

**MASSACHUSETTS INSTITUTE OF TECHNOLOGY**

Departments of Electrical Engineering, Mechanical Engineering, and the Harvard-MIT Division  
of Health Sciences and Technology

6.022J/2.792J/BEH.371J/HST542J: Quantitative Physiology: Organ Transport Systems

**PROBLEM SET 2**

**SOLUTIONS**

February 19, 2004

## Problem 1

A twenty-year-old student was involved in an automobile accident and sustained a chest injury. Upon admission to the hospital he had a rapid, weak pulse, feeble heart sounds, and a low blood pressure. Because of the suspicion of heart damage, he was evaluated in the cardiac catheterization laboratory. A left-sided cath study was performed, complete with bi-plane cine ventriculograms (X-ray movies of the ventricle obtained in orthogonal projections following injection of radio-opaque dye into the ventricle). It was discovered that the patient had a significant amount of blood in the pericardial cavity (between the heart and the pericardial sac). Three hundred milliliters of blood were removed and the patient improved considerably.

As part of the evaluation procedure, diastolic pressure-volume curves for the left ventricle were measured both before and after the pericardial tap (removal of the pericardial blood). (This was done by simultaneous measurement of LV volume from the cine data, and of the LV pressure from an intracardiac pressure transducer.) These curves are presented in Figure 1.

Figure 2A shows the LV and aortic pressures recorded prior to removal of the pericardial blood. Figure 2B shows these pressures after removal when the cardiovascular system had reached steady state. At the time indicated by the arrow, a balloon was suddenly inflated in the ascending aorta (see Figure 3), which presented an increased afterload to the left ventricle. Note that the aortic pressure was measured proximal to (on the heart side of) the balloon. The added pressure load was sudden, and compensatory mechanisms did not have time to act for several beats. Thus, the heart's contractile state may be considered constant for 10-15 seconds, and this period certainly includes beats numbered 3, 4, and 5 in the figure.

Additional data gathered during the work-up included:

A. Fick data during steady state before the pericardium was drained:

O <sub>2</sub> uptake	300 cc/min.
Arterial O <sub>2</sub> content	180 cc/liter
Mixed venous O <sub>2</sub> content	80 cc/liter

B. Individual stroke volumes during the balloon test are indicated in Figure 2B. The steady state stroke volume was 75 cc. before balloon inflation.

**Questions:**

A. From the raw data supplied, complete the table below.

	Before tap	Beat 2	Beat 3	Beat 4	Beat 5
Heart Rate (b/m)	100	60	60	60	60
Stroke Vol. (cc.)	30	75	64	70	75
Aortic Pressure (max)/(min)	82/65	115/75	140/75	157.5/87.5	167.5/107.5
Aortic valve opens (mmHg)	65	75	75	87.5	107.5
LV end systolic pressure (mmHg)	77	108	133	145	158
LVEDP (mmHg)	25	10	10	14	18
LVEDV (cc.)	51	164	164	175	185

- *HR: from Figure 2*
- *S.V.: ? S.V.  $\left[ \frac{\text{cc blood}}{\text{beat}} \right] = \frac{300 \text{ cc blood}}{\text{min}} \times \frac{1 \text{ L blood}}{(180-80) \text{ cc } O_2} \times \frac{1 \text{ min}}{100 \text{ beats}} \times \frac{1000 \text{ cc blood}}{1 \text{ L blood}} = 30 \text{ cc blood/beat}$*
- *Aortic Pressure: from Figure 2*
- *Aortic valve opens at min. Aortic Pressure*
- *LVESP: from Figure 2*
- *LVEDP: from Figure 2*
- *LVEDV: from Figure 1. (Find corresponding V from known LVEDP.)*

B. Sketch the pressure-volume loop for the heart prior to the pericardial tap (on Figure 1).

*See Figure.*

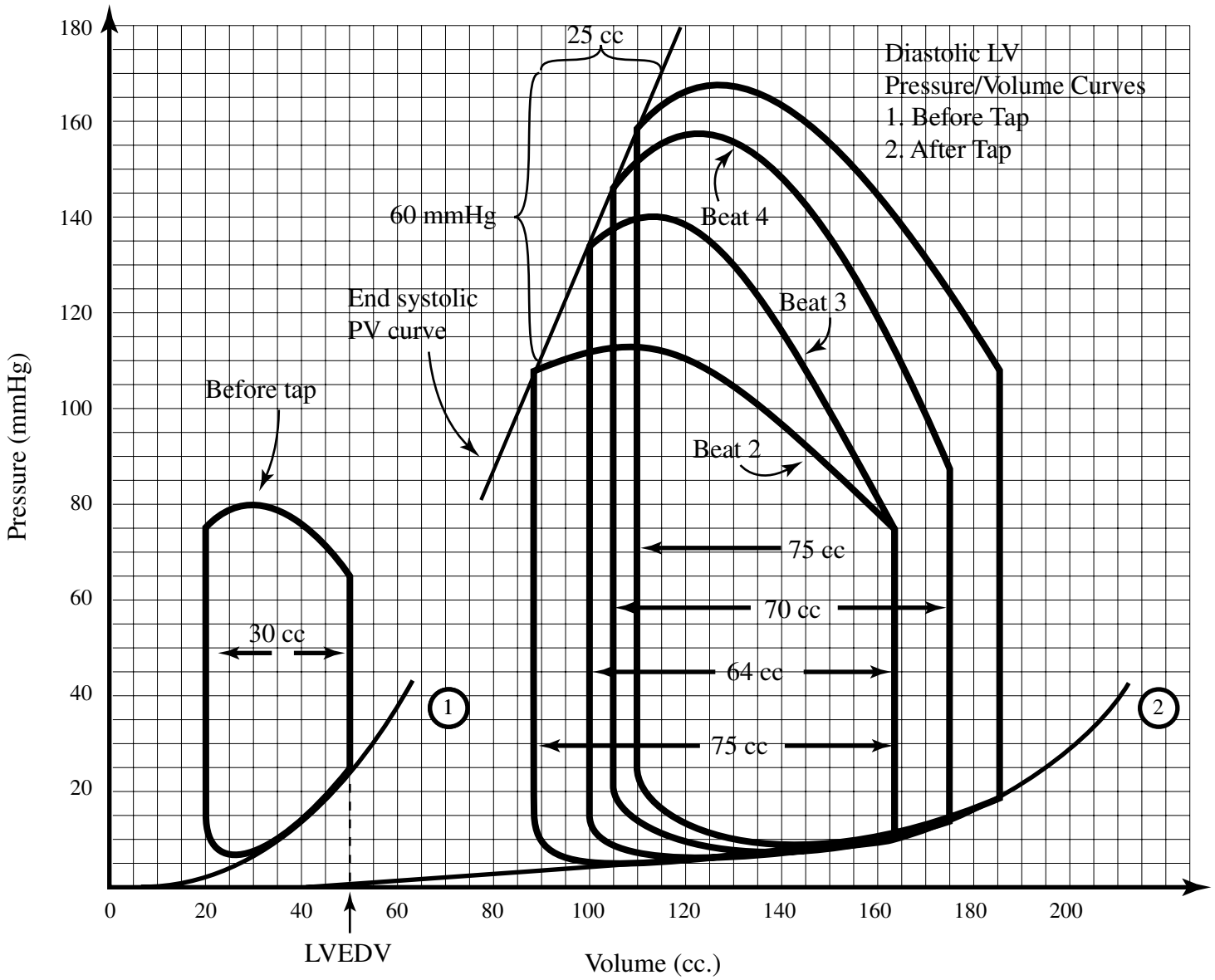
C. Plot the pressure-volume loops for beats numbered 2, 3, 4, and 5 (on Figure 1).

*See Figure.*

D. Construct the end-systolic pressure-volume curve for the normal left ventricle (on Figure 1).

*See Figure.*

Figure 1:



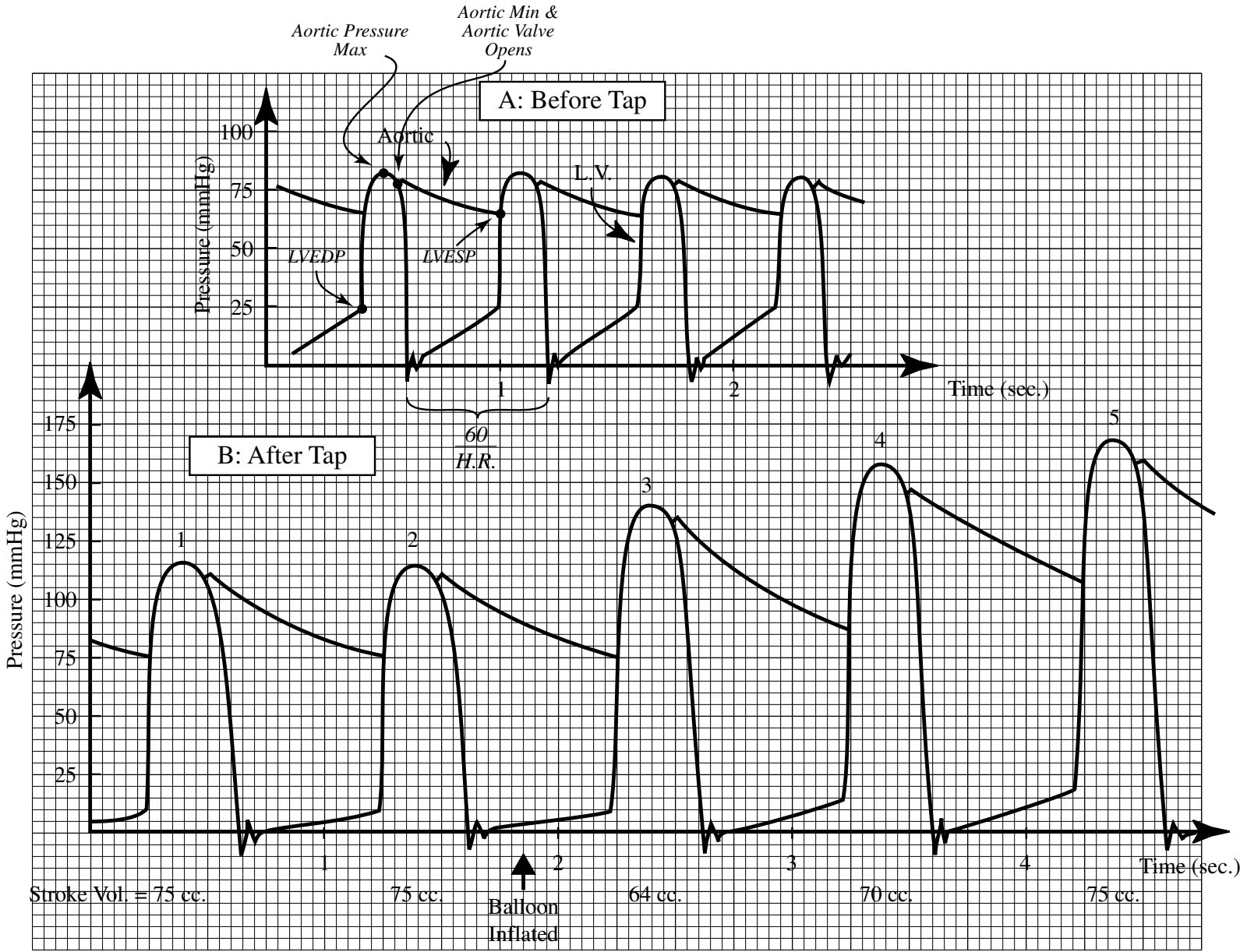
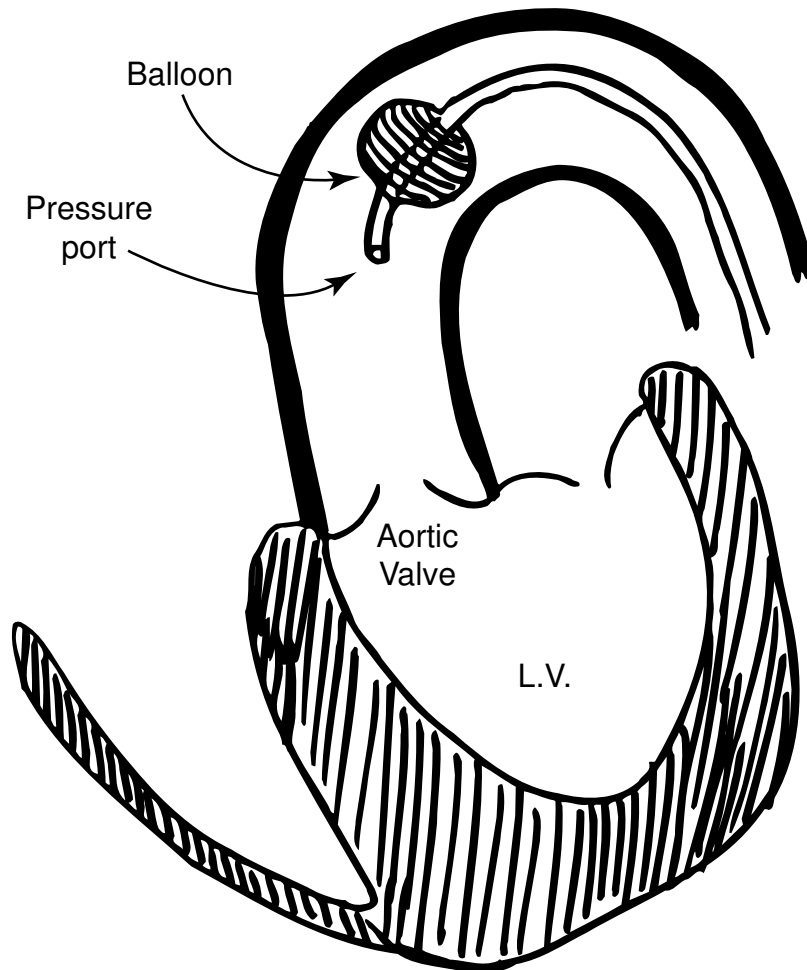


Figure 2:

Figure 3: Relative Positions of Balloon and Aortic Pressure Measurement Site



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## Problem 2

In the case study introduced at the beginning of the course, the patient's heart required the temporary assistance of a balloon pump placed in his aorta ("intra-aortic balloon pump" or IABP). This device may be life-saving in situations where the heart muscle has been weakened by disease (such as loss of blood supply).

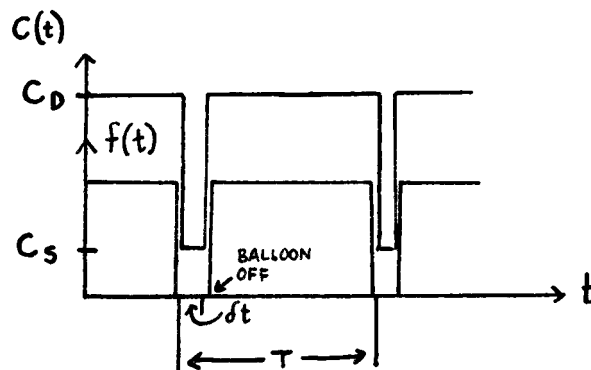
One possible design for the IABP is shown in Figure 4. It consists of a long, thin, inflatable balloon which is inserted via the femoral artery to the aortic arch. It may be in one of two states: deflated with an internal pressure of zero, or inflated at an internal pressure  $P_B$ . By appropriate timing of the two states, considerable improvement may result in circulatory function. The pressure-volume characteristics of the aorta with the balloon both deflated and inflated are shown in Figure 5.

The heart and peripheral circulation may be modeled as shown in Figure 6. The left ventricle is represented by a time-varying capacitor  $C(t)$  driven by a constant filling pressure,  $P_f$ . The peripheral circulation is represented by the Windkessel approximation where the pressure/volume relationships of  $C_a$  are shown in Figure 5. ( $C_a$  is a 2-state device.) Assume that the systolic ejection time is very short,  $dt$ .

- A. What must be the timing of the balloon inflation/deflation sequence in order to assist the heart? Plot the required switching function  $f(t)$  on the same time axis as  $C(t)$ .

Note:  $f(t)$  is defined in Figure 4, and  $C(t)$  in Figure 6.

*The balloon should be inflated during diastole; it must be deflated during ventricular systole. For aortic volumes less than 200 cc, the active balloon/aorta system behaves as a pressure source, driving blood through the periphery at a uniform rate. The balloon should not be inflated during systole, because it would present an increased afterload to the damaged heart. When inflated at the end of ventricular systole, the balloon provides a boost of pressure to increase overall flow through the periphery. During systole, the balloon should be deflated, thus lowering aortic pressure (the afterload to the LV).*



- B. Indicate on Figure 5 the pressure-volume cycle followed in the aorta

- (i) with the balloon assist device inoperative, and
- (ii) with the assist device operating as defined by you in the previous question.

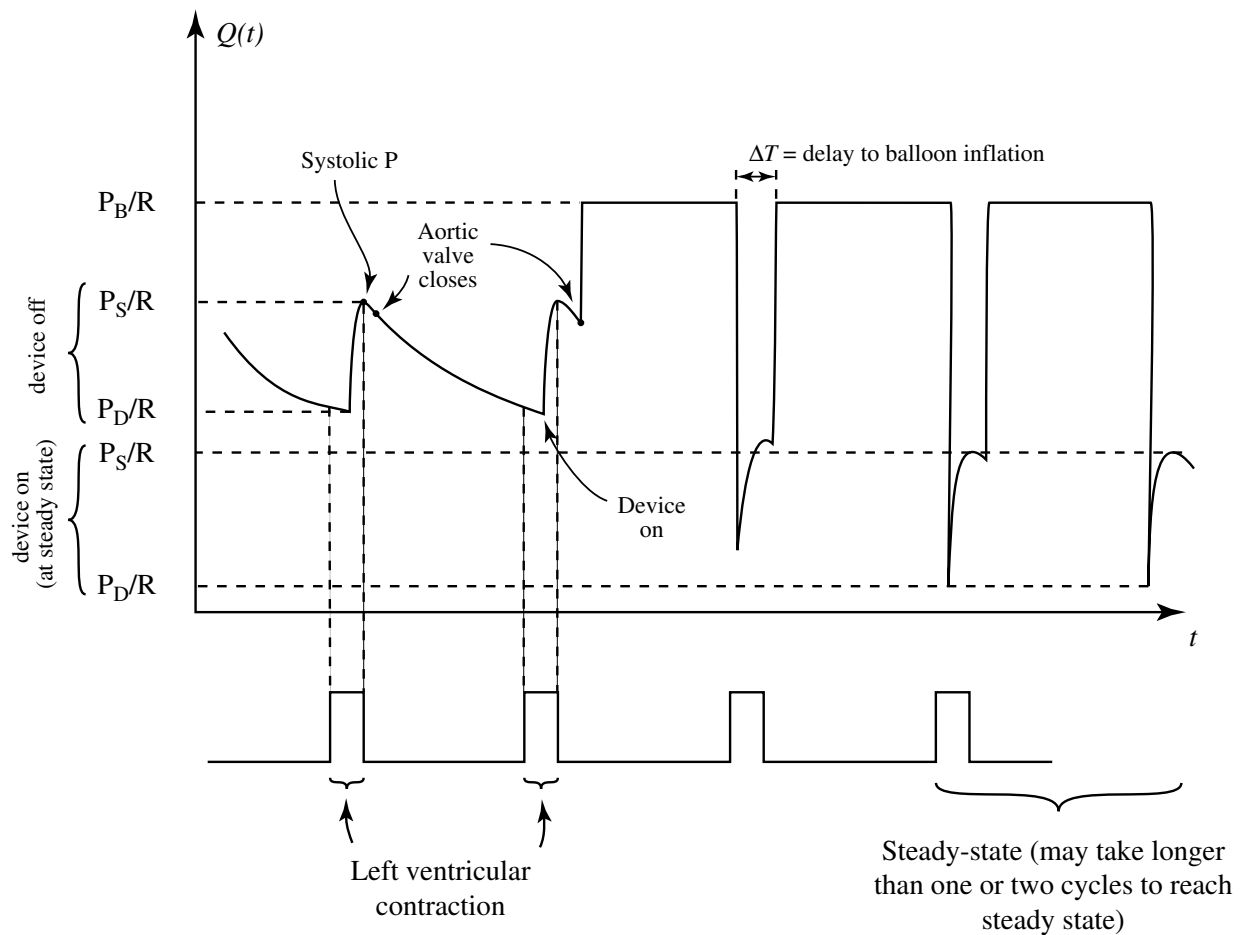
See Figure 5. Note that the balloon reduces the afterload but increases the stroke volume.

- C. Using graphical techniques, indicate on Figure 5 the area representing the net energy supplied to the circulation by the balloon device per cycle.

See Figure 5. The shaded area represents the work done by the balloon pump per cycle.

- D. Sketch the expected blood flow through the peripheral resistance,  $R$ , as a function of time with the assist device on.

$$Q(t) = \frac{P_a(t)}{R}$$

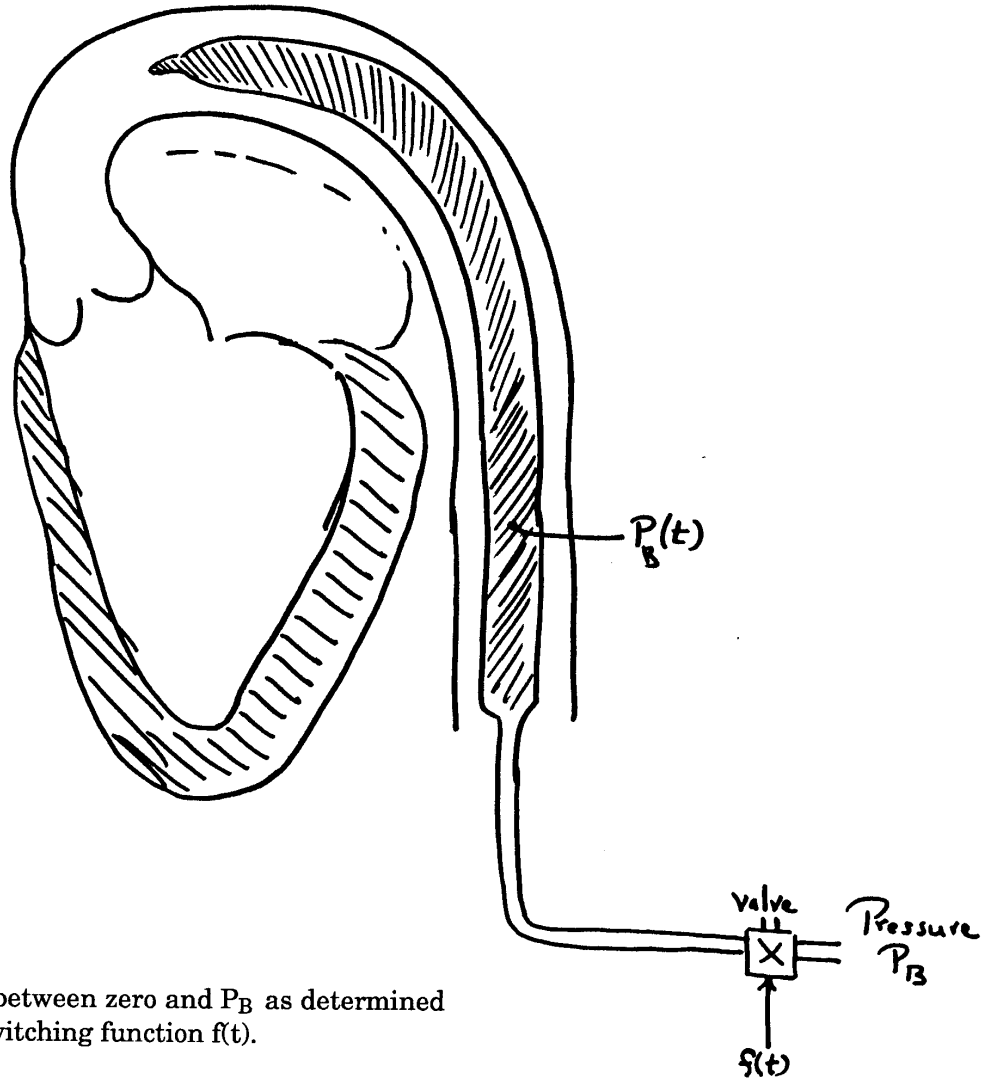


- E. A representative LV pressure-volume loop for a damaged heart is shown in Figure 7. Show qualitatively how the balloon pump will enhance cardiac output by sketching the expected new PV loop with the balloon operating.

See Figure 7. The balloon pump will reduce the afterload of the LV, permitting a larger SV even with the resultant drop in preload.



Figure 4:



$P_B(t)$  cycles between zero and  $P_B$  as determined by the switching function  $f(t)$ .

Figure 5:

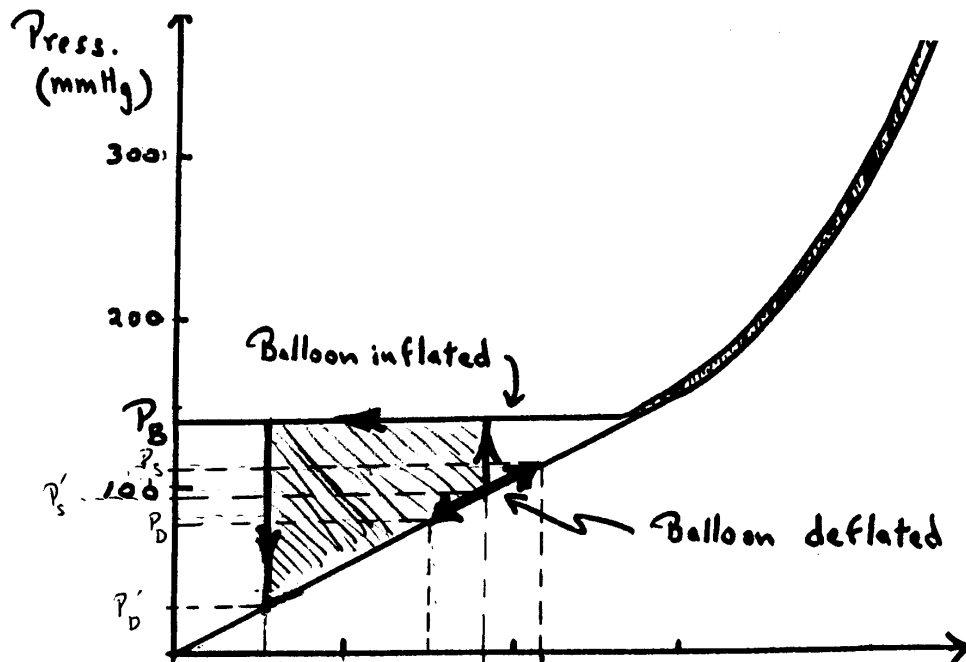


Figure 6:

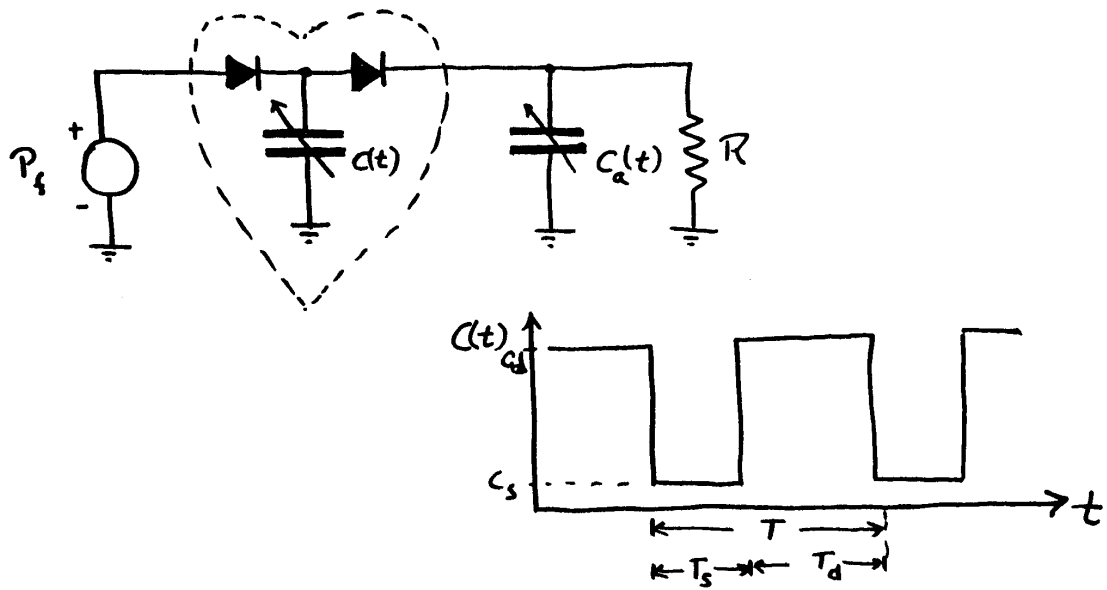
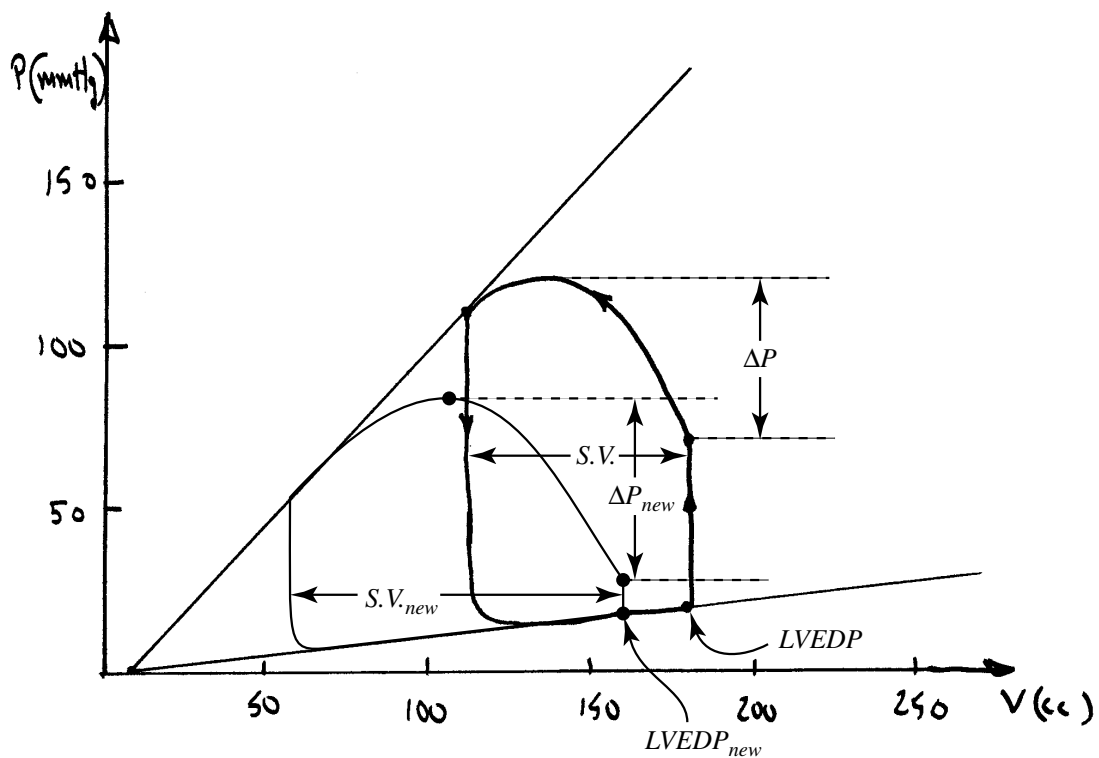


Figure 7:

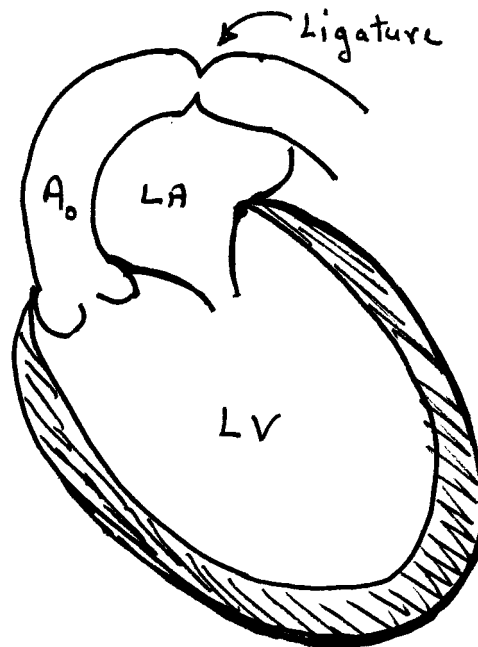


- S.V.  $\uparrow$
- $\Delta P$  (pulse pressure)  $\uparrow$  slightly
- $P_D$   $\downarrow$
- LVEDP  $\downarrow$

### Problem 3

You are a physiologist studying the effects of hypertension (high blood pressure) on the heart. Your studies involve the use of the pig, whose heart size is similar to that of humans. To evaluate the short and long-term effects, you produce an experimental increase in LV afterload by making a stricture in the aorta using a ligature as shown in Figure 8. (This is sometimes referred to as “banding”.) Assume the animal’s heart is paced at 60 beats per minute.

Figure 8:



Please answer the following:

- A. The control pressures in the LV and proximal aorta are shown in Figure 9. The LV end-diastolic volume was measured to be 140 cc. The cardiac output was 4,800 cc/min. From this data, construct the LV P-V loop using the axes provided in Figure 11.

$$HR = 60 \text{ bpm} \rightarrow S.V. = CO/HR = 80 \text{ cc}$$

$$\text{systolic} = 120 \text{ mmHg}; \text{ diastolic} = 70 \text{ mmHg}; \text{ end systolic} = 110 \text{ mmHg}$$

$$LVEDP = 10 \rightarrow LVEDV = 140, LVESV = 60$$

- B. A few seconds after placing the ligature, the pressure tracings changed as shown in Figure 10. The LV end-diastolic pressure was measured to be 20 mmHg. The cardiac output decreased only slightly to 4500 cc/min. From the data provided, construct the new LV P-V loop on the axes of Figure 11.

$$\begin{aligned}
LVEDP = 20 &\rightarrow LVEDV = 190 \\
SV = \frac{4500}{60} = 75 \text{ cc} &\rightarrow LVESV = 115 \\
BP = 230/140 &\quad \text{end syst.} = 220
\end{aligned}$$

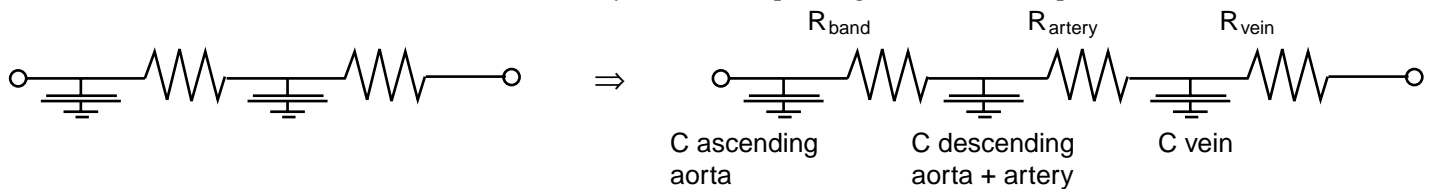
- C. Assume that the inotropic state of the heart had not changed in the few seconds following aortic banding. Draw the end-systolic PV curve, and calculate the LV systolic capacitance,  $C_s$ .

See figure for curve.

$$C_s = \frac{50 \text{ cc}}{110 \text{ mmHg}} = 0.5 \text{ cc/mmHg}$$

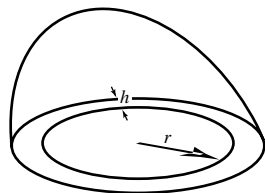
- D. How should the lumped parameter model of the systemic circulation be modified to account for the ligature? Propose and briefly justify an alternative model for the circulation which takes account of the ligature.

A new resistance has been added by the band, splitting the arterial capacitance in two.



- E. Over time, the heart adapts to its new pressure load by adding new muscle mass and changing its shape. The principle which appears to govern the adaptation is to maintain the same systolic wall stress (force per unit area) as in the control state, while also maintaining a constant stroke volume.

- (i) What is the relationship between the LV wall stress,  $\sigma$ , and the LV pressure,  $P$ ? (You may assume a spherical LV of radius,  $r$ , and wall thickness,  $h$ .)



$$\begin{aligned}
\sigma \cdot h \cdot 2\pi r &= \pi r^2 P \\
P &= \frac{2\sigma h}{r} \\
\sigma &= \frac{rP}{2h}
\end{aligned}$$

- (ii) What is the wall stress (in dynes/cm<sup>2</sup>) at end systole during the control state? Assume the wall thickness to be 0.8 cm at end-systole.

$$\text{At end systole } P = 110 \text{ mmHg} = 110 \cdot 1330 \text{ dynes/cm}^2$$

Find  $r$  from  $LVESV = 60 \text{ cc}$ .

$$\frac{4}{3}\pi r^3 = 60 \text{ cc}$$

$$\begin{aligned}
r^3 &= 60 \cdot \frac{3}{4} \cdot \frac{1}{\pi} \approx 15 \\
r &= \sqrt[3]{15} = 2.46 \text{ cm} \\
h &= 0.8 \text{ cm} \\
\sigma &= \frac{2.46 \cdot 110 \cdot 1330}{2 \cdot 0.8} = 2.2 \cdot 10^5 \text{ dynes/cm}^2
\end{aligned}$$

- (iii) As a result of the heart's compensation, the end-diastolic filling pressure falls back to its original control value despite the continued high afterload. Cardiac output also returns to its control level of 4800 cc/min. Assuming that the diastolic properties of the LV do not change, sketch the new "compensated" P-V loop on Figure 11. Draw the end-systolic P-V curve. Assume the aortic blood pressure is the same as in Figure 10.

$$CO = 4800 \text{ cc/min}$$

$$HR = 60 \text{ bpm} \rightarrow SV = 80 \text{ cc}$$

$$LVEDP = 10 \text{ mmHg}$$

$$LVEDV = 140$$

$$LVESV = 60 \text{ cc}$$

$$LVESP = 220 \text{ mmHg}; \text{ diastolic} = 140, \text{ systolic} = 230$$

- (iv) What is the LV systolic capacitance of the compensated heart?

$$C'_s = \frac{\Delta V}{\Delta P} = \frac{60 - 5}{220 - 0} = \frac{55}{220} = 0.25 \text{ cc/mmHg}$$

- (v) Based on the data provided, what would be the end-systolic wall thickness of the "compensated" heart?

*If  $\sigma$  is maintained constant, then*

$$\begin{aligned}
\sigma' &= \sigma \\
\frac{r' P'}{2h'} &= \frac{r_0 P_0}{2h_0}
\end{aligned}$$

*The conditions stated in (iii) imply*

$$r' = r_0, \quad P' = 220 \text{ mmHg}, \quad h_0 = 0.8 \text{ cm}.$$

*Thus:*

$$h' = h_0 \frac{P'}{P_0} = 2h_0 = 1.6 \text{ cm}$$

Figure 9:

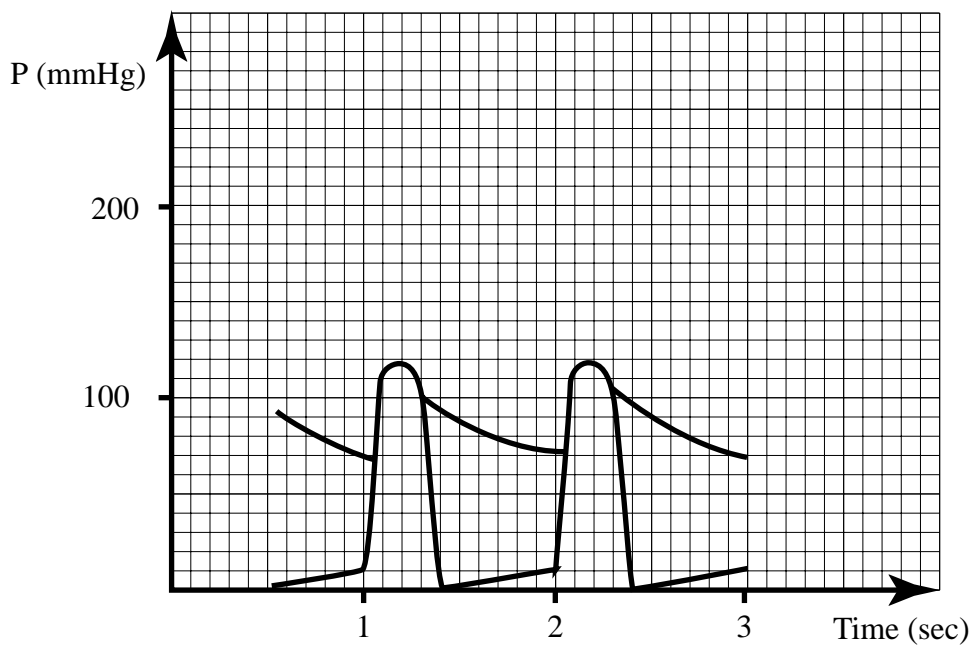


Figure 10:

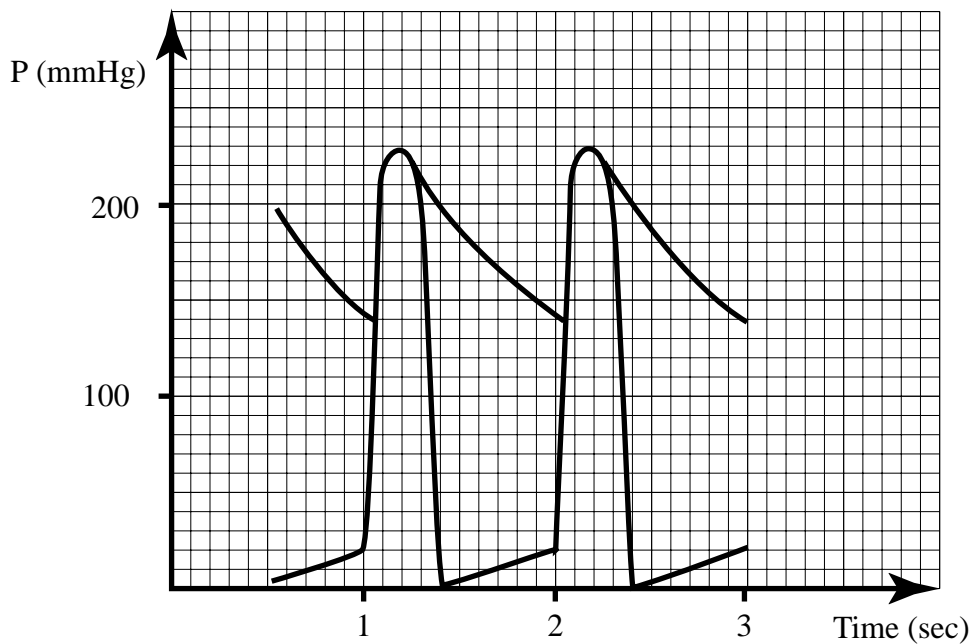
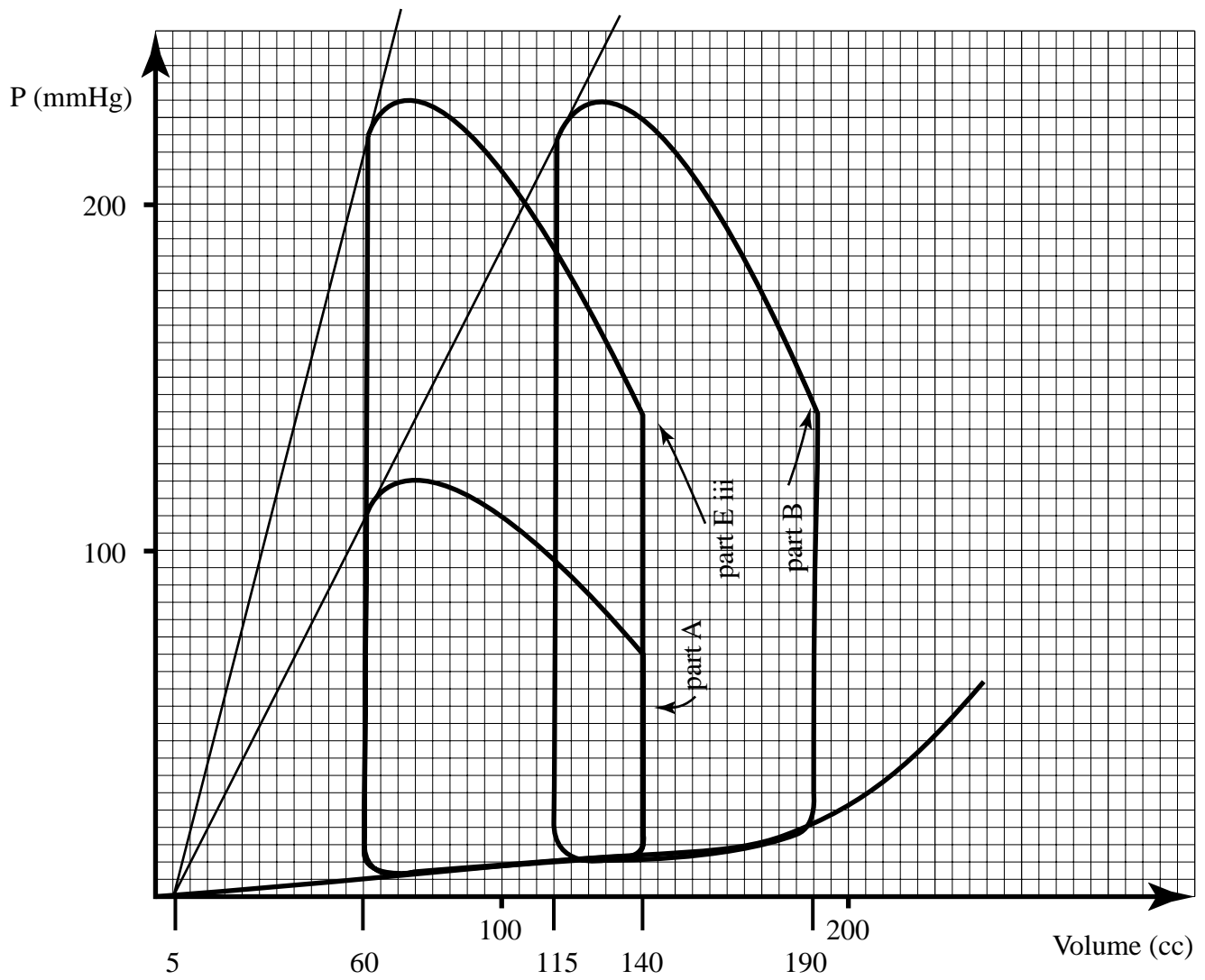


Figure 11:





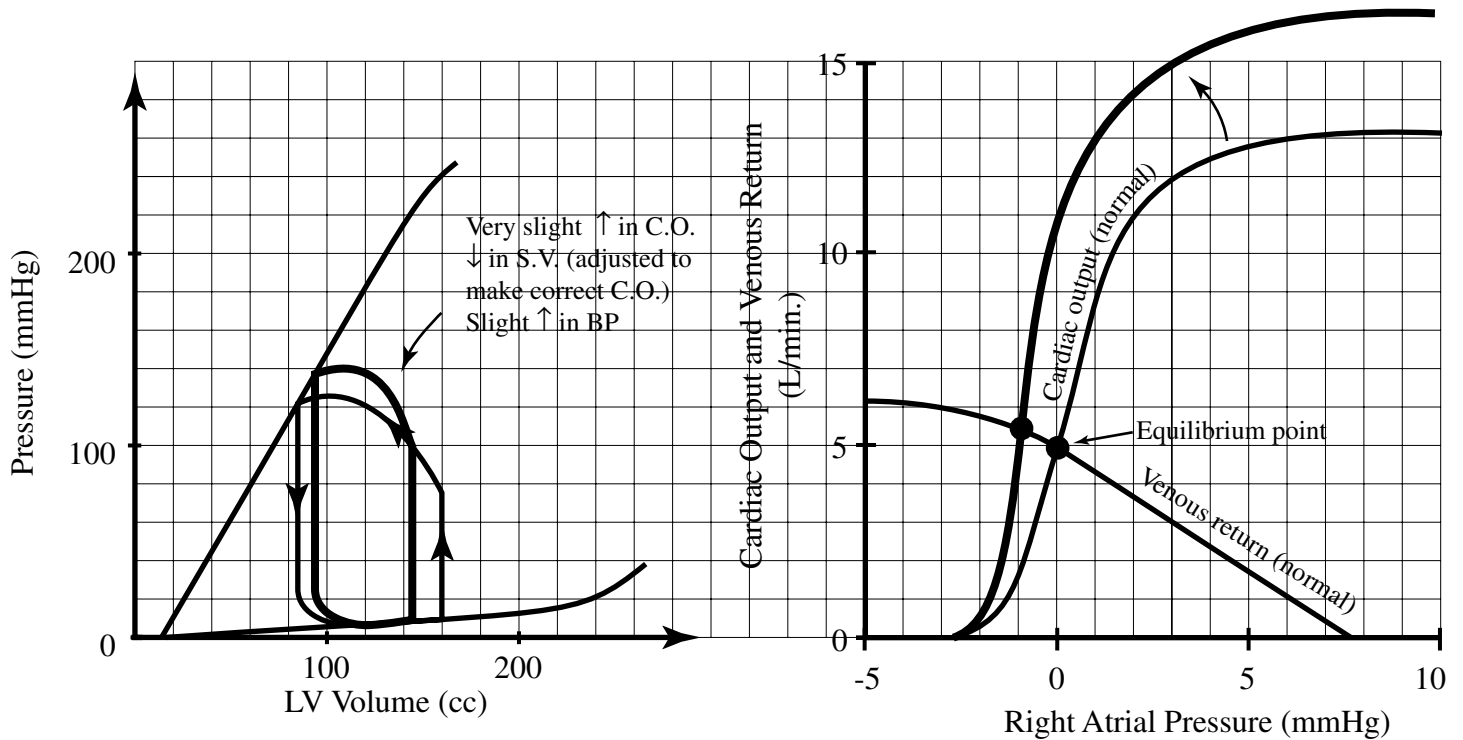
#### Problem 4

We have used several graphic techniques to represent the function of the heart and peripheral circulation. The *ventricular pressure-volume relationships* have been helpful in documenting the cardiac cycle in both transient and steady states. The *cardiac output curve* has been a convenient way to represent the average performance of the “heart-lung pumping unit”. The *venous return curve* has been used to represent the peripheral circulation. In this question you are asked to indicate the *qualitative* changes in each of the curves which would occur as a result of different interventions. Sketch your answers directly on the *normal* curves supplied for your reference. In each case: (1) assume there are *NO* extrinsic control mechanisms operating, and (2) indicate the *steady state* response, after the entire C.V. system has adapted to the imposed change. (The CV Simulator may be used as a “reference” if you wish, to test your predictions. See the CV Simulator User Manual at the end of the course notes.)

$$\begin{aligned}Q_H &= f(C_D(P_f - P_{th}) - C_S(P_a - P_{th})) \\Q_{VR} &= \frac{(P_{ms} - P_{th}) - (P_f - P_{th})}{R_v + R_a \left( \frac{C_a}{C_a + C_v} \right)} \\P_{ms} &= \frac{V_T - V_O}{C_T} \\P &= QR\end{aligned}$$

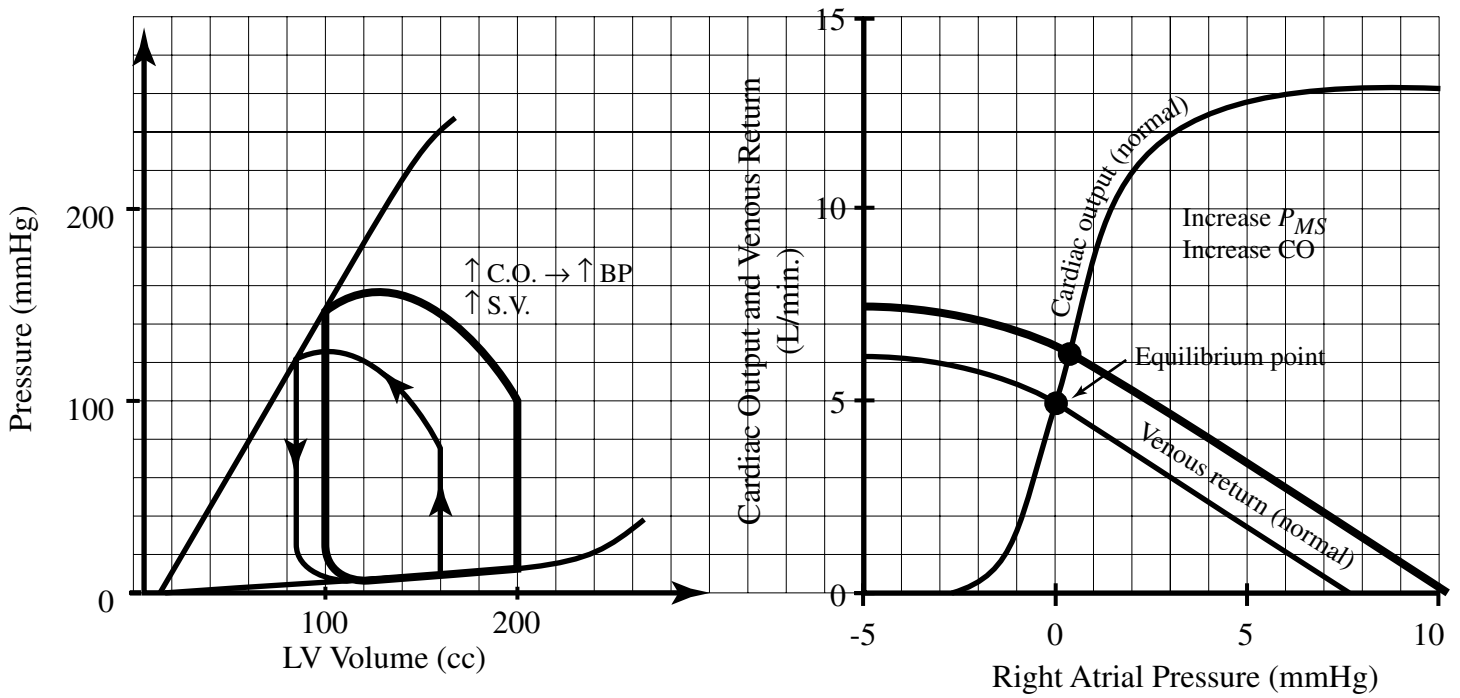
*Note: Curves in solutions are qualitative.*

A. Heart rate increases from 67 bpm to 100 bpm.



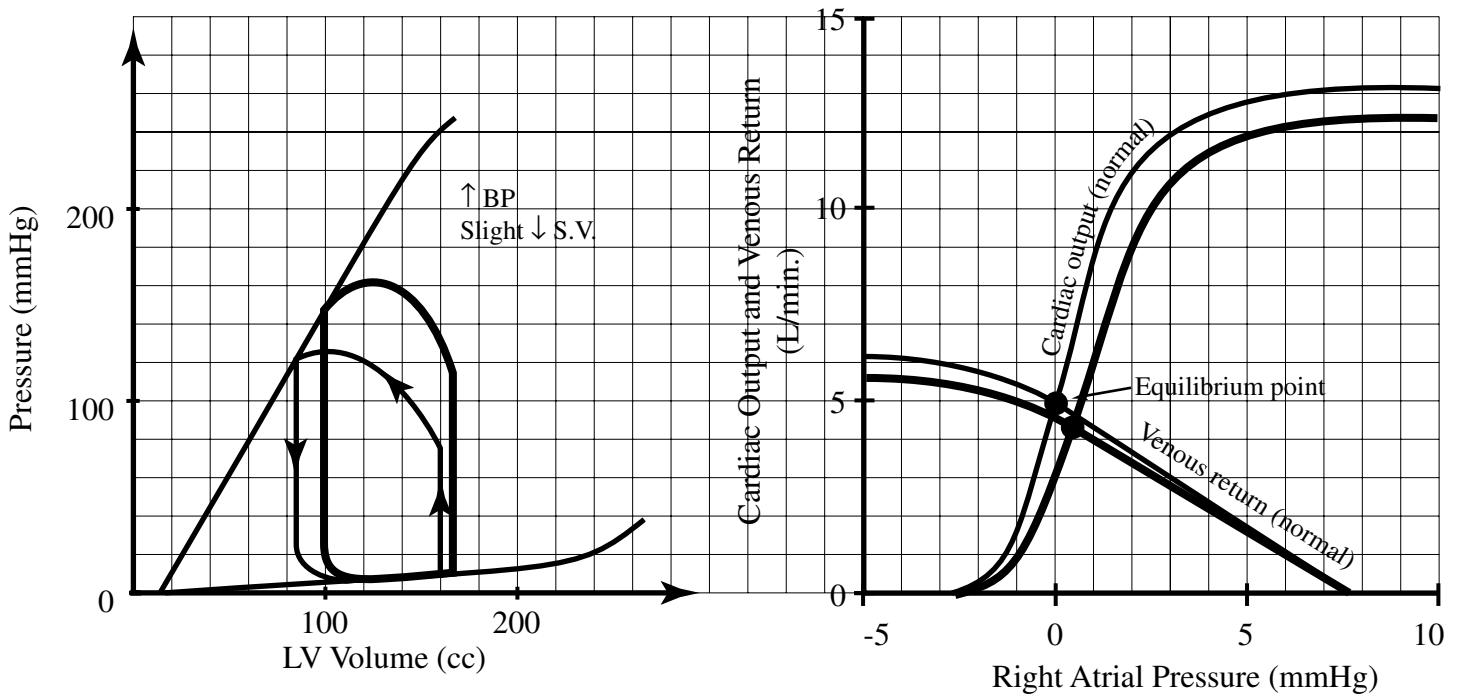
- (i) Since heart rate (HR) increases, the slope of the CO curve increases, with no change in the VR curve.
- (ii) Cardiac Output ( $Q$ ) increases slightly, and  $P_f$  decreases, as can be seen by the intersection point of the  $Q$  curves.
- (iii) Contractility curves would remain unaffected. Since  $Q$  went up slightly, and HR went up a lot, the stroke volume (SV) would decrease slightly.  
 [Note: If HR went up ridiculously high, for example 300 bpm, even though the equations don't show it, one should infer that the SV would decrease drastically, and that  $Q$  would decrease.]
- (iv) Since increase in  $Q$  with no change in peripheral resistance ( $R$ ), blood pressure (BP) would rise. Thus pressure volume (PV) loop should have a higher left ventricular end systolic pressure (LVESP).

B. The patient receives a blood transfusion.



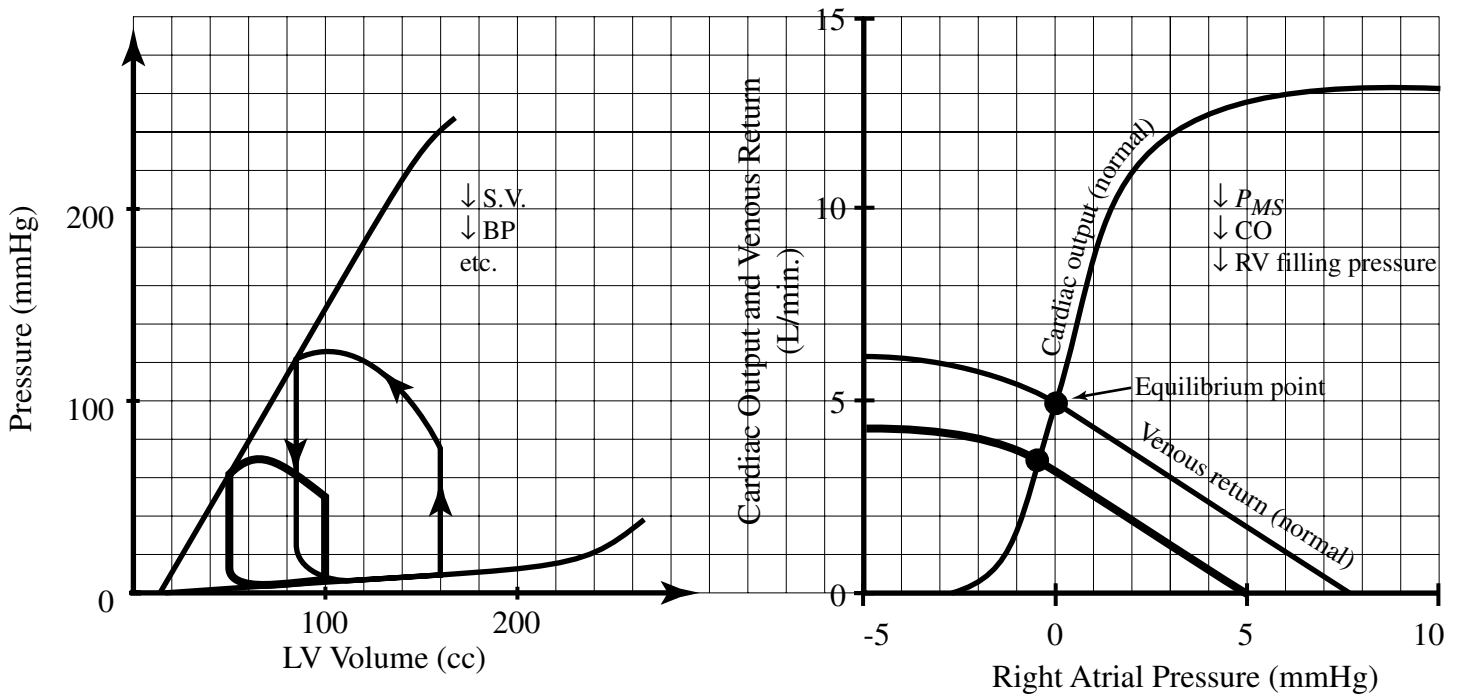
- (i)  $P_{ms}$  rises as  $(V_T - V_O)$  increases. Thus, the VR curve shifts to the right. No change in the CO curve.  $Q$  increases.
- (ii) Since  $Q$  increased, and  $R$  doesn't change, BP increases, and LVESP increases as well.
- (iii) Since HR doesn't change, and  $Q$  increased, SV increases.

C. The patient is given a drug that constricts the arterioles.



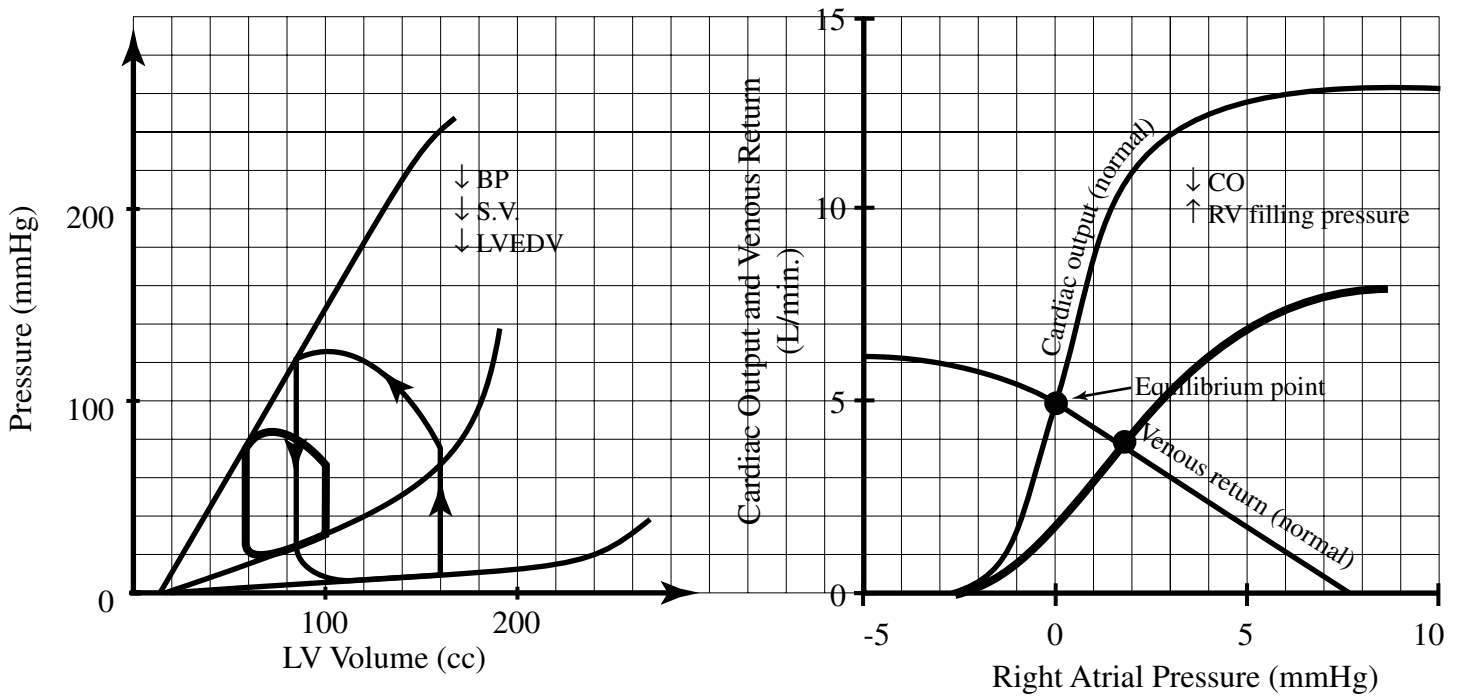
- (i) Arterioles constricting means a rise in  $R$ . Thus, the slope of the VR curve decreases slightly, without any significant change in  $P_{ms}$ .
- (ii) Since  $R$  went up, the afterload pressure,  $P_a$  goes up (as  $P = QR$ ). This causes a shift in the CO curve down. New  $Q$  is less than before.
- (iii) Since arterioles constricted, BP goes up, as does LVESP.
- (iv) Since  $Q$  decreased, and no change in HR, SV decreases slightly.

D. The patient is tipped up to the vertical position in a tilt test after lying down for 10 minutes.



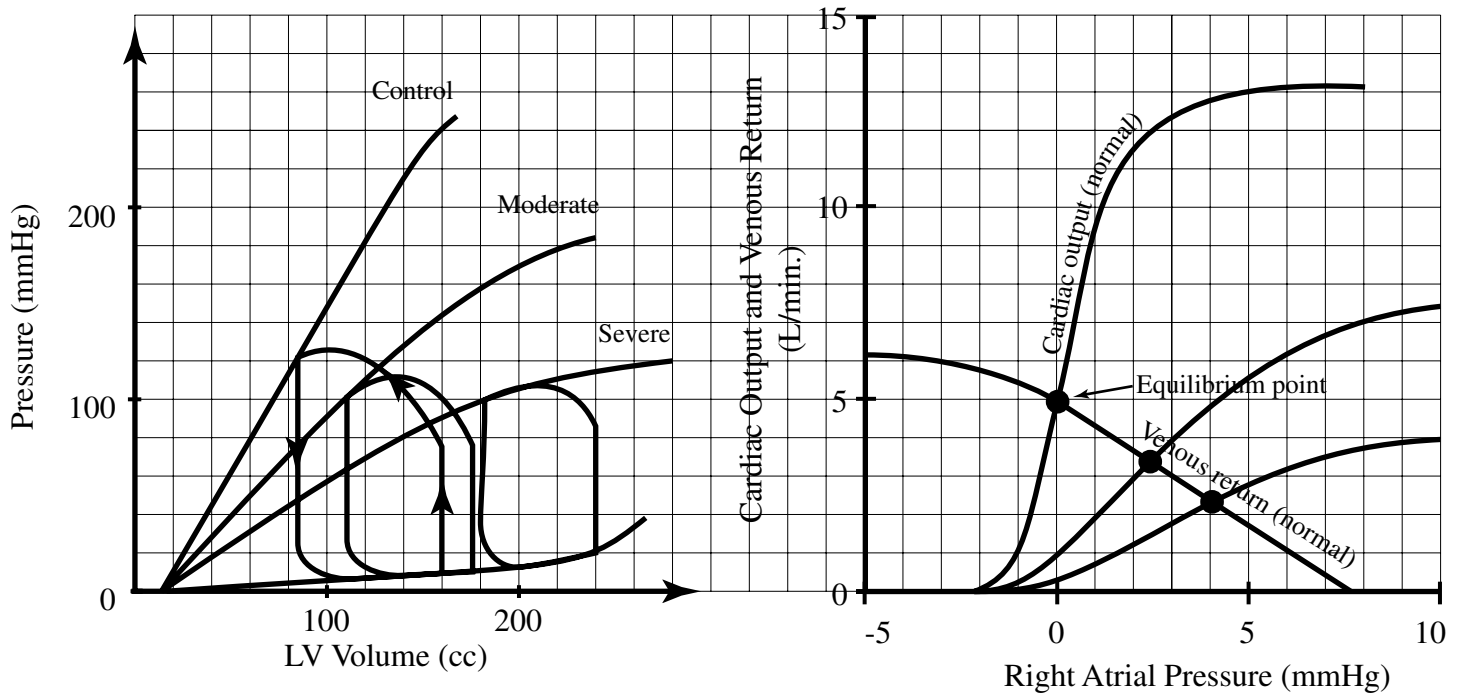
- (i) Decrease in  $P_{ms}$  due to decrease in apparent blood volume ( $V_T - V_O$ ) because of stretching of the veins when person is tipped up. VR curve shifts to the left. Slope of VR curve remains unchanged. No change in CO curve.  $Q$  decreases.
- (ii) Since  $Q$  went down, and HR unchanged, SV decreases.
- (iii) Since  $R$  is the same, and  $Q$  decreased, BP would decrease, with a lower LVESP.

E. The patient develops restrictive pericarditis, which prevents maximal diastolic filling.



- (i) Since  $C_D$  decreases, the slope of the CO curve decreases. VR curve is unaffected.  $Q$  decreases.
- (ii) Since  $C_D$  decreased, the diastolic PV characteristic curve's slope increases.
- (iii) Since diastolic filling decreases, and  $Q$  decreased without a change in HR, SV goes down.
- (iv) Since  $R$  is the same, and  $Q$  decreased, BP decreases.

F. The patient has a myocardial infarction (heart attack), which is a decrease in  $O_2$  supply caused by blocked blood flow to heart muscles.



- (i) Since cardiac tissue is dying,  $C_S$  increases,  $C_D$  decreases, i.e., the heart loses its ability to contract during systole and it gets stiffer and cannot fully relax during diastole. CO curve moves down. VR curve not affected.
- (ii) PV characteristic curves move toward each other. Systolic curve's slope decreases, diastolic curve's slope increases.
- (iii) SV decreases, and BP drops.