with 26 million people suffering from chronic heart failure of which around 4.6 million people are Indian nationals. The chronic heart failure thereby shows high fatality rate. The established therapy of end stage heart failure is heart transplantation. The type of treatment provided depends on the degree of heart failure and its availability, but the most reliable move is the heart transplantation in case of end stage heart failure. However, the limited availability of donor heart and the increasing heart failure limits the therapy of heart transplantation to a small patient population which lead to the development of Left ventricular assist devices (LVAD). LVADs are connected in parallel to the main circulation systemic loop where its inlet is connected to the apex of the left ventricle and outflow is fixed into the ascending aorta through the outflow graft thus assisting the ventricle to supply oxygenated blood to the peripheral circulatory systems through the arteries. LVAD is associated with a number of therapies depending on the requirement and physical ability of the patient e.g. Bridge to transplant, destination therapy and short duration therapy. With the advantages of heart transplantation, there are various complexities accompanied to it. The major problem being the availability of right donor. Thus, only a few numbers of people can actually receive transplantation every year.

Given the complexities tied with heart transplantation, Clinicians have moved to an alternative therapy in the form of Mechanical Circulatory Assist Devices. Mechanical circulatory assist devices are designed with the objective of assisting left ventricle of the heart to maintain required cardiac output and pressures. Hence these devices are majorly termed as Left Ventricle Assist Device (LVAD). The Clinical testing of LVAD have shown promising results as a long-term support system and have proven to be very crucial in improving the quality of life.

The LVAD being a mechanical circulatory device, has its own set of complications such as durability and Hemodynamic performance. Several reports of device complications have been reported in the recent past stating serious issues such as damage of blood cells, clots, bleeding from driveline and mechanical failure. Also, a device that is implanted in the humans is subjected to continuous changes in the orientation due to the mobile nature of the patient. The continuous changes in the orientation of the pump may alter the performance parameters like pressure head and flow rate and may affect the efficiency of the pump. It is thus imperative to study the effect of orientation on the performance of the pump. These are major design related issues and a lot of research is put in developing better pumps that expected to eradicate these issues. Thus, to design a device that along with fulfilling the intended application, gives high hemodynamic performance with least mechanical failure require intensive testing on the performance parameters in all possible working conditions. All these clinical testing require a lot of time and money before making the device available for commercial use. This in a way increases the cost of device making it inaccessible to all kinds of population. This serves as another challenge that needs to be addressed during the designing of the device.

This study is based on the fact that the axial position of rotor of the pump is affected due the effect of gravity that is imposed on it depending on its position or orientation. This study will quantify to what extent does the orientation of the pump matter in the performance analysis. The outputs obtained from testing the pump in various orientations will give the contribution of orientation and the most suitable one for the proper and efficient operation. To test the pump's performance, a pulse duplicator system was used. The role of the pulse duplicator is to replicate the pulse flow environment of the left ventricles using a piston pump with adjustable frequency of beats and stroke volume.

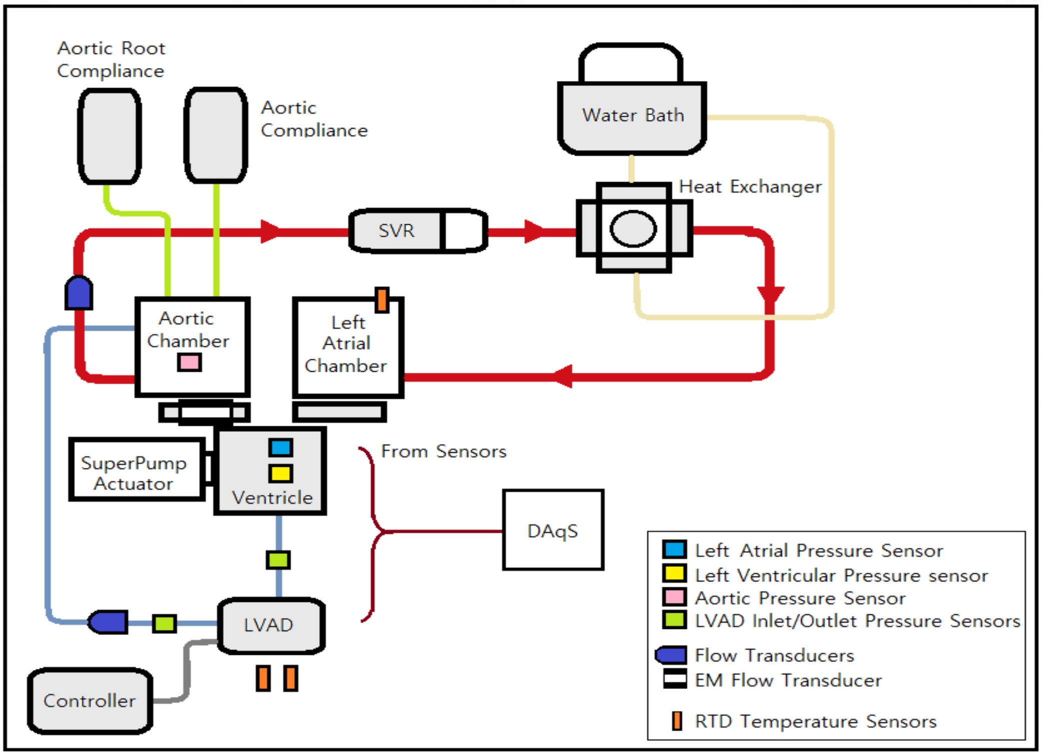



Figure 1.1: Schematic diagram of mock circulation loop.

The compliance of the arteries was mimicked by an air-trapped compliance tank, and the vascular resistance was adjusted using a Systemic Vascular Resistance (SVR) in series with the main systemic loop. The Figure 1.1 shows the schematic diagram of mock human circulation loop. The results obtained from this study can be used further in the development process of LVAD and its controller.

### 1.1 Significance and Scope

This study signifies that all the factors that contribute to altering any one or more performance parameters of LVAD are considered and documented which enables the Mechanical assist devices to be robust and do not fail when implanted. The use of pulse duplicator for testing makes the LVAD function in actual heart conditions and the output of the tests in different orientations gave data that can be used to evaluate the performance parameters of the pump.

### 1.2 Aim

This study majorly focuses on the effects of pump orientation on the performance parameters like Pressure head ($\Delta P$), Hydraulic power and efficiency., three extreme orientations -90̊, 0̊ and +90̊ were selected to broadly analyze all the variations that occur in the performance parameters when the LVAD's orientation change. All the experiments were done with constant length of pipes connecting left ventricle to inlet of the LVAD and that connecting the outlet of the LVAD to the Aortic chamber. The thesis also takes into consideration the hemodynamic study of the pump where the Pulsatility Indices at various operating conditions of Heart rate, Cardiac Output and Mean Arterial Pressure are plotted with respect to LVAD flow.

### 1.3 Thesis Outline

This thesis is divided into seven chapters which deal with the history and technological developments in the mechanical circulatory systems, basics of cardiovascular physiology which give the insight of general physiology of the heart. The theory includes the principles, design and development of LVAD along with its generations and materials used in various components of LVAD. It gives an idea of not only the pump mechanism but also the other components that go into implantation and theirs uses. Various performance parameters of continuous flow centrifugal pumps are discussed. The thesis gives the detailed specifications of the pulse duplicator system that was used to test the LVAD and also outlines the other applications and system components of pulse duplicator system. The last two chapters deal with the interpretation of bulk of data that was acquired from the experiments, aim related plots and figures and conclusion drawn from the data. The contents of each chapter are mentioned in brief ahead.

**Chapter 2: Literature Review**

- Background Information
- Design and functions of LVAD
- Previous studies done in same context

**Chapter 3: Cardiovascular Physiology**

- Basic heart physiology
- Electrical Activity of heart
- Cardiac Cycle
- Cardiac Output
- Workload of heart
- Intrinsic Property of Heart

**Chapter 4: Left Ventricular Assist Devices**

- Introduction to Mechanical circulatory systems
- Working principles and Generations
- Indications for implantation
- Components of MCS
- Materials used

**Chapter 5: Design and construction of mock circulatory loop**

- Introduction to Pulse Duplicator System
- Left heart Model and Super pump
- Data acquisition system
- Components of Pulse Duplicator system
- Specifications of Pulse Duplicator
- Applications

**Chapter 6: Methodology and Experimental Evaluation**

- Describe the method to analyze the performance parameters in different LVAD orientations
- Evaluation of LVAD in various combinations of Physiological and Heart failure conditions
- Acquire data on pressure and flow curves

**Chapter 7: Results, Discussion and Conclusions**

- State the conclusion drawn from experiments
- provide suggestions for future development

Figure 1.2: Block diagram showing the flow of the study.

### Chapter 2

This is the Literature review that informs us about the global impact of chronic heart failure and how transplantation is becoming so hard to avail. Thus, it signifies the importance of mechanical circulatory systems and how their development can provide robust left ventricle assistance. This chapter also highlights the previous studies done the LVAD in the fields of design and development, component development and their effects, performance parameter analysis under various physiological and pathological conditions.

**Chapter 3**

The basis of this chapter is to surface the cardiovascular physiology of the human heart by studying the basic anatomy of heart and histology of cardiac cell. This chapter deals with the electrical activity of heart, production and propagation of action potentials right from the SA node all the way till the ventricles. It includes explanation of important terminologies like cardiac cycle, cardiac output, Vascular resistance, Compliance, contractility. Furthermore, it enhances the reader's knowledge in the work output of heart, P-V curves and extrinsic capabilities of the cardiac muscles stated by the Frank-Starling law

**Chapter 4**

This chapter deals with the detailed study of the Left Ventricular Assist Devices. It addresses the technological developments in pumping mechanisms. This chapter majorly focuses on the continuous flow centrifugal pumps referring to the HeartMate II, HeartMate III and HeartWare CF pumps as far as the design, working principle and implantation are concerned. It also briefs focuses on each element of the LVAD circulatory system and highlights the materials used for manufacturing of these components.

**Chapter 5**

This Chapter introduces a mock circulation loop with the help of pulse duplicator system modeling a left heart which will be used in the experiments to produce all the physiological and diseased condition of the heart. Also, each component of pulse duplicator system participating in the mock circulation loop as far as producing, processing, subordinating and acquiring the data for the study is discussed in this chapter.

**Chapter 6**

This chapter proposes a methodology for testing the important performance parameters of the LVAD when subjected to different orientations under various physical, physiological and diseased condition of heart. For this purpose, a mock circulation loop is devised using pulse duplicator that acquires data for all the conditions mentioned above.

**Chapter 7**

This chapter houses the graphical interpretation of all the data obtained from experiments which in turn gives the extent of effect of orientation of pump on the performance parameters. This is the conclusion part of the thesis where a summary of outcomes is stated and corresponding recommendations are made on the most reliable orientation. This chapter also helps the future developments procedures and should be taken into consideration wherever the study of orientation is discussed.

# Literature Review | 2

Sagar Kadakia. et al. under the study, 'Current status of the implantable LVAD' stated that the standard for the treatment of end stage cardiopathy remains orthotropic heart transplantation. However, given the shortage of accessible organs and therefore the continuous inflow of patients, mechanical circulatory support devices are increasingly utilized for managing acute and chronic heart condition that's refractory to medical therapy. Particularly, the introduction and clinical validation of left ventricular assist devices (LVAD) in several pivotal studies have revolutionized the sector of cardiac therapy. Although LVAD are related to a decrease in mortality and an improvement within the quality of life, it also must be considered that LVAD implantation is related to significant complications and device-related problems. The study brings into consideration the factors like available devices, current indications, patient selection, complications and outcomes. Additionally, as long as a growing number of patients with LVAD are surviving longer and requiring non-cardiac surgery, it discusses recent advancements within the care of those patients undergoing non-cardiac surgery. Finally, it covers the topics for surgical consideration during LVAD implantation.

The indications for LVAD implantation include BTT, bridge to recovery (BTR), DT, and bridge to candidacy (BTC). The INTERMACS registry has developed patient profiles to stratify patients and permit for optimal patient selection for LVAD implantation. These range from Level 1–7. Level 1 includes patients with critical shock requiring circulatory support while Level 2 includes patients who are declining despite inotropic support. Level 3 patients show stability on inotropic support and Level 4 patients show a few resting symptoms. Level 5 patients are intolerant to exertion, Level 6 patients are those who can engage in limited exertion, and Level 7 patients have advanced NYHA III cardiopathy. As illustrated by the amount above, progressing from Level 1 to Level 6 leads to patients who are more functional and have less severe symptoms associated with their cardiopathy. The majority of patients (about 80 %) being implanted with LVAD are INTERMACS Levels 2–4.

Karen May-Newman, et al. through their study, 'The Effect of Inflow Cannula Angle on the Intra-ventricular Flow Field of the Left Ventricular Assist Device–Assisted Heart: An In Vitro Flow Visualization Study' have identified the position of inflow cannula (IC) of the left ventricular assist device (LVAD) can serve as a major risk for pump thrombosis. Thrombus development may be a consequence of altered flow dynamics, which might produce areas of flow stasis or high shear that promote coagulation. The goal of study was to find the effect of IC orientation on the heart ventricle (LV) flow field employing a mock circulatory loop, and identify flow-based indices that are sensitive measures of cannula malposition. Experimental studies were performed to quantitatively study the increased risk of thrombus as a function of IC angle in an exceedingly mock circulatory loop, which enabled a uniform comparison of fluid dynamics that was independent of LV size and therefore the level of cardiac function. The results of this study provide details on how the LV and IC flow fields are stricken by cannula angulation. Decreased regional flow velocity, pulsatility, and vortex energy were observed when the cannula was angled 15° toward the septum, which are all related to increased thrombosis.

The results confirm clinical studies that have correlated LVAD IC angulation with pathologic thrombosis. Average and systolic velocities within LVAD IC demonstrated statistical significance with angle which will be assessed with non-invasive echocardiography. This finding is very important in this it distinguishes the prediction of flow abnormalities supported cannula angulation from pump thrombus, which demonstrates a major reduction in diastolic, not systolic, IC velocity as a predictor. These indices are standard echocardiographic measurements and will be useful in anticipating problems arising from cannula malposition. Additional studies should be conducted to assess a way to apply these findings prospectively to avoid risk of thrombosis before LVAD implantation. The applying to preoperative optimization of cannula positioning using clinical imaging techniques is explored in future studies to gauge the potential for patient-specific surgical recommendations.

The American Heart Association (AHA) states that in America 5.8 million people above the age of 20 suffer from coronary failure. In LVAD assisted condition, the speed of flow of blood pumped within the Aorta is controlled by the rotational speed of the pump, which is adjusted by controlling the ability input to the pump providing support to the patient by consequently changing the blood rate of flow. The implantation of LVAD depends on three differing types of treatments. a) Bridge-to-transplantation: where the patient can wait long enough till the donor heart is on the market, LVAD provides support to the native heart temporarily. b) Bridge-to-recovery: it is intended typically for the patients whose heart disease may improve with the assistance of LVAD support. The physiological and hemodynamic changes occurring within the heart thanks to the LVAD support end in myocardial recovery. c) Destination Therapy: The patients incorporating this therapy aren't suitable for heart transplantation thanks to their age and people patients whose extent of heart disease is beyond recovery.

LVAD is meant to be implanted permanently to prolong survival and improve the patient's quality of life LVAD will be classified supported how they function mechanically: pulsatile flow or continuous flow. The primary generation LVAD, including the HeartMate XVE and Novacor, depend upon pulsatile-flow technology, mimicking the function of the center. These are called volume displacement devices. These pumps have multiple moving parts, including one-way valves and a versatile pumping chamber. Their complexity makes them liable to device breakdown and failure. The second and third generation LVADs targets continuous flow device technology. The second generation, including the Heart-Mate II and Jarvik 2000 *(Jarvik Heart Inc, New York, NY)*, relies on axial continuous flow technology. The key mechanical changes within the second generation LVAD include the elimination of valves and chambers and therefore the introduction of an interior rotor, which is suspended by contact bearings. The direct contact between the bearings and the blood, on the other hand, promotes thrombosis. The HeartWare and DuraHeart are examples of third generation LVADs that use centrifugal continuous flow. The key technological advancement within the third generation LVAD includes the introduction of noncontact bearings, which utilizes rail technology. The reduction of this contact should, in theory, reduce the risk of thrombosis. However, clinical investigations have yet to show this. Overall, second and third generation LVADs are smaller, requiring less surgical dissection and insertion time. Furthermore, because they require fewer moving components, these devices are more durable, with a lifespan of 5–10 years projected.

Nader Moazami et al. studied about the evolution of mechanical circulatory support from volume-displacement pulsatile pumps to continuous-flow (CF) rotary pumps has ushered in a very new era for treatment of end-stage heart disease. Increasing use of those pumps within the clinical arena is said to multiple positive attributes of this class of pumps, including their smaller size, improved durability, and enhanced survival with a lower rate of morbidity. As acceptance of those classes of pumps continues to grow and newer-generation pumps are developed, an entire understanding of their mechanics and the inherent differences between centrifugal and axial-flow pumps are becoming increasingly important for patient care and pump selection. This review describes the fundamental engineering differences between the two forms of Continuous Flow (CF) pumps and provides an outline of how these features translate clinically to patient management. Continuous Flow Left Ventricular Assist Devices' hydraulic performance is determined by their pressure head and rate relationships. Hydraulic characteristics of those devices are expressed by pressure head and flow loops during a pulsatile environment as they are implanted between left ventricular apex and aorta.

Selim Bozkurt figured that constant speed Continuous Flow Left Ventricular Assist Device support causes complications thanks to altered blood flow within the patients' body. Therefore, beat-to-beat varying speed Continuous Flow Left Ventricular Assist Device support algorithms are proposed to work these devices in synchronized co-pulsating or counter-pulsating modes which may generate more physiological blood flowing the vascular system. This work figures the Pressure, rate and Operating Speed Characteristics of endless Flow Left Ventricular Assist Device During Varying Speed Support However, the effect of speed variation on the pressure head and rate loops remains unclear during varying speed Continuous Flow Left Ventricular Assist Device support. During this study, pressure head, rate of flow and operating speed relations during co-pulsating and counter-pulsating pump support during a Continuous Flow Left Ventricular Assist Device were analysed utilizing numerical simulations. During varied speed heart pump support, simulation results demonstrate that pressure head – rate–operating speed loops can better represent Continuous Flow Left Ventricular Assist Device features. Pump flow-operating speed and pressure head-operating speed diagrams, on the other hand, depict the dynamic behaviour of a cardiac pump, including the speed. Understanding the relationship between pump speed, rate of flow, and pressure difference across a pump may thus aid in the development of novel beat-to-beat operating modes to improve Continuous Flow Left Ventricular Assist Device support.

Takuma Miyamoto et al. are working on designing an improved ventricular assist device (VAD) being development at their university has characteristics that allow intra-pump pressure differences to affect the axial rotor position and pump performance. However, performance may well be influenced by the pump orientation due to the effect of gravity on the rotor position. The aim of the study ‘Effects of blood pump orientation on performance: In vitro assessment of universal advanced ventricular assist device’, was to gauge the consequences of pump orientation on the pump performance, including pulse pressure and regurgitant flow through the pump when the pump was stopped. To replicate the native ventricle, the VAD was tested on a static or pulsatile mock loop with a pneumatic device. The pump performance, including pressure–flow curve, pulsatility, and regurgitant flow, was evaluated at several angles, starting from −90° (inlet pointed upward) to +90° (inlet pointed downward) at pump speeds of 2000, 2500, 3000, and 3500 rpm. The pump performance was slightly lower at +90° in the slightest degree rotational speeds, compared with −90°. Without pump support, the pulse pressure on the pulsatile mock loop (80 bpm) was 50 mmHg, stayed at 50 mmHg during pump support, and was unaffected by orientation (90°, 0°, and +90°). Regurgitant flow was approximately 0 L/min at all angles when the pump was turned off. When the pump was turned off, it had no influence on pulse pressure or regurgitant flow. This means that gravity's influence on the rotor assembly is negligible.

John C et al. in a systematic review ‘Left Ventricular Assist Device Infections: A Systematic Review’, describing infections in continuous-flow LVADs (left ventricular assist devices) which are becoming an increasingly common life-support equipment. Treatment of these patients necessitates a grasp of infection risk factors and management techniques. By device type and patient characteristics, the study looked at incidence, risk factors, related bacteria, and results. It found 90 different studies that discussed LVAD infections and outcomes. LVAD infections were shown to be more common in people who were younger and had a higher BMI. The most prevalent infection was driveline infections, which were the easiest to cure and had the fewest long-term implications. Although bloodstream infections were not as common, they were linked to stroke and mortality. Treatment methods differed, and there was no one-size-fits-all solution. Infections in LVAD patients are a leading cause of morbidity and mortality. Much of the research is based on secondary assessments of existing LVAD studies. Several regions are understudied due to a lack of infection-focused research. Bloodstream infections in this population warrant additional investigation. More research is needed by the providers to make evidence-based decisions about the prevention and treatment of LVAD infections.

# Cardiovascular Physiology | 3

This chapter discusses the functions of heart and circulation. The heart can be thought of as a combination of two separate pumps functioning independently but are tied with each other with time to bring about coordination and rhythmicity. The two pumps are connected in series and are termed as right heart and the left heart. The right heart circulates the blood through the lungs to get it oxygenated whereas the left heart supplies this oxygenated blood throughout the body. Each heart in turn is divided into two chambers namely Atria and Ventricles. The Atria serves as the weaker pump which helps to moving the blood in their corresponding ventricles hence the atria can be termed as the *primer pump* of the heart. The Ventricles then supply the blood in either the pulmonary circulation done by right ventricle, or the systemic circulation done by left ventricle by applying strong contracting force. The heart is provided with special mechanisms which allows it to continuously contract or beat in a rhythmic manner called as *Cardiac rhythmicity*. The basis of this mechanisms is to carry the action potential throughout the heart muscle that in turn allows the heart to beat rhythmically.

**3.1 Physiological anatomy of cardiac muscle**

The histology of cardiac muscle states that they divide and recombine and have striations like that of skeletal muscles. Cardiac muscles also contain myofibrils like Actin and Myosin similar to that of skeletal muscles. These myofibrils are responsible for the contraction of cardiac muscle tissue following the sliding filament theory. Along with the similarities, the cardiac muscles have their own uniqueness. The Figure 3.1 shows the histology of a typical cardiac muscle fibre made of cells connected in series and parallel which highlights the dark cell membranes that go across the muscle fibres. These disks are called as Intercalated disks which shelter a form of permeable '*Communicating*' junctions also termed as gap junctions which enable rapid diffusion of ions allowing ions to move easily throughout the intracellular fluids. This helps in rapid longitudinal movement of ions from one cell to another lead to fast propagation of action potentials. Thus, the lattice of cardiac muscle fibre acts as a functional syncytium wherein if any one cell excites, the other cells also excite with it in no time.

The heart consists of two syncytia: The *Atrial* syncytium which constitutes the wall of two adjoining Atria and the Ventricular syncytium which constitutes the walls of two adjoining ventricles. The Atria and Ventricles are separated by fibrous tissues of Atrio-ventricular valves.

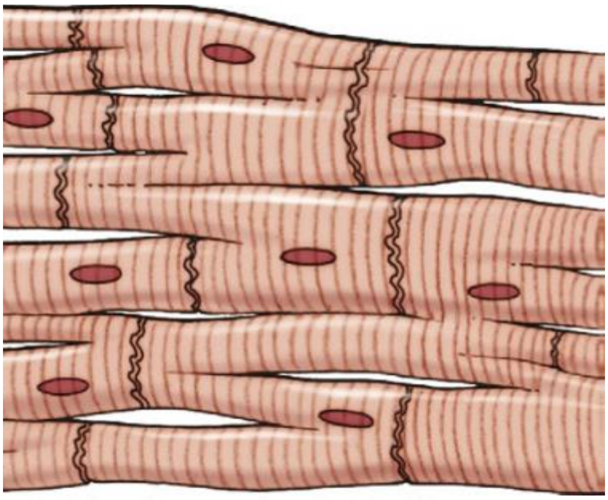


Figure 3.1: “Syncytial,” interconnecting nature of cardiac muscle fibers [Guyton and Hall]

The muscular arrangement between the two syncytia allows the atrial syncytium to contract a few milliseconds before the Ventricular syncytium which is necessary for the effective pumping of the heart. A cardiac muscle should have the following properties;

1. **Excitability**: Ability to generate action potential in response to stimulus
2. **Conductivity**: Ability to propagate/transmit electrical impulse
3. **Contractility**: Ability to contract or beat
4. **Rhythmicity**: Ability to contract in a regular constant manner with/without nerve supply
5. **Automaticity**: Ability to spontaneously generate an impulse and contract, without any external stimulus or nervous supply

**3.2 Electrical activity of heart**

3.2.1 Conducting system of heart.

The production and conduction of action potential has its roots in the right atrium where a small, flattened, ellipsoid strip of specialized cardiac muscle called as Sinus or Sino-Atrial node fires as it has the capability of self-excitation. It is in the lateral wall of right atrium near the opening of superior vena cava. The action potential produced here are carried to the Inter-nodal and Inter-atrial pathways that connect the ends of the sinus nodal fibers directly to the surrounding atrial muscle fibers. Next in line is the Atrio-ventricular (A-V) Node. A-V node and its adjacent conductive fibers brings about a delay of 0.09 sec in transmission of electrical impulse into the ventricles. The impulses are then carried to the ventricular muscles after incorporating a delay of 0.04 sec. This extra delay is brought about by Ventricular Bundle branches. Purkinje fibers run from the A-V node through the A-V bundle and into the ventricles, allowing almost instantaneous transmission of the cardiac impulse across the ventricular muscle.

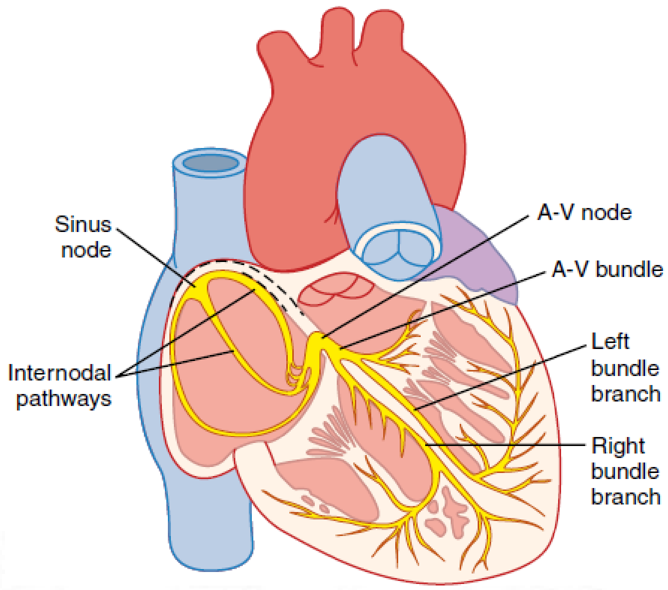


Figure 3.2: Conducting system of the heart [Guyton and Hall]

3.2.2 Spread of Cardiac impulse

The direct flow of ions to the adjacent membrane depolarizes the membrane to the threshold level initiating the action potential which is quickly conducted through the conducting system of heart. The cycle starts with atrial depolarization where the impulses are carried from SA node to the AV node. A small nodal delay is then incorporated followed by the ventricular depolarization which is parallelly accompanied by atrial repolarization. Finally, the ventricular repolarization follows ventricular depolarization.

### 3.3 Cardiac Action Potential

The cardiac action potentials have some specific features that make them different from skeletal muscle or nerve fiber action potential. So, how are Cardiac muscle action potential different? The duration of cardiac APs is longer than that of skeletal muscle Aps. The amplitudes and changes in the potentials are different. This brings about a change in overall voltage profiles of cardiac Aps. The electrical impulses travel along the Atria with the speed of 0.3 to 0.5 m/s which is one hundredth of that of skeletal muscle AP. The Ionic basis that governs the action potential are different for both cardiac muscle and skeletal muscle. The skeletal muscle AP is mostly caused by fast sodium channels which once stimulated, remain open for only few milliseconds and close almost abruptly while the cardiac muscle Aps are governed by both fast sodium as well as sloe calcium channels. So even if the sodium channels close, the calcium channels remain open for ions to transfer through membrane which increases the overall duration of cardiac action potentials. This is the very reason for the prominent plateau phase in the cardiac Aps. Also the permeability for potassium channels in decrease drastically restricting the outflow of potassium ions once the threshold is achieved adding to the duration of action potential.

3.3.1 Phases and Ionic basis of SA node Action Potential

The cardiac action potential is studied in two parts: The SA node action potential and the Ventricular action potential.

**Phase 4**: It is the phase of resting membrane potential [-60 mV] where spontaneous slow depolarization to threshold occurs which eventually develops Action Potential called the *Pacemaker potential*. There is slow decrease in K+ efflux accompanied by *Funny currents* caused by Na+ influx.

**Phase 0**: It is the depolarization phase where upstroke of SA node Action Potential occurs. The slow calcium channels open at the threshold and there is Calcium influx. This slow influx leads to *rounded tip* of AP instead of spiked.

**Phase 3**: It is the *Repolarization* phase where membrane potential returns to resting level. Here K+ efflux occurs through the K+ channels open in response to the depolarizing potential and the Calcium channels close.

It can be noted that the Phase 1 and Phase 2 are absent in SA node action potential. The Fig 3.3 shows the SA node action potential.

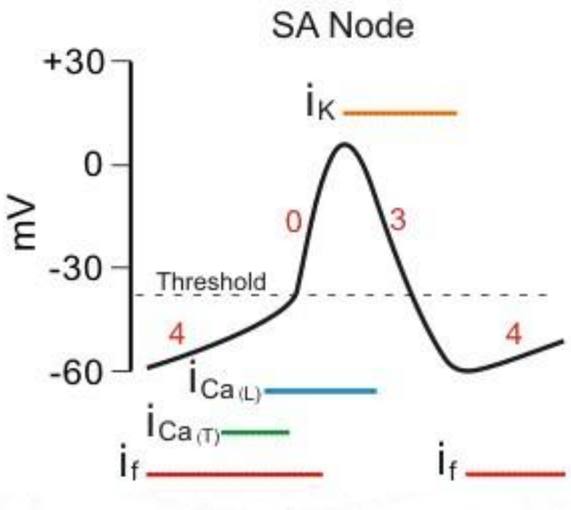



Figure 3.3: SA Node Action Potential. [Cardiac Electrophysiology]

3.3.2 Phase and Ionic basis of Ventricular Action Potential

The impulse developed at the SA Node is transferred to ventricles through AV node with the help of bundle branches and Purkinje fibres after adding a sufficient delay. The slow calcium channels thereafter change the voltage profile of electrical impulse. This can be explained by different phases of Ventricular Action Potential

**Phase 0**: This is the phase of rapid depolarization due to upstroke in membrane potential from -90 RMP to + 20 mV as the voltage gated fast Na+ channels open causing rapid Na+ influx

**Phase 1**: It is called as *Initial Repolarization* phase where Na+ channels close and K+ efflux begin due to voltage-gated fast K+ channels.

**Phase 2**: *Plateau phase*, where membrane potential remains constant at the depolarized level. This happens when Calcium influx take place through voltage-gated Calcium channels which is counter-balanced by K+ efflux hence causing no observable change in membrane potential.

**Phase 3**: This is the phase of Final Repolarization, when membrane potential returns to resting level. Here, the Calcium channels close and K+ efflux is continued through voltage-gated K+ channels.

**Phase 4**: Finally, enough K+ ions diffuse to reach the resting membrane potential.

Phase 1 and Phase 2 are specific features of Ventricular action potential and is evident from fig 3.4.

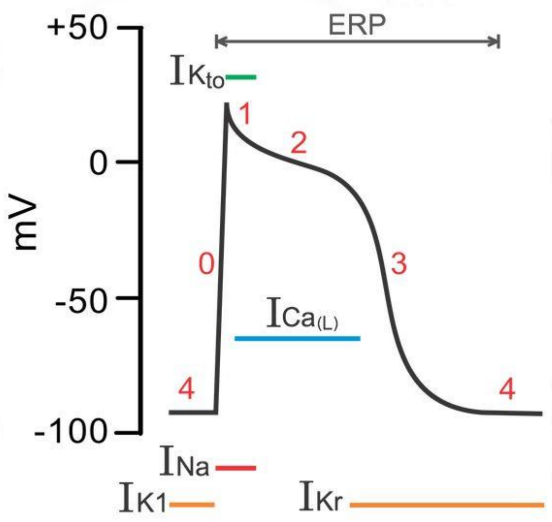



Figure 3.4: Ventricular Action Potential. [Cardiac Electrophysiology]

### 3.4 Cardiac Cycle

Cardiac cycle can be defined as the cardiac events that occur from the beginning of one heartbeat to the beginning of the next. The generation of action potential at the SA node mark the beginning of the cardiac cycle. During a cardiac cycle, the action potential developed at both the atria travel through the AV bundle all the way to the ventricles. As the atria contract ahead of ventricles, they transfer all the blood there is into the ventricles thus acting as the primer pump for the actual contraction.

### 3.4.1 Diastole and Systole

Diastole refers to the period of relaxation for a particular chamber where the blood fills the chamber whereas the Systole refers to the period of contraction where the blood is pushed out of the chamber owing to muscular contraction. The Systole and Diastole together constitutes the cardiac cycle. The total duration of systole and diastole is the reciprocal of heart rate. Thus, an increased heart rate is the marker of decreased cardiac cycle and thereby decreased duration of both diastole and systole.

### 3.4.2 Function of Atria as pump

Though systole is responsible for ejection of blood out of the chamber, in case of atrial systole most if the blood in the atrium (about 80%) readily flows into the ventricles while the remaining 20% moves due to the atrial contraction. The variations in Aortic pressure, Ventricular pressure and right Atrial pressure are shown in figure 3.5.

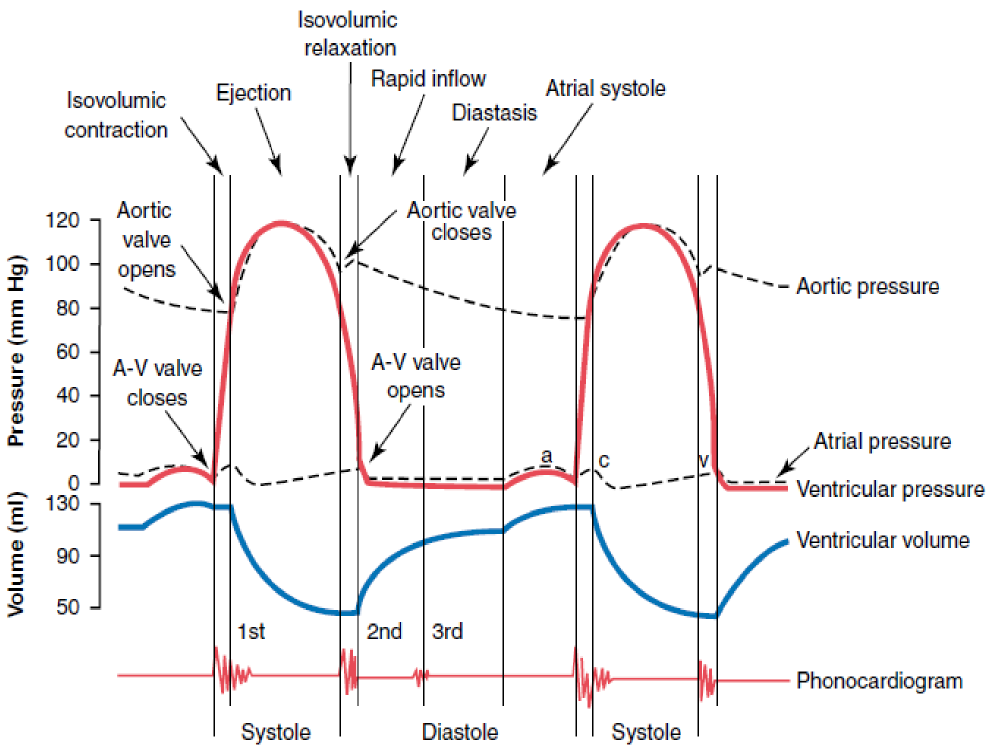



Figure 3.5: Events of the cardiac cycle for left ventricular function, showing changes in left atrial pressure, left ventricular pressure, aortic pressure, ventricular volume and the phonocardiogram. [Guyton and Hall]

### 3.4.3 Function of ventricle as pump

During ventricular systole, large amounts of blood is filled in atrium which is obstructed to enter the ventricle due to close A-V valves. When these valves open, all the blood is filled into the ventricles. As soon as the ventricle starts to contract, the ventricle pressure rises abruptly. This sudden change in the pressure closes the A-V valves close and disconnect the atrium from the ventricles. The closed ventricles contract but do not release any blood. This period is therefore called period of *iso-volumic or isometric contraction*. The ventricles then build pressures sufficient enough to push the semilunar valves open (Aortic and Pulmonary). In case of Aorta, this happens for the pressure slightly above 80 mmHg and in case of pulmonary artery the pressure is around 8 mmHg. Table 3.1 gives an idea of pressure in various chambers of the heart.

| Heart Chamber | Pressure (mmHg) |
|---|---|
| **Right Atrium** | 0 - 4 |
| **Right Ventricle** | 25/4 |
| **Pulmonary Artery** | 25/10 |
| **Left Atrium** | 8 – 10 |
| **Left Ventricle** | 120/10 |
| **Aorta** | 120/80 |

Table 3.1: Pressure distribution in heart chambers. [Mechanical design of VADs]

The emptying of ventricles happens in a non-linear fashion where 70% of them get emptied in first third of the duration of contraction making it the period of *rapid ejection* whereas the remaining 30% empty in remaining two-thirds termed as period of *slow ejection*. The Ventricle relaxes at the end of the systole which allows the intraventricular pressure to decrease rapidly thereby pushing the blood towards ventricles. This action snaps the pulmonary and aortic valves shut preventing any blood to diffuse back into ventricles. Thus, there is change in pressures but no change in volumes making this period to be called as period of *iso-volumic or isometric relaxation*.

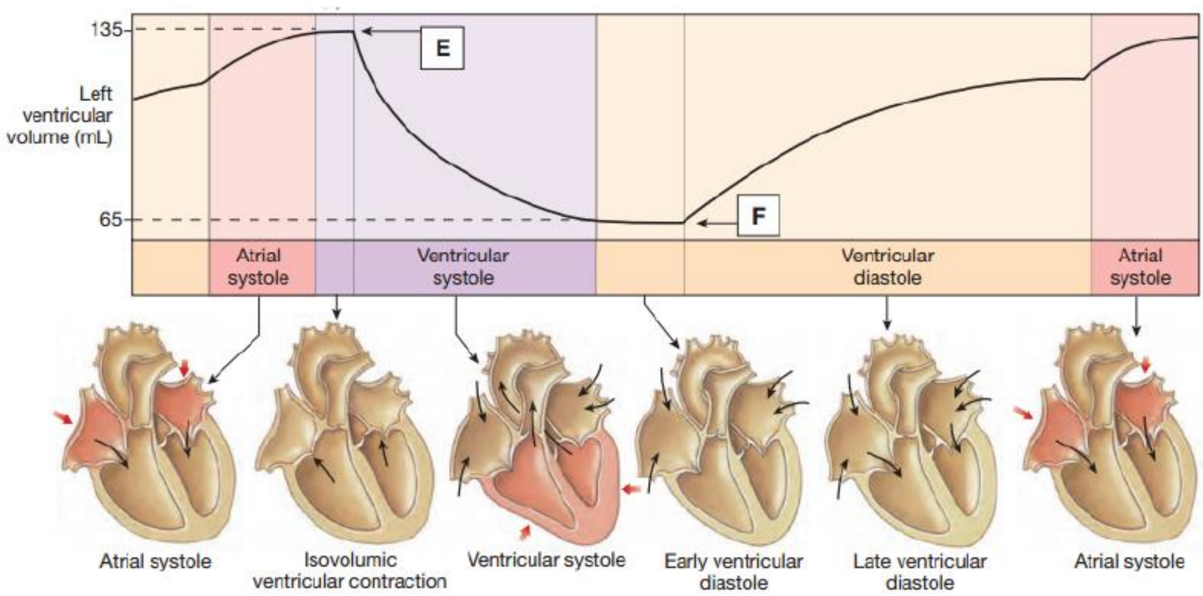



Figure 3.6: Heart events and left ventricle volume during the cardiac cycle. [Brazier, 1988]

### 3.4.4 Function of Valves

Heart valves are located superior to the ventricles attached to them. They are the one-way inlets and one way outlet of the ventricles. There are four valves, the *Tricuspid valve* separates right atrium from the right ventricle. Similarly, the *Mitral valve* separates the left atrium from the left ventricle. The *Pulmonary valve* allows deoxygenated blood to eject out from right ventricle to the pulmonary circulation whereas the *Aortic valve* lets the oxygenated blood eject out from left ventricle to the systemic circulation. They are categorized as A-V valves and Semilunar valves. During systole, the A-V valves (tricuspid and mitral valves) prevent blood from flowing backwards from the ventricles to the atria, and during diastole, the semilunar valves (aortic and pulmonary artery valves) prevent blood from flowing backwards from the aorta and pulmonary arteries into the ventricles.

Figure 3.7: Valves of the Heart. [Teach me Anatomy]

3.4.5 Terms used in cardiac cycle.

1. **Heart Rate:** Heart rate is the measure of the heart cycle per unit of time which generally is measured as beats per minute (bpm). It varies with the physical needs of the oxygen and carbon dioxide exchange and thus have a large variation from 60-80 bpm for a normal adult during rest and all the way above 180 bpm during intensive exercise.

2. **End-Diastolic volume:** During diastole, filling of the ventricles increases the volume of each ventricle to about 110 to 120 ml. This volume is called the end-diastolic volume.

3. **End-Systolic Volume:** After ventricular contraction, the remaining volume in each ventricle, about 40 to 50 ml, is called the end-systolic volume.

4. **Stroke Volume:** During systole, about 70 ml of volume of blood is ejected out through ventricles, this is termed as stroke volume.

5. **Ejection fraction:** The fraction of the end-diastolic volume that is ejected is called the ejection fraction. [Usually equals to about 60 percent]

**3.5 Cardiac output**

Cardiac Output represents the volume of blood pumped into the Aorta by left ventricle in *one minute*. The Normal physiological value of cardiac output is 5L/min. It is the marker of how efficient the cardiovascular system is. Mathematically, Cardiac Output is given by;

C.O = Heart rate (beats/min) x Stroke Volume (ml)

Cardiac output monitors the blood dynamics which is represented by the pressure vs. flow curves. It helps to find the amount of oxygen carried by blood and provides means to assessing the blood flow into the tissue. A detailed idea on the cardiac output enables the clinicians to learn how to best support the failing circulation system of the patient.

**3.6 Factors regulating cardiac output**

Cardiac output can vary with respect to various physiological and pathological factors. These factors individually or in multiple govern the CO.

3.6.1 Primary Factors:

1. **Blood Volume Reflexes:** *Atrial/Bainbridge Reflex:* The atrial reflex, also referred to as the right heart reflex or *Bainbridge* reflex, is triggered by an increase in *venous return* to the heart. Baroreceptors in the superior and inferior venae cava sense pressure changes and send impulses to the SA node, increasing heart rate. *Ventricular Reflex:* The amount of blood expelled is

determined by the amount of blood filling the ventricle during diastole (end-diastolic volume) and the amount of blood remaining in the ventricle after systole (end-systolic volume).

2. **Frank-Starling Law:** The amount of blood in the ventricles, the amount of stretching, and the force of contraction are directly proportional i.e. an increase in blood volume results in greater fiber stretching and then a more powerful contraction. This relationship is referred to as the *Frank-Starling law*.

3. **Autonomic Innervation:** The heart rate is mainly established by SA nodal cells, but the most important control of heart rate and strength of contraction is provided by autonomic innervation. *Cardio-acceleratory Centre:* Sympathetic fibers that begin in the CAC innervate the SA node, the AV node, and parts of the myocardium. CAC stimulation causes these fibers to release norepinephrine, thereby increasing heart rate and contraction strength. *Cardio-Inhibitory Centre:* CIC stimulation results in the transmission of nerve impulses along the parasympathetic fibers and the release of acetylcholine, which decreases heart rate.

4. **Hormones:** In response to sympathetic stimulation, *norepinephrine* is released in the myocardium, and norepinephrine and epinephrine are released by the adrenal medullae. *Norepinephrine* raises the heart rate and the contractility of the myocardium. *Epinephrine* stimulates the SA node, which speeds up and strengthens myocardial contractions. The release of *acetylcholine,* which reduces heart function by lowering the intensity of cardiac contractions, is a consequence of parasympathetic stimulation.

3.6.2 Secondary Factors:

1. **ECF Ion Concentration**: Elevated levels of Na+ and k+ can decrease **Heart rate** and **Stroke volume**

2. **Calcium ion Concentration:** calcium ion concentrations affect the strength and duration of cardiac contractions, which then affects stroke volume

3. **Temperature and Emotions**

4. **Sex and Age**: The heartbeat of females is generally faster than that of males. Heart rate is fastest at birth and decreases throughout life.

### 3.7 Mean Arterial Pressure (MAP)

Due to the nature of pulse flow, there is always a fluctuation in the pressures. Thus, an average pressure is generally used as a reference for the studies and calculations of arterial pressure. However, as the diastolic phase is normally longer than the diastole, the mean arterial pressure (MAP) is calculated based on the diastolic pressure plus one-third of the pulse pressure.

$$\text{MAP} = P_{dias} + \frac{1}{3}\,\text{(Pulse Pressure)}$$

Where: Pulse Pressure = Systolic pressure – Diastolic pressure

The typical value of mean arterial pressure for a healthy adult, whose systolic pressure is 120 mmHg and diastolic pressure is 80 mmHg, is calculated as follows:

$$\text{MAP} = 80 + \frac{(120-80)}{3} = 93.33 \text{ mmHg}$$

The pulmonary artery pressure is approximately 6 times lower than the aortic pressure.

### 3.8 Vascular Resistance

A linear relationship exists between the pressure drop and blood flow through the vessels.

$$\Delta P \;\alpha\; Q$$

$$\Delta P = RQ$$

where: $\Delta P$ = pressure drop in dynes/sq.cm

$Q$ = flow rate in cc/cm

The Vascular resistance is dependent on factors like geometry of the vessel and viscosity of blood. Thus,

$$R = \frac{8\mu l}{\pi r^4}$$

where: $\mu$ = viscosity of blood

r = Radius of vessel

l = Length of Lumen

### 3.9 Compliance

The walls of the vessels are not rigid and they expand in response to increased trans-mural pressure. They are made of four major elements; *Endothelial Lining* are the active sensors of fluid shear stresses. The *Elastin fibers* produce an elastic tension automatically as the vessel expands with any biochemical energy expenditure. *Collagen fibers* are stiffer than elastin fibers but are slack and do not produce tension until the vessel expands. *Smooth muscles* serve to produce an active tension by contracting under physiological control and changing the diameter of the lumen. As the transmural pressure increases, blood vessel expands, stores more volume and thus acts as a capacitor. Thus, compliance can be realized as the slope of pressure-volume curve in arteries and veins.

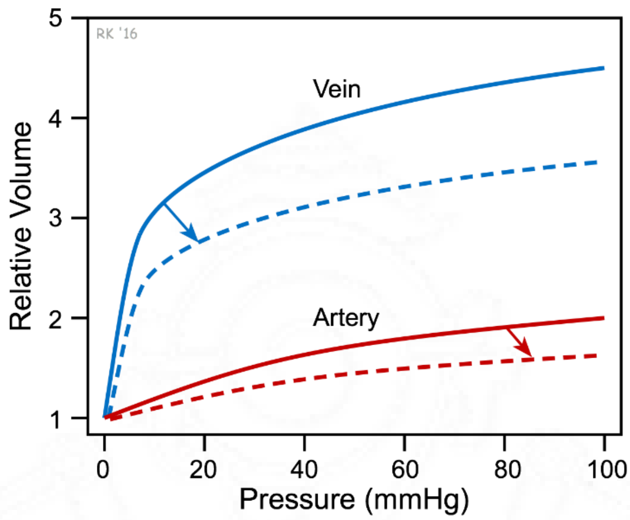



Figure 3.8: Vascular Capacitance or Compliance. [Cardiovascular physiology concepts]

### 3.10 Work output of Heart

The amount of work done by heart in each heartbeat is called the stroke work output of the heart. The work output of the heart has two components. The first part of the work is done to shift the blood from low pressure veins to high pressure arteries. This work is referred as the *Volume pressure work* or the *external work output. The second component of this work is that required to attain the velocities at the time of ejection from the ventricles into the aorta and pulmonary artery*. This component is the kinetic energy part of the net work output.

Figure 3.9 graphically represents the work output of the heart. The main components of this diagram are the two blue and green curves respectively named as the Diastolic P-V curve and the Systolic P-V curve. The Diastolic P-V curve is the plot of pressures recorded just before ventricular contraction at end-diastolic volume. Same procedure is followed for multiple volumes taken in increasing order while the Systolic P-V curve is plotted by marking systolic pressure for every value of volume taken to fill the ventricle.

Initially, for low flow the systolic pressures rise rapidly with gradual decrease at the higher flows while in the diastolic state, even low pressures are sufficient to pull large volumes of blood.

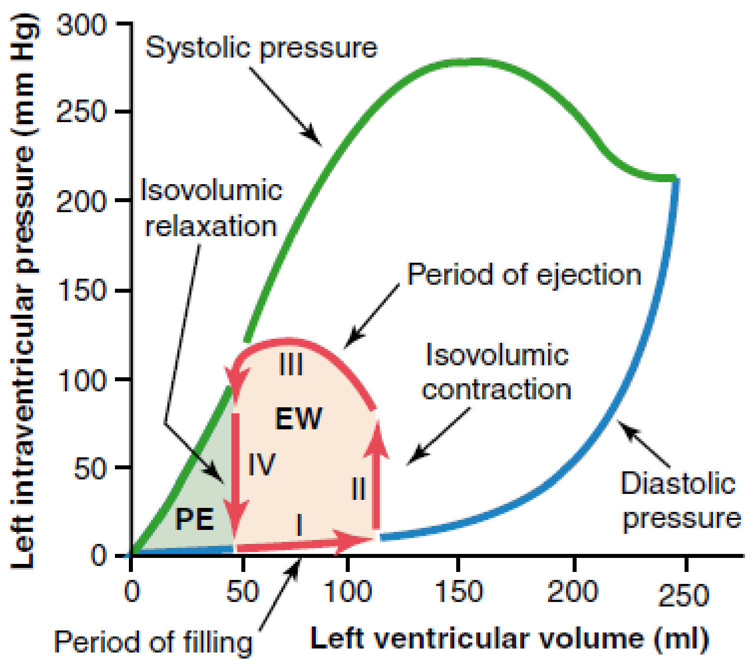



Figure 3.9: Relationship between left ventricular volume and intraventricular pressure during diastole and systole. [Guyton and Hall.]

As the cardiac cycle consisting of systole and diastole keeps on repeating itself, a loop of pressure and volume change is formed referred to as *Pressure-Volume curve*. The Pressure volume curve has four phases mentioned below;

**Phase 1**: Period of filling : During ventricular systole, blood flows rapidly from right atrium to ventricle as the A-V valve open called period of rapid filling.

**Phase 2**: Period of Isometric Contraction: Due to ventricular contraction, the ventricular pressure rises abruptly till the time the pressure is not high enough to push the semilunar valves open. At this time the ventricle undergoes contraction, but no blood comes out of it hence this period is called the period of isometric contraction.

**Phase 3**: Period of ejection: When the left ventricle pressure rises above 80 mmHg, the aortic valve open pouring about 70 % of volume present in ventricle in about a third of systole called as period of rapid ejection. The remaining 30 percent is emptied in next two-thirds of the systole.

**Phase 4**: Period of Isometric Relaxation: At the end of systole the ventricles relax decreasing the intraventricular pressure. As a result, the aortic and pulmonary valves shut closed thus the ventricle face expansion with no net increases in blood volume. This period is called as period of isometric expansion.

### 3.10.1 Concepts of Preload and Afterload

While the contractile properties of muscle are assessed, it is important to have the information on the *degree of tension* on the muscle when it begins to contract, which is called the *preload*, and to determine the *load* against which the muscle exerts its contractile force, which is called the *afterload.* The end-diastolic pressure when the ventricle has been filled is normally called the preload for cardiac contraction. The pressure in the aorta leading from the ventricle is known as the ventricle's afterload.

The preload and afterload are very sensitive to any functional changes in the heart. Any abnormality in the normal functioning of heart will be clearly seen in the ventricular volumes and aortic pressures thus making preload and afterload a very important marker of any factor leading to heart failure.

### 3.10.2 Cardiac Contractility

Cardiac contractility can be defined as the ‘tension developed and velocity of shortening of myocardial fibers at a given preload and afterload (i.e. the ‘strength’ of contraction)’. It represents a unique and intrinsic ability of cardiac muscle to generate a force that is independent of any load or external stretch applied to it. Sympathetic nervous system is responsible for the activation of cardiac contractility and is affected by factors like heart rate, metabolic activities like Hypercalcaemia and drugs like Digoxin.

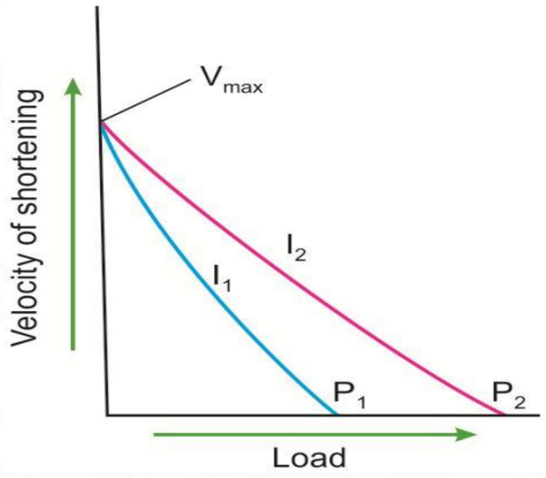



Figure 3.10: Velocity of Shortening vs. Afterload at constant Preload. [Jaypee Digital]

### 3.10.3 Intrinsic Regulation of heart pumping: 'The Frank-Starling Mechanism'

In certain circumstances, the amount of blood pumped by the heart per minute is almost entirely dictated by the rate of blood flow into the heart from the veins, a process known as venous return. This means that each peripheral tissue of the body regulates its own local blood flow, which all combine and return to the right atrium through the veins. This incoming blood is then automatically pumped into the arteries by the heart, allowing it to circulate around the circuit again.

The Frank-Starling function of the heart refers to the heart's inherent ability to respond to increasing amounts of inflowing blood.

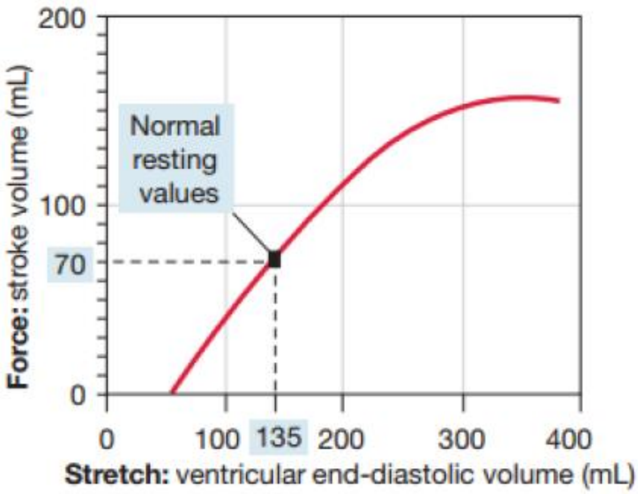



Figure 3.11: A Starling Curve. [Brazier, 1988]

When there is an increase in the amount of blood flows into the ventricles, the cardiac muscle is stretched by itself to *greater length*. As a result of this, the muscle to contract with *increased force* as the actin and myosin filaments are brought to a more nearly *optimal degree of overlap* for force generation. Therefore, the ventricle, because of its increased pumping, automatically pumps the extra blood into the arteries.

# Left Ventricular Assist Devices | 4

Congestive heart failure (CHF) or chronic heart failure is a heart condition where the muscles responsible for contraction of ventricles become weak over time resulting in to decreased cardiac output and blood flow. This condition falls short for maintaining required blood pressure and result into low organ blood perfusion. Inadequate perfusion leads to fatigue and breathlessness causing hypoxia. Chronic heart failure is mainly caused by coronary artery disease, hypertension and diabetes. Most commonly observed in old age people. CHF has become a worldwide health concern, as it has been one of the leading causes of death in the past decade with an estimated 38 million patients worldwide and the number is still rising. According to the World Health Organization, the total number of deaths from all the cardiovascular diseases could rise to 23.3 million by 2030.

The most successful treatment for end stage heart failure remains the heart transplantation. However, it is not possible to provide the right donor every time. As a result, the mechanical circulatory devices emerge as the alternative for heart transplantation. These mechanical circulatory device in the form of pumps assist the left ventricle to maintain the required flow and blood pressure through the vasculature. These pumps came to be known as Left Ventricle Assist Devices (LVAD) owing to their assistance to the left ventricle. So, An LVAD is a mechanical circulatory pump used to assist the left ventricle with patients having very weak hearts or end stage heart failure. An LVAD takes blood from left ventricle and pumps it to the body through the aorta. Its function is to assist the heart and not replace it. Being a mechanical circulatory device, it works on electrical power sourced from either battery or AC power. It is connected to Controller that monitors the LVAD’s functions. The power batteries are carried in Holster in vest and controller is fitted around waist.

This chapter deals with the functions of LVADs, their classifications and components. It also brings a light to the selection of patient and some important indications

### 4.1 Implantation of LVAD

With the currently available technologies, implantation of the VAD can be done either externally for short-term support after a cardiac operation, or implanted internally for patients who require long-term support. If the device is to be implanted intra-corporeal, it can be placed sub-diaphragmatically in pre-peritoneal or in abdominal positions and connected to the control unit and batteries outside the body with the driveline tunnelled through the skin of the abdominal wall as shown in figure 4.1.

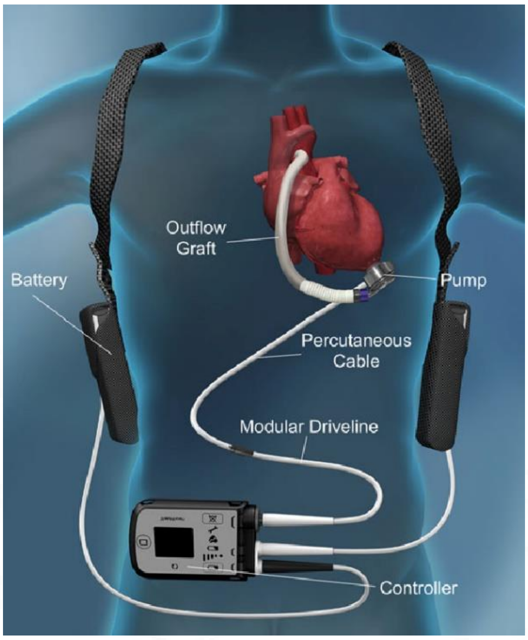



Figure 4.1: Mechanical Assist system. [Stanford Healthcare]

The pump is typically connected to the circulatory system by the inflow and outflow cannula. In the LVAD support, this inflow cannula or inlet of the device is normally attached to an apex of the left ventricle and the outflow cannula is connected to the aorta for additional blood pumping in parallel with the native flow from the heart.

**4.2 Classification of LVADs**

With the technological advancements, requirement of the patient and studies done on the previous models, various advancements have been brought in the performance and design of the LVADs. LVADs are mainly classified on the basis of their mechanical functionality. So it can be pulsatile flow pump or a continuous flow pump.

With the incorporation of this functionalities, there are three generations of LVAD.

The first generation pumps rely on pulsatile-flow technology where they mimic the function of the heart. With every pulse, a certain amount volume of blood is displaced hence these are also known as volume displacement devices. The pulsatile pumps are accompanied by multiple moving parts which include one-way valves and a flexible pumping chamber. It is the complexity of these devices that make them prone to device breakdown and failure. The figure 4.2 below shows the Heartmate XVE of first generation

Figure 4.2: First generation pulsatile pump HeartMate XVE. [ResearchGate]

The second and third generation LVAD are continuous flow devices. These pumps rely on axial continuous flow technology. The key mechanical changes brought in the second generation LVAD are the elimination of valves and chambers which are replaced by an internal rotor, suspended by contact bearings as shown in figure 4.3. With the clinical trials it was observed that this direct contact between the bearings and blood causes thrombosis.

Figure 4.3: Continuous Flow axial pump HeartMate II. [ResearchGate]

The third generation LVAD, which rely on centrifugal continuous flow. The key technological advancement in the third generation LVAD is the introduction of noncontact bearings that rather suspends the impeller using magnetic levitation. Theoretically, the elimination of this contact would only lessen the incidence of thrombosis. Figure 4.4 illustrates heartware LVAD which is a continuous flow centrifugal pump with magnetically levitated impeller.

Figure 4.4: CF centrifugal flow LVAD, Heartware. [Journal of Cardiothoracic and Vascular Anesthesia]

Overall, the second and third generation LVAD are smaller in size and require less surgical dissection and time for implantation. In addition, the fewer moving parts allow these devices to have greater durability with an expected lifespan of 5–10 years. Table 4.1 briefly summarizes the difference in the parameters of three generations of the pump.

| | Pulsatile Pump | Centrifugal | Axial Flow |
|---|---|---|---|
| Speed | ~ 60 bpm | 2000 – 4000 rpm | 6000 – 12000 rpm |
| Size | Large | Medium | Small |
| Hemolysis (NIH) | High | 0.0007 – 0.009 | 0.0028 – 0.003 |
| Thrombosis | Low | Medium | High |

Table 4.1: Comparison of the important parameters of rotary pump [Kafagy & Gitano-Briggs, 2013]

Although there have been tremendous advancements in the LVAD design and principle since its first generation, some of the serious issues still persist. Most of these problems are related to pump design and float around the blood damage from blood clot and shear stress subjected on the blood cells which later results into various infections. Despite the pump being improved in terms of rotor clearance using magnetic levitation, these problems surface in the long run. Other problems are related to the controlling, battery backup and cost. The open driveline is prone to various infections which might later become fatal. The pump requires high power which in turn reduces the backup capabilities of the battery and thereby hinders the idea of making LVAD mobile and durable in long run.

4.2.1 Future Directions

Studies have suggested that development in myocardial treatment using stem cells can later lead to a significant turning point in the direction of the development of VADs. One of the major problems that needs to be addressed for the LVADs is that the unit cost is expensive thereby preventing patients from having access to these devices. The idea of successful cardiac recovery using stem cell injections could prove to be the future of CHF treatment. Studies have suggested that it takes around 6-12 weeks for the heart muscles of heart failure patients to regenerate after injecting bone marrow cells. If this technology comes into practice, it would reduce the requirement of long-term support such as the Bridge to Candidacy (BTC) and Destination therapy (DT) while decreasing the waiting time for patients on the Bridge to Transplantation (BTT) significantly. This can divert the entire focus on a wearable blood pump which could provide support for up to only 6 months rather than investing large amount of time and capital on the development of implantable LVADs for long-term support that are more durable but are yet expensive. The cost per unit should also be lowered greatly as compared to that of commercial pump to make it become more widely accessible for patients

### 4.3 Indications for LVAD Implantations

The indications for LVAD implantation include BTT, bridge to recovery (BTR), bridge to candidacy (BTC) and Destination Therapy (DT). The INTERMACS registry has developed patient profiles to classify patients as per the clinical implications and allow for optimal patient selection for LVAD implantation. These range from Level 1–7. The majority of patients (about 80 %) that are suggested with LVAD implantation are INTERMACS Levels 2–4.

1. **Bridge to recovery (BTR):** It is an indication for LVAD implantation in patients with acute decompensated heart failure. These patients typically have reversible causes of heart failure, such as medication-induced cardiomyopathy, post-partum cardiomyopathy, postcardiotomy syndrome, and viral myocarditis with refractory cardiogenic shock. The patients are expected to get their cardiac muscles to recover and that’s why require assistance for a limited duration of time.
2. **Bridge to transplantation (BTT):** BTT is the most common indication for LVAD implantation. As per the reports provided by Seventh INTERMACS, the BTT accounted for 51 % of biventricular and univentricular assist device implantation in the year 2014. The survival rates are high for patients that have undergone LVAD implantation as a BTT path. The United Network of Organ Sharing (UNOS) database shows that patients who underwent LVAD implantation prior to being listed for heart transplantation had improved survival compared to those who were medically managed. This survival benefit extended to those who were implanted with a LVAD while being listed and awaiting heart transplantation. Implantation of a LVAD as a BTT also allows a patient with end stage heart failure to leave the hospital, have

an improved quality of life, and have an improved functional status, while awaiting heart transplantation.

**3. Bridge to candidacy:** BTC, is another growing indication for LVAD placement. BTC refers to the patients that are awaiting to get physically eligible to undergo implantation. Thus, it is the LVAD placement in individuals who do not meet transplant criteria may allow them to become eligible for a transplant in the future. Patients with secondary pulmonary hypertension who are unable to receive a transplant have also been shown to benefit from the use of an LVAD to unload the left ventricle, allowing them to become transplant candidates in the future.

**4. Destination therapy:** Given the severe donor organ shortage and improved device durability, increasing numbers of LVAD are implanted as DT. Due to advanced age, frailty, advanced liver or kidney failure, obesity, extreme pulmonary hypertension, and malignancy, these patients typically do not meet the requirements for heart transplantation. The criteria for LVAD consideration as DT included the following: left ventricular ejection fraction of less than 25 %, peak oxygen consumption of less than 14 mL/kg/min, NYHA class IIIB or IV, and dependence on accessories like an intra-aortic balloon pump for 7 days or inotropes for 14 days.

### 4.4 Patient Selection

LVAD Implantation is advised for people having;

1. Left Ventricle Ejection Fraction (LVEF) less than 25%
2. Advanced Heart Failure patients that cannot be managed by medications alone
3. Class III/IV NYHA Heart Failure: The New York Heart Association has classified heart failure into four classes. The patients belonging to class III are those who have very limited physical activities. For a Class III patient, less than ordinary physical activity can cause undue fatigue, palpitations and/or dyspnea. The patients belonging to Class IV experience fatigue and palpitations even at rest.
4. Dilated Cardiomyopathy (Ischemic and Non-Ischemic)
5. Diabetes, Hypertension, Chemotherapy, Pregnancy, Congenital, Viral, Heart Attack

### 4.5 Circulatory System Components

The system components of mechanical circulatory system can be broadly classified into two parts: (i) The internally implanted pump and (ii) External components.

The internal pump is a combination of:

- Inflow Cannula
- Pump Mechanism
- Outflow Graft
- Driveline tunnelled into Abdomen

While the External components includes:

- System Controller
- System Monitor (Used only in Hospital)
- Power Sources (Power Module, Battery)
- Driveline/ Percutaneous lead/ Power Cord
- Accessories

The Figure 4.5 below shows the complete mechanical circulatory systems in function assisting the left ventricle using the continuous flow centrifugal pump with all the components in place.

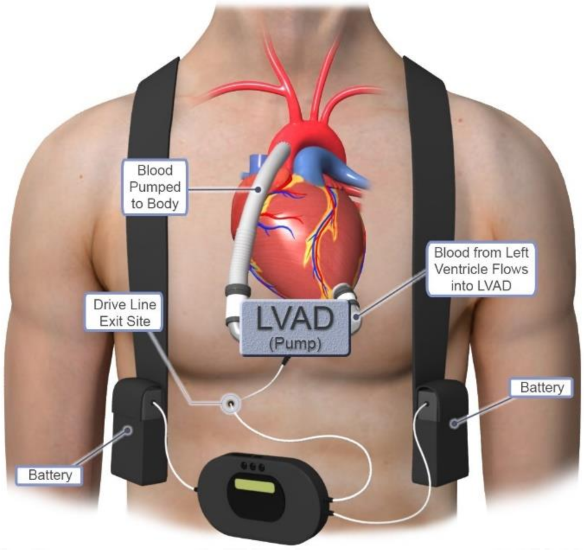



Figure 4.5: LVAD system. [Patient guide to Heart, Lung, and Oesophageal surgery]

### 4.5.1 Centrifugal pump

The Centrifugal pump is an assembly of three parts; 1) The Impeller, 2) The Spiral casing and 3) The Motor. The Impeller has a shape of a disc with blades arranged in regular manner giving rise to vanes. The Blades of the impeller are backward curved in order to provide least displacement to the blood flowing through the vanes. The inflow of the impeller is located at the centre of circular disc along the axis of rotation. The inflow of the impeller is called as eye of the impeller. The centrifugal force of the rotating impeller pushes the fluid circumferentially and the fluid spirals out and discharges through the outlet. The figure 4.6 a below, shows the volute of the centrifugal pump.

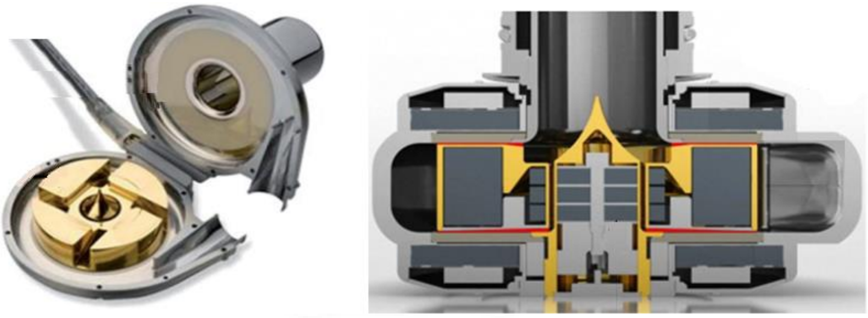


Figure 4.6.a Volute and impeller set of Centrifugal pump. 4.6.b Magnetic levitation and hydrodynamic thrust of HeartWare CF pump. [Axial and centrifugal continuous-flow rotary pumps, Nader Moazami *et al.* 2013]

The Motor of the pump comprises of the passive magnets attached in the inner part of rotor while the stator comprises of active electromagnets which are excited with the appropriate phase difference which creates rotating magnetic field around the impeller causing the impeller to rotate in the same direction of the field. The rotor uses magnetic levitation to maintain a certain clearance from the stationary stator as shown in figure 4.6 b. The base of the impeller is kept from the stationary base by forming a thin layer of fluid creating a hydrodynamic thrust. This thin layer of fluid is generally blood.

### 4.5.2 System Controller

The main function of the system controller is to supply regulated power the pump however the controller also *regulates* and monitors the pump functioning. It also Identifies alarm conditions and initiates Hazard and Advisory alarms in case of any power lag caused by low battery or any other system malfunction. Figure 4.7 features a controller of Heartmate III .The User Interface of the LVAD controller displays roughly following information however it differs with controller to controller. 1) Pump Parameters (Flow, Speed, Power and PI) 2) Status of Backup Battery Charge. 3) Visual alarms with actionable instructions. Modern controllers are provided with a backup battery is housed within the case. The other important function of controller is to carry out driveline diagnostic capability and records alarm data and device performance.

Figure 4.7: System Controller of LVAD HeartMate III. [Abbott Cardiovascular]

### 4.5.3 Power Module

A power module is designed with the virtue of allowing patient to be mobile. The Module houses two batteries are connected to system controller. These batteries provides backup of 6-12 hours a pair however, battery backup depends on the type of instrument used. Equipment can be carried in several different ways depending on the type of accessory. The figure 4.8 below shows the power module of *Heartmate III*. The Power Module (PM) provides AC mains electrical power to the HeartMate III LVAD system. In addition to powering the LVAD, the PM can simultaneously power the HeartMate Display Module or System Monitor. Before being used to power the system, the PM power cord and patient cable first need to be attached.


Figure 4.8: Power Module of LVAD HeartMate III. [Michigan Medicine]

### 4.5.4 Accessories

The other important components of mechanical circulatory system are *Inflow cannula* which is inserted into the orifice made in the ventricle that draws blood into the impeller. Similarly, the *Outflow Graft* carries the discharged blood all the way into the *ascending aorta*. An additional *strain relief* is attached around the outflow graft to nullify any stress the graft may be subjected to. The Driveline or *percutaneous driveline* supplies the power from the controller to the pump piercing through the skin. To keep all the components in place while the patient is mobile, various accessories are provided like *belt attachment, travel bag or battery holster* as shown in figure 4.9

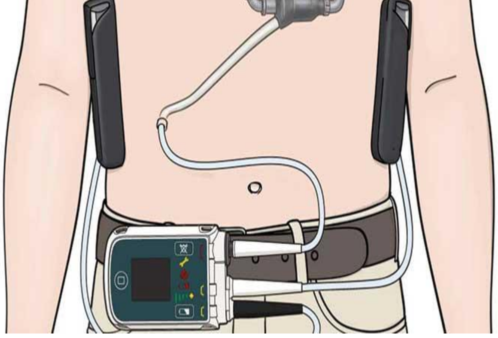


Figure 4.9: LVAD Holster Vest. [Michigan Medicine]

### 4.6 LVAD Hydraulic Performance parameters

The Hydrodynamic performance of LVAD is carried out by analysing important parameters like;

1) **Pressure Head:** Pressure head is typically identified as the difference of pressure between outlet and inlet pressures of the pump. Qualitatively, it represents the work performed by the pump on the liquid. Pressure head can be calculated by following equation;

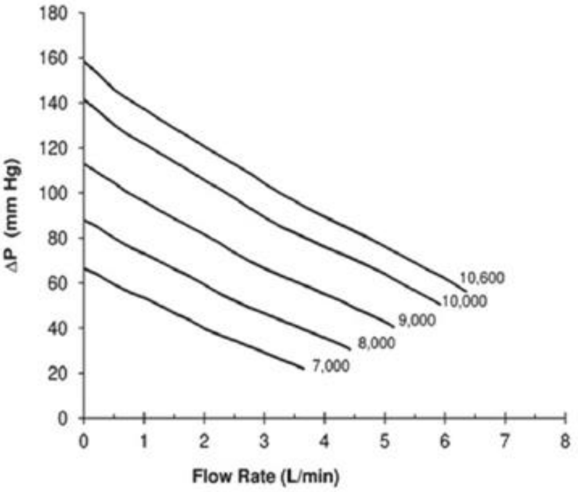
$$H = \frac{\Delta P}{\rho g}$$

Where: $\Delta P$ = Pressure difference

$\rho$ = Density of fluid

$g$ = Acceleration due to gravity

2) **Pressure vs. Flow curve:** It is a plot between pressure head and volumetric flow rate at one operating speed which serves as the major pump performance characteristics. The key point is in case of centrifugal pump, the characteristics show a flat head whereas the curve is steep in case of axial pumps. This Flat characteristics provide a large flow range for a very little change in the pressure head. The figures 4.10.a and 4.10.b typically represent the Pressure flow curves of axial and centrifugal flow pumps respectively.



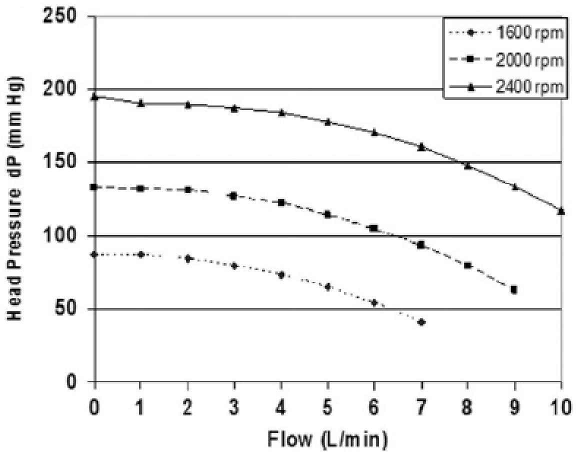




Figure 4.10.a H-Q Curve of Axial HeartMate II. 4.10.b H-Q Curve of Centrifugal Terumo DuraHeart LVAD. [Axial and centrifugal continuous-flow rotary pumps, Nader Moazami *et al.* 2013]

**3) Hydraulic power:** Hydraulic power indicates the amount of fluid that the pump can move; in one cycle that is the amount of work done by the pump per beat. It can be calculated by the following equation

$$P_h = Q\Delta P \text{ or}$$

$$P_h = \rho g Q H$$

Where: H = Pressure Head (mmHg)

$\rho$ = Density of fluid

$\Delta P$ = Pressure difference

Q = Flow rate (L/m)

**4) Hydraulic Efficiency:** The hydraulic efficiency identifies how well the mechanical power of the pump is transferred into hydraulic power. For the continuous flow pump, the efficiency is the ratio of fluid power (output) to the shaft power (input). Efficiency is calculated as;

$$\eta_h = \frac{P_h}{P_s} = \frac{\rho g Q H}{T\omega}$$

Where: 1. $\eta_h$ = Hydraulic efficiency

2. $P_h$ = Hydraulic power

3. $P_s$ = Shaft power

4. T = Impeller torque

5. $\omega$ = Impeller angular velocity

The figure 4.11 show the variation of efficiency with respect to flow through the centrifugal pump. It is evident from the figure that for the low values of flow, the efficiency is directly proportional to the flow rate however as the flow increases, after a certain point the efficiency starts to decline this because at higher flow rates, the flow distributions inside the impeller are disturbed and the turbulence of the fluid inside the pump prevents the conversion of mechanical input by the shaft to effectively convert into the hydraulic power and result into wastage of energy. The flow rate that allows the pump to operate at highest efficiency is called best efficiency point (BEP) vest.

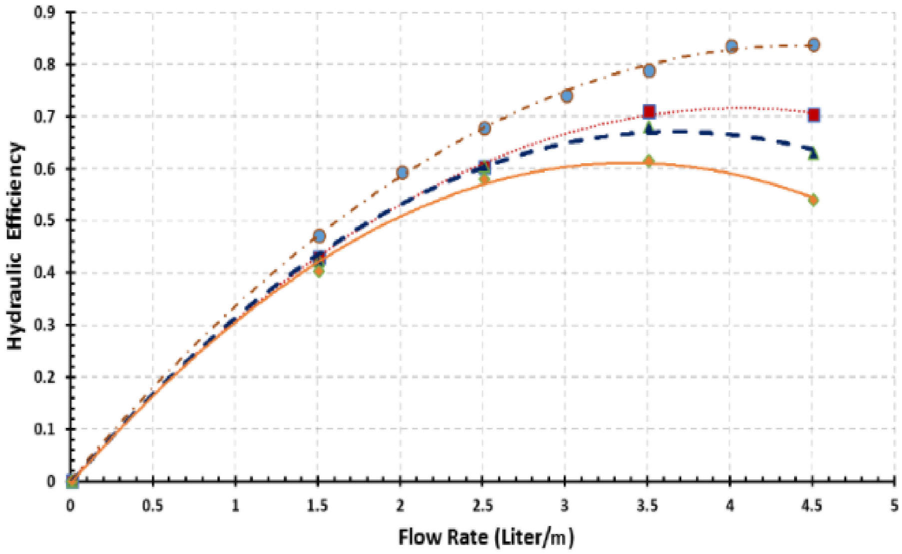



Figure 4.11: Efficiency Vs. Flow rate plot for centrifugal flow pump. [Pumps and System]

### 5) Overall Efficiency

The overall efficiency refers to considering all the losses occurring in the pump. In other words, it is the ratio of the hydraulic power developed (output) and the electrical input power to the machine.

$$\eta_o = \frac{P_h}{P_{in}} = \frac{\rho g Q H}{VI}$$

Where: 1. $\eta_o$ = Hydraulic efficiency

2. $P_h$ = Hydraulic power

3. $P_{in}$ = Electrical input to the machine

### 4.7 LVAD Materials:

The impellers of the centrifugal and axial blood pump is mostly made of ceramics and titanium. The impeller of the flow pumps can be fabricated from epoxy. For prototype LVADs, impeller may be polished to give smooth surfaces. The inner surface of the pump housing may be coated with segmented polyurethane and the impeller are sprayed with a black coating except for the top (shroud) surfaces of blades. The shaft and bearing are usually made of titanium or stainless steel with varying hemolytic properties depending on the design of the bearing. To prevent water infiltration, the stator was moulded with epoxy resin. The surface of the shaft and bearing are coated with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer, this make the surface of the shaft sufficient enough to avoid thrombus formation. Careful treatment of the antithrombogenic material coating is necessary to prevent the risk of thrombosis. Polytetrafluoroethylene

On the motor side, a layer of (Teflon) polymer is mounted between the impeller and the casing to reduce friction. Impeller wall can sometimes be made of the transparent acrylic. The pump materials in contact with the blood are primarily Polycarbonate (PC), and the pivot bearing is a combination of stainless steel (SUS) ball and a receptacle of ultra-high-molecular-weight polyethylene (UHMWPE). The table 4.2 and 4.3 shows materials used in production of some commercialized devices axial and centrifugal LVADs respectively along with their manufacturers.

| Device | Manufacturer | Materials |
|---|---|---|
| **HeartMate II** | Thoratec | Polished Titanium |
| | | Textured Titanium |
| | | Microsphere |
| | | textured material |
| | | Ceramic – Aluminium oxide |
| **Jarvik 2000** | Jarvik Heart | Ceramics for bearing |
| **Flowmaker** | | Titanium |
| | | Polyester for the sewing ring |
| **Heart Assist 5** | MicroMed | Titanium |
| **Adult VAD** | Cardiovascular | Cameda® |
| **InCOR** | Berlin Heart | Biocompatible coating |
| | | Heparin coated with carmeda® |
| **HeartMate III** | Thoratec | Polished Titanium |
| | | Textured Titanium |
| | | microsphere |

Table 4.2: Materials and Manufacturers of Clinical axial CF pumps. [Biocompatible materials of pulsatile and rotary blood pumps, Azzam Ahmad et al. 2020]

| Device | Manufacturer | Materials |
|---|---|---|
| **WorldHeart** | Levacor | Polished Titanium |
| **Duraheart** | Terumo | Titanium |
| | | Stainless steel |
| | | Heparin coating |

| | | |
|---|---|---|
| **HVAD** | HeartWare | Ceramics |
| | | Titanium |
| | | Woven Polyester fabric |
| | | Polyether Ether Ketone |
| **VentrAssist** | Ventracor | Titanium |
| | | Silicone |
| | | Diamond-like carbon |
| **MITiHeartLVAD** | Mitiheart | Polycarbonate |
| **MVAD** | Heartware | 1 - Ceramic |
| | | 2 - Titanium |
| | | 3 – Woven Polyester Fabric |

Table 4.3: Materials and Manufacturers of Clinical centrifugal CF pumps. [Biocompatible materials of pulsatile and rotary blood pumps, Azzam Ahmad et al. 2020]

# Pulse Duplicator System | 5

This chapter focuses on the description of Human Mock Circulation Loop (MCL), which is used for in-vitro evaluation of LVAD. The Mock Circulation system must be able to imitate the basic physiological circumstances of a normal heart and the cardiac functions of CHF, which are primarily defined by pulsatile flow, the compliance of the venous and arterial system, and resistance of the blood vessels, to achieve all aspects of evaluation.

## 5.1 Physical parameters of human circulatory system

To imitate the flow characteristics of the human circulatory system, numerous physical parameters must be investigated and appropriately selected to reproduce, as closely as possible, the state that occurs in the human body. The flow circulation pathways, cardiac functionality, pressure and flow dispersion, and compliance and resistance to the flow are among these parameters.

### 5.1.1 Human Circulatory System

The human heart is a two-pump system with each pump having its own circulatory loop that includes arteries, arterioles, capillaries, venules, and veins. The human circulatory system is seen in Figure 5.1, with the left side of the heart pumping blood through the systemic circulation and the right-side pumping blood through the pulmonary circulation.

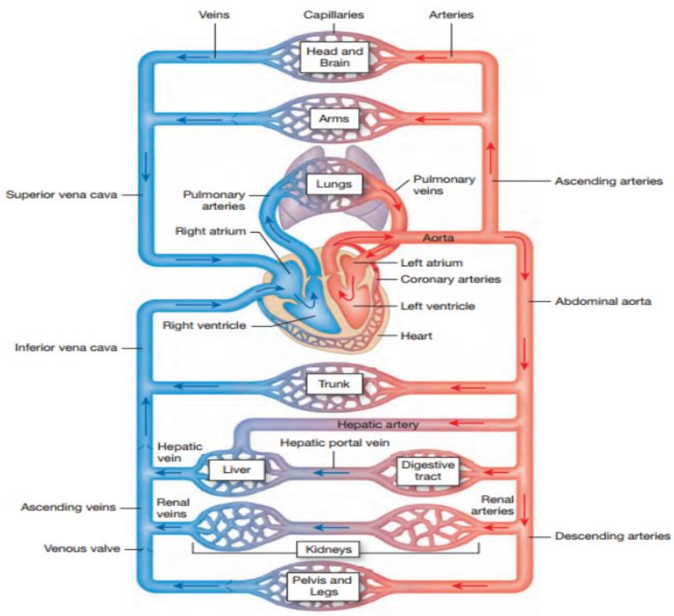



Figure 5.1: Human circulatory system [Brazier, 1988]

The systemic circulation transports oxygen-rich blood containing nutrients and other essential elements to all bodily tissues and organs, as well as carbon dioxide and organic waste from cell metabolism back to the heart via the vena cava. The right atrium, which serves as a weak starter pump to regulate venous flow to the right ventricle before pumping to the pulmonary circulation, receives this return blood.

The pulmonary circulatory system is a more compact system. It transports oxygen-poor, carbon dioxide-rich dark red blood from the end of the systemic circulation to the lungs' air sacs termed alveoli, where it is exchanged, and oxygen levels are enriched. The blood turns deep crimson when the gases are exchanged and travels back to the left atrium via the pulmonary veins to enter the systemic circulation again.

## 5.2 Pulse Duplicator System

The Pulse Duplicator is an In-vitro cardiovascular hydrodynamic testing equipment that mimics the heart's action (left or right). It simulates natural and complicated flow changes by generating pulsatile flow through prosthetic heart valves installed in the model heart. Data on pressure and flow is obtained through ports in the aortic and mitral valves. The transparent viewpoints allow multiple viewing angles of the valve including inflow and outflow.

5.2.1 Features of the Pulse Duplicator System

1. Simulates cardiac conditions like arrhythmia, normal, hypo and hypertensive states at specified CO and beat rates
2. Measures wall pressures in the atrium, ventricle, and aortic outflow
3. Measures flow at aortic and mitral states
4. Ventricle membrane replicates natural chamber flow
5. Quality data acquisition which meets verification and testing in accordance with ISO 13485 requirements and aids in the collection of data to meet ISO 5840 to FDA requirements through the use of ViViTest software.
6. Optional components enable testing of various cardiac valve types and cardiac structures, viscoelastic simulated behaviour to produce realistic ventricle pressure waveforms and operate test fluid at 37ºC to simulate physiological conditions.

5.2.2 The Pulse Duplicator system can be configured for the following tests and applications

1. Heart valve function testing
2. Peripheral devices

3. Aortic Valve By-pass
4. LVADs simulator
5. Flow transducer Evaluation/Calibration
6. Isolated heart Driver
7. Neurovascular flow studies
8. Blood vessel flow studies
9. MRI studies

### 5.2.3 Specifications

The following are the technical specifications of the Pulse Duplicator system

| | |
|---|---|
| Pump and Model Left Heart | 53 x 92 x 45 cm |
| DAS and Flow system | 48 x 33 x 32 cm |
| Dry weight: Actuator + MLH + VIA | 18 kg |
| Temperature Range | Ambient up to 40̊ C ± 1.0̊ C |
| Flow Rate | 0 – 15 L/min |
| Heartbeat Rate | 3 – 200 Bpm |
| Valve Size<br>Aortic<br>Mitral | <br>Up to Ø 35 mm<br>Up to Ø 35 mm |

Table 5.1: Pulse duplicator system specification table

## 5.3 Left heart model

Simulates pressures and flows of the left heart allowing insertion of cardiovascular devices into pulse duplicator system. Transparent walls allow complete view of functioning valves. Pressures ports measure pressures in the atrium, ventricle and aortic outflow tract and downstream of aortic valves

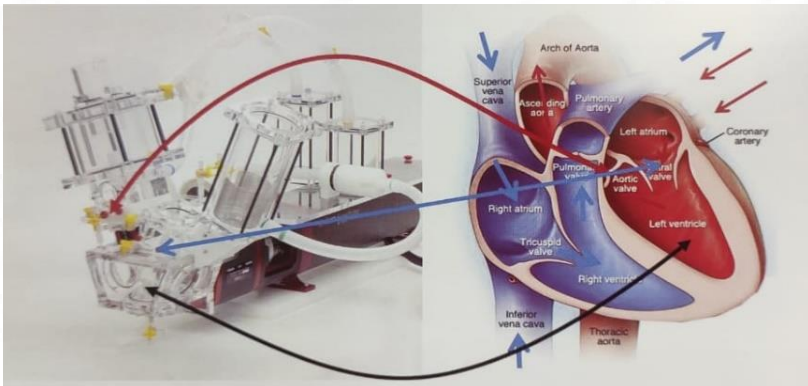



Figure 5.2: Left heart model marking various chambers of heart. [Vivitro Labs]

System components and accessories

- SuperPump
- Vivitest Data Acquisition System (DAS)
- Vivitest Software
- Viscoelastic Impedance Adapter
- Electromagnetic flow meter
- Pressure Transducers
- Heat Exchanger and Heat bath
- Digital Thermometer

5.3.1 Superpump

The Vivitro Superpump is a digitally controlled hydraulic piston pump that creates the physiological cardiac flow. The AR series of these pumps uses a digital technology that provides maximum control and precision accuracy. It is pre-loaded with 5 waveforms in the controller making it a standalone system. Custom waveforms can be stored externally (external function generators and smartphones). The ViVitro SuperPump AR Series can be driven by external waveform sources giving flexibility for waveform input. Function generators, personal computers with I/O functionality, custom hardware, microcontroller development boards, and even smartphones can directly control the flow output of the pump. SuperPump feedback can be captured using an oscilloscope or other acquisition device to monitor waveform accuracy.

Figure 5.3: Vivitro Superpump AR and Controller unit [Vivitro labs Inc. Canada]

5.3.1.1 Super pump specifications

| | |
|---|---|
| Dimensions | |
| Pump | 15 x 55 x 17 cm |
| Controller | 11 x 48 x 33 cm |
| Dry weight | |
| Pump | 7.65 kg |
| Controller | 4.7 kg |
| Voltage | 90 – 240 VAC/ 50-60 Hz |
| Cycle Rate | 3 – 200 bpm |

| | |
|---|---|
| Displacement Volume | 0 – 180 mL |
| Piston Area | 38.32 cm$^2$ |
| Waveform Accuracy | < 4% of stroke volume at 70 bpm (±3 mL @ 75mL/stroke) |
| | < 5% of stroke volume at 200 bpm (±3.8 mL @ 75mL/stroke) |
| Standard Waveforms | Physio at 70 bpm – (Complex physiological waveform) |
| | Sine 30% at 45 bpm |
| | Sine 35% at 70 bpm |
| | Sine 50% at 70 bpm |
| | Sine 50% at 120 bpm |
| Sync Pulse | +5V signal for 10ms duration |
| | Adjustable from 0 – 2000ms delay |

Table 5.2: Technical Specification of Superpump and Controller. [Vivitro labs Inc, Canada]


Figure 5.4: Superpump Controller Display. [Vivitro labs Inc, Canada]

### 5.3.2 Vivitest Data Acquisition System (DAS)

ViVitest is part of the ViVitro Data Acquisition System (DAS) family of software products. Combined with the Pulse Duplicator System it collects hydrodynamic testing data to meet ISO 5840 requirements. ViVitest software controls the SuperPump while simultaneously measuring pressure and flow data. It monitors, processes, and reports data such as regurgitant fraction, effective orifice area (EOA), and other valve performance indicators. A calibration wizard walks new users through the set-up process for quick system preparation for testing. Output files are available in .CSV format for easy analysis in Excel and MATLAB. The software is pre-installed on a laptop

Each system includes the following components:

- I/O Module – inputs/outputs signal from the software
- AmPack - Pressure Measuring System including transducers and amplifier
- Connecting cables
- Laptop with ViVitest Software (compatible with Windows 7 & 10)

Figure 5.5: Vivitro Data Acquisition system [Vivitro labs Inc. Canada]

### 5.3.3 Vivitest Software

The ViVitest software program is designed to acquire data from the ViVitro Labs Pulse Duplicator System in characterizing heart valves and testing mechanical circulatory devices. A primary reference document for the various elements of the Pulse Duplicator System is provided with the ViViTest software. ViViTest is designed for monitoring, acquisition and analysis of data generated by laboratory systems for assessment of heart valves, LVADs and other extracorporeal and implantable devices. This software is primarily developed for the Pulse Duplicator System from ViVitro Labs. An Image representing the user interface of the software is shown below.


Figure 5.6: The user Interface of the Vivitest Software. [Vivitro labs Inc. Canada]

#### 5.3.3.1 Software Features

The software consists of four primary processes:

- Waveform Acquisition
- Waveform Analysis

- Waveform Comparison
- Waveform Review

and one secondary utility:

- Sensor Calibration

### 5.3.4 Viscoelastic impedance Adapter (VIA)

The ViVitro Viscoelastic Impedance Adapter (VIA) is an accessory of the PDS that works in conjunction with the SuperPump to produce more realistic physiological ventricular pressures. These realistic physiological pressures are a result of a fixed resistive element around 200 mmHg/lpm and two adjustable compliance chambers working in subordination to simulate ventricular viscoelastic behaviour. The adjustable dp/dt ratio of the VIA produce both physiological and diseased cardiac models. It has capability to filter out high frequency noise when testing prosthetic valves and aortic conduits. Compliance has a source air volume of 0-120 mL and output of 0-60 mL which is syringe adjustable making a Total Liquid Volume 500 mL with SOURCE / OUTPUT compliance air volumes. Materials used for making VIA are Acrylic, Polycarbonate, Delrin, Nylon, Polyethylene, Stainless Steel, Viton etc.


Figure 5.7: Viscoelastic Impedance Adapter (VIA7991). [Vivitro Labs Inc. Canada]

5.3.5 Flowmeters

There are typically two types of Flowmeters used in this experiment,

5.3.5.1 Electromagnetic flowmeter

An electromagnetic flow meter is a transducer that measures fluid flow by the voltage induced across the liquid by its flow through a magnetic field. A magnetic field is applied to the metering tube, which results in a potential difference proportional to the flow velocity perpendicular to the flux lines. The physical principle at work is electromagnetic induction. The magnetic flow meter requires a conducting fluid, for example, water that contains ions, and an electrical insulating pipe surface, for example, a rubber-lined steel tube. The figure 5.8.a shows an Electromagnetic flowmeter *(EM Flowmeter, Carolina Medical Electronics, Inc., NC).*


Figure 5.8.a: Electromagnetic Flowmeter [EM Flowmeter, Carolina Medical Electronics, Inc., NC]

5.3.5.2 Transit time Ultrasonic flowmeter

Transit time ultrasonic flow meters measure the difference in time from when an ultrasonic signal is transmitted from the first transducer until it crosses the pipe and is received by the second transducer. A comparison is made of upstream and downstream measurements. If there is no flow, the travel time will be the same in both directions. When flow is present, sound moves faster if traveling in the same direction and slower if moving against it. The transit time flowmeter *(Transonic Systems Inc., Ithaca, NY)* used in the experiment is shown in figure 5.8.b. Since the ultrasonic signal must traverse the pipe to be received by the sensor, the liquid cannot be comprised of a significant amount of solids or bubbles, or the high frequency sound will be abated and too weak to travel across the pipe.


Figure 5.8.b: Transit time Flowmeter. [Transonic Systems Inc., Ithaca, NY]

### 5.3.6 Pressure transducers

The Data Acquisition System includes three (*Utah Medical 6069)* Pressure Transducers at the aortic and mitral sites to measure Aortic, Left Ventricle and Left Atrial pressure. It also possesses a Cable test-port that allows easy verification of monitoring system accuracy. The transducers are interfaced to the DAS with the help of I/O module and a system called AmPack. This Module is suitable for Pulse duplicator system and is also employed for use with EV Simulator, Real-time wear tester or the HiCycle.

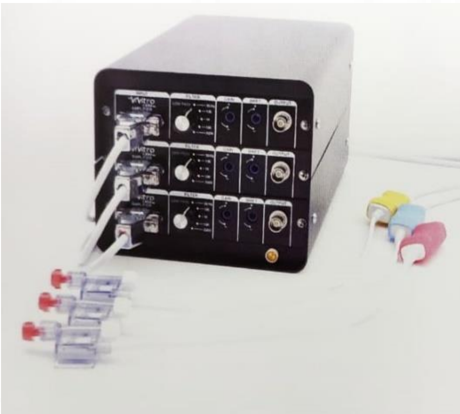


Figure 5.9: Pressure Transducer (HCMO18). [Vivitro labs Inc. Canada]

### 5.3.7 Heat Bath and heat exchanger

The ThermoScientific Heat exchanger used in the study, allows heating of test fluid to the required temperature with a variance of ± 5 ˚C with minimal interference of fluid flow. It features isolated inflow and outflow metal channels that prevents the test fluid to come in contact with the hot water from the bath. Figure 5.9 shows the heat exchanger and the heater and the water bath. The Heat exchanger comes with the feature that can automatically cut off system for over temperature and low reservoir level to prevent damage to the circulation loop or to itself. It has a rreservoir volume of 6 Litres and a wide Temperature Range (Ambient 15˚C to 150˚C). The Heater power requirement is 1000 W and can be powered by a source 230 VAC, 50 Hz, 10 Amps. The hot water used for heating the test fluid can be pumped around the loop at around 12 L/min at 0 psig.


Figure 5.10: Heat Exchanger [ThermoScientific, CA]

### 5.3.8 Temperature sensors

The Resistance temperature detectors (RTD) sensors allow easy fluid temperature, motor casing and Volute temperature measurement. The fluid temperature is measured by submerging a sensor in the Left atrium reservoir while the casing and volute temperatures are measured by keeping the RTD sensors in contact with surface. The sensors used are traceable to standards provided by NIST and have Accuracy/ Resolution of 0.1 ˚ from -20 ˚ to +100 ˚ C. The sensor data is acquired and displayed with the help of Agilent Data Acquisition System. The ambient temperature is read using Hygro-thermometer. Figure 5.10 shows the sensors and display system for temperature.


Figure 5.11: Hygro-Thermometer and RTD Temperature probe with Agilent DAS [ Agilent Technologies]

## 5.4 Mock Circulation Loop

The Mock Circulation Loop used for the orientation study includes the left heart model actuated by the SuperPump producing the required pulsatile flow at adjustable heart rate. The fluid pooled at the left atrium chamber moves through the mitral valve into the ventricle chamber and from there it is expelled out into the aortic chamber through the aortic valve. The aortic chamber consists of Aortic root compliance chamber connected to it through the 3/8 PVC pipes providing variable compliance to the aortic chamber. The fluid from the aortic chamber passes through the tubing and the systemic Vascular Resistance knob is used to control the peripheral resistance to the flow. The temperature of fluid is maintained at 37 ˚C with the help of heat exchanger that is shunted along the main flow of the fluid. A parallel path, from the apex of the ventricle is provided that connects LVAD in parallel to the main pump. The outlet of LVAD is connected to the aortic chamber. Pressure transducers are connected at the aortic and mitral sites in the main loop and the Inlet and outlet of LVAD in the bypassed route to measure hemodynamic pressure variations. Similarly Flow sensors are connected in the main and supplementary route to measure aortic and LVAD flows. The RTD temperature sensors measure temperature of the motor casing, volute and fluid. The Figure 5.11 shows the detailed schematic diagram of Mock Circulation Loop.

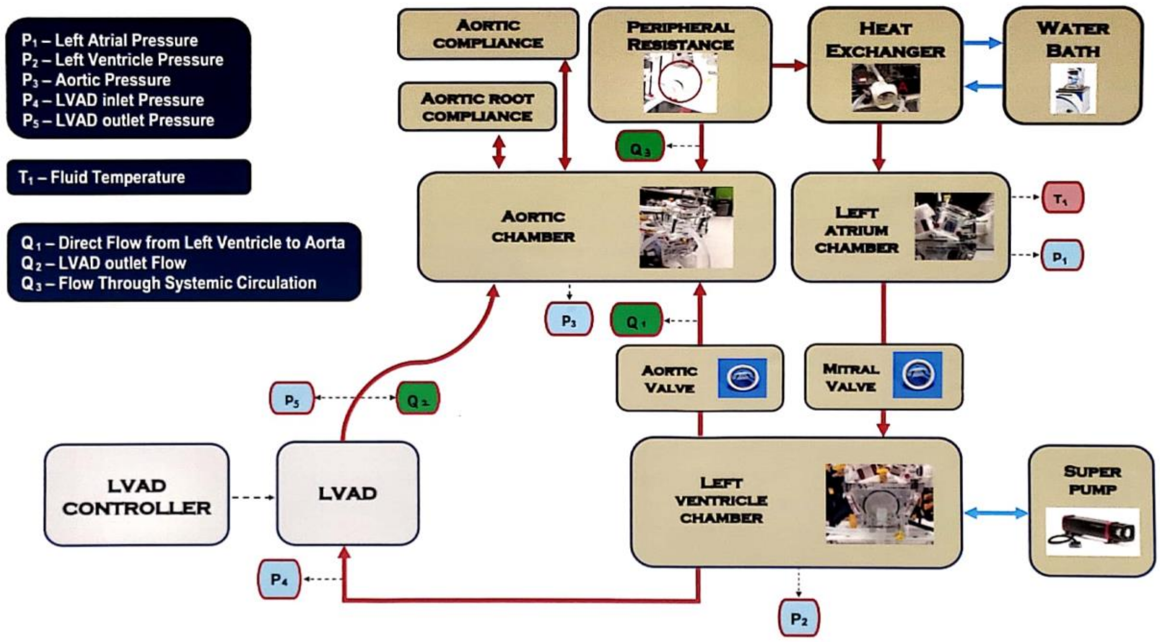



Figure 5.12: Mock Circulation loop established using pulse duplicator system.

This MCL can simulate both the normal heart function for establishing the baseline condition to validate the output from the loop, and the heart failure condition for the heart pump testing. The normal heart condition was simulated with the average parameters from a healthy adult while the cardiac output and aortic pressure are reduced for the heart failure condition.

# Experimental Evaluation | 6

A continuous flow centrifugal LVAD prototype of the design described in chapter 4 was produced for conducting the experiments. The orientation study on this prototype was done with the help of pulse duplicator system as described in chapter 5. The pulse duplicator was used to mimic the normal and diseased functioning of the human heart to acquire data on the hemodynamics and pump performance parameters at all the prescribed orientations. The information obtained on hemodynamics can be used for further development of the LVAD.

## 6.1 System Description

### 6.1.1 LVAD

The LVAD used in the experiments is in its intermediate stages of development and has pump casing is 48 mm in diameter and 57 mm long. It has a priming volume close to 15 mL. The rotor of the motor houses the impeller with passive magnets while the stator has the arrangement of six active (electromagnets) magnets. The pump works on the magnetic levitation principle and the bottom of the impeller is separated by hydrodynamic thrust. The rotor speed varies with a performance range of 1600-2800 rpm and flow up to 5 L/min. The base of stator houses a hall sensor which feeds back the rotor position to calculate speed.

The pump is controlled using a custom-built control unit comprised of a microcontroller-based motor drive circuit and rotary dial speed selector. The impeller comprise of six regularly placed backward curved blades at the top making curved vanes for the blood flow. The axial spacing between the impeller and housing varies between 1 and 2 mm. The magnetic levitation can maintain the separation between rotating impeller and stationary axle to as low as 20-25 microns.

### 6.1.2 Mock Circulatory Loop

The pump orientation test was performed on a pulsatile mock loop, using *Vivitro Labs Pulse Duplicator System* which can be used to obtain or physiological and pathological conditions of heart. The loop uses a linear pump device *(Vivitro SuperPump AR, Canada)* to simulate the native ventricle. The working fluid is called *blood analogous fluid* (BAG) which is a glycerine/water mixture with 0.9 Sodium chloride and has a density of 1047 kg/m3at 37̊ C. The left heart Model consists of three chambers 1) The atrial chamber which acts as the reservoir for the fluid, 2) The ventricle chamber that houses the ventricle sac which is having a volume of 150 ml which is immersed in the fluid distilled water solution with biocide *Proclin* to reduce bioburden, 3) The Aortic chamber where the fluid from both the ventricle and the pump is collected and circulated to the vascular system.

Systemic Vascular Resistance is controlled with peripheral resistance controller which will alter the resistance to flow, arterial compliances are modelled with closed pneumatic reservoirs called as aortic compliance and aortic root compliance. The pump inlet is connected to the apex of the left ventricle sac and pump outlet is connected to the aortic chamber. Pressures are monitored at all the three chambers of the model heart and the inlet and outlet of the pump using the *pressure measuring system (AP9991)* and three units of *pressure transducers (HCM018)*. The cardiac output through the ventricle is measured using the *Transonic flow probe (ME 11 PXL)* and *(ME 9 PXL)* of electromagnetic Flowmeter *(EM Flowmeter, Carolina Medical Electronics, Inc., NC).* The Total flow and the pump flow are measured by transonic flow probe *(Transonic Systems Inc., Ithaca, NY).* The polyvinyl tubes (3/8 inches in inner diameter) are used to connect the pneumatic ventricle and the inlet and outlet of the pump, to change the orientation without any obstruction. The fluid temperature is always maintained at $37^{\circ}$ Celsius with the help of Heat Exchanger *(Thermoscientific, CA).* The temperature of the fluid, volute and the motor casing are continuously measured by RTD sensors.

### 6.2 Methodology

The schematic diagram shown in the figure 6.1 below, gives experimental setup where the left heart model is actuated by the SuperPump and LVAD at three proposed orientations is placed. The Data on Pressure and Flow is obtained from the DAQ and fed to the system using Vivitro LHS DAQ software. LVAD is powered and controlled by the controller shown in the figure The performance parameters are tested for three orientations covering all the extreme cases and data from pressure transducers installed in both the left heart model and the LVAD is acquired by the data acquisition system.

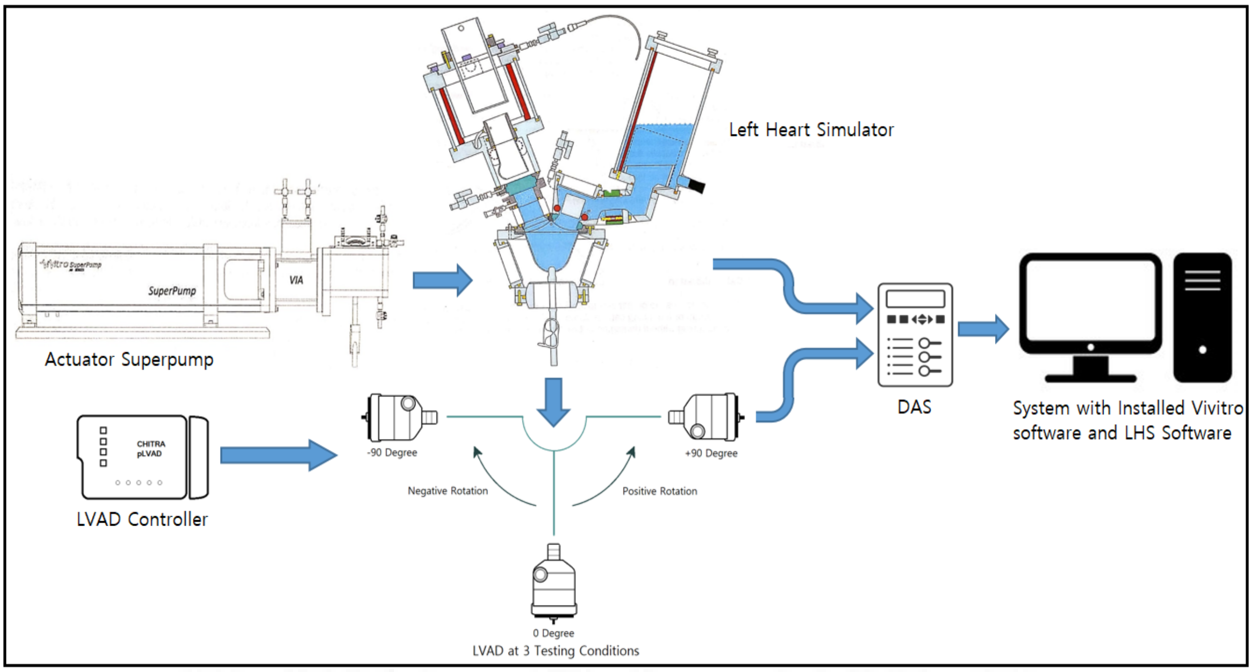



Figure 6.1: Schematic diagram orientation study.

### 6.2.1 Procedure of In-vitro study

This study takes into consideration a vast number of physiological and diseased conditions involving parameters in wide range. The experiments is planned for three orientations [-90°,0°,+90°] which roughly considers all the possible positions of LVAD with respect to ventricle. Considering the left heart model in lateral plane, the position of pump exactly below the ventricle is the 0 degree position. Rotating the pump in clockwise direction will decrease the angle to -90 degree whereas rotating in counter clockwise direction will increase to +90 degree. In all the cases, the inlet of the pump is strictly facing the ventricle. For each orientation, a set of three heart rates [80 bpm, 100 bpm, 120 bpm] are taken into evaluation. The diseased or pre-implantation Mean Arterial Pressure (MAP) is taken to be 55 mmHg for all the combinations. The pre-LVAD conditions are set with diseased mean arterial pressure and Cardiac Output (CO) for instance 1.5 lpm and then once the LVAD is switched on, the target MAP is acquired by adjusting the Systemic Vascular Resistance (SVR) and speed of rotation of LVAD. The target Cardiac Output is set to 4 lpm. The pressure transducers at right atrial, left ventricle and Aortic chambers acquire the pressure values from right atrium, left ventricle and Aortic chamber, respectively. Also, the pressures at inlet and outlet of the LVAD are acquired by the pressure transducers.

The Cardiac Output before switching the LVAD ON is measured by electromagnetic Flowmeter and the total flow and the LVAD flow is measured by Transonic Flowmeters. The RTD temperature sensors are placed in right atrial chamber to measure the fluid temperature whereas those fixed in contact with the LVAD, measure the temperature of motor casing and volute. The

Vivitest and Left Heart Simulator LHS-DAQ Software save the readings of sensor in .acq, .csv and .xlsx file in the system. Once the data for one set is saved, the Cardiac Output is then gradually increased to 4.5 lpm by increasing the speed through the controller and keeping the targeted MAP same as previous. This step is repeated with step of 0.5 lpm until the LVAD speed reaches its maximum. This procedure is repeated for three different target MAPs [80mmHg, 100mmHg, 120mmhg] and for four different initial cardiac outputs [1.5 lpm, 2.5lpm, 3.5 lpm, 4.5 lpm]. At lower cardiac outputs (1.5lpm), if the total cardiac output does not reach to 4lpm even for the maximum LVAD speed, the maximum value of cardiac output is considered. For higher cardiac outputs (4.5 lpm), if the target MAP does not reach 80mmHg, the minimum attained MAP is considered. Once all the combinations for one orientation are successfully acquired, the orientation is changed, and the entire process is repeated for next orientation. The figure 6.2 below is the block diagram of the flow of experiment.

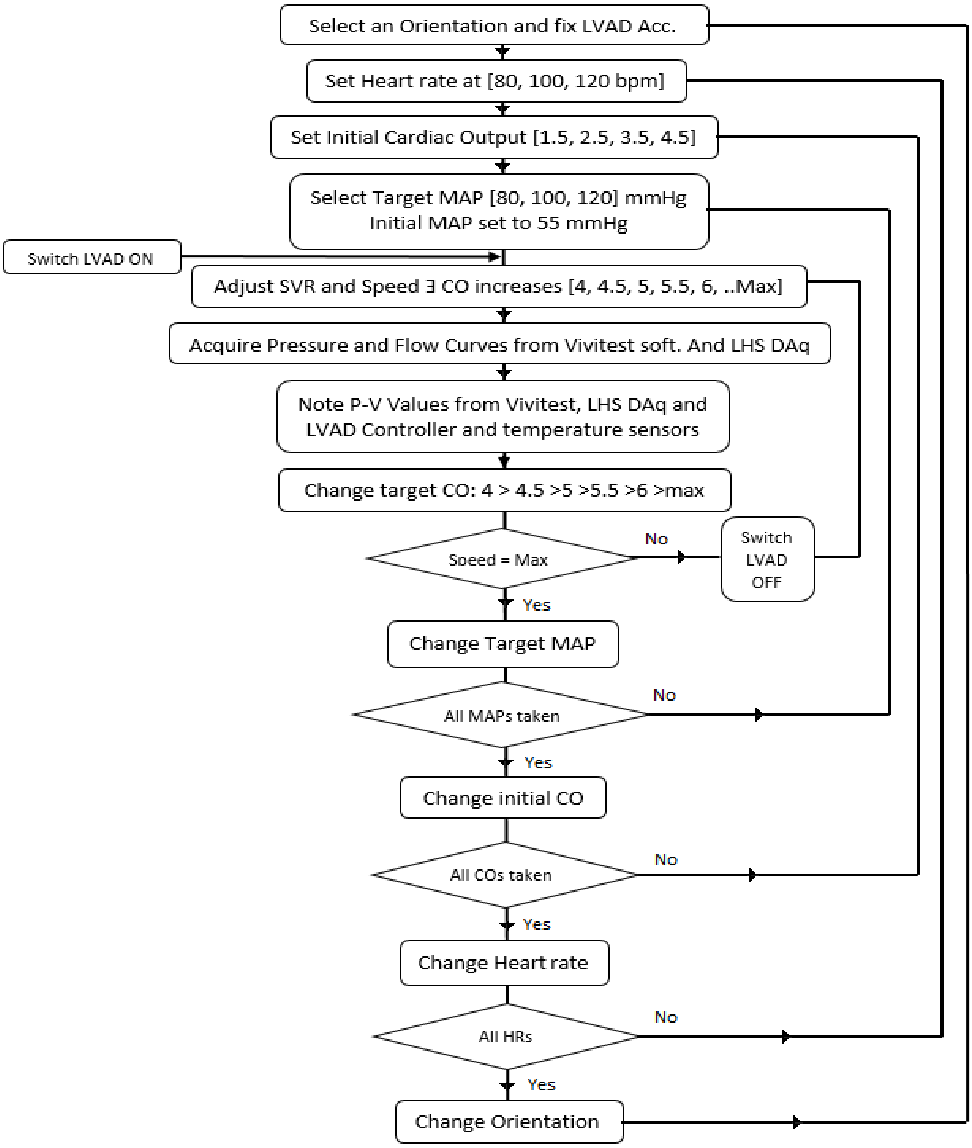



Figure 6.2: Block Diagram showing the flow of Experiments.

An experimental layout is created to track the finished, ongoing and upcoming experiments. The finished experiments are marked as green while the ongoing and remaining are unmarked. The running time of the LVAD is noted with the remarks stating any abnormal conditions (if present). The Figure 6.3 below shows the experimental layout of the experiments and LVAD running time.

| | Initial Patient Settings on LHS | | | | | |
|---|---|---|---|---|---|---|
| Orientation | HR(bpm) | MAP (mmHg) | CO (L/min) | Target MAP (mmHg) | | |
| | | | | 80 | 100 | 120 |
| -90 degree | 80 | 55 | 1.5 | | | |
| | | | 2.5 | | | |
| | | | 3.5 | | | |
| | | | 4.5 | | | |
| | 100 | 55 | 1.5 | | | |
| | | | 2.5 | | | |
| | | | 3.5 | | | |
| | | | 4.5 | | | |
| | 120 | 55 | 1.5 | | | |
| | | | 2.5 | | | |
| | | | 3.5 | | | |
| | | | 4.5 | | | |

| Date | pLVAD Running time (Hrs:mins) | Remarks |
|---|---|---|
| 30-03-2021 | | |
| 31-03-2021 | | |
| 01-04-2021 | | |
| 02-04-2021 | | |
| 03-04-2021 | | |
| 04-04-2021 | | |
| 05-04-2021 | | |
| 06-04-2021 | | |
| 07-04-2021 | | |
| 08-04-2021 | | |
| 09-04-2021 | | |
| 10-04-2021 | | |
| 11-04-2021 | | |
| 12-04-2021 | | |
| 13-04-2021 | | |
| 14-04-2021 | | |
| 15-04-2021 | | |
| 16-04-2021 | | |
| 17-04-2021 | | |
| 18-04-2021 | | |
| 19-04-2021 | | |
| 20-04-2021 | | |
| 21-04-2021 | | |
| 22-04-2021 | | |
| 23-04-2021 | | |
| 24-04-2021 | | |
| 25-04-2021 | | |
| 26-04-2021 | | |
| 27-04-2021 | | |
| 28-04-2021 | | |
| 29-04-2021 | | |
| 30-04-2021 | | |

Figure 6.3: Experimental Layouts at three different orientations.

### 6.2.2 Acquired data

For each set of experiment, static and dynamic data of the Atrial Pressure vs. time, Ventricle pressure vs. time, Aortic pressure vs. time, LVAD inlet and Outlet pressure vs. time LVAD and Aortic flow vs. time curves for 10 cycles are acquired by the data acquisition softwares. The table 6.1 below, shows the data that is acquired for one set of experiment.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Patient condition: CO-2.5; 80bpm; MAP: 55mmHg to 100mmHg** | | | | | | | | | |
| **Device ID:** | | | | | | | | | |
| **Test Fluid- Blood analogus Fluid( 50%+50% W/W)** | | | | | | | | | |
| **Aortic Flow (L/min)** | Lvad Speed (rpm) | LVAD Flow (L/min | Systolic Pressure (mmHg) | Diastolic Pressure (mmHg) | **MAP (mmHg)** | LVAD Inlet Pressure (mmHg) | LVAD Outlet Pressure (mmHg) | LVAD Diff Pressure (mmHg) | Current (A) |
| **2.5** | | | | | | | 0 | 0 | 0 |
| **4** | | | | | | | | | |
| **4.5** | | | | | | | | | |
| **5** | | | | | | | | | |
| **Max** | | | | | | | | | |
| **Controller ID:** | | | | | | **Motor:** | | | |
| | **Starting Time** | | | | **Date** | | | | |
| Voltage (V) | Power (W) | Efficiency (η) | Fluid Temp (°C) | Time (Hrs:min) | Motor Casing Temp (°C)(102) | Volute Casing Temp (°C)(101) | Pulsatility Index (PI) | Ambient Condtion (°C) | User Adjusted Sensor Gain-Transonic Flow meter |
| | | | | | | | | | 90% |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

Table 6.1: Format table of the data acquired.

### 6.3 Precautions

The Pulse Duplicator system is a sophisticated left heart simulator which can be used as a testing tool for multiple cardiovascular devices and is designed for long working hours, though few necessary precautions are needed to be taken while working with it.

- All the chambers must be made free from air bubbles after the fluid is poured into the atrial chamber. A clinical syringe can be used to de-bubble the chambers
- After filling the chambers with the fluid, the pressure transducers attached at each of the chambers must be made free from trapped air
- After filling the fluid, the LHS must be run for few minutes and heat exchanger must be turned ON to keep the fluid temperature maintained at 37 degree Celsius
- All the pressure and flow sensors must be re-zeroed before taking readings for each experiment
- For changing the heart rate, the actuator must be still and stationary
- While running, the pressure and fluid levels in the Aortic chamber must be continuously monitored. If these levels are disturbed, the pneumatic compliance chambers must be used to brings the levels back to normal
- A sudden rise in ventricular pressure can be relaxed adjusting the SVR
- All the flow transducers at any stage should NOT be reading when there is no fluid in the system. Thus, before draining the system, flowmeters are turned OFF
- The system should always be monitored for any leaks

# Results and Discussion | 7

To understand the effects of the orientation, all the performance parameters of LVAD were examined in three different orientation. Parameters like Pressure difference (ΔP), Power and Efficiency were plotted with respect to LVAD flow and the variation of LVAD flow with respect to speed was examined.

### 7.1 Variation of LVAD output parameters

To examine the output parameters mentioned above, the extreme conditions of heart rate [80 bpm and 120 bpm] were selected. The diseased Cardiac Outputs of 2.5 lpm and 4.5 lpm were selected to understand if there any variation for initial low and high cardiac output. The Mean Arterial Pressures of 80 mmHg and 120 mmHg were taken as the target MAPs with the virtue of covering all the extreme cases.

#### 7.1.1 LVAD Flow vs. Pressure Difference (ΔP)

The plots below show the variation of Pressure Difference (ΔP) with respect to LVAD Flow for all the conditions mentioned above for all three orientations.

| Condition: 2.5+ lpm 80bpm 80mmHg | | | | | |
|---|---|---|---|---|---|
| Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) |
| -90 Degree | | 0 Degree | | +90 Degree | |
| 3.09 | 51.6 | 3.12 | 55.53 | 2.89 | 42.8 |
| 3.58 | 62.8 | 3.69 | 66.39 | 3.51 | 56.1 |
| 4.11 | 72.46 | 4.27 | 77.67 | 4.12 | 66.75 |
| 4.49 | 83.1 | 4.69 | 88.08 | 4.45 | 74.9 |

| Condition: 2.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|
| Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) |
| -90 Degree | | 0 Degree | | +90 Degree | |
| 2.86 | 57.33 | 3.12 | 56.09 | 2.16 | 43.69 |
| 3.52 | 69.29 | 3.71 | 67 | 3.4 | 54.99 |
| 4.13 | 80.35 | 4.31 | 80.14 | 4.02 | 67.4 |
| 4.33 | 85.61 | 4.73 | 88.7 | 4.52 | 78.3 |

Table 7.1: LVAD Flow vs. Pressure Difference curve for 2.5+ lpm.

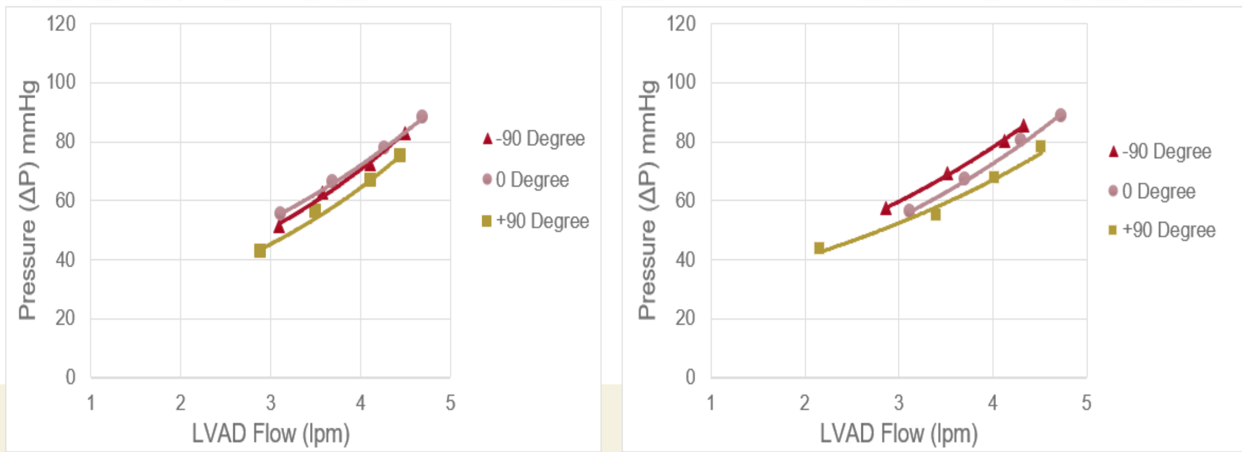



Figure 7.1: LVAD Flow vs. Pressure Difference curve for 2.5+ lpm.

| Condition: 4.5+ lpm 80bpm 120mmHg | | | | | | Condition: 4.5+ lpm 120bpm 120mmHg | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) | Lvad Flow(lpm) | ΔP (mmHg) |
| -90 Degree | | 0 Degree | | +90 Degree | | -90 Degree | | 0 Degree | | +90 Degree | |
| 2.45 | 62.48 | 2.29 | 67.68 | 2.19 | 51.94 | 1.86 | 51.48 | 2.08 | 60.46 | 1.9 | 49.2 |
| 3.01 | 71.1 | 2.98 | 78.545 | 2.95 | 70.57 | 2.71 | 64.2 | 2.95 | 72.93 | 2.68 | 59.6 |
| 3.7 | 77.36 | 3.56 | 86.17 | 3.58 | 76.26 | 3.53 | 75.91 | 3.75 | 85.87 | 3.41 | 71.83 |
| 4.05 | 91.2 | 4.23 | 100.77 | 4.11 | 93 | 3.98 | 85.03 | 4.41 | 97.96 | 4.14 | 86.04 |

Table 7.2: LVAD Flow vs. Pressure Difference curve for 4.5+ lpm.

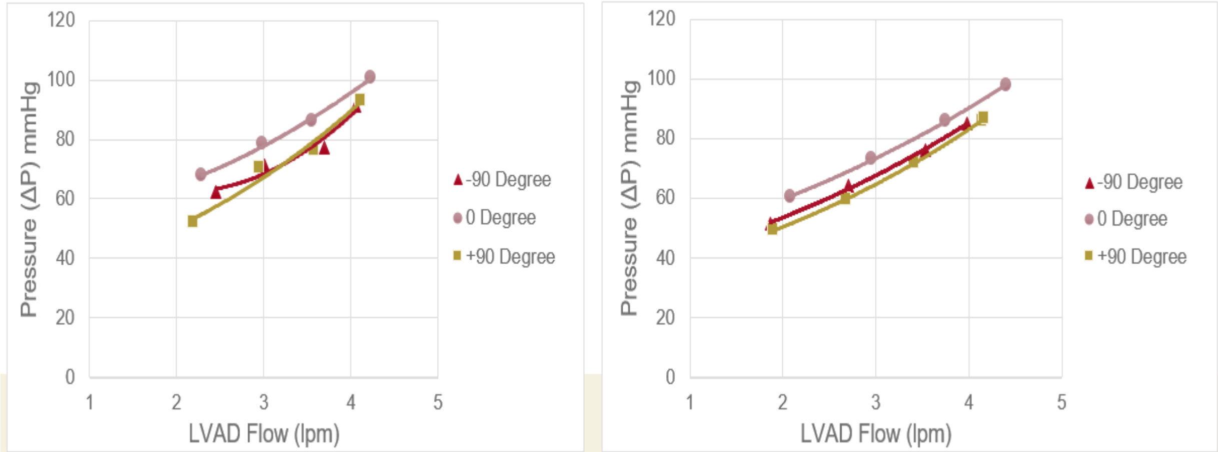



Figure 7.2: LVAD Flow vs. Pressure Difference curve for 4.5+ lpm.

From the above figures it can be observed that for the lower diseased cardiac output (2.5 lpm), the Pressure Difference does not show variation with the orientation whereas the variation is evident for the higher value of diseased cardiac output (4.5 lpm) and is more for 0 degree orientation than the other two. This variation is observed for both values of heart rate and MAPs.

### 7.1.2 Speed vs. LVAD Flow:

The plots in the figure 7.3 below show the variation of LVAD flow with respect to Speed of the rotor for all the conditions mentioned above for all three orientations;

| Condition: 2.5+ lpm 80bpm 80mmHg | | | | | | Condition: 2.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) |
| -90 Degree | | 0 Degree | | +90 Degree | | -90 Degree | | 0 Degree | | +90 Degree | |
| 2160 | 3.09 | 2160 | 3.12 | 2130 | 2.89 | 2100 | 2.86 | 2160 | 3.12 | 2070 | 2.16 |
| 2310 | 3.58 | 2340 | 3.69 | 2280 | 3.51 | 2340 | 3.52 | 2370 | 3.71 | 2280 | 3.4 |
| 2520 | 4.11 | 2550 | 4.27 | 2490 | 4.12 | 2520 | 4.13 | 2580 | 4.31 | 2460 | 4.02 |
| 2640 | 4.49 | 2670 | 4.69 | 2610 | 4.45 | 2610 | 4.33 | 2700 | 4.73 | 2670 | 4.52 |

Table 7.3: Speed vs. LVAD Flow for lower CO (2.5 lpm)

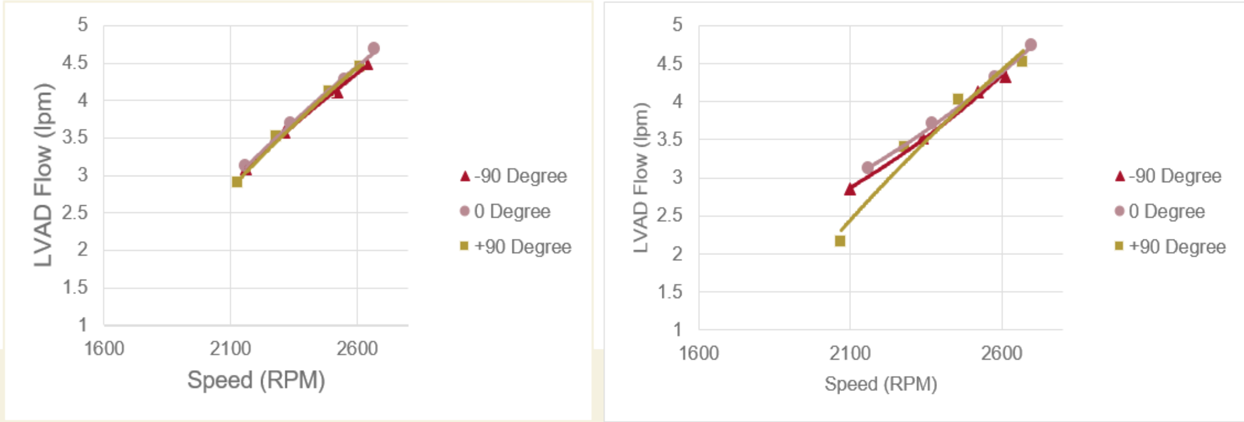



Figure 7.3: Speed vs. LVAD Flow for lower CO (2.5 lpm)

| Condition: 4.5+ lpm 80bpm 120mmHg | | | | | | Condition: 4.5+ lpm 120bpm 120mmHg | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) | Speed (rpm) | Lvad Flow(lpm) |
| -90 Degree | | 0 Degree | | +90 Degree | | 90 Degree | | 0 Degree | | +90 Degree | |
| 2310 | 2.45 | 2190 | 2.29 | 2220 | 2.19 | 2100 | 1.86 | 2130 | 2.08 | 2100 | 1.9 |
| 2370 | 3.01 | 2370 | 2.98 | 2430 | 2.95 | 2310 | 2.71 | 2370 | 2.95 | 2250 | 2.68 |
| 2520 | 3.7 | 2490 | 3.56 | 2550 | 3.58 | 2520 | 3.53 | 2550 | 3.75 | 2460 | 3.41 |
| 2700 | 4.05 | 2610 | 4.23 | 2700 | 4.11 | 2670 | 3.98 | 2760 | 4.41 | 2610 | 4.14 |

Table 7.4: Speed vs. LVAD Flow for Higher CO (4.5 lpm)

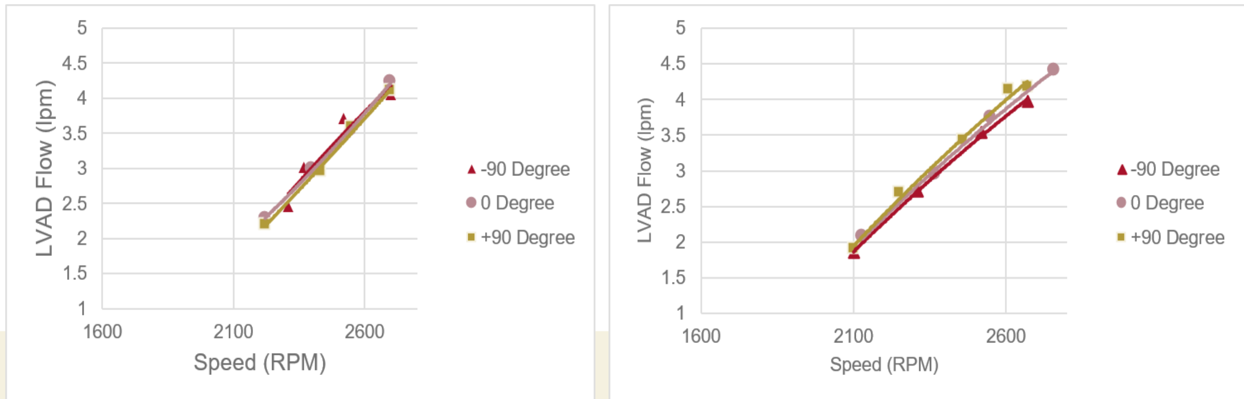



Figure 7.4: Speed vs. LVAD Flow for Higher CO (4.5 lpm)

From the above figure, it can be observed that the flow of the LVAD has a linearly increasing trend of Flow for all the orientations and it does not vary or has very insignificant variation with orientation.

### 7.1.3 LVAD flow vs. Input Power

The values of current taken by LVAD at certain speeds is fed back to the controller through the driveline and is used to calculate power which is displayed by controller. The graphs below, show the variation of input power to LVAD with the flow.

| Condition: 2.5+ lpm 80bpm 80mmHg | | | | | | Condition: 2.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) |
| -90 Degree | | 0 Degree | | +90 Degree | | -90 Degree | | 0 Degree | | +90 Degree | |
| 3.09 | 5.57 | 3.12 | 5.1 | 2.89 | 5.1 | 2.86 | 4.93 | 3.12 | 4.55 | 2.16 | 4.25 |
| 3.58 | 6.83 | 3.69 | 5.57 | 3.51 | 6.26 | 3.52 | 6.23 | 3.71 | 5.64 | 3.4 | 5.46 |
| 4.11 | 8.69 | 4.27 | 7.9 | 4.12 | 8.24 | 4.13 | 8.04 | 4.31 | 8.01 | 4.02 | 7.17 |
| 4.49 | 10.4 | 4.69 | 9.79 | 4.45 | 10 | 4.33 | 9.38 | 4.73 | 10 | 4.52 | 9.57 |

Table 7.5: Power input to LVAD with respect to LVAD flow for 2.5 lpm.

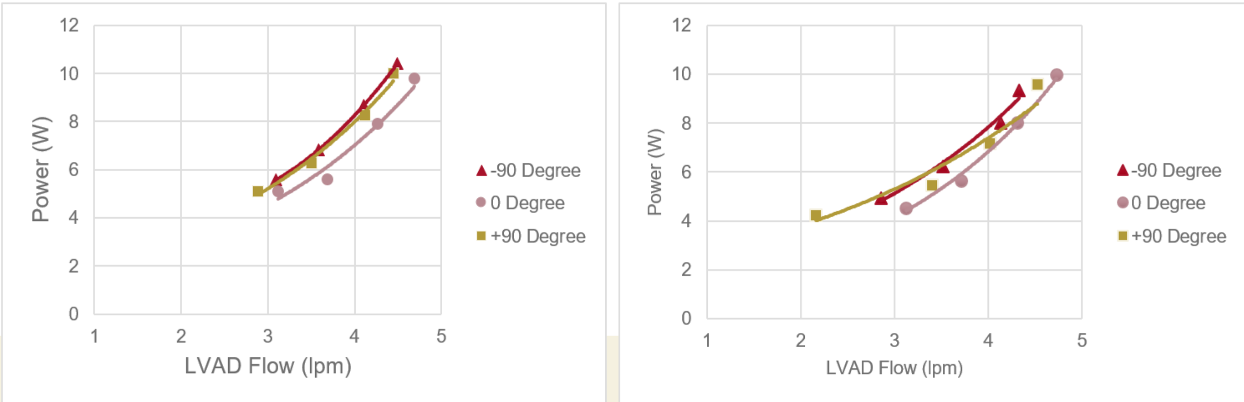



Figure 7.5: Power input to LVAD with respect to LVAD flow for 2.5 lpm

| Condition: 4.5+ lpm 80bpm 80mmHg | | | | | | Condition: 4.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) | Lvad Flow(lpm) | Power In (W) |
| -90 Degree | | 0 Degree | | +90 Degree | | -90 Degree | | 0 Degree | | +90 Degree | |
| 1.76 | 3.38 | 1.96 | 3.75 | 1.8 | 3.59 | 1.48 | 3.29 | 1.7 | 3.51 | 1.59 | 3.15 |
| 2.52 | 4.29 | 2.69 | 4.42 | 2.55 | 4.41 | 2.31 | 3.96 | 2.6 | 4.33 | 2.37 | 3.83 |
| 3.25 | 5.14 | 3.37 | 5.33 | 3.22 | 5.36 | 3.04 | 4.87 | 3.35 | 5.3 | 3.09 | 4.9 |
| 3.81 | 6.75 | 3.9 | 6.49 | 3.77 | 6.78 | 3.78 | 6.51 | 3.9 | 6.54 | 3.65 | 6.25 |

Table 7.6: Power input to LVAD with respect to LVAD flow for 4.5 lpm

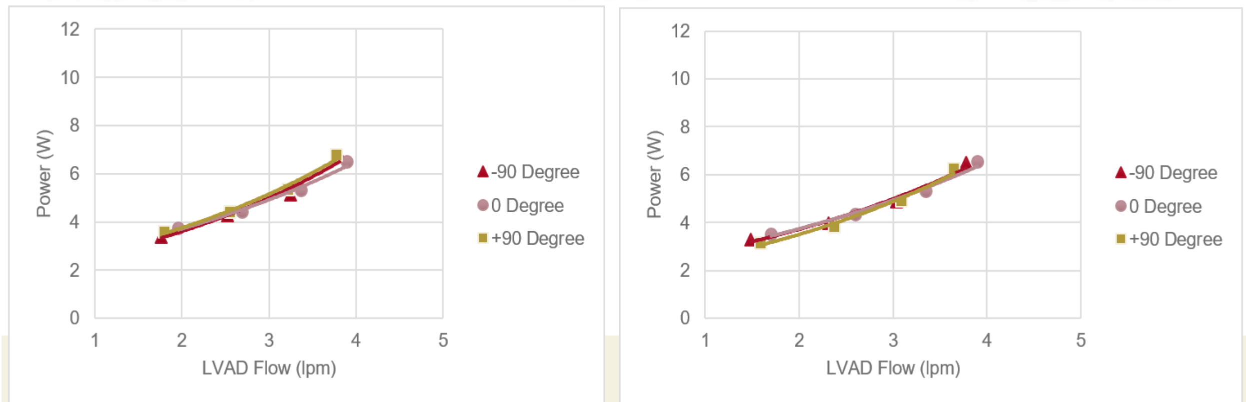



Figure 7.6: Power input to LVAD with respect to LVAD flow for 2.5 lpm

The above graphs state that for most of the combinations of parameters, the input power to LVAD motor shows significant variation with not only orientation but also the diseased cardiac outputs. For the initial cardiac output is low (2.5 lpm), power required for the pump to produce a certain flow at 0 degree orientation is less than that required in the other two orientations. However, for higher diseased cardiac output (4.5 lpm), the variation of input power to pump with respect to orientation becomes insignificant. It is also evident that there is no contribution of heart rate or target MAP in the variation of power input to the pump.

### 7.1.4 LVAD flow vs. Efficiency

The efficiency of LVAD is the ratio of hydraulic power to input power. The variation of efficiency with respect to LVAD flow is plotted for all the conditions mentioned before.

| Condition: 2.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|
| Lvad Flow(lpm) | Efficiency (η) % | Lvad Flow(lpm) | Efficiency (η) % | Lvad Flow(lpm) | Efficiency (η) % |
| -90 Degree | | 0 Degree | | +90 Degree | |
| 2.86 | 7.3168 | 3.12 | 8.4615 | 2.16 | 4.8850 |
| 3.52 | 8.6128 | 3.71 | 9.6951 | 3.4 | 7.5334 |
| 4.13 | 9.0803 | 4.31 | 9.4867 | 4.02 | 8.3136 |
| 4.33 | 8.6942 | 4.73 | 9.2301 | 4.52 | 8.136 |

| Condition: 4.5+ lpm 120bpm 80mmHg | | | | | |
|---|---|---|---|---|---|
| Lvad Flow(lpm) | Efficiency (η) % | Lvad Flow(lpm) | Efficiency (η) % | Lvad Flow(lpm) | Efficiency (η) % |
| -90 Degree | | 0 Degree | | +90 Degree | |
| 1.48 | 2.5543 | 1.7 | 3.6803 | 1.59 | 2.4985 |
| 2.31 | 4.6212 | 2.6 | 5.9934 | 2.37 | 4.4107 |
| 3.04 | 6.5026 | 3.35 | 7.8427 | 3.09 | 6.0072 |
| 3.78 | 8.0988 | 3.9 | 8.6455 | 3.65 | 7.1344 |

Table 7.7: LVAD flow vs. Efficiency curve for 2.5 lpm and 4.5 lpm

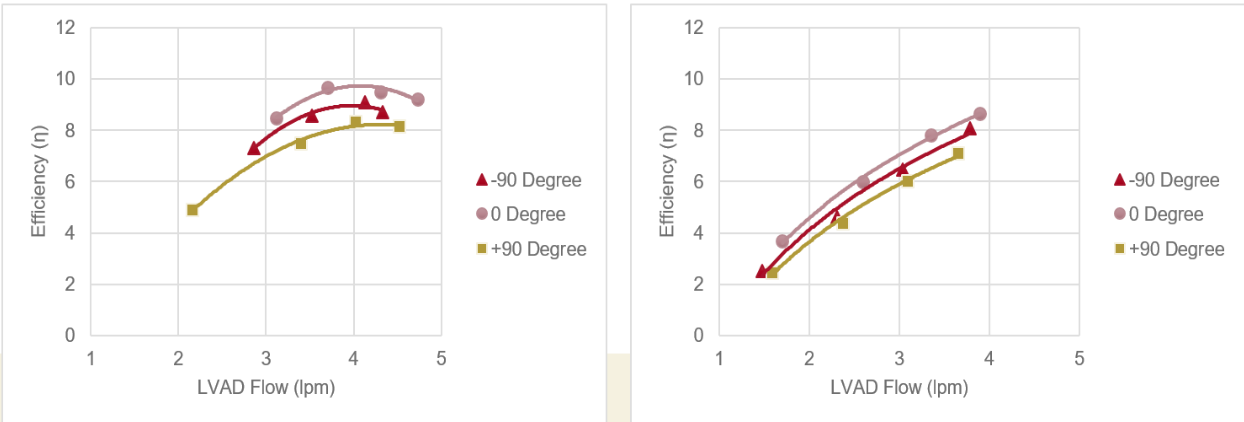



Figure 7.7: LVAD flow vs. Efficiency curve for 2.5 lpm and 4.5 lpm

For all the conditions studied above, it is very clear that the overall efficiency is affected due to orientation. The efficiency for all the conditions mentioned above is obtained highest for 0 degree orientation than that obtained in other two orientations. However, the reason for the efficiency being maximum is different for different initial cardiac outputs. For lower initial cardiac outputs (2.5 lpm), the efficiency is highest for 0 degree due the increased value of ΔP whereas in case of higher initial cardiac output (4.5 lpm), the requirement of least power input to the pump at 0 degree contributes to overall increase in the efficiency.

### 7.2 Variation of Pulsatility Index (PI) with respect to Cardiac Outputs

Pulsatility Index is a dimensionless quantity and is defined as the ratio of difference of maximum and minimum LVAD flow to the mean LVAD flow. To analyse how pump orientation affects the PI, a set of initial cardiac outputs ranging from 1.5 lpm to 4.5 lpm are taken. With the three target MAPs [80 mmHg, 100 mmHg, 120 mmHg] and target CO taken as 5 lpm, The PI for each condition is calculated and plotted against corresponding initial cardiac output. In cases where final CO is less than 5 lpm, maximum attained CO is taken. The same readings are taken for all three orientations.

80 Bpm-80 mmHg MAP- 5lpm Final CO

$$\text{Pulsatility Index (PI)} = \frac{(\text{LVAD Flow})_{max} - (\text{LVAD Flow})_{min}}{(\text{LVAD Flow})_{avg}}$$

| CO | -90 Degree | 0 Degree | +90 Degree |
|---|---|---|---|
| 1.5 | 0.392 | 0.384 | 0.304 |
| 2.5 | 0.618 | 0.645 | 0.674 |
| 3.5 | 0.908 | 0.952 | 0.974 |
| 4.5 | 1.658 | 1.925 | 1.625 |

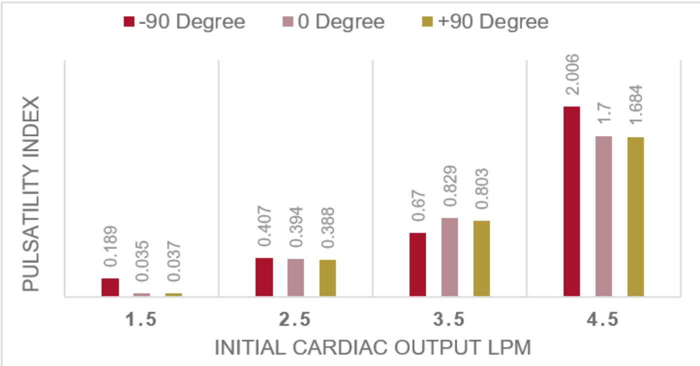



Figure 7.8.a: Cardiac Output vs. PI at 80 mmHg target MAP.

80 Bpm-100 mmHg MAP- 5lpm Final CO

$$\text{Pulsatility Index (PI)} = \frac{(\text{LVAD Flow})_{max} - (\text{LVAD Flow})_{min}}{(\text{LVAD Flow})_{avg}}$$

| CO | -90 Degree | 0 Degree | +90 Degree |
|---|---|---|---|
| 1.5 | 0.163 | 0.126 | 0.119 |
| 2.5 | 0.459 | 0.536 | 0.468 |
| 3.5 | 0.965 | 0.949 | 0.88 |
| 4.5 | 1.483 | 2.334 | 1.896 |

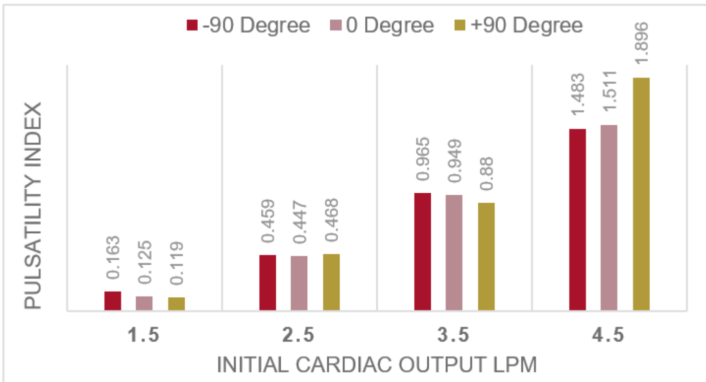



Figure 7.8.b: Cardiac Output vs. PI at 100 mmHg target MAP.

80 Bpm-120 mmHg MAP- 5lpm Final CO

$$\text{Pulsatility Index (PI)} = \frac{(\text{LVAD Flow})_{max} - (\text{LVAD Flow})_{min}}{(\text{LVAD Flow})_{avg}}$$

| | -90 Degree | 0 Degree | +90 Degree |
|---|---|---|---|
| 1.5 | 0.392 | 0.384 | 0.304 |
| 2.5 | 0.618 | 0.545 | 0.674 |
| 3.5 | 0.908 | 0.952 | 0.974 |
| 4.5 | 1.658 | 1.844 | 1.625 |

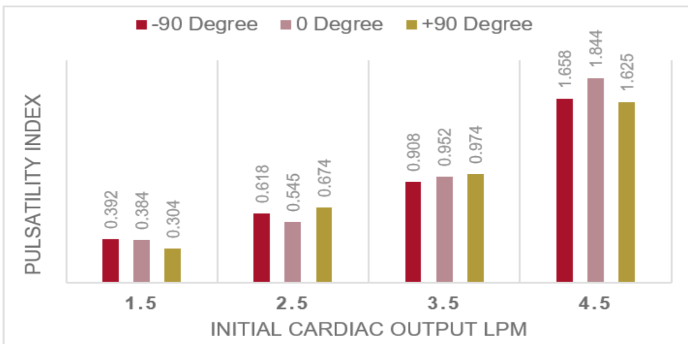



Figure 7.8.c: Cardiac Output vs. PI at 120 mmHg target MAP.

As observed from the figures above, for lower values of initial cardiac outputs, the orientation of pump does not have a significant impact on the pulsatility index that is it is similar for all the three orientations while for higher values of initial cardiac outputs, there is lot of inconsistency in the variation of pulsatility index. However, it can be observed that PI is highest for -90 degree, least for +90 degree and somewhere in between for 0 degree orientation at 120 bpm.

### 7.3 Hemodynamic Performance (Pressure variations)

Hemodynamics refers to the study of pressure distribution and flow through the various components of cardiovascular system. In the case of left heart model, the hemodynamics would refer to the measure of pressure variations at the concerned three chambers of the model viz. the left atrial chamber, the ventricular chamber and the aortic chamber and the flow study would involve the net flow rate from the aortic chamber and the contribution of the LVAD. The measurements were taken from the simulations of both diseased and improved conditions. The calculation of pressure is done by the pressure measuring system. The flow through the aorta and LVAD is calculated by the flowmeters. Before taking each reading, the sensors were re-calibrated or re-zeroed which is done by making the sensors open to atmosphere using manual valves and setting them to zero through the Vivitro software.

The hemodynamic performance analysis is done for two extreme heart rates [80bpm and 120bpm]. For each heart rate, a pair of initial cardiac outputs was taken [2.5 lpm, 4.5 lpm]. The selection of one lower and one higher cardiac output ensures that all the probable physiological and pathological conditions are considered. The graphs for the highest possible final cardiac outputs common to all three orientations are plotted with the interval of 0.5 lpm. Each of the readings were taken for 80mmHg and 120mmHg final MAPs. The following pages contain plots of aortic pressure, ventricular pressure and atrial pressure as the pressure data and Aortic flow and LVAD flow as the flow data for all the conditions mentioned above for all three orientations.

The Pressure data includes two cycles of diseased condition with initial cardiac outputs of 2.5lpm and 4.5 lpm. The next two cycles in the same curve represent the assisted condition. This helps in figuring out the variation in the pressure and flow curves that was incorporated due to change in orientation.

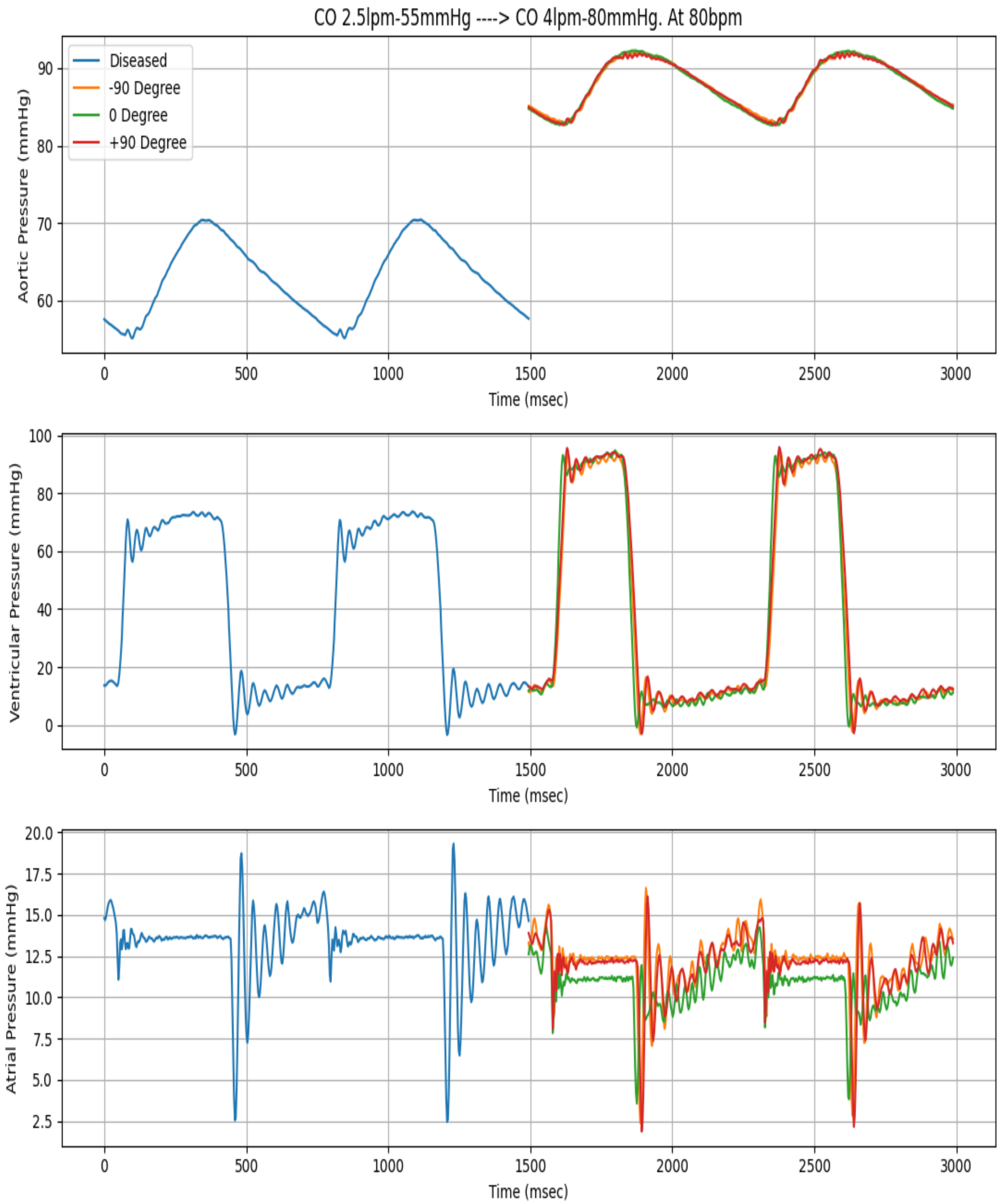



Figure 7.9: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

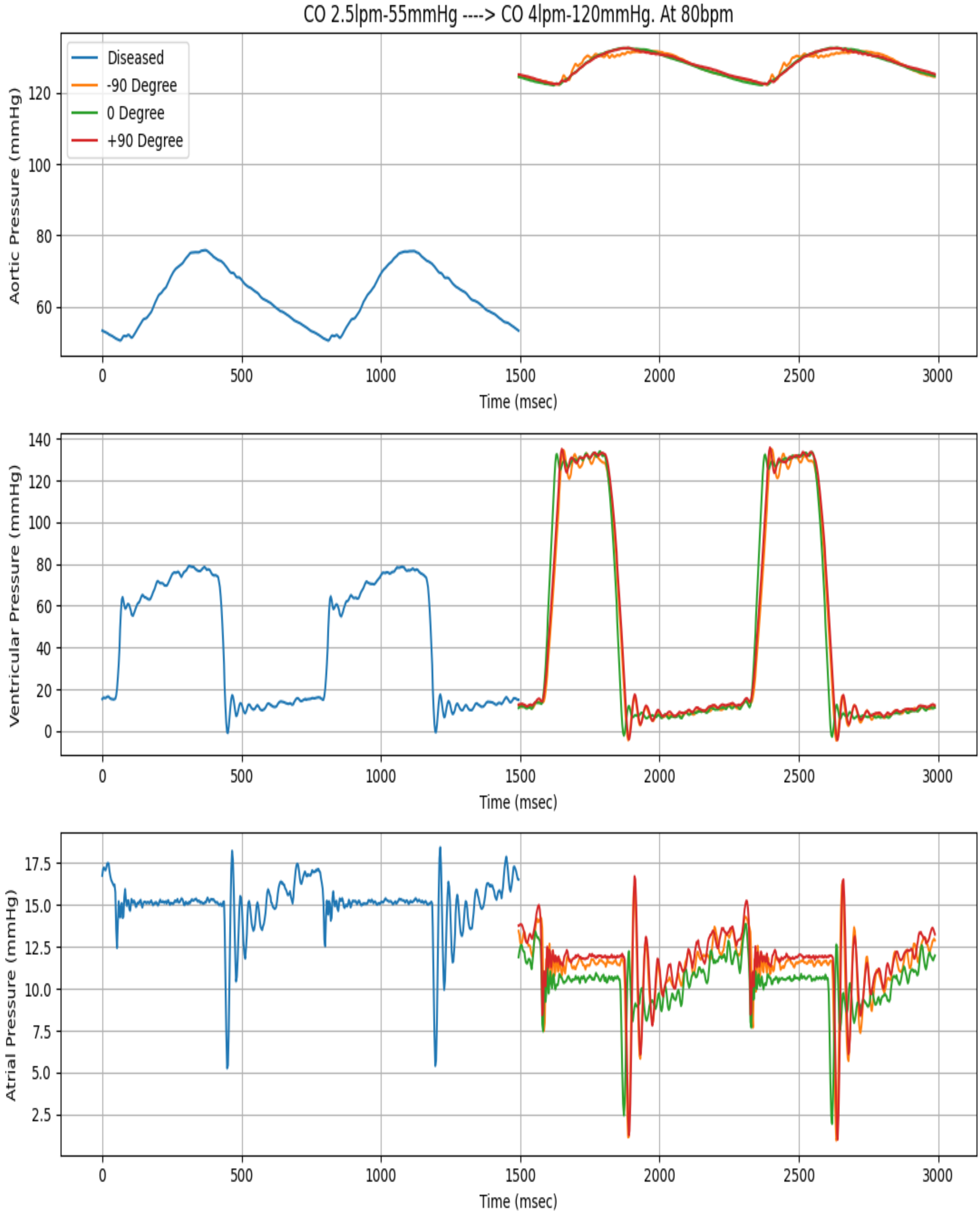



Figure 7.10: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

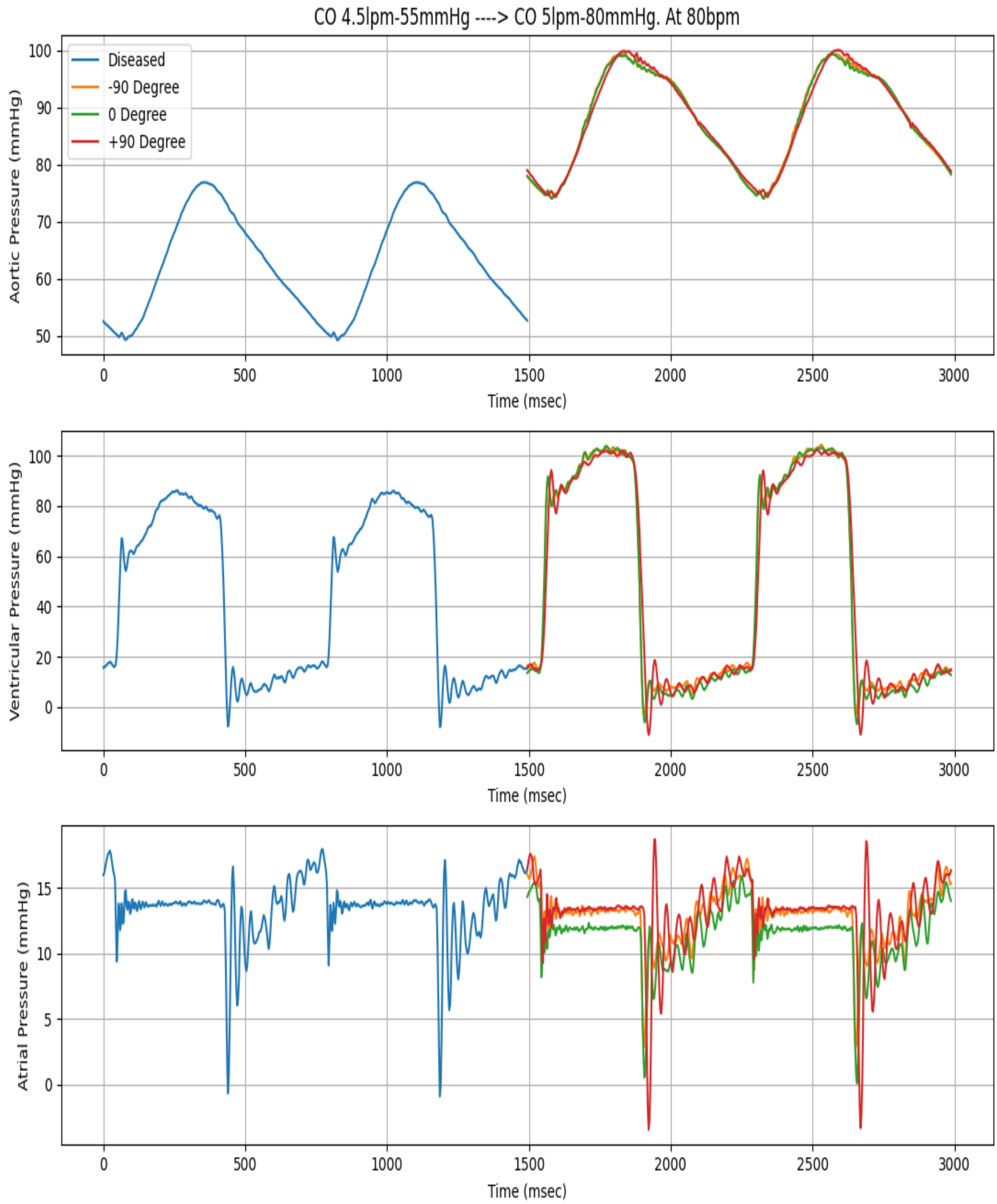



Figure 7.11: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

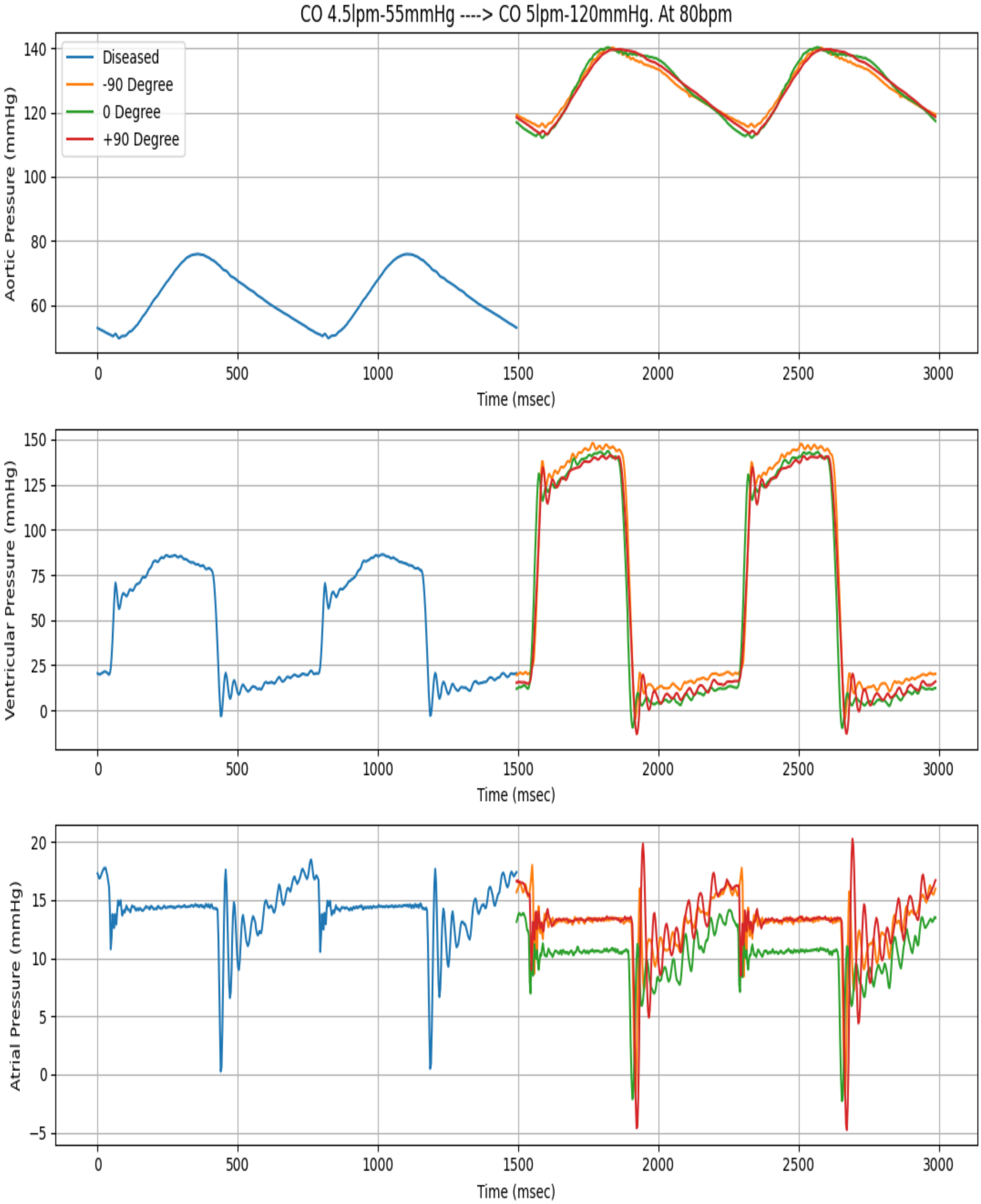



Figure 7.12: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

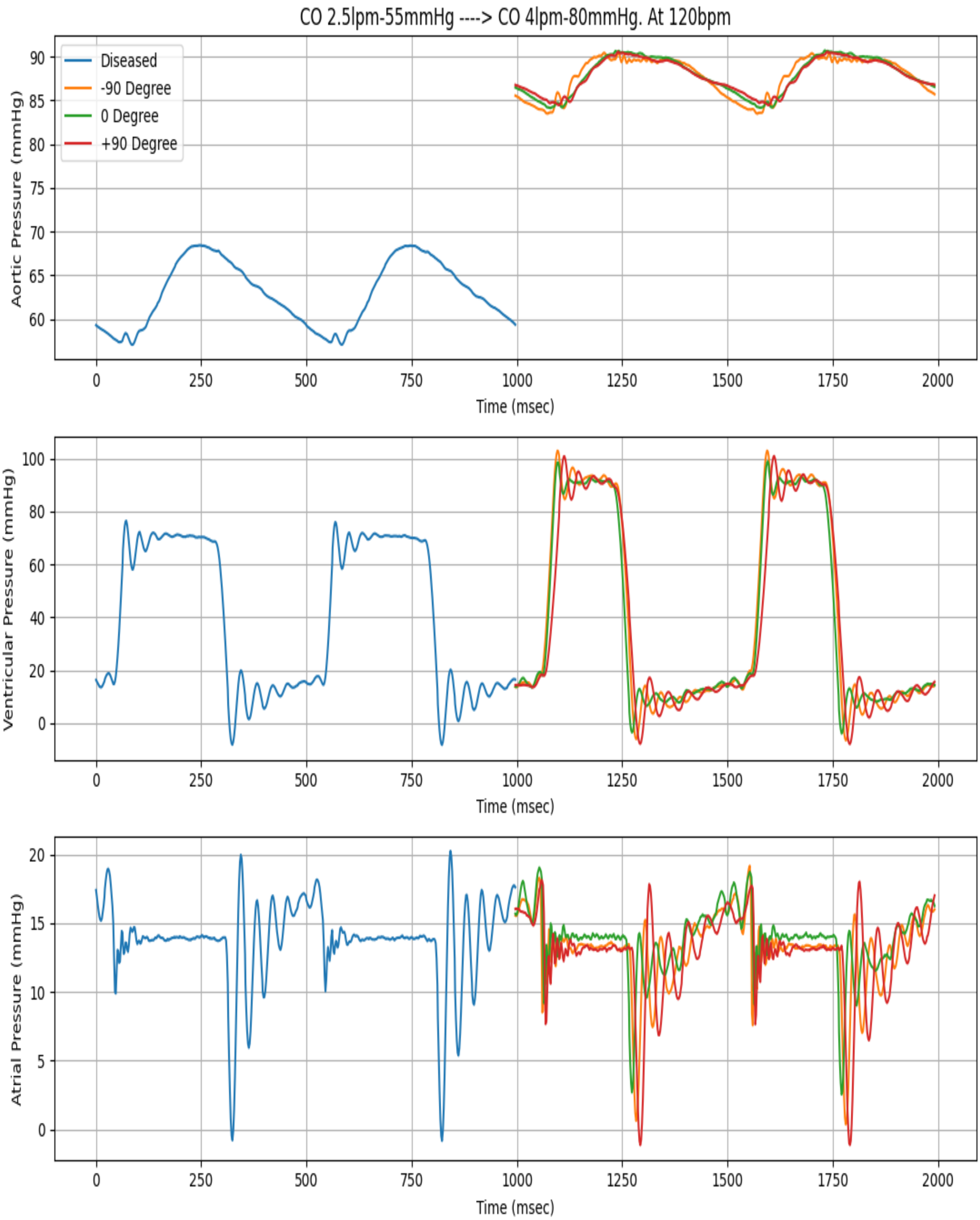



Figure 7.13: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

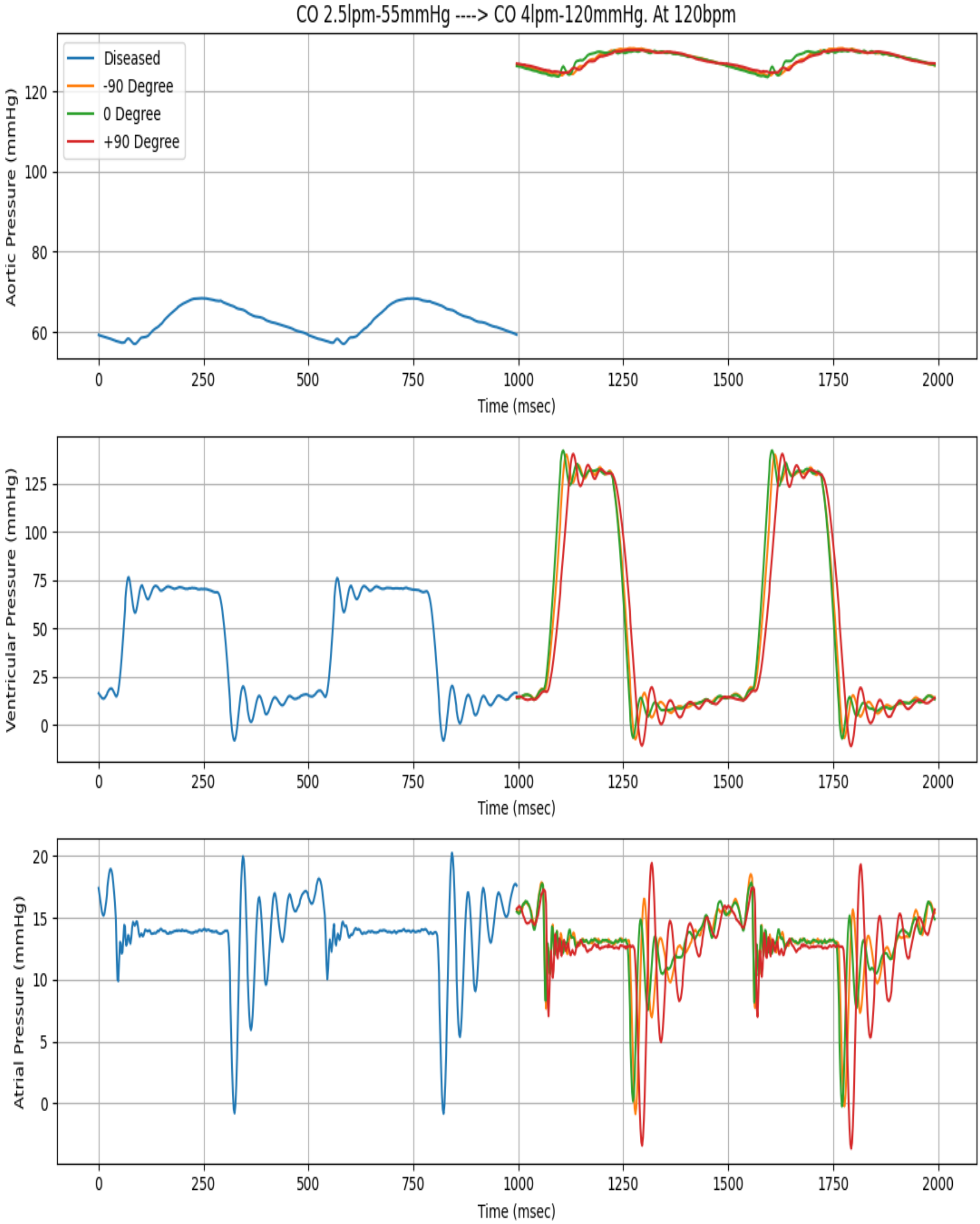



Figure 7.14: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

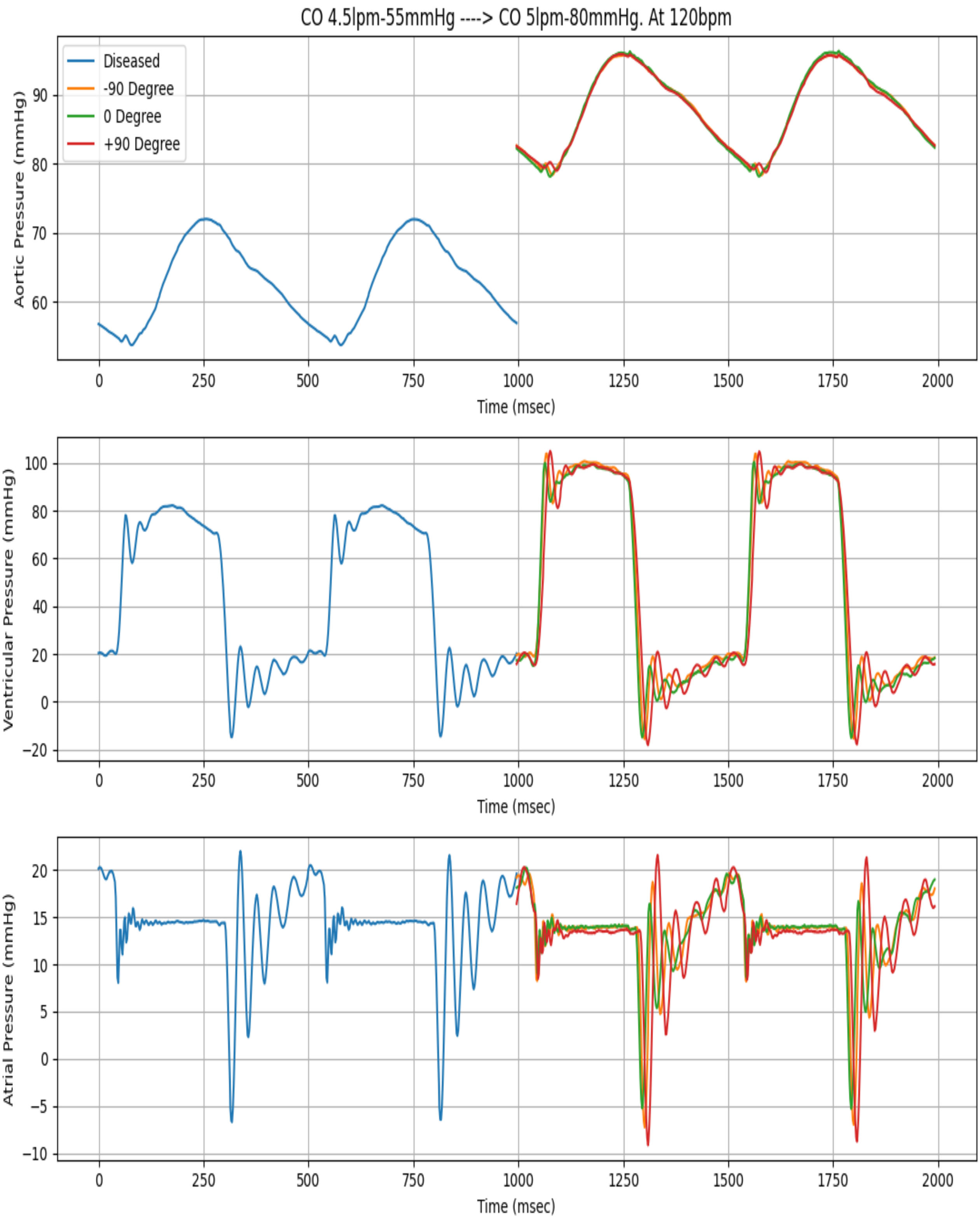



Figure 7.15: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

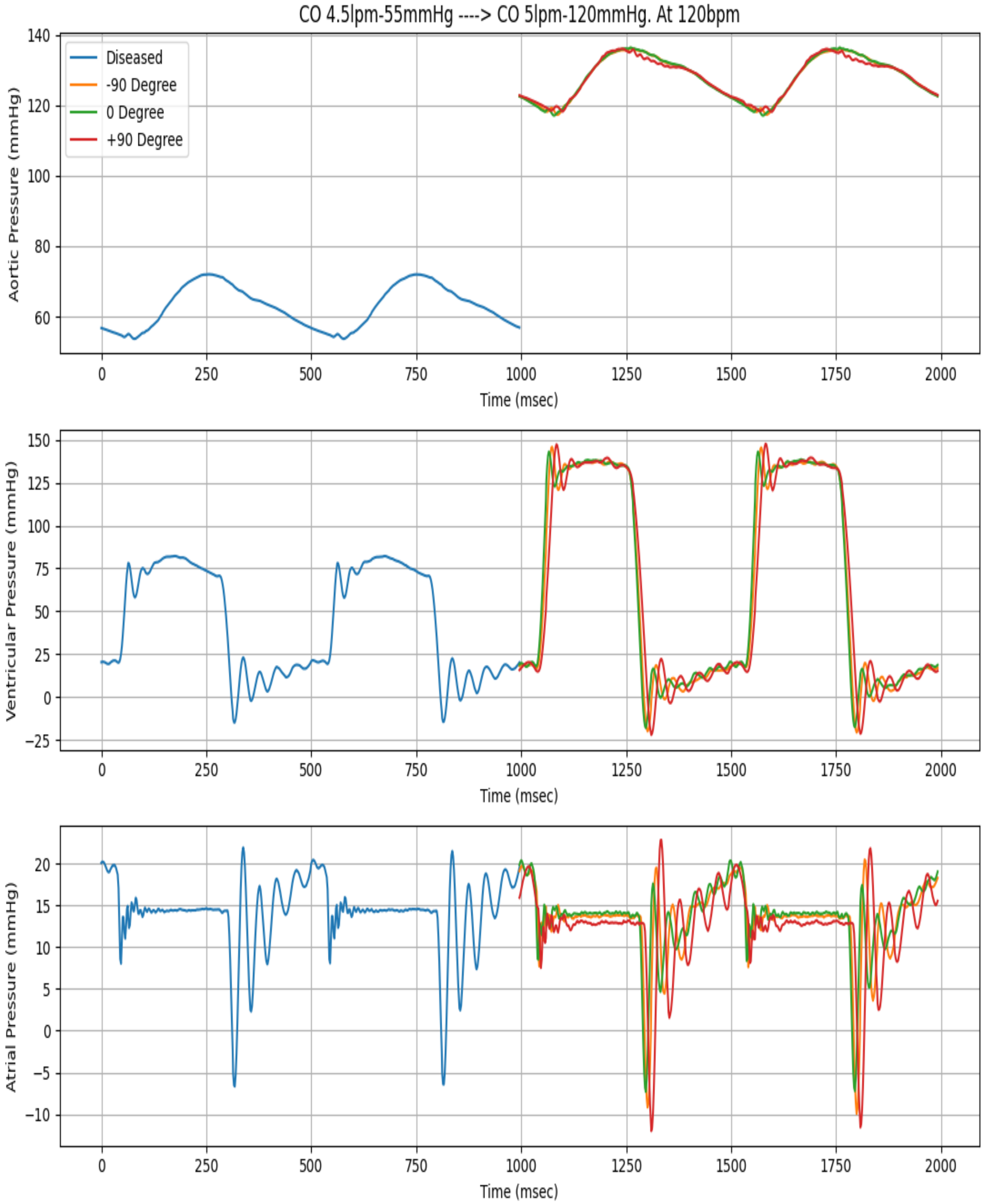



Figure 7.16: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

After observing the variation of aortic pressure, left ventricular pressure and the left atrium pressure for all three orientations, it can be observed that at 80 bpm, the left atrial pressure is minimum for 0 degree when compared with the left atrial pressures at other two orientations [-90 degree and +90 degree]. However, when same conditions of initial cardiac outputs, final cardiac outputs and target MAPs are observed at 120 bpm, the profile of left atrial pressure has no effect of orientation and is same for all orientations. The aortic pressure and the left ventricle pressure can be said to have no effect of orientation whatsoever for all the conditions considered for experiments.

### 7.4 Hemodynamic performance (Flow variations)

Flow variations denote the improvement in the flow profile on assisting with LVAD. To understand this, different stages of initial (Diseased) and final (Improved) cardiac outputs are taken into consideration. The improved cardiac output is taken as 4 lpm for an initial cardiac output of 2.5 lpm and 5 lpm for initial cardiac output 4.5 lpm. Each condition for diseased cardiac outputs mentioned above are repeated for 80 mmHg and 120 mmHg as target MAPs and 80 bpm and 120 bpm as heart rate. The other parameter like initial MAP is set to 55mmHg considering the natural values for a CHF patient. The following figures on the left shows the time vs. Aortic flow curve and that on the right shows the time vs. LVAD flow curve for selected combinations of conditions mentioned above.

**2.5 lpm - 55 mmHg to 4 lpm - 80 mmHg at 80 bpm**

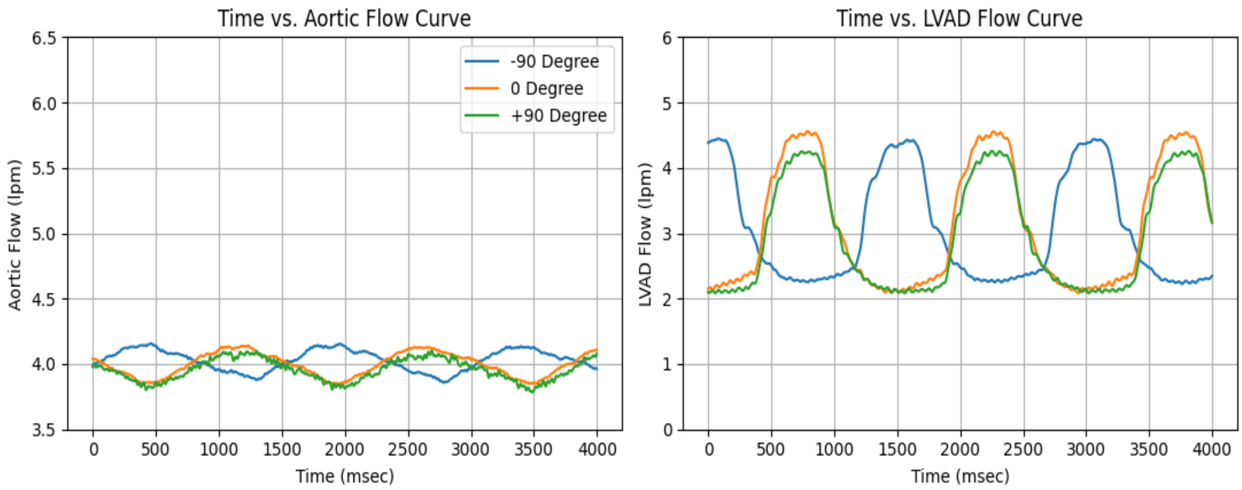



Figure 7.17: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

## 2.5 lpm - 55 mmHg to 4 lpm - 120 mmHg at 80 bpm

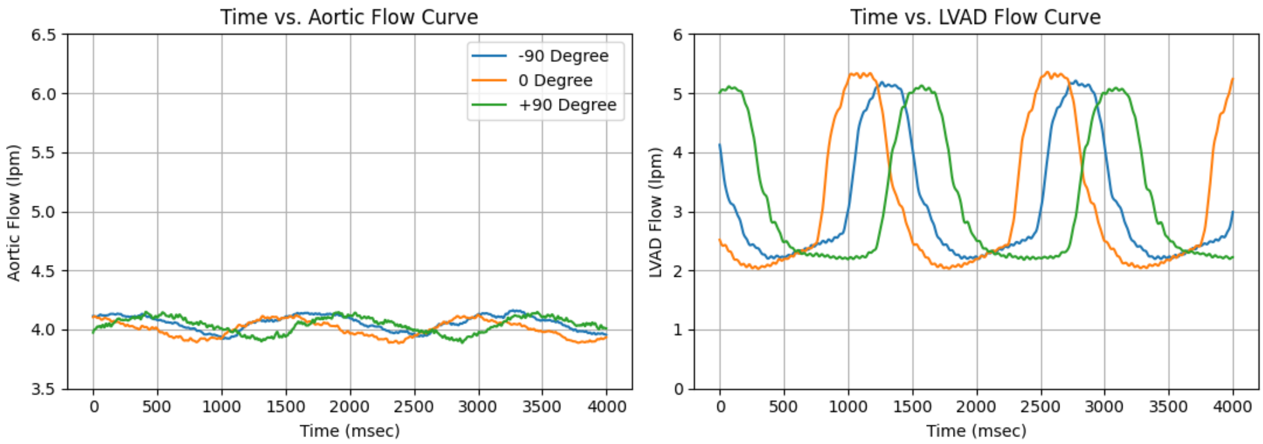



Figure 7.18: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

## 4.5 lpm - 55 mmHg to 5 lpm - 80 mmHg at 80 bpm

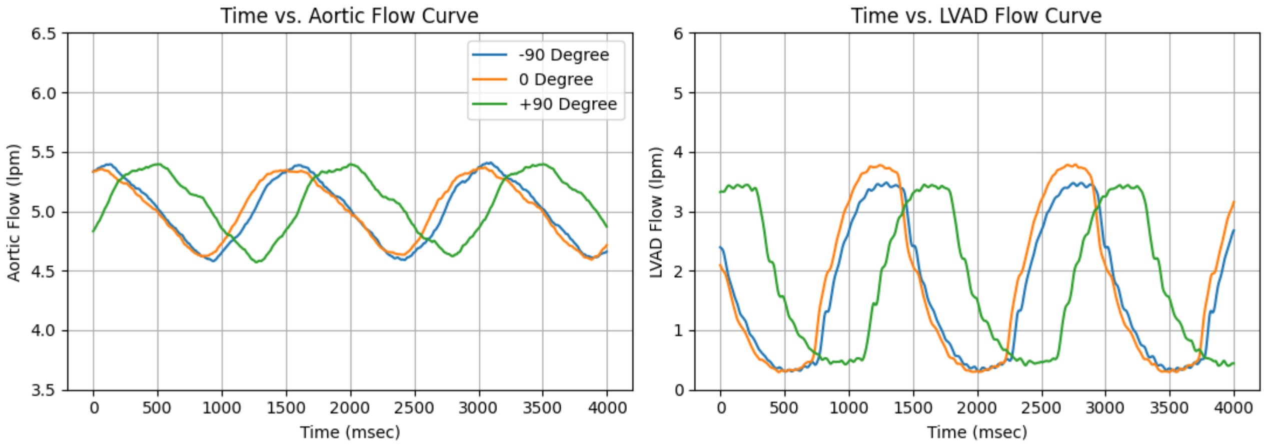



Figure 7.19: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

## 4.5 lpm - 55 mmHg to 5 lpm - 120 mmHg at 80 bpm

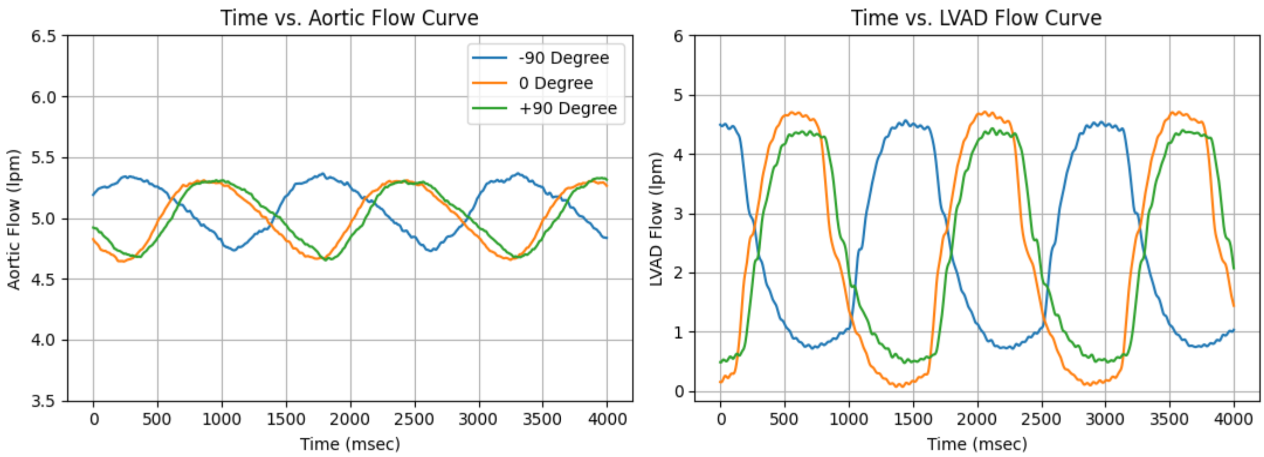



Figure 7.20: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

## 2.5 lpm - 55 mmHg to 4 lpm - 80 mmHg at 120 bpm

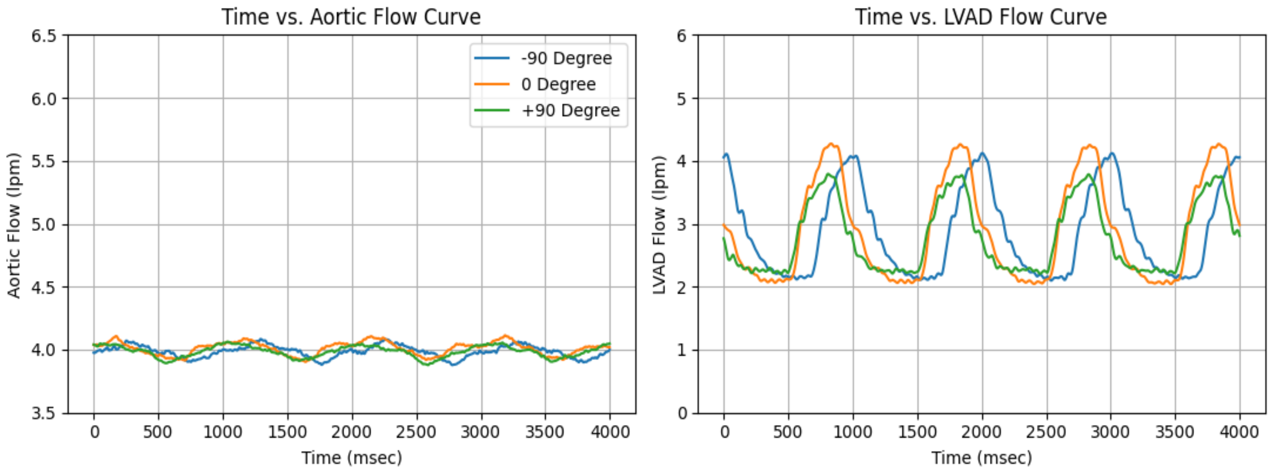



Figure 7.21: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition

## 2.5 lpm - 55 mmHg to 4 lpm - 120 mmHg at 120 bpm

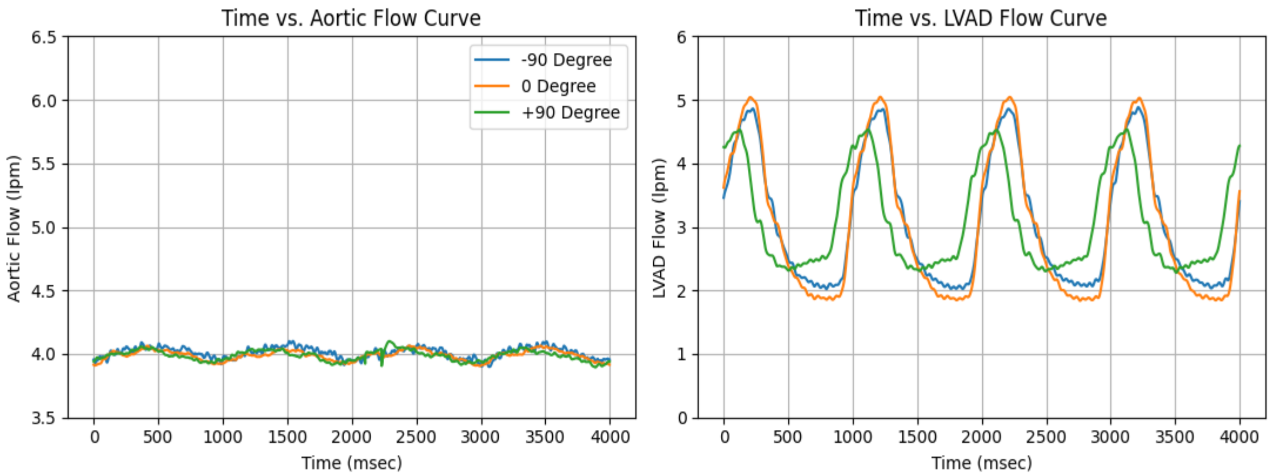



Figure 7.22: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

## 4.5 lpm - 55 mmHg to 5 lpm - 80 mmHg at 120 bpm

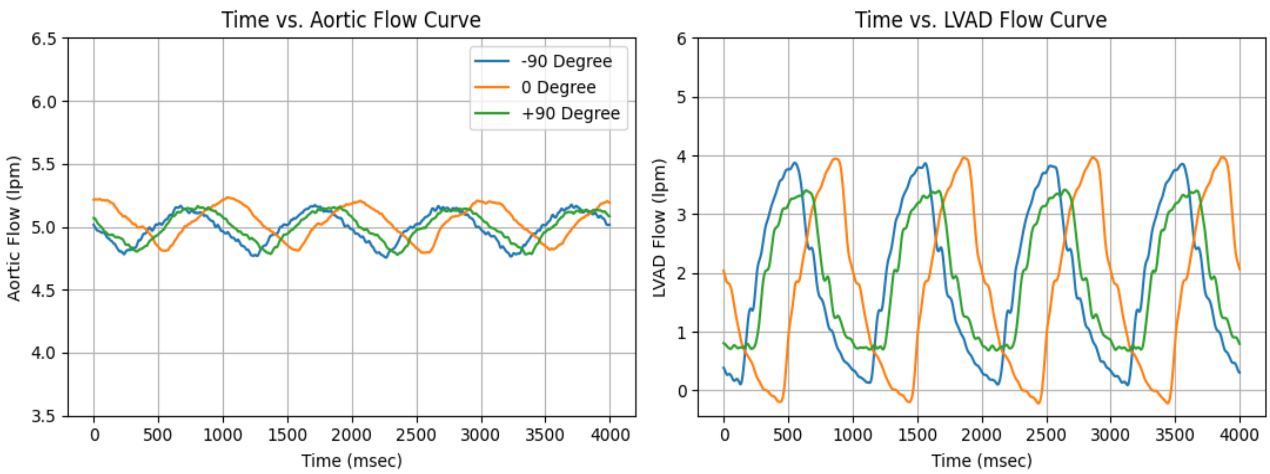



Figure 7.23: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

**2.5 lpm - 55 mmHg to 4 lpm - 120 mmHg at 120 bpm**

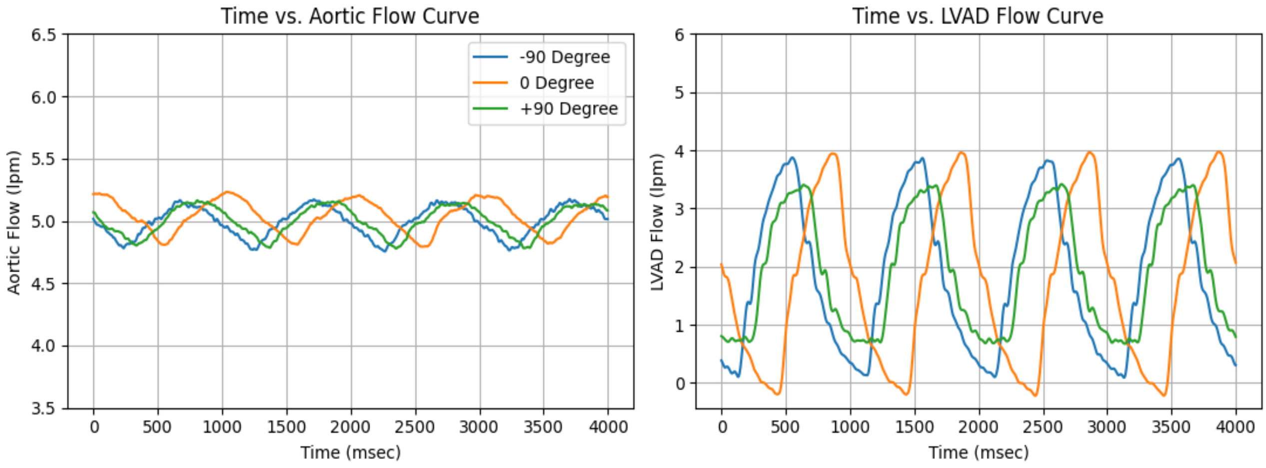



Figure 7.24: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for above condition.

The average values of Aortic Flow and LVAD Flow have insignificant effect of orientation which is also supported by the Speed vs. LVAD Flow curves mentioned in the parameter plots. However, it can be observed that when the variation is plotted at instantaneous levels, the amplitude of LVAD flow for some conditions is more for 0 degree orientation than the other two orientations [-90 degree and +90 degree]. On the other hand, the Aortic flow has no effect of orientation even at the instantaneous scale. A slight phase difference is observed in the curves which can be the result of many reasons including the start and stop time of LVAD controller, the instant at which the outputs are acquired, LVAD speeds etc.

### 7.5 Discussion

In this study, an attempt was made to understand the effect of pump orientation on its performance parameters by considering the Chitra pLVAD that is in its developing stage at the institute. The mock circulation loop established using the pulse duplicator system could successfully produce the physiological and diseased conditions required for the experiments. In developing the noncontact bearing mechanism with the help of magnetic levitation technology and hydrodynamic thrust, it becomes very important to understand the effect of orientation of pump on the impeller or rotor under the influence of gravity. The rotor position must be studied to understand its effects on blood cells, wearing of the pump and the performance parameters.

The experiments carried out in this study mainly focus on the performance parameters like pressure difference, LVAD flow, input and hydraulic power, efficiency and how they vary with respect to three extreme orientations [-90 degree, 0 degree, +90 degree] with the pump inlet always facing the ventricle of the model left heart. Other factors that might affect the performance of the pump like hydrostatic pressure and length of the pipes connecting pump to the loop have been taken into consideration. The pump used in this study is a continuous flow centrifugal pump which has a rotating assembly such that the axial suspension is provided by the magnetic levitation and is radially suspended with the help hydrodynamic thrust. This study establishes the effect of postural changes on the performance parameters of the pump once it is implanted. This study focuses on the effect of orientation on the pulsatility index of the pump calculated at different initial cardiac outputs and MAPs. The hemodynamic analysis performed on the left heart model and pump at all the proposed conditions are studied at all three orientations

## 7.6 Conclusions

From the series of experiments performed at different orientations, it can be concluded that the difference of pressure (ΔP) between the outlet and inlet of the pump and the Input power to the pump vary with the orientation under certain conditions. Both the factors mentioned above contribute for higher efficiency at 0 degree orientation. However, no change in flow rate of the pump was observed under any orientation. The pulsatility Index vary insignificantly with the orientation for a large range of initial or diseased cardiac output. The hemodynamic studies of pressures and flows show that there is minimum or no effect of orientation on the Aortic pressure, Left ventricular pressure or LVAD flows at any speed.

### 7.6.1 Limitations

The limitation of this study is that it takes only one value of initial MAP (55 mmHg) and the LVAD speed has a variation of ± 60 rpm at a particular set speed.

### 7.6.2 Future Research

As the study was conducted to broadly understand the effect of orientation on performance parameters, the error analysis was not done which require multiple outcomes for same condition. Thus, an error analysis on the same set of experiments can be done in the future to quantify the error present in the outputs. The experiments can be performed by including more orientations to support the existing outcomes for example, the same set of readings can be taken for +45 degree and -45 degree orientation. The results obtained from this study can be used to optimize the pump design to produce same efficiency and consume low power at all orientations. This study can also help to improve pulsatility index variation at high initial cardiac outputs.

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# Appendices

Appendix 1: Cardiovascular parameters for adults. [Goodwin et. al.]

Appendix 2: Electrical Connection Diagram for Pulse Duplicator system. [Vivitro Labs Inc. Canada]

Appendix 3-A: LVAD Flow vs Pressure Difference (ΔP) at 100 bpm

Appendix 3-B: Speed vs LVAD Flow at 100 bpm

Appendix 3-C: LVAD Flow vs Input Power at 100 bpm

Appendix 3-D: LVAD Flow vs Efficiency at 100 bpm

Appendix 4-A: Hemodynamic Study of Pressure

Appendix 4-B: Hemodynamic Study of Flow

## Appendix 1: Cardiovascular parameters for adults. [Goodwin et. al.]

| Part of circulation | Compartment | Parameter description | Adult value |
|---|---|---|---|
| Total circulation | | Initial total blood volume | 4740 |
| Heart | Atria and ventricles | Heart rate | 72 |
| Intrathoracic | All intrathoracic | Average intrathoracic pressure | -4.0 |
| Left heart | Left atrium | Resistance to forward flow of the inflow tract | 0.00300 |
| | | Mitral valve resistance | 0.00300 |
| | | Diastolic elastance | 0.120 |
| | | Maximum systolic elastance | 0.280 |
| | | Unstressed volume | 30.0 |
| | Left ventricle | Aortic valve and intrathoracic artery resistance | 0.00800 |
| | | Diastolic elastance | 0.0900 |
| | | Maximum systolic elastance | 4.00 |
| | | Unstressed volume | 60.0 |
| Systemic circulation | Intrathoracic arteries | Elastance | 1.43 |
| | | Unstressed volume | 140 |
| | Extrathoracic arteries | Blood flow inertia | 0.000700 |
| | | Resistance | 0.0600 |
| | | Elastance | 0.556 |
| | | Unstressed volume | 370 |
| | Systemic peripheral vessels | Resistance | 1.00 |
| | Extrathoracic veins | Resistance (to forward flow) | 0.0900 |
| | | Elastance | 0.0169 |
| | | Unstressed volume | 1000 |
| | Intrathoracic veins | Elastance | 0.0182 |
| | | Unstressed volume | 1190 |
| Right heart | Right atrium | Resistance to forward flow of the inflow tract | 0.00300 |
| | | Tricuspid valve resistance | 0.00300 |
| | | Diastolic elastance | 0.0500 |
| | | Maximum systolic elastance | 0.150 |
| | | Unstressed volume | 30.0 |
| | Right ventricle | Pulmonic valve and pulmonary artery resistance | 0.00300 |
| | | Diastolic elastance | 0.0570 |
| | | Maximum systolic elastance | 0.490 |
| | | Unstressed volume | 40.0 |
| Pulmonary circulation | Pulmonary arteries | Elastance | 0.233 |
| | | Unstressed volume | 50.0 |
| | Pulmonary peripheral vessels | Resistance | 0.110 |
| | Pulmonary veins | Elastance | 0.0455 |
| | | Unstressed volume | 350 |

Table: cardiovascular parameters of Circulation for Adults. [Goodwin et. al.]

## Appendix 2: Electrical Connection Diagram for Pulse Duplicator system. [Vivitro Labs Inc. Canada]

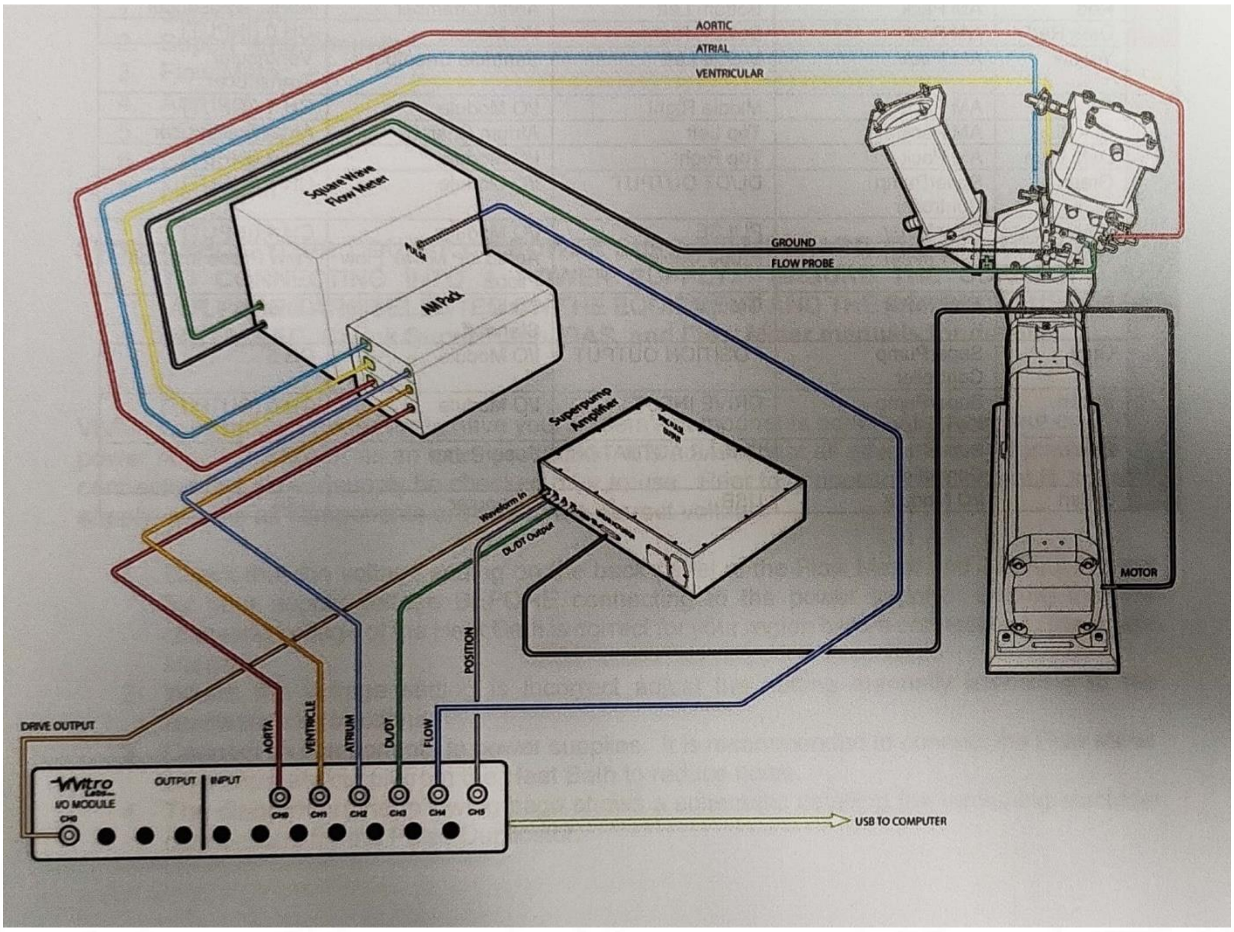


Figure: Electrical Connection Diagram of Pulse Duplicator System. [Vivitro Labs Inc. Canada]

## Appendix 3-A: LVAD Flow vs Pressure Difference (ΔP) at 100 bpm

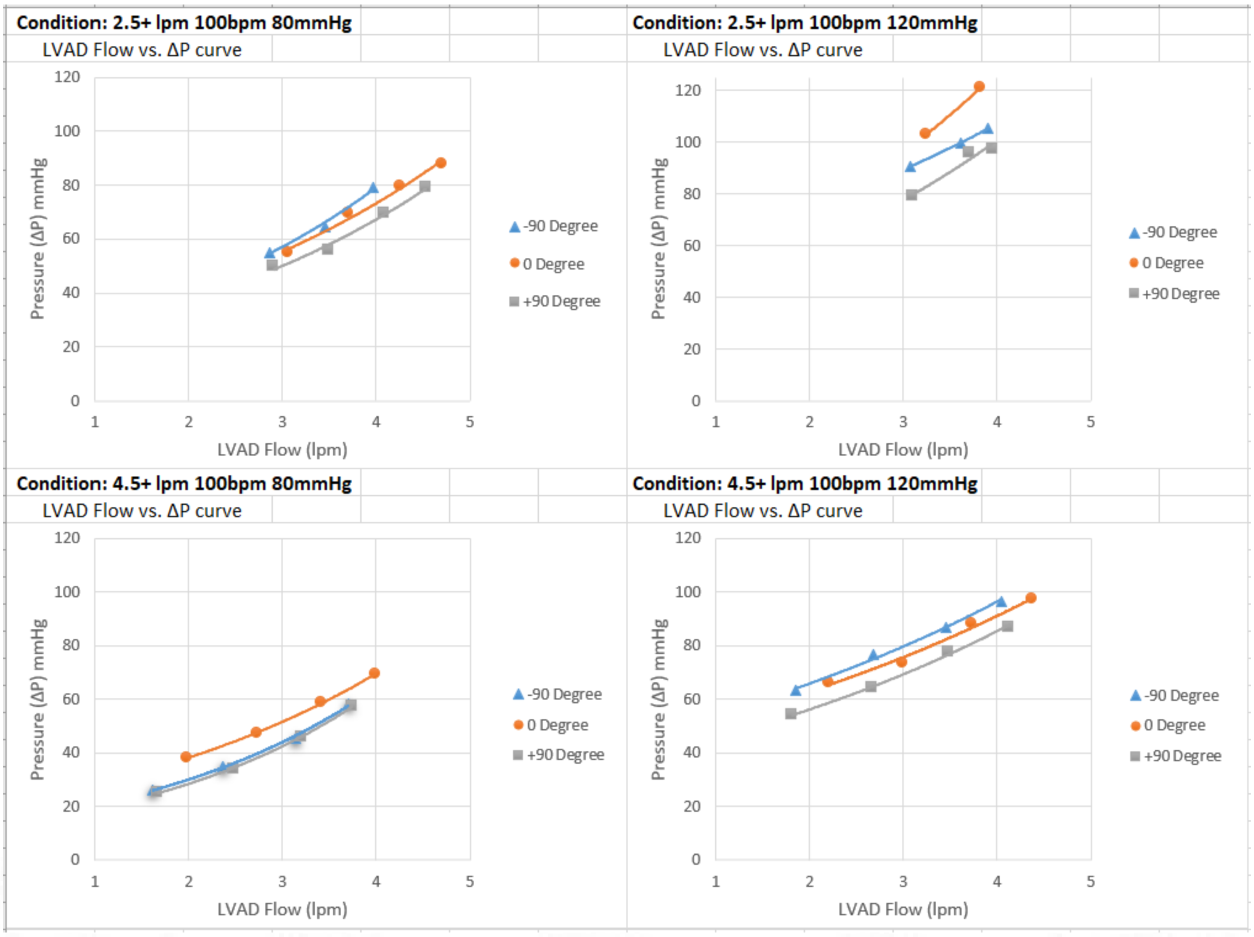


Figure: LVAD Flow vs. Pressure Difference curve for 100 bpm.

## Appendix 3-B: Speed vs LVAD Flow at 100 bpm

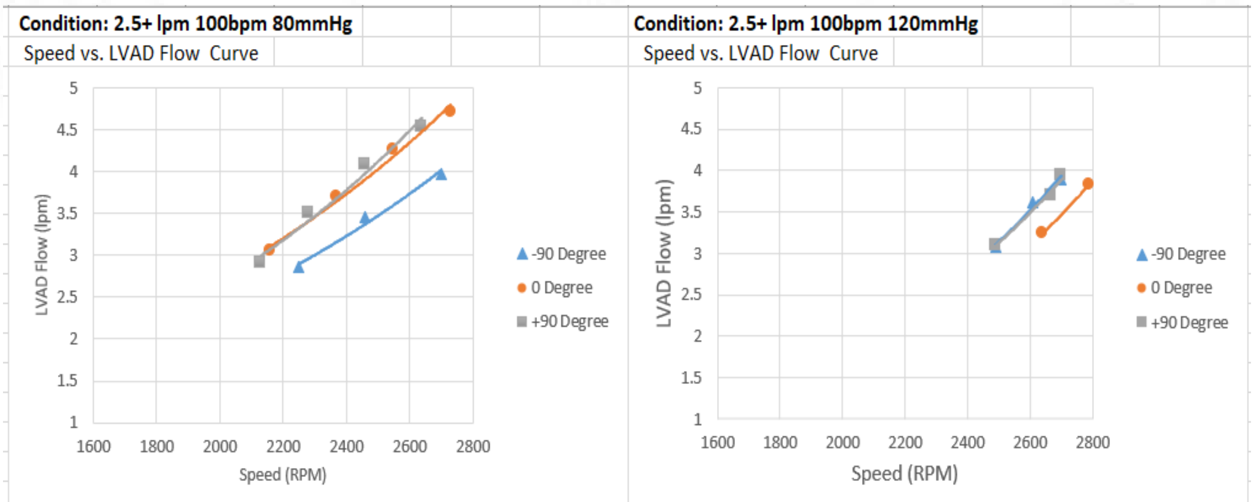


Figure: Speed vs. LVAD Flow for lower (2.5 lpm) initial CO at 100 bpm.

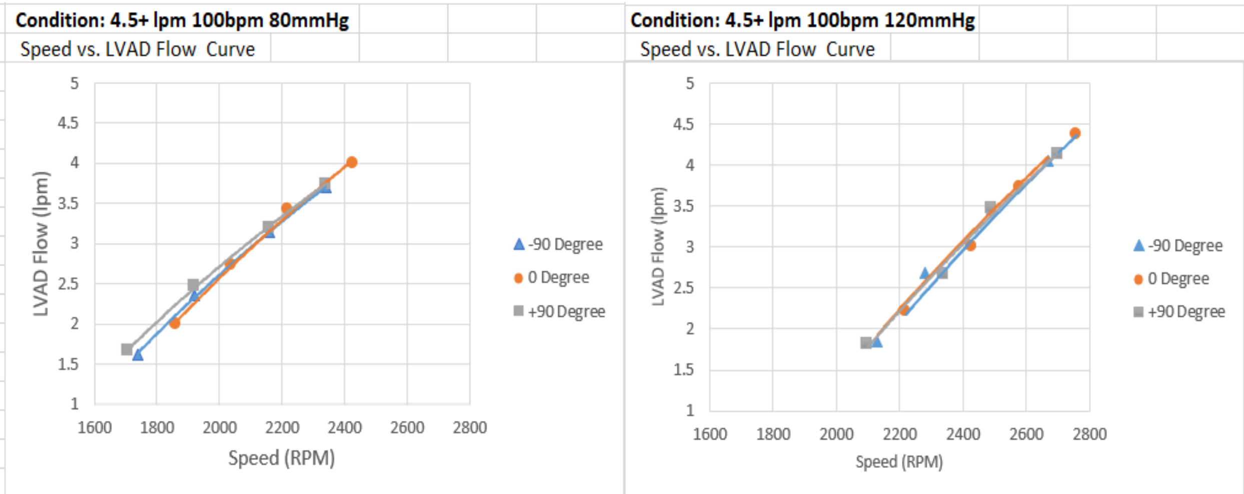


Figure: Speed vs. LVAD flow for Higher (4.5 lpm) initial CO at 100 bpm.

## Appendix 3-C: LVAD Flow vs Input Power at 100 bpm

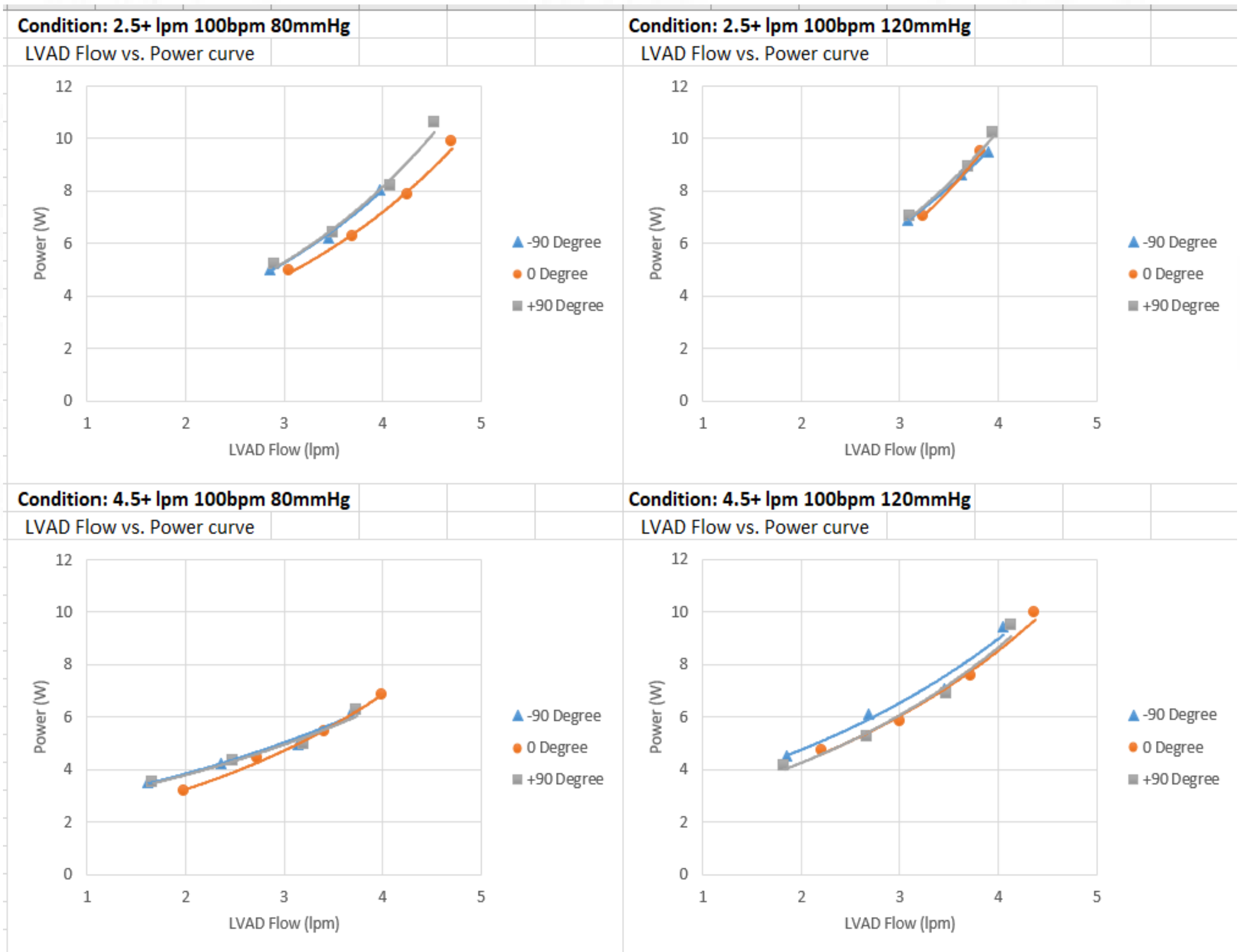


Figure: Power input to LVAD with respect to LVAD flow at 100 bpm

## Appendix 3-D: LVAD Flow vs Efficiency at 100 bpm

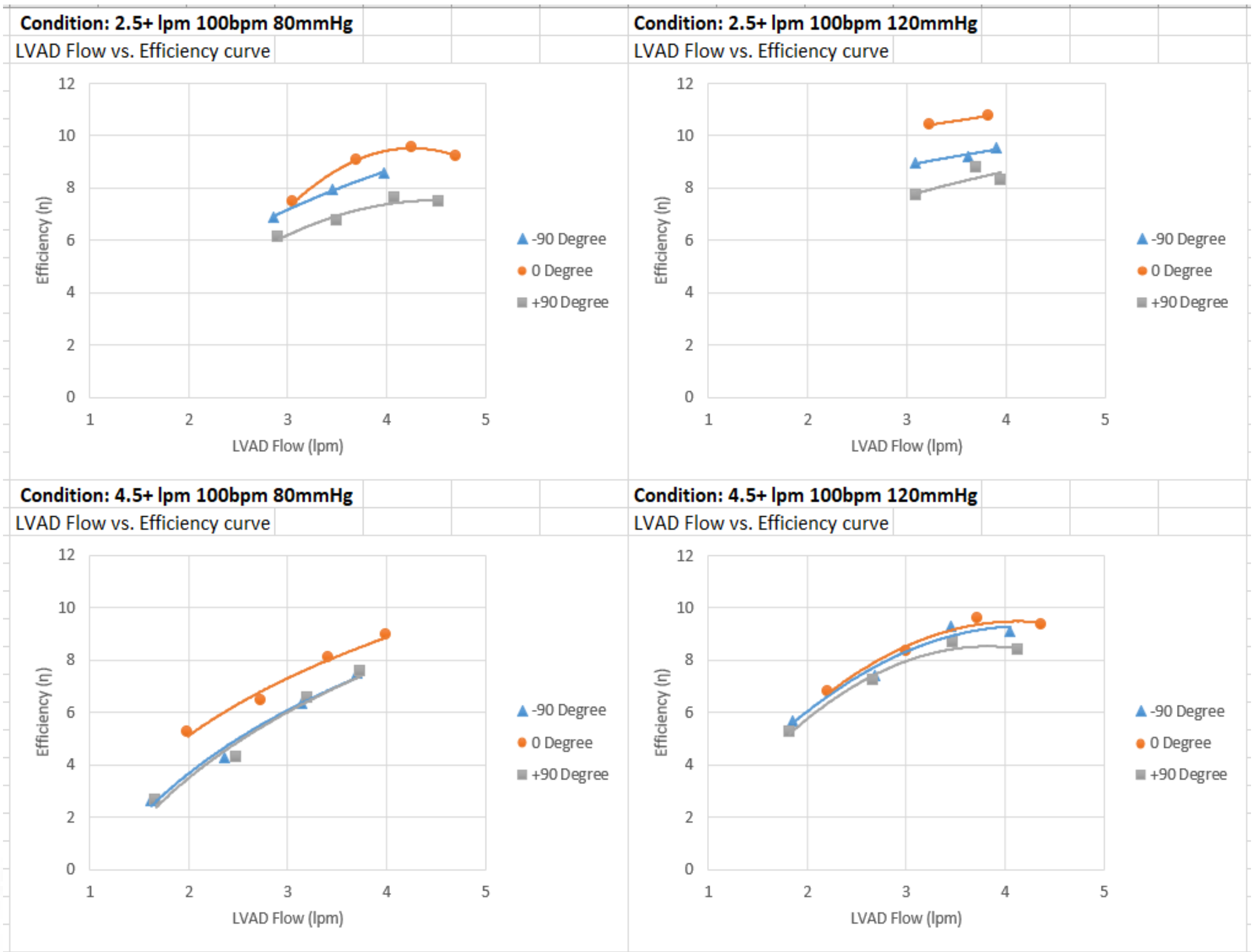


Figure: Power input to LVAD with respect to LVAD flow at 100 bpm

## Appendix 4-A: Hemodynamic Study of Pressure

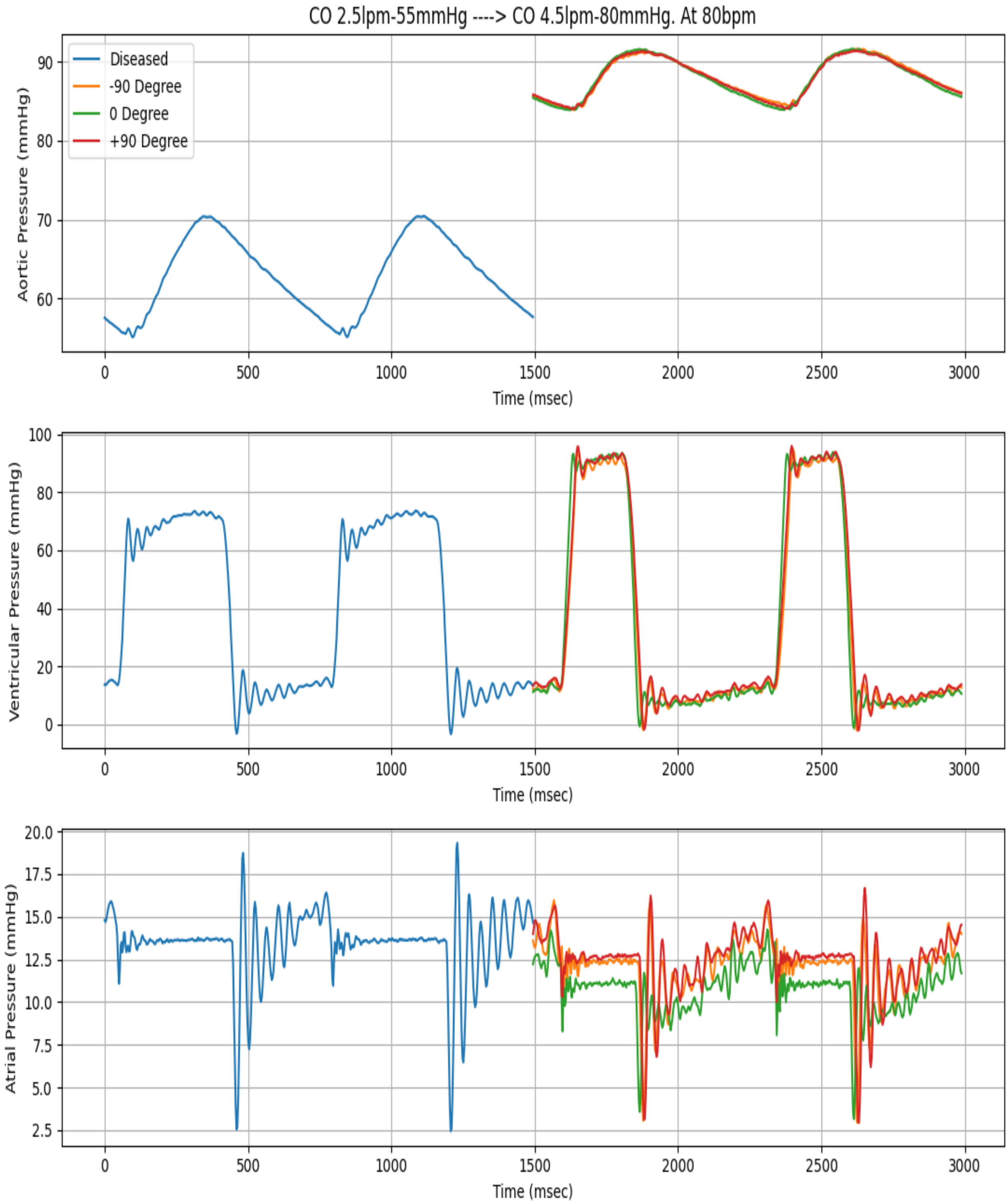


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

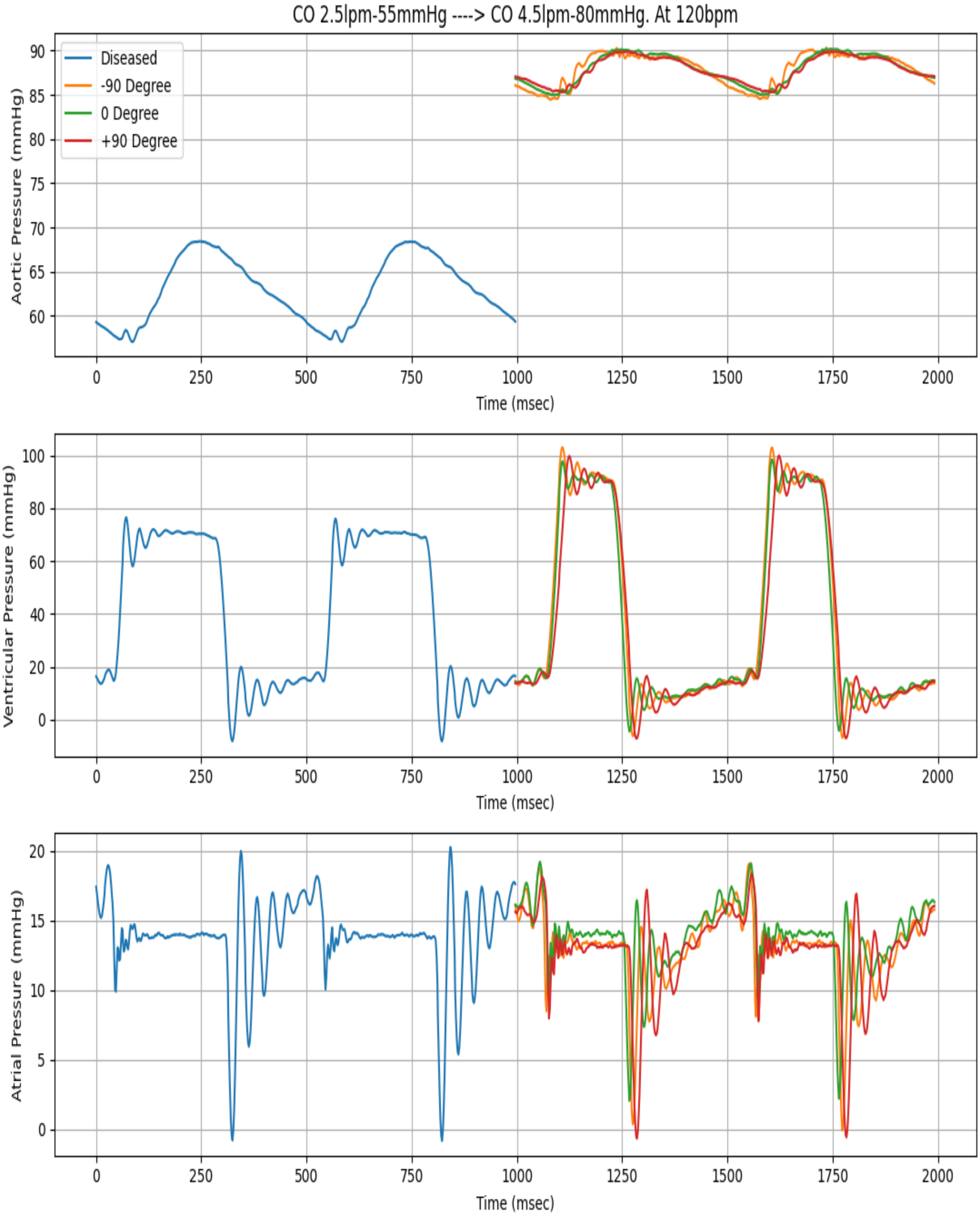


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

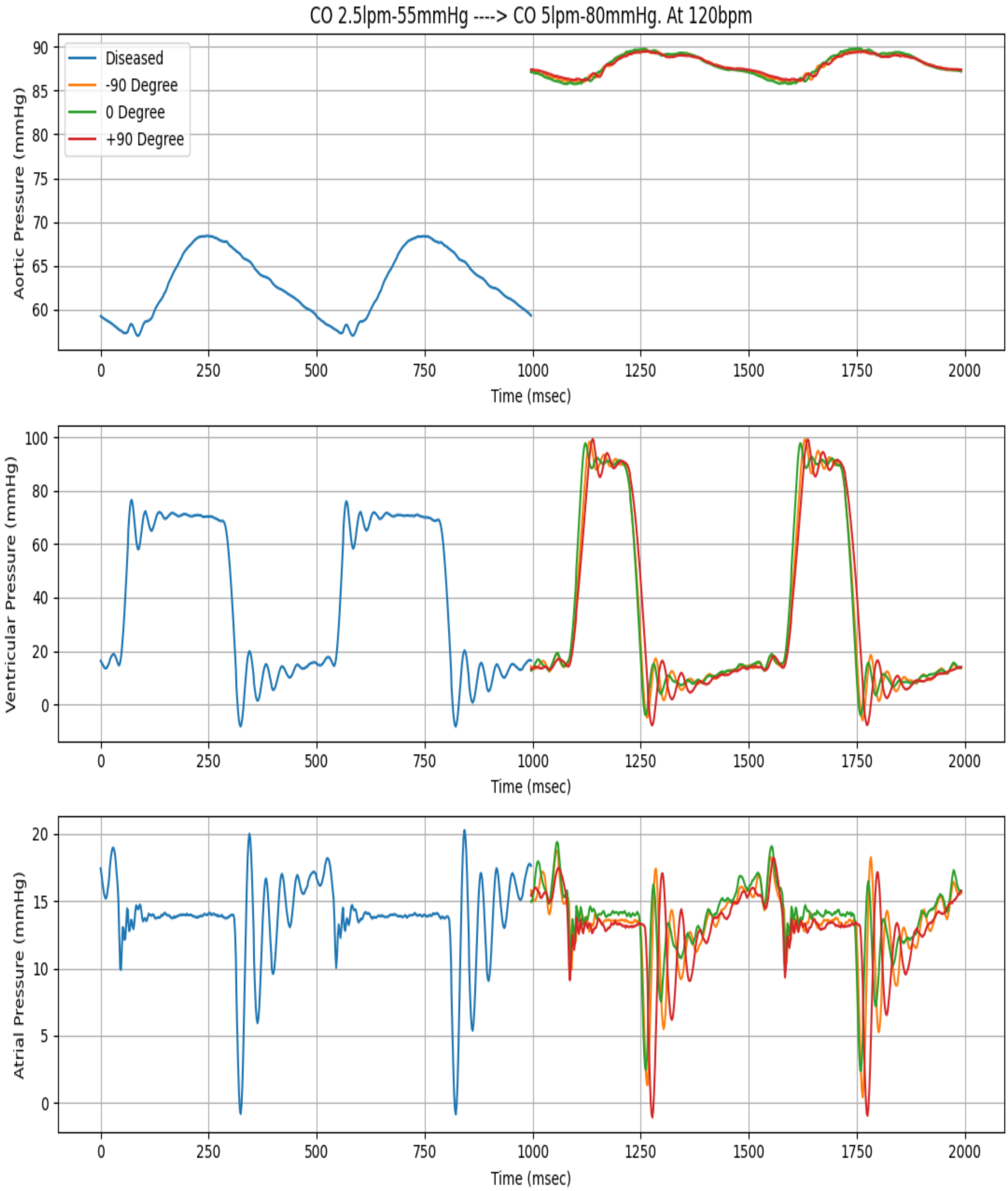


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

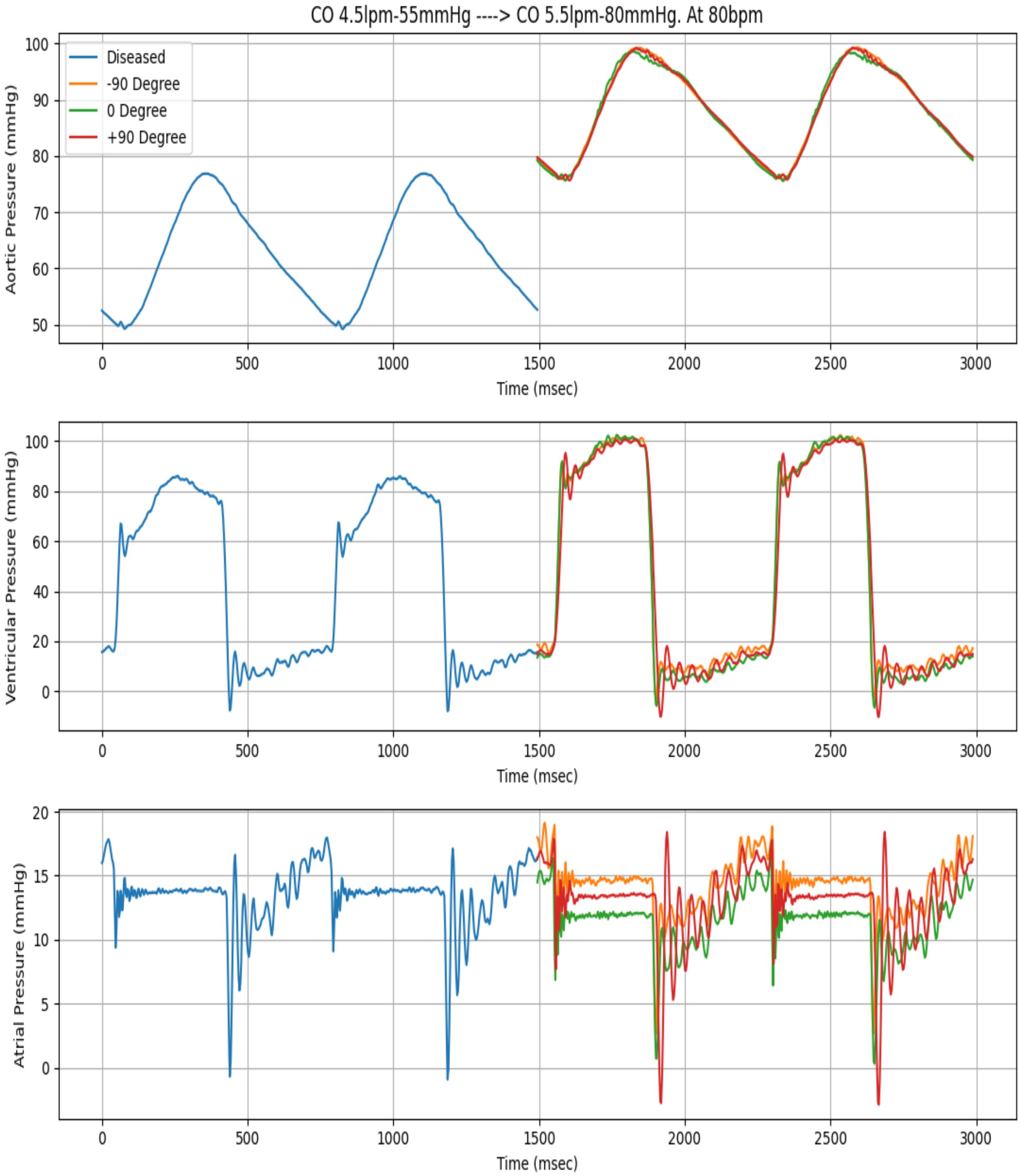


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

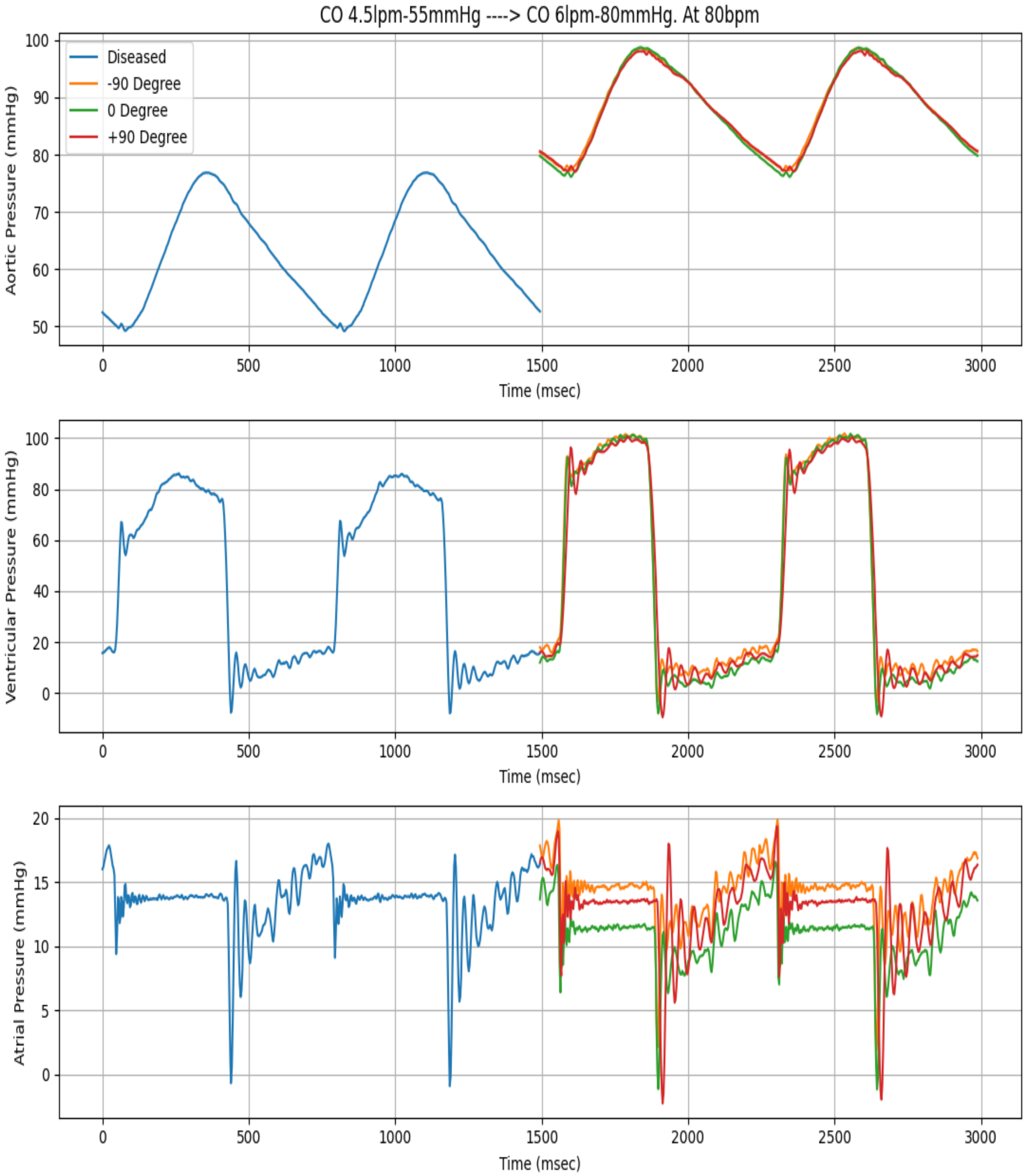


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

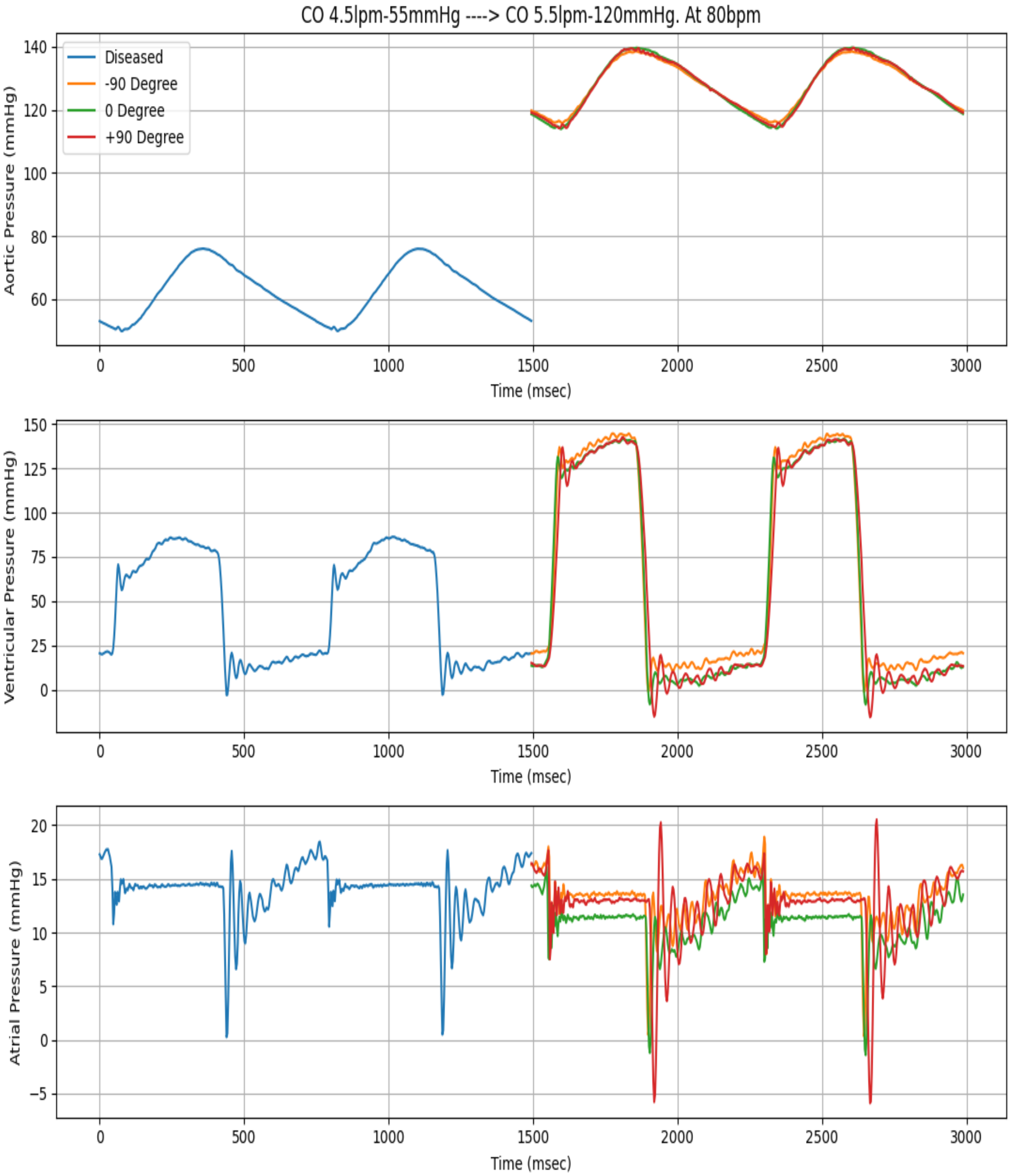


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

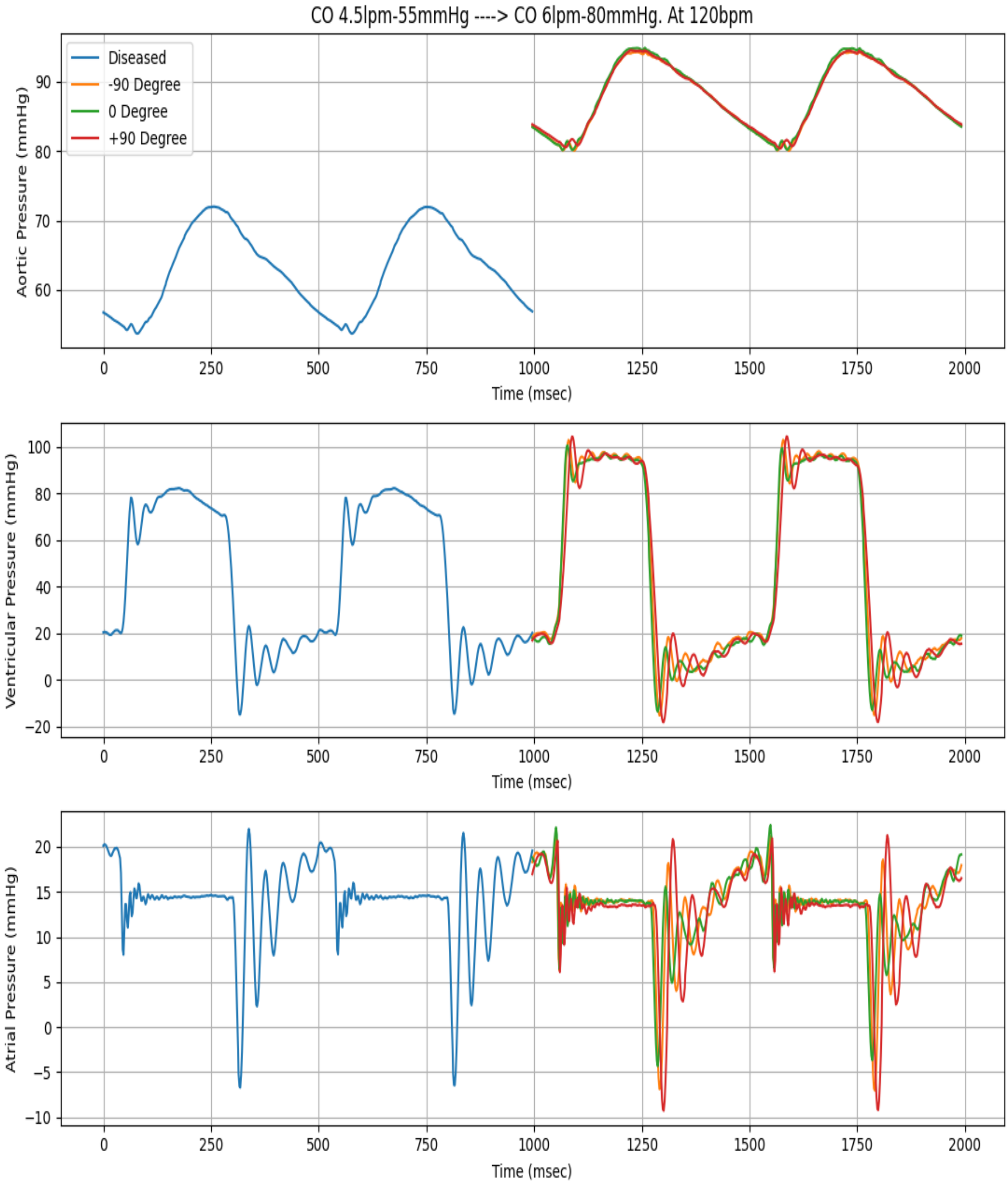


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

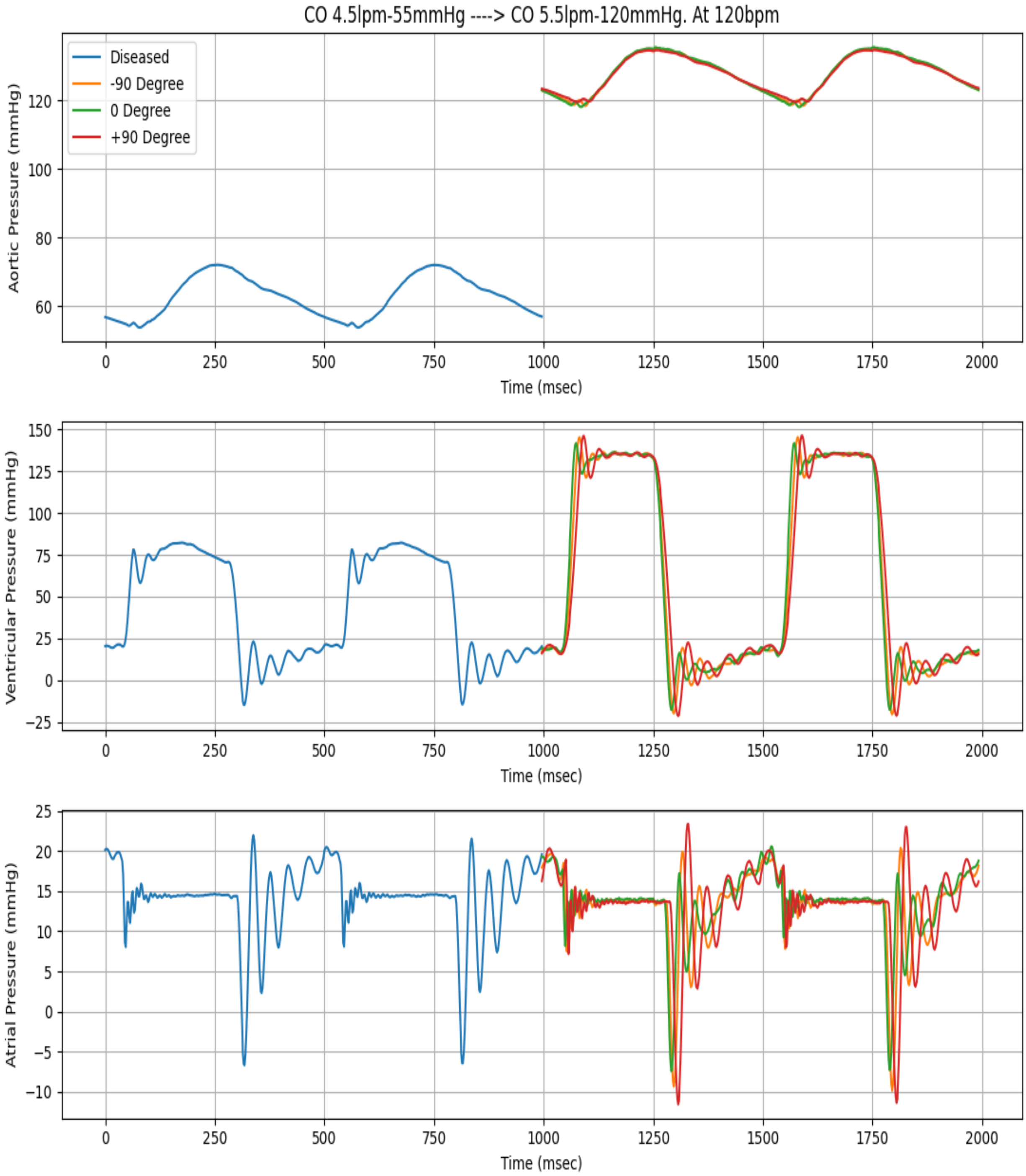


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

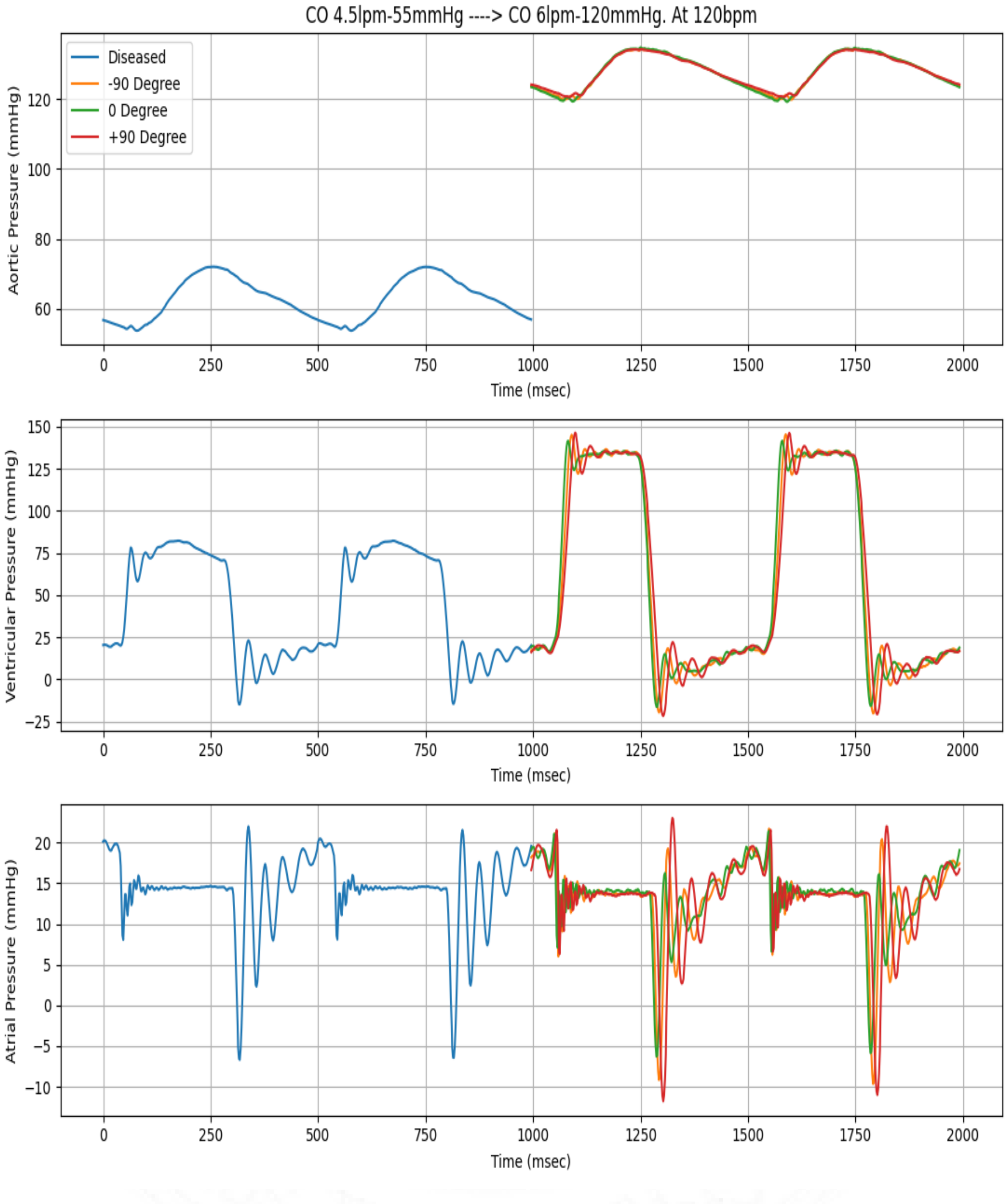


Figure: a) time vs. Aortic Pressure, b) time vs. Ventricular Pressure and c) time vs. Atrial Pressure for the condition given above.

## Appendix 4-B: Hemodynamic Study of Flow

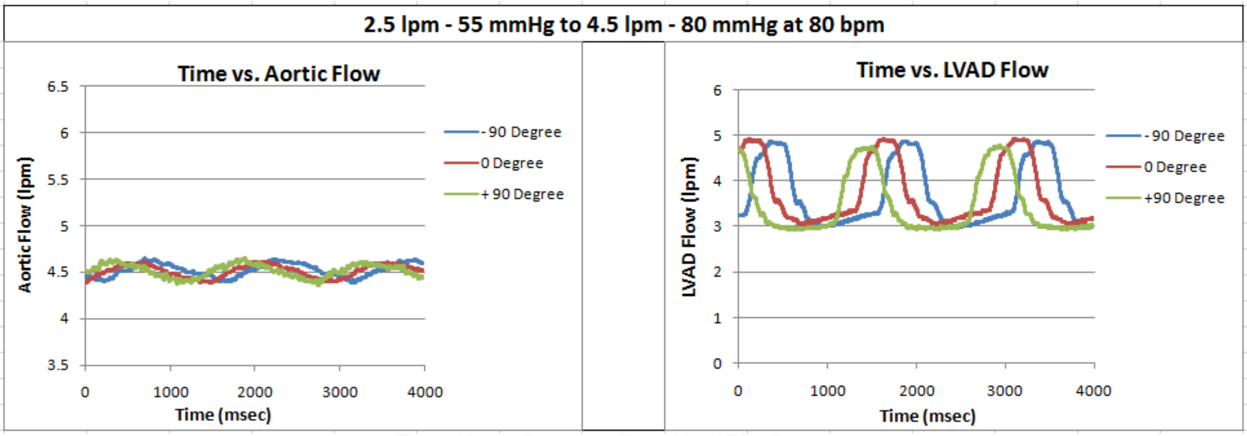


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

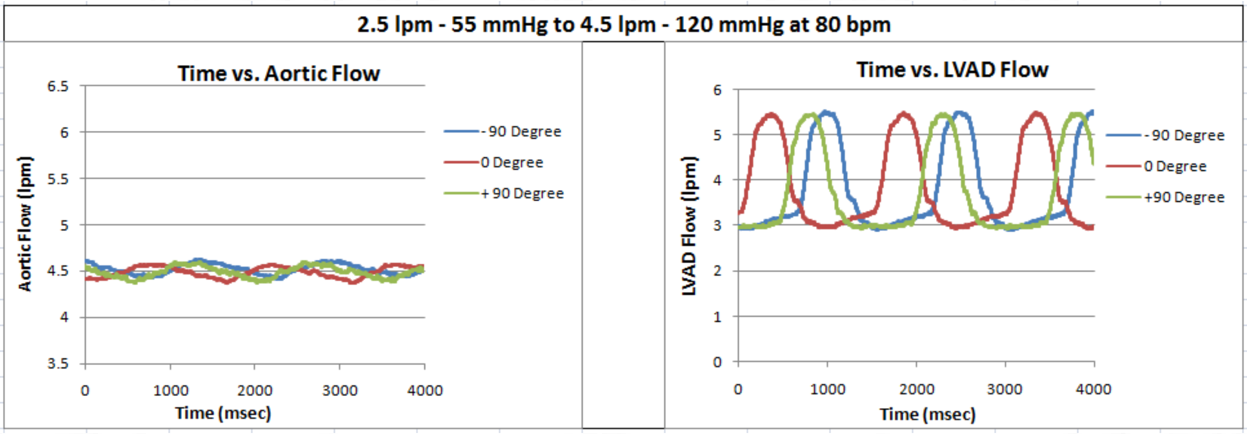


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

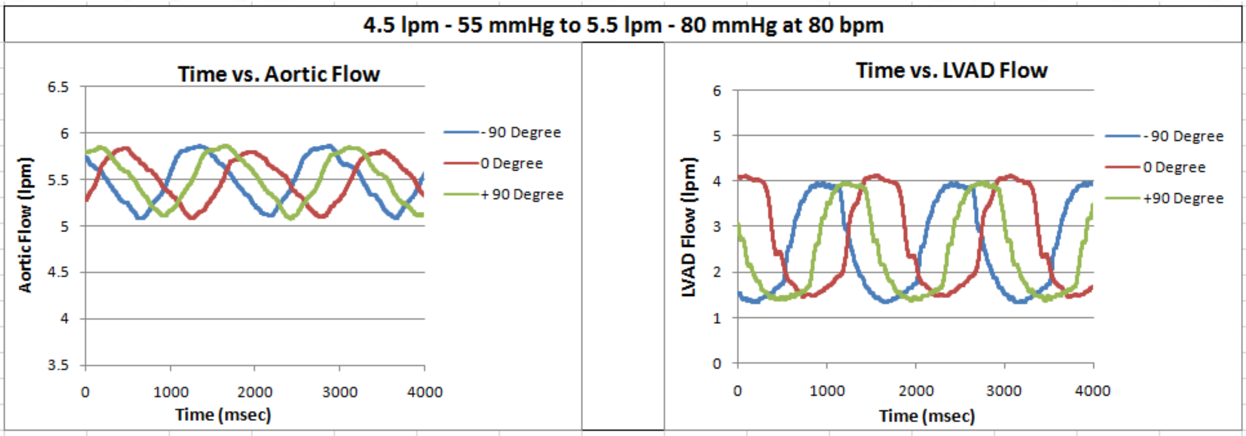


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

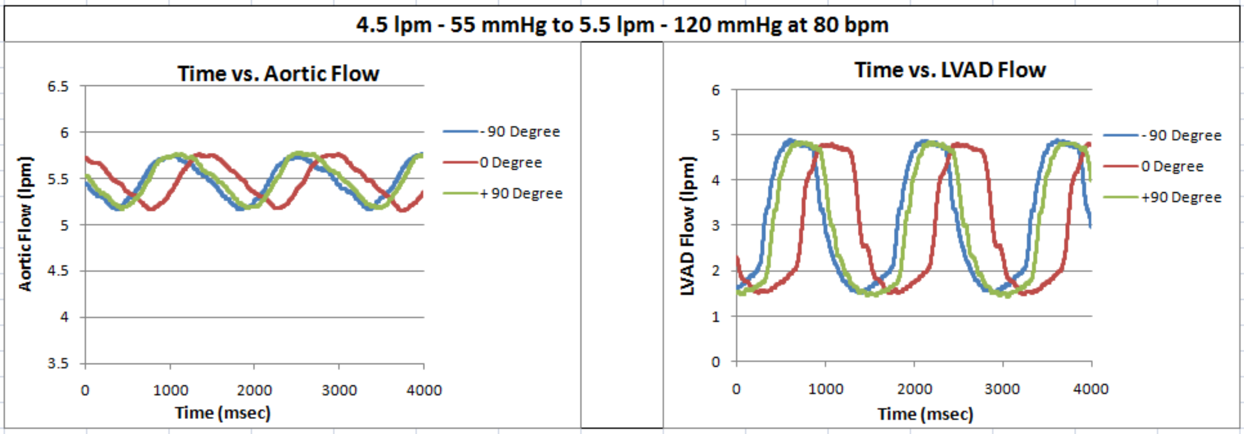


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

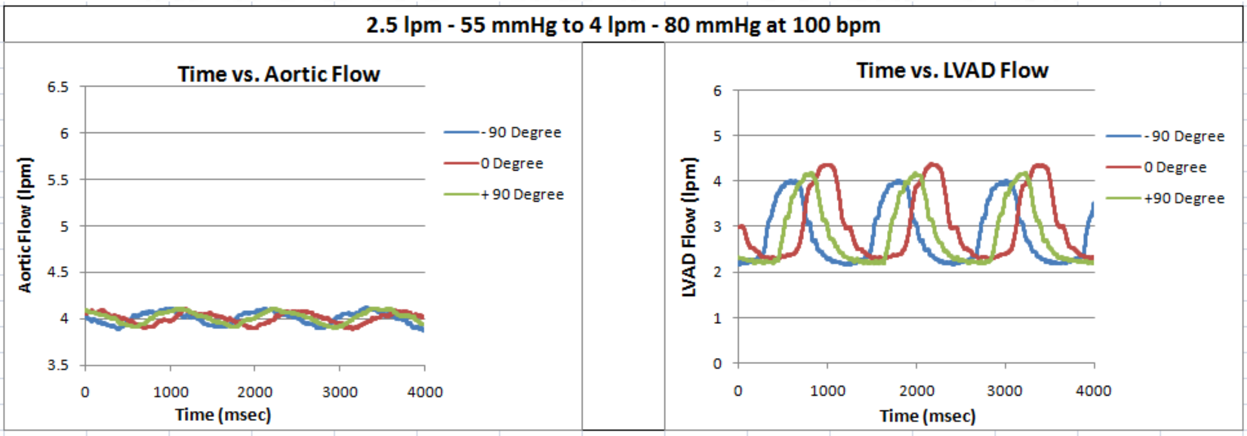


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

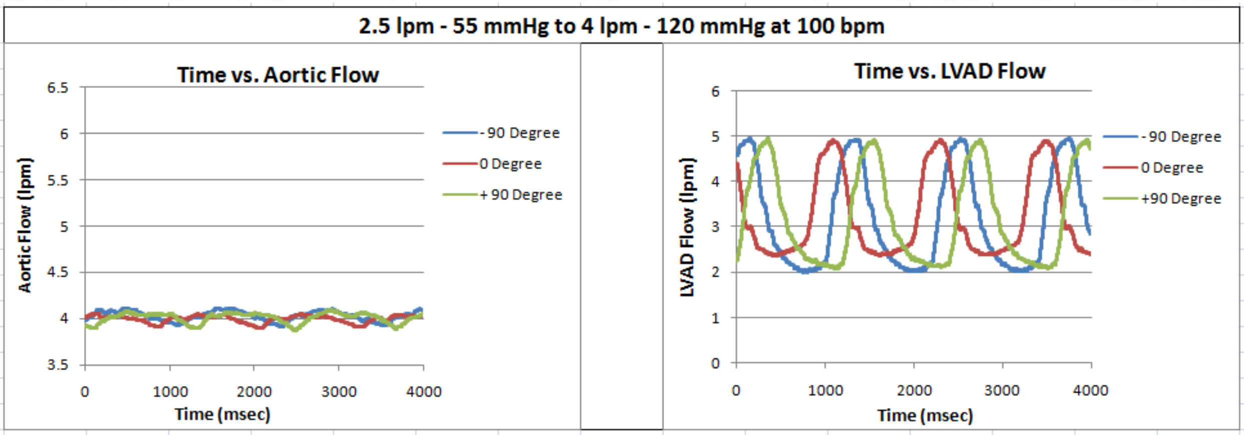


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

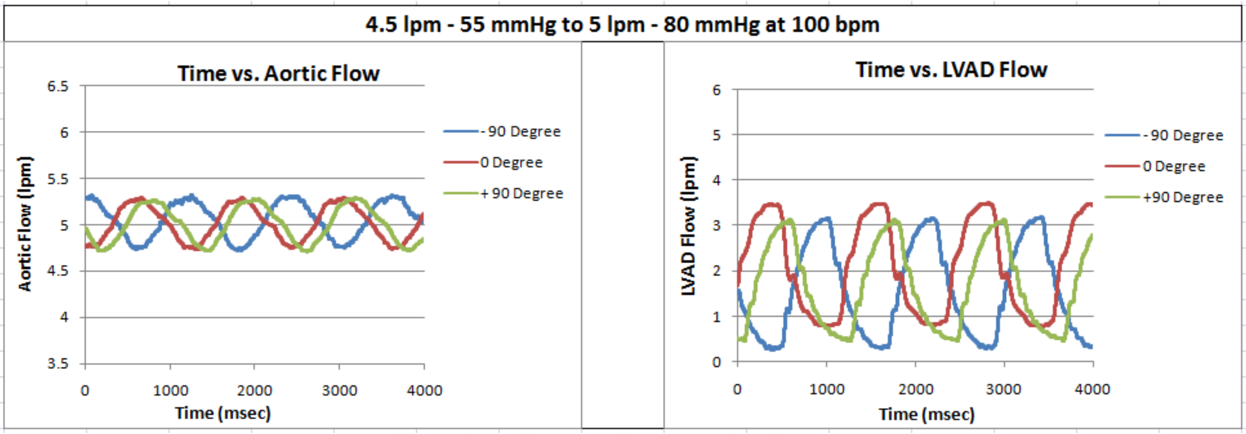


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

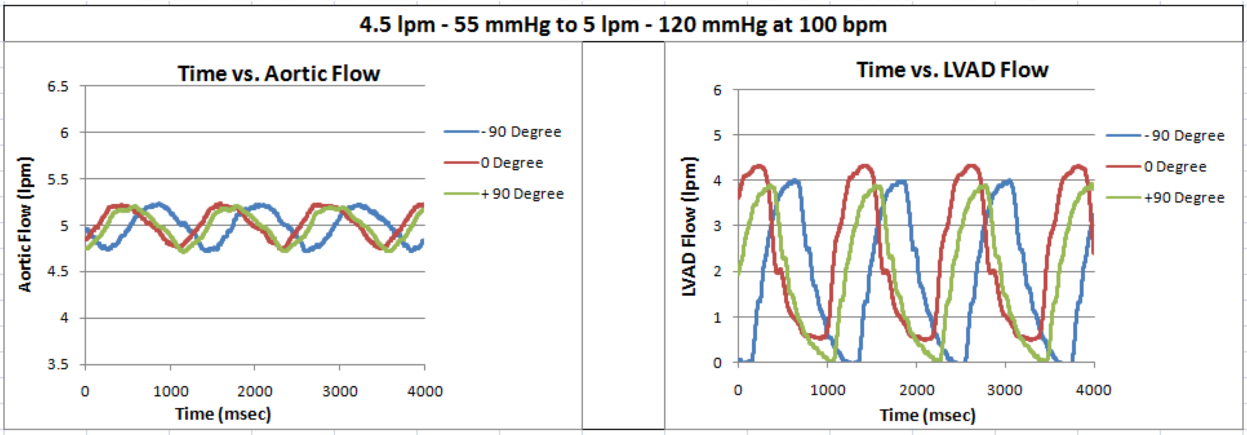


Figure: Time vs. Aortic Flow [left] and Time vs. LVAD Flow [right] for condition shown in the diagram.

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