PROJECT 1: CARDIOVASCULAR MODELLING

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INTRODUCTION

Coronary Artery Disease

The coronary artery is the blood vessel responsible for oxygenating the myocardium of the heart. Coronary artery disease (CAD), or heart disease, occurs when artherosclerotic deposits such as lipids are present in abnormal quantities on the inner walls of the vessel. This causes stenosis in the artery via the narrowing radius of the vessel. The vasculature in proximity may experience turbulence and large pressure drops in regional blood flow.[1]

In the case of coronary arteries, the reduction of blood flow to the heart is concurrent with ischemic effects faced by myocardium. There is an associated weakening of tissue due to the implications of necrosis and tissue death with more severe cases (cardiac infarctions, stroke, thrombosis). In literature the effects of diastole and hypoxic conditions are considered in modelling CAD with symptoms of angina as a reference.[2] Angina is a hypoxic symptom of reduced blood flow to the heart. In practice, it is predicted that the heart will overstretch and require more afterload to eject the blood over time due to the weakening of myocardium under hypoxic conditions (i.e. cardiomegaly).

A few studies and overviews of literature describe haemodynamics of systemic vascularization under similar conditions. Models of CAD are useful in the simulation of heart failure and comorbidities to better understand pathophysiology, diagnosis, and potential outcomes of medication use. Similarly, parameters for cardiovascular simulation (CVS) are informed by mechanics of the ischemic myocardium of the heart in this study.

Vascular Occlusion

Blood is a primary carrier of oxygen and other essential compounds in the vascular system to remain living in organs, including the heart.[1] Vascular occlusion describes when a blood vessel has been blocked by a clot, thus prohibiting blood flow to a localized region. A lack of oxygen is commonly associated with necrosis. In cases where the blocked artery is a limb resulting in critical limb ischemia, there is a need to revascularized the limb or, in the worst case, amputate.[3]

For the purpose of this study, this described occurrence will be referenced as a nearly anoxic event to any region of the body.

Concurrent Diseases

When vascular occlusion occurs leading to myocardial infarction or stroke, it is due to the tearing or erosion of a fibrous cap. Blood platelets aggregate this region and cause this fatal blockage. The preceding lesion or fibrous cap is often formed in lieu or as a symptom of coronary artery disease which will also be explored in scope of this study. Therefore, vascular occlusion will be simulated both independently, generally to systemic arteries, and in the presence of coronary artery disease. [4] It was difficult to find studies separating these hemodynamics from others (independently). In this experiment it is aimed to see covariance between the two independent diseases.

It is the objective of this study to compare the evolution of coexisting heart dysfunction in the form of hemodynamics and heart related effects of vascular diseases using the cardiovascular simulator (CVS) from Cornell University by Dr. James Antaki.

MATERIALS AND METHODS

Cardiovascular Simulator and Healthy Baseline

The CVS is a cardiovascular simulator that allows users to simulate and compare normal and disease oriented conditions in the heart, as well as ventricular assist devices (VAD). For the purpose of this experiment all VAD related settings were not used. In preliminary use, baroreceptor control was set to "all," but was settled to "non-heart" due to the inflexibility of reading the rapidly adjusting parameter outcomes of the simulation. All settings followed the recommended baseline parameters for a healthy individual. These were already defaulted values.

Simulating Coronary Artery Disease

As prefaced in the description of CAD, properties of moderate ischemic myocardium will be the focus for simulation parameters. For the purpose of simplification and the known dominance of left ventricle (LV) function, CAD is simulated in the left coronary artery. Since the coronary arteries are a part of systemic circulation, under the "Heart Disease" tab of CVS, the systemic resistance labelled "LV Afterload" was increased from the default 0.06 to .1125 mmHg•s•ml^{-1} [5] based on study measuring symptoms from heart diseases, including CAD.

Related clinical studies have demonstrated decreased LV compliance[6] which informed left ventricular compliance decrease in CVS. Taking "LV Elastance" as the reciprocal of compliance, elastance was increased to its simulated max of 2.7 mmHg/mL from 2.4. This value was estimated and the midpoint of maximum compliance which is used in the combined simulation case.

Dilated heart failure parameters were intuitive based on discussed ischemic physiological effects, but it contains too many variables and assumptions for this experiment. Only left ventricular compliance/ elastance and systemic resistance were used as altered parameters.[7]

Simulating Vascular Occlusion

Based on vascular occlusion pathophysiology, common physical laws used in description of occlusive hemodynamics will be referenced for use of simulating vascular occlusion. Predicted measures use concepts of fluid dynamics, including Poiseuille's Law, turbulent flow, and equations for compliance, and laws of serial and parallel resistance.[8] The following parameters were adjusted accordingly: systemic pressures decreased by greatly increasing the systemic resistance without impacts on compliance because the heart tissue is untargeted.

To exclude the coronary artery, to show ischemic effects outside of the heart, the femoral artery was an example for simulation, causing critical limb ischemia (CLI). A corresponding study with hemodynamic data is used for simulation. The ankle-brachial index (ABI) used in reference was 0.4, which indicates severe arterial stenosis. Valvulo-arterial resistance is found to be 1,810 dyne·s·cm^{-5} or 0 .1375 mmHg•s•mL^{-1} in groups with severe arterial stenosis.[9] This value was used as the "LV Afterload" (systemic resistance). Systemic arterial compliance is shown to be 0.89 mL/mmHg and was used for Csa in the "Dilated HF" tab.

Simulating Coronary Artery Disease Progressed to Coronary Occlusion

To stimulate the concurrency, vascular occlusion was reduced to follow a scenario in study which included total vascular occlusion of the left main coronary artery. A case study patient (Case 6) who suffered a myocardial infarction was used in reference of realistic parameters.[10]

In simulation the combined parameters from both CAD and vascular occlusion were unioned and adjusted in extremity. Thus, overlapping parameters were maximized. In summary, LV compliance from CAD simulation was used and Csa and systemic resistance parameters were used from vascular occlusion simulation. To account for drastic changes in the heart structure, from ischemia and infarction due to coronary occlusion, the linear end-systolic pressure-volume relationship (ESPVR) was changed to the first non-linear LVF (left ventricular failure).

Table 1. CSV parameters for each variation of simulated cardiovascular function. Variables/ variations highlighted in yellow.

Parameters	Case of Simulation			
Heart Disease Tab	**Normal Baseline**	**Coronary Artery Disease**	**Vascular Occlusion**	**Combined Disease**
Left Ventricular, LV Elastance (Elvmax: mmHg/ml)	2.4	2.7	2.4	2.7
LV afterload (Systemic Resistance: mmHg•s•ml-1)	0.06	**0.1125**	**0.1375**	**0.1375**
Heart Rate (HR: bpm)	83	83	83	83
Total Blood Volume (TBV: ml)	5300	5300	5300	5300
Dilated HF				
Systemic Arterial Compliance, Csa (ml/mmHg)	0.28	0.28	0.89	0.89
Left Ventricle End-Systolic Pressure Volume Relationship, LV ESVPR Hypothesis	Linear	Linear	Linear	Non-Linear (ESVPR 1)

RESULTS

From raw pressure and volume vs. time curves, we can compare the four simulated cases – normal baseline, CAD, vascular occlusion, and combined disease (*Figures 1-2*). The CAD simulation resulted in elevated LV pressure while vascular occlusion did not affect this parameter. The combined or concurrent result did lower the LV pressure. Aortic valvular blood flow was normal in vascular occlusion but with halved aortic flow. Both flows were similarly affected in the concurrent case. CAD only led to a slight decrease in both metrics.

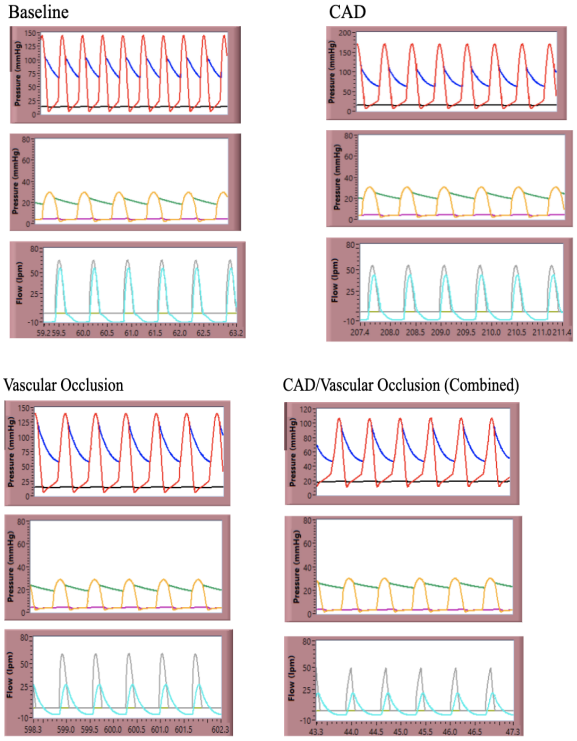

Figure 1/2. Depiction of left and right heart pressures (mmHg) and volumes according to time (minutes) for the conditions normal baseline, CAD, vascular occlusion, and combined CAD/vascular occlusion. For red = left ventricular, black = left atrial, blue = aortic; gold = right ventricular, green = pulmonary arterial, pink = right atrial; light blue = aortic flow, grey = aortic valvular flow, light green = pump flow.

Stroke volume is visible by the difference in the bottom left and right corners of the pressure loops. Combined disease had the most significant decrease from the healthy baseline. MAP, an average of blood pressure metrics, decreased in the same fashion. All ejection fractions decreased from the normal baseline, but values were low and skewed. Cardiac output had the same relationship.

Table 2. The output parameters for each variation of simulated cardiovascular function. Ejection fraction calculated from the stroke volume and end-diastolic volume from the PV curves.

	Case of Simulation			
Measurements (from PV Curve)	**Normal Baseline**	**Coronary Artery Disease**	**Vascular Occlusion**	**Combined Disease**
Right Atrial Pressure (ml/mmHg)	3.94	3.76	3.69	2.73
Left Atrial Pressure Mean (ml/mmHg)	12.99	14.68	14	12.66
Max Left Atrial Pressure (mmHg)	15	15	16	19
Mean Arterial Pressure (ml/mmHg)	96.63	99.67	90.56	56.72
Max Aortic Flow (L/min)	57	18	27	20
Max Aortic Valve Flow (L/min)	75	55	60	50
Max Left Ventricular Pressure (mmHg)	145	170	140	107
Stroke Volume (mL)	57.54	55.18	50.43	36.02
Total Cardiac Output (L/min)	4.88	4.68	4.28	3.06
Ejection Fraction	0.2996875	0.2801015228	0.2654210526	0.1774384236

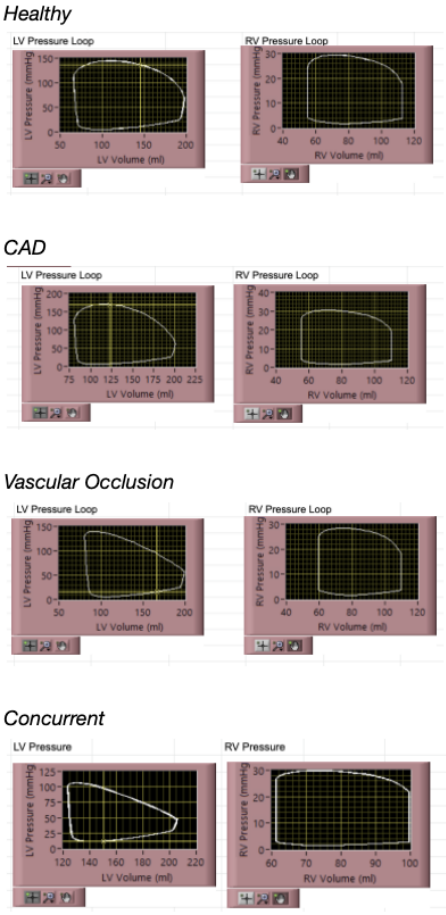

Figure 3. Side by side comparison if left and right ventricular PV curves per one stable cycle.

DISCUSSION

Pulsatile Pressure and Flow

It was predicted that the LV pressure needed to eject blood would be increased due to the elasticity parameter increase. Mechanically, it was expected for a stiffer object to contract more force against the blood's load. Similarly this follows mean arterial pressure (MAP) being the most elevated for CAD (*Table 2*). In order for the aortic valves to open the aorta/systemic arteries must reach the same pressure as the systolic LV. CAD is commonly associated with hypertension which is displayed theoretically within the results.

Aortic valvular blood flow was normal in vascular occlusion but with halved aortic flow which would suggest that the heart is able to properly contrast and mechanically eject the stroke volume (SV), but there may not be enough blood making it to or out of the heart via a systemic blockage.

PV Curves and Derivations

From CAD to vascular occlusion, to the concurrent condition, there are decreasing SV and somewhat smaller work volumes output by the left heart. Additionally, the work from the right heart seems to increase in vascular occlusion because of the increased systemic resistance parameter. There is overall commonality in increased LV pressures across disease variations. The concurrent disease has its worst effects in overlapping regions of pressure differences between CAD and occlusion (such as LV pressure, SV, cardiac output).

In comparative applications to studies, increased MAP were found to be greater in patients with CAD (98.07 ± 11.67).[11] Since relaxation is required for ventricular filling, there was a suspected decrease in stroke volume. A prediction of LV pressure can be given by the time relaxation constant (tau) which is dependent on this loading factor. Prolongation of tau led to higher LV pressures as measured in cases of coronary ischemia.

There is overlap in the results of the simulation with existing literature. However, current doppler radars and sensors can measure some hemodynamics in existing patients without fully recognizing which risk factor in a disease contributes to a certain preventative process. In this study, which precursor of combined conditions, occlusion and CAD, most greatly affects the heart in disease outcomes was discussed, in context of cardiac infarctions and the start of cardiomegaly.

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