SymBioSys Exercise 2 – Cardiac Function
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The goal of this exercise to explore the behavior of the heart as a mechanical pump. For the purposes of this exercise, the heart can be considered to exist in either a relaxing state (diastole) or a contracting state (systole). Cardiac filling occurs during diastole, while systole begins when the sinoatrial node initiates a heart beat. The primary determinants of cardiac function are preload, afterload, contractility, and heart rate. As a first approximation, the term *preload* refers to the left ventricular volume at the end of diastole, while the term *afterload* represents the aortic pressure, against which the ventricle must contract. The term *contractility* refers to the intrinsic strength of the mechanical pump, and *heart rate* is obvious. In this exercise, we will examine each of these concepts in more detail.

If left ventricle's (*LV*) pressure is plotted against its volume, the result is a loop (see Figure 1). In either systole or diastole, pressure inside the left ventricle is a function of the volume it contains and its compliance. In diastole, the ventricle tends to be highly compliant (i.e., floppy), while in systole its compliance is relatively small (i.e., it tends to be stiff). In mechanical terms, contraction appears as a transition between these two states. After a contraction, the relaxed ventricle begins to fill. As the left ventricle begins to contract, the pressure in the ventricle increases until it exceeds the diastolic pressure in aorta, at which point the aortic valve opens and the ventricle begins to eject. Ejection continues against the afterload (effectively the aortic pressure) until the pressure in the ventricle decreases to less than the aortic pressure. At this point, the aortic valve closes and ejection ceases. The end of systole is defined as the upper left corner of the PV-loop, and precedes the end of ejection by several milliseconds. For the purposes of this discussion, we will not further distinguish between the end of systole and the end of ejection. Following the end of ejection, the ventricle relaxes back to the diastolic curve and filling begins again.

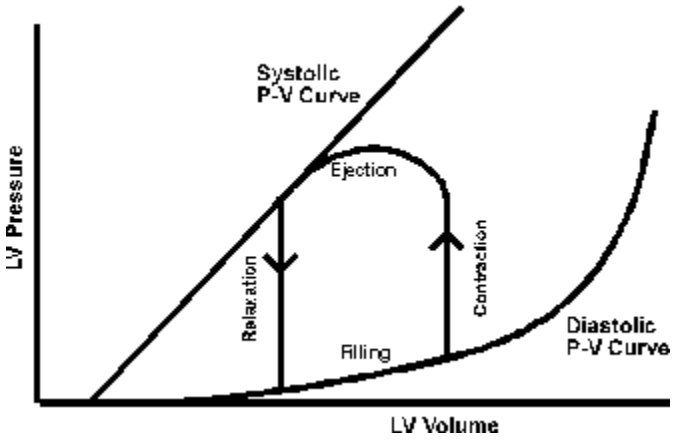

Figure 1: Left ventricular compliance curves and P-V loop.

The end-systolic pressure volume relationship represents the maximum pressure that can be generated by the ventricle at any given volume.

Exercises

If you haven't done so yet, minimize the clinical tools window and load exercise E02.EXR from the File menu. Loading this exercise file will set up several viewers, will disable the autonomic nervous system and the lungs so you can study the heart in isolation, and will accelerate infusion rates so that you can give or remove blood or drugs much faster than you could under real clinical circumstances.

1. Diastolic PV Relationships

Focus attention first on the end-diastolic pressure volume relationship, shown in the viewer marked LV Diastolic Pressure Volume Relationships. The parameters at the bottom determine the shape of the curve. You will adjust the *Beta* parameter, and see what happens to other cardiovascular quantities.

a. Examine the PV loop and identify the end-systolic and end-diastolic points on the tracings. Record LV_{EDV} and LV_{ESV}. Calculate stroke volume from the difference between end-diastolic and end-systolic volumes. Compare it to the stroke volume (*SV*) shown by the program. Multiply the *SV* by the heart rate (*HR*) and compare the result to the cardiac output.

b. Predict what will happen to LV_{EDV}, LV_{ESV}, and *SV* when the diastolic pressure volume curve becomes steeper.

c. Close the help window (if it is open), as you will need the space so you can see several viewers at once. Restore the *LV* P-V curve window, and arrange your desktop to see the PV loop and the P-V curves at the same time. Now change the parameter labeled *Beta* from 0.02 to 0.029 by pressing the increase button on the toolbar. You will see the curve change immediately. Note the new values of LV_{EDV}, LV_{ESV}, and *SV*. Then, reset the value of *Beta* for the next exercise, and restore this window.

What happened and why did it happen?

2. The End-Systolic PV Relationship

Contractility is defined qualitatively as the strength of contraction developed by the ventricular muscle, and quantitatively as the position of the end-systolic pressure volume relationship. The end-systolic relationship is usually represented by a line whose slope is generally cited as measuring contractility. Thus, steeper slopes represent increasing contractility. Sympathetic stimulation increases contractility while hypoxia and acidosis decrease cardiac contractility. In humans, the most common cause of impaired

contractility is cardiac damage due to myocardial infarctions, where portions of the ventricular wall die from lack of blood supply.

a. Record the current values of *LV* end-diastolic volume, end-systolic volume, stroke volume and cardiac output.

b. Predict what will happen to LV_{EDV}, LV_{ESV}, and *SV* when *LV* contractility is reduced.

c. Once again, read these instructions in advance, because you will need to minimize this window. Rearrange your desktop so see the PV curves and the PV Loops at the same time. Select LV Contractility and decrease it to approximately 0.5. This will produce a decrease in LV contractility, manifested as a decrease in the slope of the end-systolic pressure-volume relationship. Allow the patient to stabilize and record the new values of *LV* end-diastolic volume, end-systolic volume, stroke volume and cardiac output. Finally, reset the value of *LV* contractility and restore this window.

Why did LV_{ESV} change? Why did *SV* change? Why did LV_{EDV} change?

3. Cardiac Preload

Preload is defined qualitatively as the stretch of the cardiac muscle before contraction, and quantitatively as the end-diastolic volume. The higher the end-diastolic volume, the more blood can be ejected in each cardiac stroke (known as the Frank-Starling effect). Thus, maximizing preload maximizes stroke volume. During normal exercise, an important mechanism for increasing cardiac output is an increase in preload, which occurs because of the increase in venous return from the systemic vessels. In preparation for this exercise, minimize the PV Curves window: you will primarily observe the Loop window.

a. Record the current values of LV_{EDV}, LV_{ESV} and Cardiac Output (*Q*).

b. Infuse 1000 ml of whole blood at 5000 ml per hour. Start the infusion and watch it infuse; remember that all infusion rates are artificially increased by a factor of 20 in this exercise, so you can see effects without waiting as long. Inside the body, where is the blood going?

c. Record the new values of LV_{EDV}, end-systolic volume and cardiac output. What happened? By what mechanism did this rapid blood transfusion change cardiac output? Apart from blood transfusion or withdrawal, how else could you change cardiac preload? Now, in preparation for the next stage, perform a 1000 ml blood withdrawal (a phlebotomy, to remove the blood you gave in the last stage).

4. Cardiac Afterload

Afterload is defined qualitatively as the opposition encountered by the left ventricle during ejection, and is often taken to be the instantaneous pressure in the aorta during ejection. Alternative indices of afterload are the end-systolic pressure or the end-systolic wall stress; the "best index" is still controversial. Recall that ventricular ejection continues until pressure inside the ventricle equals pressure in the aorta. At that point, ejection stops and the aortic valve closes. When aortic pressure (afterload) increases suddenly, end systolic pressure and end-systolic volume also increase, because the ventricle cannot eject as far against a greater afterload. This causes a decrease in stroke volume on the subsequent contraction (heart beat). Because venous return continues, the end-diastolic pressure on the next heart beat will be greater, resulting in a greater preload and an increase in stroke volume. This exercise explores the effects of vascular resistance on cardiac output and stroke volume.

a. Record the current values of LV_{EDV}, LV_{ESV}, *SVR*, *Q*, *HR* and mean arterial pressure.

b. Infuse nitroprusside at 4 mcg/kg/min (nitroprusside is a drug that relaxes vascular smooth muscle, and has significant effect on systemic vascular resistance). Allow the patient to stabilize, and record new values of LV_{EDV}, LV_{ESV}, *SVR*, *Q*, *HR* and mean arterial pressure. Why did LV_{ESV} change?

c. Why did cardiac output change? Stop the nitroprusside infusion in preparation for the next exercise.

Nitroprusside relaxes the tone of arteriolar smooth muscle, which decreases systemic vascular resistance. This tends to reduce blood pressure at any given level of cardiac output, an effect seen clearly in this example. Hypotension ordinarily elicits a reflex increase in sympathetic tone, but this is disabled in this exercise to simplify thinking about cardiac function.

5. Heart Rate (*HR*)

The last major characteristic of the heart is the heart rate. During exercise, both stroke volume and heart rate increase, and together they increase the cardiac output. But what happens if you vary the heart rate without independently changing venous return?

a. Record heart rate, stroke volume, LV_{EDV}, LV_{ESV}, mean arterial pressure, and cardiac output.

b. Select *Sinus Rate* increase heart rate to 105 beats/minute. Again, record heart rate, stroke volume, LV_{EDV}, LV_{ESV}, mean arterial pressure, and cardiac output.

c. Increase heart rate to 140 beats/minute and record data. Why didn't the cardiac output double? Why did LV_{EDV} and LV_{ESV} change in the manner that they did?

Appendix A – Terminology

Parameter in LV end-systolic P-V relationship (?): *LV Contractility*.
Parameter in LV end-diastolic P-V relationship (?): *LV Beta*.
Stroke Volume, the blood pumped in each heartbeat (ml): *SV*.
Left ventricular end-diastolic volume (ml): LV_{EDV}.
Left ventricular end-systolic volume (ml): LV_{ESV}
Total flow or cardiac output (ml/min): *Q*.
Heart Rate (/min): *HR*.

Appendix B – Required Formulas

$$SV = Q/HR$$

$$SV = LV_{EDV} - LV_{ESV}$$