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SOURCEBOOK OF LABORATORY ACTIVITIES IN PHYSIOLOGY

Use of an iPad App to simulate pressure-volume loops and cardiovascular physiology

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Leisman S, Burkhoff D. Use of an iPad App to simulate pressure-volume loops and cardiovascular physiology. *Adv Physiol Educ* 41: 415–424, 2017; doi:10.1152/advan.00204.2016.—The purpose of this laboratory exercise is to model the changes in preload, afterload, and contractility on a simulated pressure-volume loop and to correlate those findings with common measurements of clinical cardiovascular physiology. Once students have modeled these changes on a healthy heart, the students are asked to look at a simulated case of cardiogenic shock. Effects on preload, contractility, and afterload are explored, as well as the hemodynamic effects of a number of student-suggested treatment strategies.

pressure-volume loops; starling curves; mean arterial pressure; physiology; simulation

Objectives and Overview

CARDIAC PRESSURE-VOLUME (PV) loops are physiological concepts that are taught extensively in medical schools and are used clinically to understand the changes in PV relationships in cardiac muscle. Fundamentals of PV loops, blood volume, and systemic vascular resistance can be found in almost any preclinical physiology or pathophysiology textbook (10, 12) and are required knowledge for both clinical medicine and the *U.S. Medical Licensing Examination* exams (7). However, in our experience, we have found that, when students are taught these complex topics in a didactic, lecture-based approach, they often have difficulty understanding how the multiple different variables can be integrated into whole body physiology and how they interrelate. We have developed a simulator session using a commercially available cardiovascular simulation App (developed by D. Burkhoff) to highlight the connection between the changes in the various fundamental components (preload, afterload, and contractility) and the effects on measurable clinical parameters, such as stroke volume (SV), blood pressure (BP), and cardiac output (CO). The simulation, which is based on the experimental work of Guyton, builds on prior cardiovascular simulation models and has been extensively validated in a recent paper (6).

We use the simulator to explore the basic concepts of preload, afterload, and contractility, and then we tie them together using a case of acute cardiogenic shock. This allows students to see how these concepts are relevant to clinical medicine, and how they can be manipulated in treatment strategies. It also shows that treatment strategies often come at a cost, that almost all strategies have untoward side effects.

Background

This laboratory exercise was initially written by S. Leisman in conjunction with the Harvi App created by D. Burkhoff (3). It was used in the cardiovascular laboratory portion of the Icahn School of Medicine first-year Human Physiology course. Students were taught PV loops in a traditional lecture format, supplemented with the required textbook. What we observed was that students could understand each individual component of the PV loop, but had trouble implementing them in specific clinical scenarios, or seeing how changes in preload, afterload, and contractility correlated with changes in output parameters, such as mean arterial pressure (MAP) and CO. We created a laboratory designed to teach those more in depth. Studies using other, proprietary-based cardiovascular simulators have shown a significant improvement in posttest scores compared with didactic lectures (2).

Laboratory software packages do exist, such as Biopac, that show simulations of cardiovascular phenomena and teach students real-time physiology. Additionally, medical schools have created their own proprietary cardiovascular simulator software, which students have subjectively reported helpful in understanding PV loops (11). However, these are limited in many cases by cost, need to purchase or develop hardware or software, need to train preceptors, or changes in technology rendering programs obsolete. Alternatively, animal laboratories can be used to teach relevant physiology, but these are becoming phased out for basic education, and studies have shown that students prefer computer simulations to animal demonstrations (14).

A major strength of this laboratory exercise is that it retains many of the strengths of a simulation program, but only requires an iPad, a free App, and can be run directly on an iPad or via projection. There is no need for expensive hardware, and App updates are available without additional cost. Our laboratory guide also provides suggested questions and answers to guide the facilitators as they teach. Although an expanded and paid version of the App has been developed and is available through iTunes (Harvi), the entire exercise described in this laboratory manual was designed and developed for the free, student version to increase its reach and range. All components and instructions are designed for the student app, and the colors and parameters described in the exercise refer to the student

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(free) version, not the paid version. Many of the features on the paid version are above and beyond the scope of a first-year physiology course, and purchase of the software will not result in an enhanced experience, nor is it required.

Improvements in hardware and software have rendered other simulation programs obsolete (5, 13–15), and we are hoping this simplified version will overcome that limitation. The App is regularly updated, and the exercise can also be done in a limited fashion (without requiring the App or iPad) using the figures provided.

Many medical schools are now requiring students to have iPads, and, among schools that do not require them, the proportion of ownership is high, with the most recent data available suggesting that 75% of preclinical students use the iPad (1). However, for students or institutions without access to an iPad or iTunes, instructions and figures are provided to allow students to use this exercise in a more limited fashion that will still accomplish many of the same goals.

Learning Objectives

After completing this activity, the student will be able to:

1. Visualize and describe the changes to the basic PV loop after alterations in preload, afterload, and contractility.
2. Understand and describe how changes to preload, afterload, and contractility will affect output variables, such as systolic BP (SBP) and diastolic BP (DBP), CO, and SV.
3. Give examples on how to use pharmacological and physiological mechanisms to change preload, afterload, and contractility.
4. Understand and describe the changes to the cardiac muscle after an acute myocardial infarction (MI).
5. Understand how a decrease in cardiac relaxation leads to a rise in end-diastolic pressure (EDP), left atrial pressure (wedge pressure), and pulmonary edema.
6. Understand and describe how a loss of cardiac muscle leads to a decrease in MAP and CO.
7. Predict treatment strategies to improve MAP and CO after acute heart failure.
8. Understand the limitations of available treatment strategies for heart failure.

Activity Level

This activity is suitable for preprofessional, allied health students, and graduate students enrolled in a Human or Cardiovascular Physiology course. We run this laboratory exercise in a first-year medical school Human Physiology course.

Prerequisite Student Knowledge or Skills

Before doing this activity, students should have a basic understanding of the human cardiovascular system and the autonomic nervous system, specifically their impact on the heart and vasculature. The students should have had prior knowledge of the following topics:

- Pressure-volume loops
- Cardiac output
- Preload, afterload, and contractility
- Mean arterial pressure, stroke volume, and ejection fraction
- Sympathetic and parasympathetic nervous system, including receptors

Skills students should have before the laboratory include:

- Calculating mean arterial pressure, ejection fraction, and stroke volume
- Interpretation of pressure-volume loops

Time Required

The exercise is designed to take 40 min to 1 h. However, it can be adapted to be longer or shorter, depending on the interest of the students and their prior knowledge base.

METHODS

We perform this activity 12 times, in groups of 8–12 students. We have found that this is the ideal number of students to encourage participation: with too many, quieter students may not speak up, and with too few, the discussion can be limited. The students are led through the activity by a facilitator who is an expert in Cardiovascular Physiology and can guide them through the various scenarios.

Equipment and Supplies

The following equipment and supplies are needed:

- iPad with iOS 7.0 or later
- Harvi-Student App, *PVLoops LLC* (free, via iTunes)
- iPad-compatible projector (we connect the iPad to a desktop computer using an Apple VGA adaptor and project from the desktop computer onto a large screen)

Human or Animal Subjects (If Applicable)

Not applicable.

Instructions

1. Connect the iPad to the projector screen and open the Harvi Student App. To access the "Interactive Simulation," you will need to turn the iPad horizontally. As we are only going to discuss PV loops and not utilize the Wiggers diagram in this simulation, you can hide the diagram by clicking "Layout" in the *bottom right* corner and unchecking "Time." You will now have a screen that shows "Inputs" on the *left*, "Pressure Volume Loops" in the *middle*, and "Outputs" on the *right*. You can click "Pause" to get the black dot to stop moving. (see Fig. 1).

2. Using laboratory guide, preceptor should facilitate and engage student discussion of terminology and PV loops. Suggested questions for discussion are provided below, but, because this is a simulator, students may request inputs that are not covered in the guide.

3. Orientation to terminology used in the simulator. Begin by orienting students to the terminology and program. Note that, because the simulator uses clinical terminology and not experimental terminology [i.e., pulmonary capillary wedge pressure (PCWP) can be seen on the simulator, but left atrial pressure cannot], preclinical students may not have familiarity with them.

3a. Input variables (ask students to define each one; definitions are below). Variables are on the *left* side of screen/figure under "Basic Left Ventricle."

PRELOAD: "STRESSED VOLUME". The total blood volume is functionally divided into two pools: the "unstressed" and the "stressed" volumes. The unstressed volume (or "dead volume") is the volume required to fill the capacitances of all vessels to a point at which the pressure inside just exceeds 0 mmHg at a CO of 0 l/min. The stressed volume is the blood volume in excess of the unstressed volume. For a typical person, there are 5 liters of blood, of which ~4 liters are in the unstressed pool, and ~1.2 liters (here noted as 1,200 ml) are in the stressed pool. In circumstances in which more preload is required (i.e., hemorrhage, exercise), blood in the unstressed pool can be recruited to

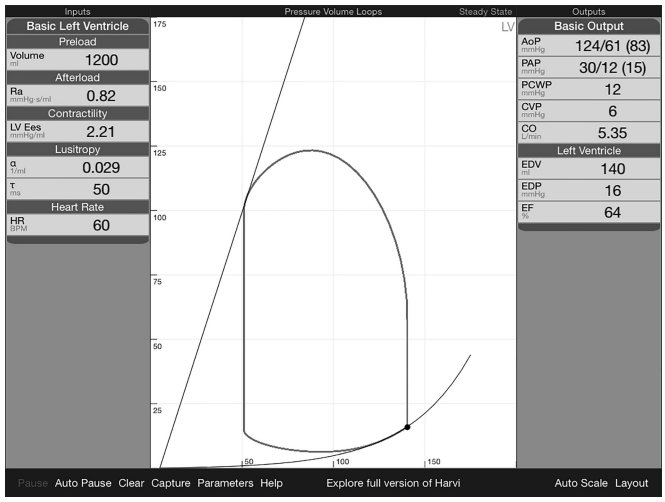

Fig. 1. Basic pressure-volume loop as modeled by Harvi. Inputs can be seen on the *left*, and pressure-volume loop in the *center* (volume in ml on *x*-axis, pressure in mmHg on *y*-axis). Basic outputs can be found on the *right*. AoP, aortic pressure; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CVP, central venous pressure; CO, cardiac output; EDV, end-diastolic volume; EDP, end-diastolic pressure; EF, ejection fraction.

augment the stressed volume via sympathetic stimulation. Similarly, the unstressed pool can be increased in some cases where there is too much preload.

AFTERLOAD. Ra is systemic arterial resistance (SAR), sometimes called "total peripheral resistance" or TPR. (In the afterload exercise, we will discuss how SAR is not the only component of afterload.)

CONTRACTILITY. The term contractility refers to the intrinsic strength of the heart muscle, independent of changes in preload and afterload. The purest index of left ventricular (LV) contractility is LV end-systolic elastance (LV Ees). It is the slope of the end-systolic PV relationship, which is the black diagonal line on the simulator under the "Pressure Volume Loops" column.

Remind students that, for a given contractility, you are constrained by the end-systolic PV line (or the LV Ees line): moving upward on the line (e.g., as occurs with increase in preload or afterload) will increase ventricular pressure generation, but the intrinsic ventricular (and muscle) contractility is unchanged. This is one expression of the Starling Relation, where an increase in preload increases myofiber stretch and thus increases contractile force, analogous to how increasing the stretch on a rubber band will increase the force with which it snaps back. Changing contractility, an intrinsic property of the muscle, is typically done by changing the calcium fluxes (or, in the analogy, changing the rubber band to a rubber band made of different material).

LUSITROPY. Lusitropy refers to diastolic properties of the heart, generally including the rate and extent of relaxation. In this simulation, changes to lusitropy are modeled via changes in the slope of the end-diastolic PV relationship (EDPVR). The model uses the equation $EDP = Po + \beta V^{\alpha}$ (4), where EDP is end-diastolic pressure, Po is the ventricular pressure at low volumes, V is the ventricular volume, and α and β are constants that refer to the curvature of the line and are determined by the mechanical properties of the heart. When α is increased, the βV^{α} term increases, resulting in a higher EDP for a given ventricular volume and a steeper EDPVR. Thus an increase in α will result in a stiffer, less compliant ventricle, which is shown on the PV loop by a steeper slope in the EDPVR. This means that, to increase lusitropy, you will decrease the α term: a decrease in α results in a "positive lusitropy."

HEART RATE (HR). HR is the number of times the heart beats per minute.

3b. PV loops: center panel. Depending on the time available, you may choose to review the components of the PV loop, including isovolumic contraction, ejection, isovolumic relaxation, and filling, etc. Students can be asked where the aortic and mitral valve open. We choose to leave this section out to keep the laboratory within a 45-min time period. Students are told before the laboratory to have facility with the basic PV loop.

3c. Outputs: right panel. Click "Capture" on the *bottom* menu to have a full set of outputs appear in the *right* panel. You will see two columns (orange and gray) with identical numbers. Only those variables that will be explored in the laboratory will be defined. (If you are using the figures instead of the App, see Fig. 2 and look at the dark gray "Capture" column).

- HR: Heart rate [60 beats/min (BPM)]
- EF: Ejection fraction (64%)
- CO: Cardiac output (5.35 l/min)
- PCWP: Pulmonary capillary wedge pressure (12 mmHg). The students should be taught that this is the surrogate for left atrial pressure, because clinically, measuring left atrial pressure would be extremely invasive. Instead a "wedge pressure" is used as a substitute clinically.
- AoPs/d/m: Systolic, diastolic, and mean aortic pressure (124/61/83 mmHg).
- MVO_2: Myocardial oxygen consumption is the amount of oxygen the myocardium requires per minute to regenerate the ATP that is used in contraction and active transport. As this number increases, it means the heart is requiring more oxygen.

SUGGESTED DISCUSSION QUESTIONS FOR THE ORIENTATION SECTION 3.

Question 3a: What mechanisms does the body use to mobilize the unstressed volume?

Question 3b: How much of the preload ("stressed volume") is in the LV at the end of diastole and at the end of systole in this simulated

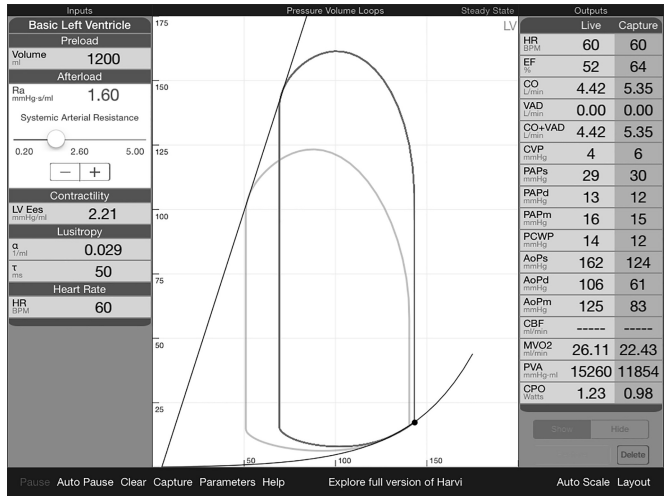

Fig. 2. Modeling increased afterload. *Left*: the increase in SVR (systemic vascular resistance) from 0.8 to 1.60 $mmHg \cdot s \cdot ml^{-1}$. *Middle*: original pressure-volume loop (light gray) and new, higher afterload pressure-volume loop (dark gray). *Right*: quantitative clinical measurements at baseline (dark gray/"Capture") and higher afterload (light gray/"Live"). HR, heart rate; EF, ejection fraction; CO, cardiac output; VAD, ventricular assist device; CVP, central venous pressure; PAPs, pulmonary artery systolic pressure; PAPd, pulmonary artery diastolic pressure; PAPm, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; AoPs, systolic aortic pressure; AoPD, diastolic aortic pressure; AoPm, mean aortic pressure; CBF, coronary blood flow; MVO_2, myocardial oxygen consumption; PVA, pressure volume area (stroke work); CPO, cardiac power output.

patient? What is the SV in this patient? What are two ways it can be calculated from the data provided?

Question 3c: How does the body alter SAR?

Question 3d: How would the body change the contractility of the cardiac muscle (and thus change the slope of the line)?

Question 3e: What are the determinants of EF? How can you mathematically verify the value seen here?

Question 3f: What is the patient's CO? How can you calculate it using the values provided?

Question 3g: Where on the PV loop can you find the SBP? Where can you find the DBP?

4. Modeling the classic changes to the PV loop (preload, afterload, and contractility). Note: Most textbooks teach a simplified version of PV loops, in which one parameter is changed while keeping all other variables constant (12), or only show changes to the loop after the first beat, but not subsequent beats (10). This results in the generation of PV loops in which only the end-systolic volume (ESV) is altered (changes to afterload or contractility) or only the end-diastolic volume (EDV) is altered (changes to preload). However, because the cardiovascular system is a closed loop, it is impossible to only change one parameter without affecting the others. When one parameter (such as LV contractility) is changed, there are volume shifts of blood between pulmonary and circulatory circuits that creates a new state of equilibrium throughout the circuit, leading to a more complex array of alterations to the heart and PV loop (6, 9).

The simulator takes a "whole body" approach, in which the changes to the classic variables will have multiple effects on cardiac pressures and volumes. Specifically, changes to preload, afterload, contractility, or lusitropy will result in changes to both EDV and ESV and will result in loops and physiology closer to what are seen in a real-world setting.

4a. Using the simulator to model changes in afterload. Have students first define afterload. In our experience, students will tend to say "afterload is equivalent to the systolic blood pressure" or "afterload is equal to total peripheral resistance." We stress that afterload is the impedance to ejection that the LV faces as it contracts. We use this definition because it encompasses both changes in Ra and changes in valvular resistance. We ask them to come up with a scenario where a patient could have a very high afterload and a normal or low SAR, such as aortic stenosis.

For this simulator, however, we use changes in SAR to model changes in afterload. To do this:

1. Screen should have "Basic Left Ventricle" inputs on the *left*, an orange PV loop in the *center*, and the "Live" and "Capture" columns on the third "Outputs" panel.
2. Click "Afterload" (*left* panel) to expand the size; then increase the SAR from 0.82 to 1.6 $mmHg \cdot s \cdot ml^{-1}$, either by sliding the circle or by using the + and – buttons.
3. In the *top right* corner of the panel, you will see the word "Transitioning" in red font. After a short time, it will change to the words "Steady State" in green font. Once the simulator is in "Steady State," click "Pause" on the *bottom* menu. Click "Pause" again to stop the black dot from moving.
4. You will now see two loops in the *middle* panel, which correspond to the output variables in the *right* panel:
   - *4a*. An orange loop (the original PV loop), which corresponds to the "Capture" column in orange.
   - *4b*. A red loop (the new PV loop with the higher afterload setting), which corresponds to the gray "Live" column in the "Outputs" section. (Fig. 2. In the figures, the original loop is light gray and corresponds to the dark gray/"Capture" column. The higher afterload loop is dark gray and corresponds to the light gray/"Live" column.)

Once students are oriented to the new loop and corresponding numbers, they can be divided into smaller groups and answer the following questions regarding the changes that they see. Students may notice that HR remains the same, and ask why the HR has not decreased in the face of a higher MAP. The answer is that this program does not have a baroreceptor reflex.

SUGGESTED QUESTIONS FOR SECTION 4A: MODELING CHANGES IN AFTERLOAD.

Question 4a-1: What happens to contractility when afterload is increased?

Question 4a-2: What happens to SV when afterload is increased? What are two different ways you can use to determine SV using the simulator?

Question 4a-3: What happens to EF when afterload is increased? Why?

Question 4a-4: What happens to SBP and DBP when afterload is increased? Where can you find this on the PV loop? What happens to MAP? What are two ways it can be calculated?

Question 4a-5: What happens to MVo_2 when afterload is increased?

Question 4a-6: Describe the differences in the shapes of the two PV loops.

Question 4a-7: What drugs could mimic these changes?

Once students have answered questions, they should come together to discuss as a group, and the facilitator can ensure all students have answered the questions correctly and can ensure any additional questions are answered.

4b. Using the simulator to model changes in contractility. In this simulation, we simulate contractility changes by changing the slope of the Ees. In this case, we will double contractility and look at the effects on a variety of hemodynamic parameters.

1. Click "Parameters" on the *bottom* of menu; then choose "Normal" under the list of "Presets."
2. Click "Load Preset," and you should now see both PV loops (higher afterload and normal) in red.
3. Click "Clear" on the *bottom* menu; the higher afterload (red) PV loop should disappear, and only the original PV loop should remain; it will be in orange. The "Live" and "Capture" values in the *right* panel should show equivalent values.
4. Increase contractility by clicking on "Contractility" in the *left-hand* panel; the value is preset to read 2.21 mmHg/ml. The box size should expand. Increase the contractility using the slide bar or the + key to 4.42 mmHg/ml, doubling the contractility.
5. Wait for the red "Transitioning" to turn into the "green" steady-state notification; when this happens, click "Pause." Click "Pause" again to have the dot stop moving.
6. You should now see two loops in the *middle* panel:
   - *6a*. An orange loop (the original PV loop), which corresponds to the values in the orange "Capture" column on the *right* panel.
   - *6b*. A red loop (higher contractility) that corresponds to the values in the gray "Live" column in the *right* panel (Fig. 3. In the figures, the original loop is light gray and corresponds to the dark gray/"Capture" column. The higher contractility loop is dark gray and corresponds to the light gray/"Live" column).

Once students are oriented to the new loop and corresponding numbers, they can be divided into smaller groups and answer the following questions regarding the changes that they see. Again, HR remains unchanged.

SUGGESTED QUESTIONS FOR SECTION 4B: MODELING CHANGES IN CONTRACTILITY.

Question 4b-1: What drugs could mimic these changes?

Question 4b-2: Describe the changes seen in the PV loop.

Question 4b-3: What happens to SV with increases in contractility?

Question 4b-4: What happens to EF with increases in contractility?

Question 4b-5: What happens to SBP, DBP, and MAP with an increase in contractility?

Question 4b-6: What happens to MVo_2 with higher contractility?

4c. Using the simulator to model changes in preload. In this simulation, we simulate preload changes by increasing the "Stressed

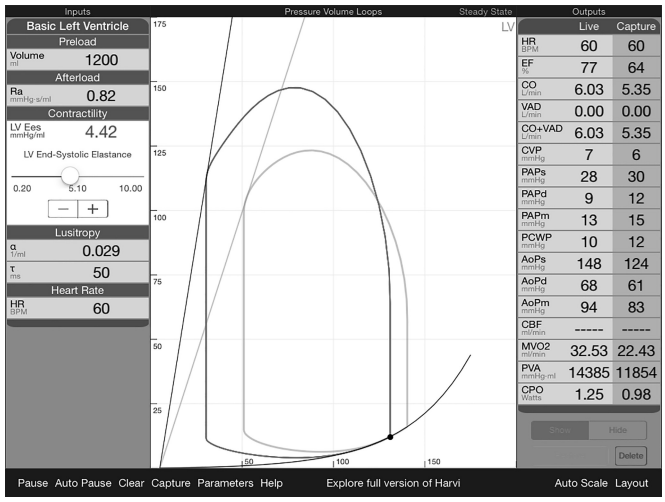

Fig. 3. Modeling increased contractility. *Left*: the increase in contractility/LV end-systolic elastance from 2.21 to 4.42 mmHg/ml. *Middle*: original pressure-volume loop (light gray) and new, higher contractility pressure-volume loop (dark gray). *Right*: quantitative clinical measurements at baseline (dark gray/"Capture") and higher contractility (light gray/"Live"). HR, heart rate; EF, ejection fraction; CO, cardiac output; VAD, ventricular assist device; CVP, central venous pressure; PAPs, pulmonary artery systolic pressure; PAPd, pulmonary artery diastolic pressure; PAPm, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; AoPs, systolic aortic pressure; AoPD, diastolic aortic pressure; AoPm, mean aortic pressure; CBF, coronary blood flow; MVO_2, myocardial oxygen consumption; PVA, pressure volume area (stroke work); CPO, cardiac power output.

Volume" or the amount of blood in the arterial system. In this case, we are increasing the stressed volume from 1,200 to 1,700 ml.

1. Click "Parameters" on the *bottom* of menu; then choose "Normal" under the list of "Presets" and click "Load Preset."
2. You should now see both PV loops (higher contractility and normal) in red, with the circle tracing the normal PV loop.
3. Click "Clear" on the *bottom* menu. The higher contractility PV loop should disappear and only the original PV loop should remain; it will be in red. The "Live" and "Capture" values in the *right* panel should show the same values.
4. Increase preload by clicking on "Preload" in the *left-hand* panel; the value is preset to read 1,200 ml. The box size should expand. Increase the preload ("Stressed Blood Volume") by 500 ml using the slide bar or the + key to 1,700 ml.
5. Wait for the red "Transitioning" to turn into the "green" steady-state notification; when this happens, click "Pause."
6. Click "Pause" to have the dot stop circling the loops.
7. You should now see two loops in the *middle* panel:
   - *7a*. An orange loop (the original PV loop), which corresponds to the values in the orange "Capture" column on the *right* panel.
   - *7b*. A red loop (higher preload) that corresponds to the values in the gray "Live" column in the *right* panel (Fig. 4. In the figures, the original loop is light gray and corresponds to the dark gray/"Capture" column. The higher preload loop is dark gray and corresponds to the light gray/"Live" column).

Once students are oriented to the new loop and corresponding numbers, they can be divided into smaller groups and answer the following questions regarding the changes that they see. Again, HR remains unchanged.

SUGGESTED QUESTIONS FOR SECTION 4C: MODELING CHANGES IN PRELOAD.

Question 4c-1: Is a stressed volume increase of 500 ml equivalent to giving 500 ml of isotonic saline? Of colloid? Of blood? Is there a way to increase the stressed volume without giving fluids?

Question 4c-2: Describe the changes seen in the PV loop. How are these changes similar and different from the higher contractility example?

Question 4c-3: What happens to SV with increases in preload?

Question 4c-4: What happens to EF with increases in preload? Why?

Question 4c-5: What happens to SBP, DBP, and MAP with an increase in preload?

Question 4c-5: What happens to MVO_2 with higher preload?

5. Putting it all together: a case of acute cardiogenic shock. In this simulation, we will simulate a case of cardiogenic shock and look at the hemodynamic changes that ensue. We will also attempt to treat the patient using a variety of student-suggested methods.

1. Click "Parameters" on the *bottom* of menu; then choose "Normal" under the list of "Presets."
2. Click "Load Preset," and you should now see both PV loops. The baseline loop will be in orange, and the higher preload loop in red.
3. Click "Clear" on the *bottom* menu. The higher preload PV loop should disappear, and only the original PV loop should remain; it will be in orange. The "Live" and "Capture" values in the *right* panel should show the same values.
4. Load the case by clicking on "Parameters" on the *bottom* menu, and choose "Acute Heart Failure." Then select "Load Preset." Click "Pause" to have the new loop appear, and "Pause" again to have the dot stop circling the loop.
5. You should now see two loops in the *middle* panel:
   - *5a*. An orange loop (the original PV loop), which corresponds to the values in the orange "Capture" column on the *right* panel.
   - *5b*. A red loop (acute heart failure) that corresponds to the values in the gray "Live" column in the *right* panel. You will also see a new end-systolic PV relationship (ESPVR) line in black.
6. Click "Clear" to have the red loop disappear.

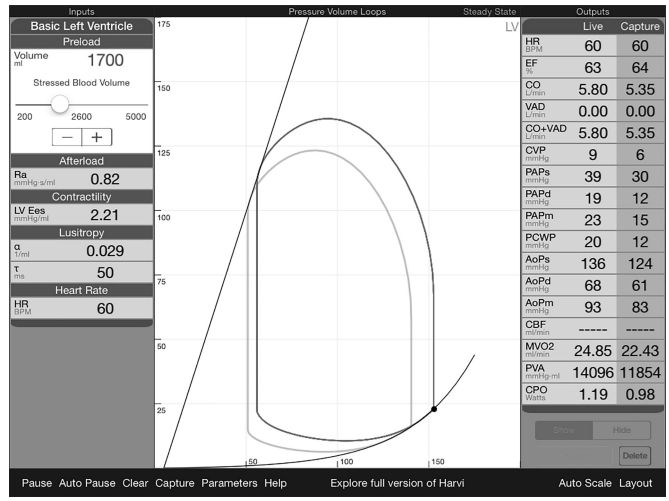

Fig. 4. Modeling increased preload. *Left*: the increase in preload from 1,200 to 1,700 ml. *Middle*: original pressure-volume loop (light gray) and new, higher preload pressure-volume loop (dark gray). *Right*: quantitative clinical measurements at baseline (dark gray/"Capture") and higher preload (light gray/"Live"). HR, heart rate; EF, ejection fraction; CO, cardiac output; VAD, ventricular assist device; CVP, central venous pressure; PAPs, pulmonary artery systolic pressure; PAPd, pulmonary artery diastolic pressure; PAPm, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; AoPs, systolic aortic pressure; AoPD, diastolic aortic pressure; AoPm, mean aortic pressure; CBF, coronary blood flow; MVO_2, myocardial oxygen consumption; PVA, pressure volume area (stroke work); CPO, cardiac power output.

7. In the *left* panel, click on "Lusitropy" to open the box. Increase the α from 0.029 to 0.039 1/ml.
8. Again, wait for "steady state," and, once reached, click "Pause" on the *bottom* menu. Click "Pause" again to have the dot stop moving.
9. You should now see two loops in the *middle* panel:
   - 9a. An orange loop (the original PV loop), which corresponds to the values in the orange "Capture" column on the *right* panel.
   - 9b. A red loop (acute heart failure) that corresponds to the values in the gray "Live" column in the *right* panel. You will also see a new ESPVR line and a new EDPVR curve in black (Fig. 5. In the figures, the original loop is light gray and corresponds to the dark gray/"Capture" column. The postinfarction loop is dark gray and corresponds to the light gray/"Live" column).
10. Go back to "Parameters" and enter "Custom 1" under "Parameter Set Name" and then click "Save." This will allow you to recall the postinjury PV loop between simulations.

Once the two loops are visible, provide the following case to the students. A 65-yr-old man is shoveling snow when he feels an intense pressure on his chest and radiating down his left arm. He begins to feel extreme shortness of breath, which improves slightly with sitting straight up. He also starts feeling lightheaded. He calls 911 and is rushed to the ER. He is diagnosed with a MI. You now see his original (orange/"Capture") and postevent (red/"Live") PV loops.

SUGGESTED QUESTIONS SECTION 5: ACUTE CARDIOGENIC SHOCK.

Question 5-1: What are the changes to the cardiac muscle that happen as a direct result of the myocardial infarction (MI)? Why did these happen? How are they represented on the curve?

Question 5-2: What are the hemodynamic impacts of the cardiac changes? Why?

Question 5-3: How do these changes relate to his symptoms of shortness of breath and lightheadedness?

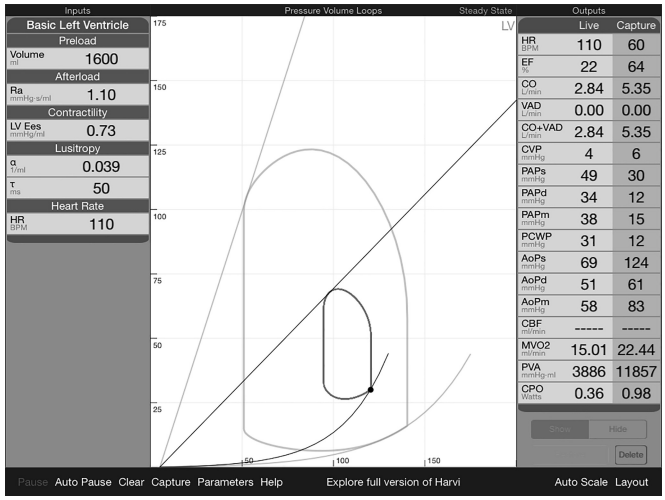

Fig. 5. Modeling acute heart failure. *Left*: qualitative values for the post-acute infarction heart. *Middle*: original pressure-volume loop (light gray) and post-acute infarction pressure-volume loop (dark gray). *Right*: quantitative clinical measurements at baseline (dark gray/"Capture") and post-acute infarction (light gray/"Live"). HR, heart rate; EF, ejection fraction; CO, cardiac output; VAD, ventricular assist device; CVP, central venous pressure; PAPs, pulmonary artery systolic pressure; PAPd, pulmonary artery diastolic pressure; PAPm, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; AoPs, systolic aortic pressure; AoPD, diastolic aortic pressure; AoPm, mean aortic pressure; CBF, coronary blood flow; MVO_2, myocardial oxygen consumption; PVA, pressure volume area (stroke work); CPO, cardiac power output.

Question 5-4: What are the compensatory responses the body uses to attempt to restore homeostasis? On what receptors do they act? In this particular simulation, the baroreceptor is engaged.

6. Simulation of treatment of acute cardiogenic shock. Students should now be asked for potential treatment strategies to manage the patient's symptoms. When a student makes a suggestion, use the input settings to mimic that change. For example, if a student says, "increase preload," use the simulator to increase preload. With each change, look at the output parameters and discuss the helpful and harmful effects of the intervention. Students should be encouraged to pay attention to what they are trying to improve and how they will improve it.

Depending on their level, they may know drugs that act on the cardiovascular system. If a student suggests a drug, use the input parameters to mimic those changes. For example, if a student says to give high-dose epinephrine, change the input parameters to increase the HR, contractility, and TPR to model the effects of a high dose of epinephrine.

A list of frequently seen suggestions follows, as well as pros, cons, and potential teaching points for each one.

Before starting to simulate the suggestions:

- Click "Capture" on the *bottom* menu to capture the post-MI, pretreatment PV loop. The acute cardiogenic shock loop will now turn light blue. The "Outputs" column should now be a gray "Live" column and a blue "Capture" column. The changes the students suggest will appear as "Live" and will be compared with the blue "Capture" column. Remind students that they are unlikely to be able to get the patient back to the pre-MI state, but can hopefully improve the post-MI parameters with their treatments.
- For all suggested treatment strategies, change the parameters in the *left* column ("Basic Left Ventricle"). After the treatment change, you will have three loops: the orange pre-MI, the turquoise post-MI, and the red post-MI, posttreatment.

Between each scenario:

- Click "Clear" to start a new treatment (alternatively, you can add on to a treatment by not pressing "Clear").
- Go to "Parameters" and choose "Custom 1" to get back to the post-MI state.

Compare the variables in the turquoise "Capture" column with the "Live" gray column to see the effects of the changes.

A. INCREASE PRELOAD OR GIVE FLUIDS. (Most students will suggest this, because they have been taught that an increase in preload will increase SV, MAP, and CO in a healthy person.) Simulate this by increasing the preload from 1,600 to 2,000 ml.

Pros: CO increased (modestly), MAP increased (modestly).

Cons: Worsening of pulmonary edema, evidenced by the rise in PCWP from 31 to 40 mmHg (it was 12 mmHg before the acute event). Students often will forget that increasing preload when you are already at the plateau of the Frank-Starling curve will minimally increase SV and CO. However, because you are adding preload to an already stiff ventricle, you are going to increase the left atrial pressure, which will increase the hydrostatic pressure in the pulmonary capillaries, and lead to movement of fluid from the pulmonary capillaries into the alveoli.

B. INCREASE SYSTEMIC VASCULAR RESISTANCE/GIVE AN α_1-AGONIST. (Students often pick this strategy in an attempt to increase MAP.) Simulate this by increasing Ra (Afterload) from 1.10 to 2 $mmHg \cdot s \cdot ml^{-1}$.

Pros: Increased MAP (58 to 67 mmHg).

Cons: Decreased CO, increased PCWP (it is harder for the heart to pump blood out with a higher afterload). You are asking a sick, ischemic heart to work harder to overcome the higher afterload. Patient's angina will increase.

Students may wonder why a loss of CO matters if the overall MAP has risen. Although cerebral perfusion pressure has improved, it has done so by severe vasoconstriction of peripheral vessels. This can lead to ischemia, especially of the digits.

C. DECREASE SYSTEMIC VASCULAR RESISTANCE/GIVE AN α_1-ANTAGONIST. (This strategy is typically chosen after the "increase SVR" one, to decrease cardiac work.) Simulate this by decreasing Ra (afterload) from 1.10 to 0.6 mmHg·s·ml^{-1}.

Pros: Increased CO, decreased PCWP.

Cons: Decreased MAP (patient now has a BP of 61/38 mmHg), and shock is worsened.

This scenario is useful to point out that increases in CO alone are not always beneficial to patients; in fact, this patient has a worsening of MAP with the decreased afterload. You can use vasodilatory shock as an example of a high CO state with a low SVR, leading to hypotension and shock.

D. INCREASE CONTRACTILITY/GIVE AN INOTROPE.

Increase from 0.73 to 1 mmHg/ml.

Pros: Increased CO, increased MAP, decreased PCWP.

Cons: Increased MVO_2 in an already ischemic heart.

If students suggest giving a β_1-agonist, such as high-dose epinephrine, dobutamine, or isoproterenol, make sure to increase contractility and HR. This will more accurately mimic those drugs and will show the additional cons of tachycardia: a decrease in diastolic filling time, lower SV, and increased risk of arrhythmia.

E. INCREASE LUSITROPY.

Decrease α from 0.039 to 0.032 1/ml.

Pros: Increased MAP, increased CO, decreased PCWP (improvement of pulmonary edema and cerebral perfusion).

Cons: Increased MVO_2, and (unlike the above scenarios) there is no way to increase LV compliance in practice.

Troubleshooting

The main challenge can be pressing a wrong button on the simulator and getting an unwanted view. Common errors are:

- Accidentally pressing the main "PV Loop" screen and getting a view of all four chambers. Click on the desired chamber (LV), and the others will disappear.
- Having the black dot continue to circle the loops. This can be eliminated by pressing "Pause."
- Having the loop disappear. Try pressing "Pause," and the loop will get retraced.
- Forgetting to reset between simulations and seeing the effects of two alterations. Choosing "Normal" under "Parameters" will reset to the beginning values.

If these do not work, the program can be closed and restarted.

Safety Considerations

None.

RESULTS

Expected Results and Evaluation of Student Work

Suggested questions and answers for section 3: orientation to the simulator and variables.

Question 3a: What mechanisms does the body use to mobilize the unstressed volume?

[Answer 3a: Activation of sympathetic nervous system via α_1-receptors on the large-capacitance veins causes venoconstriction and results in a functional shift of blood from one pool to the other. The vascular beds where most of the unstressed volume is derived include the splanchnic bed and the spleen.]

Question 3b: How much of the preload ("stressed volume") is in the LV at the end of diastole and at the end of systole in this simulated patient? What is the SV in this patient? What are two ways it can be calculated from the data provided?

[Answer 3b: Students may say "1,200 ml" as that is the number listed for preload. However, using the PV loop, it can be determined that the EDV is 140 ml and the ESV is 50 ml, so that the SV is (140 ml − 50 ml = 90 ml). Alternatively, you can calculate from the variables on the "Outputs" column. EF = SV/EDV, 0.64 = SV/140 ml, or SV = 89.6 ml.]

Question 3c: How does the body alter SAR?

[Answer 3c: Sympathetic stimulation of the α-adrenergic receptors on the smooth muscles within the arterial system, particularly those of the arterioles, which are the main drivers of systemic vascular resistance. Remind students that there is no parasympathetic innervation to the vascular system.]

Question 3d: How would the body change the contractility of the cardiac muscle (and thus change the slope of the line)?

[Answer 3d: Changes in sympathetic tone, inotropes, damaging heart muscle as in myocardial ischemia and infarction.]

Question 3e: What are the determinants of EF? How can you mathematically verify the value seen here?

[Answer 3e: EF is (EDV − ESV)/EDV, or SV/EDV. You can verify the answer using 90 ml/140 ml.]

Question 3f: What is the patient's CO? How can you calculate it using the values provided?

[Answer 3f: The patient's CO is given to us as 5.35 l/min. CO is calculated by SV × HR. 90 ml × 64 beats/min = 5.4 l/min.]

Question 3g: Where on the PV loop can you find the SBP? Where can you find the DBP?

[Answer 3g: The systolic pressure, or the maximum pressure in the aorta, is represented as the maximum pressure on the PV loop. In this example, the peak pressure on the loop is 119 mmHg. The diastolic pressure is the lowest pressure in the aorta and is where the aortic valve opens. Here it is seen at 62 mmHg (the inflection point on the right side of the PV loop when the vertical line starts to curve).]

Suggested questions and answers for section 4a: modeling changes in afterload.

Question 4a-1: What happens to contractility when afterload is increased?

[Answer 4a-1: Contractility will not change, because the intrinsic properties of the heart muscle have not been altered. We see this as the slope of the ESPVR remaining constant. A higher afterload will cause the PV loop to move higher up the same ESPVR (Ees, black) line. However, the pressure generated by the heart has increased. The loop appears taller, and the inflection point between isovolumic contraction and ejection at a higher pressure (the aortic valve opens at a higher pressure). This is reflected in the higher diastolic pressure (AoPd) (62 mmHg to 106 mmHg) seen in the "Outputs" section.]

Question 4a-2: What happens to SV when afterload is increased? What are two different ways you can use to determine SV using the simulator?

[Answer 4a-2: SV = (EDV – ESV). The SV decreases with an increase in afterload. This can be calculated in two ways. You can qualitatively see the width of the loop is narrower in the higher afterload scenario; the increase in the ESV means that the SV has decreased. This can be measured qualitatively

using the numbers on the *x*-axis. It can also be measured by dividing CO by HR:

Old: 5.35 l/min divided by 60 beats/min = 89 ml.

New: 4.40 l/min divided by 60 beats/min = 73 ml.

Note that most classic textbook diagrams will show that increases in afterload lead to decreased ESV and a constant EDV. This is because, in textbooks, changes in afterload are seen in an artificial system in which preload and contractility are held constant. In the simulator, there will be changes in preload when afterload is altered.]

Question 4a-3: What happens to EF when afterload is increased? Why?

[Answer 4a-3: EF decreases. EF = SV/EDV and the decrease in SV leads to a decrease in EF. Despite the small increase in the EDV compared with the original PV loop, the much larger decrease in SV results in a lowering of EF.]

Question 4a-4: What happens to SBP and DBP when afterload is increased? Where can you find this on the PV loop? What happens to MAP? What are two ways it can be calculated?

[Answer 4a-4: SBP is the highest BP during a given cardiac cycle. It is the maximum pressure seen in the aorta. In this simulation, the SBP is 162 mmHg for the higher afterload, and 124 mmHg for the original scenario. These values also correspond on the PV loop to the highest point on the curve (trace the highest point on curve to the *y*-axis).

DBP is the lowest pressure in the aorta. It can be represented as the pressure that needs to be generated in the heart to open the aortic valve (assuming normal valve). In the simulator, the DBP corresponds to the inflection point on the PV loop where the isovolumic contraction becomes ejection and can be found either in the "Outputs" panel or from the curve. For the original simulation, the DBP is 61 mmHg, and, for the high afterload simulation, the DBP is 107 mmHg.

The MAP can be calculated using two methods.

$$MAP = CO \times TPR$$

or

$$MAP = 2/3\ DBP + 1/3\ SBP$$

In this simulation, we see that MAP increases with a higher afterload. Both SBP and DBP are increased, and, using the numbers provided:

$$\text{Original MAP} = 2/3 \times 61 + 1/3 \times 124 = 82\ \text{mmHg}$$

$$\text{Higher Afterload MAP} = 2/3 \times 107 + 1/3 \times 162 = 125\ \text{mmHg}$$

Note that, for the second calculation, both the SBP and the DBP are higher, as is the MAP. For the second calculation, the CO has decreased in the higher afterload condition, but the increase in TPR is great enough to cause a higher MAP.]

Question 4a-5: What happens to MVO_2 when afterload is increased?

[Answer 4a-5: Cardiac work increases with higher afterload. The heart requires more oxygen to achieve the pressures required to eject blood with a higher SAR.]

Question 4a-6: Describe the differences in the shapes of the two PV loops.

[Answer 4a-6: Compared with the original PV loop, the increased afterload loop is taller (higher SBP) and narrower (decreased SV).]

Question 4a-7: What drugs could mimic these changes?

[Answer 4a-7: Increased TPR would be expected after administration of an α_1-agonist. Examples of these include phenylephrine, vasopressin, and norephinephrine. These drugs would be expected to cause a reflex bradycardia.]

Suggested questions and answers for section 4b: modeling changes in contractility.

Question 4b-1: What drugs could mimic these changes?

[Answer 4b-1: Drugs that can increase contractility are termed "positive inotropes" and include agents such as digoxin, β_1-agonists, phosphodiesterase inhibitors, and calcium.

A β_1-agonist would be expected to also increase the HR.]

Question 4b-2: Describe the changes seen in the PV loop.

[Answer 4b-2: Changes include an increase in height (higher SBP) and an increase in width (higher SV). The increase in SV is due to a decrease in the ESV: more blood is ejected in systole for the same preload. Although the EDV has decreased (due to a decreased venous return as more blood remains in the stressed component), the decrease in the ESV is greater and so the net SV has increased.

Students may ask why the EDV has decreased, when most textbooks will show a constant EDV, despite an increase in contractility. The reason for this is most basic physiology textbooks will assume an artificial scenario in which contractility is changed and preload remains constant. In reality, the change in contractility will lead to a decrease in EDV.

The slope of the Ees line has also increased; this means that, for a given lengthening of the cardiac myocyte fiber, more tension can be generated.]

Question 4b-3: What happens to SV with increases in contractility?

[Answer 4b-3: SV increases with increases in contractility. Here we can attempt to view the change in SV qualitatively: the PV loop is wider. We can also attempt to calculate it given the numbers provided:

Old: 5.35 l/min divided by 60 beats/min = 89 ml.

New: 6.03 l/min divided by 60 beats/min = 100.5 ml.]

Question 4b-4: What happens to EF with increases in contractility?

[Answer 4b-4: EF increases from 64 to 77%. Again, the EF increases, despite a decrease in EDV.]

Question 4b-5: What happens to SBP, DBP, and MAP with an increase in contractility?

[Answer 4b-5: The SBP, DBP, and MAP all increase. The SBP (the highest point on the PV loop) increased from 124 to 148 mmHg. This is attributable to the increased contractile force ejecting more blood into the aorta, resulting in a higher pressure. In contrast to the higher afterload example, the DBP does not increase as much as the SBP (61 to 68 mmHg). The slight increase in DBP is due to the increased volume of blood transferred to the aorta, which will increase the pressure against which the aorta has to push to open. Overall, the increase in SBP and DBP has led to a higher MAP.

Alternatively, we can use CO × TPR to calculate MAP. Although TPR remains constant, the increase in CO leads to a higher MAP.]

Question 4b-6: What happens to MVO_2 with higher contractility?

[Answer 4b-6: The increase in contractility comes at a price: more oxygen is required to generate the additional ATP needed to increase the calcium fluxes. The MVO_2 increases.]

Suggested questions and answers for section 4c: modeling changes in preload.

Question 4c-1: Is a stressed volume increase of 500 ml equivalent to giving 500 ml of isotonic saline? Of colloid? Of blood? Is there a way to increase the stressed volume without giving fluids?

[Answer 4c-1: No. When crystalloids are given to patients, they will not stay in the intravascular space alone. Due to hydrostatic pressures, 500 ml of isotonic saline administered into the intravascular space will eventually distribute to 375 ml of saline in the interstitial space and 125 ml in the intravascular space: isotonic fluids will distribute 75% into the interstitium and 25% into the intravascular space. To get 500 ml of isotonic saline in the intravascular space, you would need to administer 2 liters of isotonic saline.

Although 500 ml of administered colloid and blood would remain in the intravascular space (the rise in intravascular oncotic pressure due to the blood and colloid will counteract the hydrostatic pressure of the fluid), this still will not result in an increased preload of 500 ml.

Because fluid in the intravascular system can distribute into the stressed (arterial) and unstressed (venous) systems, 500 ml of colloid/blood into the vascular system will result in only a small increase in the stressed volume: the majority will distribute into the higher capacitance veins. This will not contribute to the preload. Instead, an increase in stressed volume of 500 ml would result from a much larger volume of colloid/blood being administered to the patient. In the case of isotonic saline, 500 ml of saline would only lead to 125 ml of fluid in the intravascular space, and even less of this would remain in the stressed volume.

The body can increase the stressed volume as a response to low BP. Baroreceptor sensing of a low MAP leads to higher sympathetic tone, which will venoconstrict the veins. By lowering the capacitance (decreasing the compliance) of the veins, more blood will be transferred to the arterial system, increasing the stressed blood volume.]

Question 4c-2: Describe the changes seen in the PV Loop. How are these changes similar and different from the higher contractility example?

[Answer 4c-2: Changes include an increase in height (higher SBP) and an increase in width (higher SV). Note that this is different from the increase in height and width seen in the higher contractility example because:

- The increase in width/SV results primarily from an increase in EDV in the higher preload example. In the example of higher contractility, the increase in SV is mediated by a decrease in the ESV.
- The PV loop is constrained by the LV Ees with higher preload, but, with higher contractility, the Ees increases (noted by a second Ees line on the graph, at a steeper slope). Although an increase in preload results in a greater stretch to the myocytes and more forceful ejection of blood, this is not the same as an increase in contractility. In a change in contractility, you get a more forceful contraction for the same amount of preload.

The higher preload curve shows a slight increase in ESV; again, this is in contrast to most physiology texts that will show a constant ESV with changes in preload. This is because textbooks often show changes in preload in an artificial system in which contractility and afterload are held constant.]

Question 4c-3: What happens to SV with increases in preload?

[Answer 4c-3: SV increases with increases in preload. We can see this qualitatively via the increase in the width of the PV loop. We can also attempt to calculate it given the numbers provided:

Old: 5.35 l/min divided by 60 beats/min = 89 ml.

New: 5.80 l/min divided by 60 beats/min = 96.7 ml.]

Question 4c-4: What happens to EF with increases in preload? Why?

[Answer 4c-4: EF is effectively unchanged, despite an increase in preload (64% in normal, 63% in increased preload).

Remember that EF is the fraction of blood ejected compared with the amount present at the end of diastole. It is calculated dividing SV by the EDV. In this case, the increase in SV (7.7 ml) is matched by the proportional increase in EDV.]

Question 4c-5: What happens to SBP, DBP, and MAP with an increase in preload?

[Answer 4c-5: The SBP, DBP, and MAP all increase. The SBP (the highest point on the PV loop) increased from 124 to 136 mmHg. This is attributable to the increased CO exerting pressure in the aorta. The diastolic pressure increases as well, due to the increased volume of blood transferred to the aorta, which will increase the pressure against which the aorta has to push against to open. Overall, the increase in SBP and DBP has led to a higher MAP.

Alternatively, we can use CO $\times$ TPR to calculate MAP. Although TPR remains constant, the increase in CO leads to a higher MAP.]

Question 4c-6: What happens to MVO_2 with higher preload?

[Answer 4c-6: There is a higher MVO_2, but not as significantly increased as in the contractility or afterload examples.]

Suggested questions and answers for section 5: modeling a case of acute cardiogenic shock.

Question 5-1: What are the changes to the cardiac muscle that happen as a direct result of the myocardial infarction (MI)? Why did these happen? How are they represented on the curve?

[Answer 5-1: *1*) Decreased contractility (shallower ESPVR). *2*) Increased ventricular stiffness (steeper EDPVR curve).

Myocardial contraction is an active process: it requires ATP and oxygen. When coronary perfusion decreases, less oxygen is available, the heart becomes ischemic, and it cannot contract as well. The reduction in contractility is seen in the shallower ESPVR. However, relaxation is also an active process: moving calcium from the cytoplasm back into the sarcoplasmic reticulum requires energy to activate the ATP-consuming calcium pumps. Without adequate oxygen, these pumps will not be able to run optimally, and calcium will not be able to be sequestered. Without the active sequestration of calcium, the actin-myosin bridges cannot break, and the cardiac muscle will not relax as efficiently. This is reflected in the increased slope of the EDPVR curve (from orange to black).]

Question 5-2: What are the hemodynamic impacts of the cardiac changes? Why?

[Answer 5-2: The cardiac changes have multiple implications, which can be seen by comparing the pre- and post-"Outputs" columns on the *right*:

- The decrease in LV compliance means that, for a given volume, the LDEVP is much higher: less blood can fill the ventricle in diastole. EDV decreases.
- Cardiac contractility decreases, meaning less blood can be ejected, and ESV increases. This is represented by the shallower slope of the ESPVR (black) line.
- SV decreases due to the higher ESV and lower EDV (width of loop decreased).
- The fall in SV leads to a decrease in CO (5.35 to 2.84 l/min).
- MAP, which is dependent on CO and TPR, decreases. Later we will infer what happened to the TPR, but we can see that the MAP fell from 83 to 58 mmHg.

Students, depending on their level, may also point out the changes in EF, MVO_2, HR, or the pulmonary pressures/wedge pressures. Some of these are discussed below.]

Question 5-3: How do these changes relate to his symptoms of shortness of breath and lightheadedness?

[Answer 5-3: His lightheadedness is due to the fall in MAP: his cerebral perfusion pressure has decreased.

The shortness of breath is because the stiffer LV can neither pump blood well, nor can it relax well enough to accommodate the venous return. The pressure in the LV rises, which is transmitted back into the lungs. The right ventricle, which normally pumps into the low-pressure pulmonary system, begins to fail, and the increased hydrostatic pressure in the pulmonary capillaries leads to pulmonary edema. This is manifested as the rise in PCWP from 12 to 31 mmHg.]

Question 5-4: What are the compensatory responses the body uses to attempt to restore homeostasis? On what receptors do they act? In this particular simulation, the baroreceptor is engaged.

[Answer 5-4: We can infer that, with the initial insult, the patient's MAP fell from 83 mmHg to a much lower value. The drop in MAP is sensed by the baroreceptors, which increase sympathetic firing and decrease parasympathetic firing. This will have a number of effects, some of which can be seen in the simulator, and some of which need to be inferred, but will all act to increase the MAP to a higher value than after the initial insult:

- HR will rise (60 to 110 beats/min) as a result of β_1-stimulation of the heart.
- TPR will increase (0.8 to 1.1 $mmHg \cdot s \cdot ml^{-1}$), as a result of α_1-stimulation of the vasculature.
- Cardiac contractility will increase, due to β_1-stimulation of the heart.
- Venous return will increase, due to α_1-stimulation of the capacitance veins. This is likely maladaptive.]

Inquiry Applications

This session is a combination of facilitated and guided inquiry. The facilitator leads the session and can modify the simulator. However, it can be made into a guided or open inquiry by increasing the number of iPads and providing students with instructions on how to use the software, as well as questions to answer by manipulating the simulator.

Additional Resources

For additional information on this topic, please see the following:

1. "Assessment of systolic and diastolic ventricular properties via PV analysis: a guide for clinical, translational, and basic researchers" (4).
2. *Guyton and Hall Textbook of Medical Physiology*, chapter on "Cardiac muscle: the heart as a pump and function of the heart valves" (8).

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DISCLOSURES

D. Burkhoff developed the iPad App and obtains fees from the paid version of it. This paper described experiments using a free version.

AUTHOR CONTRIBUTIONS

S.L. and D.B. conceived and designed research; S.L. performed experiments; S.L. analyzed data; S.L. interpreted results of experiments; S.L. prepared figures; S.L. drafted manuscript; S.L. edited and revised manuscript; S.L. and D.B. approved final version of manuscript.

REFERENCES

1. **Association of American Medical Colleges.** *Summary and Select Results from the AAMC Medical School Tablet Device Summary, Feb 2013*. Washington, DC: AAMC, 2013.
2. **Benharash P, Frank P, Hoy B.** Development and use of a novel cardiovascular simulator: time for a paradigm shift? *Am Surg* 78: 1132–1136, 2012.
3. **Burkhoff, D.** *Harvi by PVLoops LLC (version 2.1.1)* (Online). https://itunes.apple.com/us/app/harvi/id568196279?mt=8 [7 April 2017].
4. **Burkhoff D, Mirsky I, Suga H.** Assessment of systolic and diastolic ventricular properties via pressure-volume analysis: a guide for clinical, translational, and basic researchers. *Am J Physiol Heart Circ Physiol* 289: H501–H512, 2005. doi:10.1152/ajpheart.00138.2005.
5. **Davis MJ, Gore RW.** Determinants of cardiac function: simulation of a dynamic cardiac pump for physiology instruction. *Adv Physiol Educ* 25: 13–35, 2001.
6. **Doshi D, Burkhoff D.** Cardiovascular simulation of heart failure pathophysiology and therapeutics. *J Card Fail* 22: 303–311, 2016. doi:10.1016/j.cardfail.2015.12.012.
7. **Federation of State Medical Boards of the United States, National Board of Medical Examiners.** *USMLE Content Outline* (Online). http://www.usmle.org/pdfs/usmlecontentoutline.pdf [7 April 2017].
8. **Hall JE.** Cardiac muscle: the heart as a pump and function of the heart valves. In: *Guyton and Hall Textbook of Medical Physiology*. Philadelphia, PA: Saunders Elsevier, 2016, chapt. 9, p. 101–110.
9. **Katz AM.** Influence of altered inotropy and lusitropy on ventricular pressure-volume loops. *J Am Coll Cardiol* 11: 438–445, 1988. doi:10.1016/0735-1097(88)90113-1.
10. **Katz, A.** The working heart. In: *Physiology of the Heart*. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, chapt. 12, p. 319–335.
11. **Kelsey R, Botello M, Millard B, Zimmerman J.** An online heart simulator for augmenting first-year medical and dental education. *Proc AMIA Symp* 2002: 370–374, 2002.
12. **Miranda D, Lewis GD, Fifer MA.** Heart failure. In: *Pathophysiology of Heart Disease: A Collaborative Project of Medical Students and Faculty*. Philadelphia, PA: Lippincott Williams & Wilkins, 2016, chapt 9, p. 220–248.
13. **Rothe CF, Gersting JM.** Cardiovascular interactions: an interactive tutorial and mathematical model. *Adv Physiol Educ* 26: 98–109, 2002. doi:10.1152/advan.00031.2001.
14. **Samsel RW, Schmidt GA, Hall JB, Wood LD, Shroff SG, Schumacker PT.** Cardiovascular physiology teaching: computer simulations vs. animal demonstrations. *Am J Physiol* 266: S36–S46, 1994.
15. **Wildhaber RA, Verrey F, Wenger RH.** A graphical simulation software for instruction in cardiovascular mechanics physiology. *Biomed Eng Online* 10: 8, 2011. doi:10.1186/1475-925X-10-8.