

Cardiopulmonary interactions

M Ngwenya 

Department of Anaesthesia, School of Clinical Medicine, Faculty of Health Sciences, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, South Africa

Corresponding author, email: kngwenya@yahoo.com

The goal of the heart and lungs is to deliver oxygen at a tissue level, and this is determined by cardiac output (CO) and the oxygen content of arterial blood (CaO_2), $\text{DO}_2 = \text{CO} \times \text{CaO}_2$.¹ The heart and lungs share the same intrathoracic space: mechanically this is akin to having a pump within a pump.² Cardiopulmonary interactions refer to the relationship between airway pressures, lung volumes, and CO.³ In health, the effect of cardiopulmonary interactions is minimal. It is important to look at each part of the heart separately as phasic changes in intrathoracic pressures (ITP) have differing effects.

In a spontaneously breathing person, a negative ITP is transmitted to the right atrium. The flow of blood to the right atrium is governed by Ohm's law, $\text{flow} = \Delta P/R$, where ΔP is the driving pressure to the right atrium and R is the resistance of the capacitance vessels.⁴ With positive pressure ventilation (PPV) the increased ITP is transmitted to the right atrium, which results in a reduction of the driving pressure and ultimately the venous return (VR). The right ventricle afterload is the pressure that the heart must work against to eject blood during systole, and this is determined by the pulmonary vascular resistance (PVR).

PVR is determined by the extra-alveolar vessels and the intra-alveolar vessels. The total PVR is the addition of the two and lowest at functional residual capacity.⁵ The left ventricle preload is essentially equal to the right ventricle output. There is a time lag as blood must traverse the pulmonary circulation. Left ventricle afterload can be expressed as left ventricular (LV) wall stress. Afterload increases as transmural pressure and vascular resistance increase. Positive pressure reduces the transmural pressure needed for the ejection of the stroke volume. With negative ITP there is a pressure pulling outwards as the ventricle attempts to eject its stroke volume, therefore higher transmural pressures are needed.⁴ Knowing how the heart and lungs work in the normal physiological state will help guide decision-making about heart-lung interactions in critically ill patients therefore mitigating any adverse consequences.

Keywords: cardiopulmonary interactions, intrathoracic pressure, spontaneous ventilation, positive pressure ventilation, pulmonary vascular resistance

Introduction

The heart and lungs work together to meet the body's tissue oxygen demands. The effect of pulmonary physiology on cardiac function is not always appreciated and this article aims to examine how the lungs may affect the cardiovascular function in healthy individuals. It is important to note that in diseased states these effects can be exaggerated, and may ultimately lead to an imbalance between tissue oxygen demand and supply resulting in tissue hypoxia and cell death.⁶

The mechanical interplay between the respiratory and cardiac systems was first observed some 300 years ago by English physiologist Stephen Hales. He noted that the level of a blood column in a glass tube inserted into a horse's carotid artery varied cyclically with respiration.² Hales also first documented that the blood pressure of healthy individuals fell during spontaneous respiration.⁶ Cardiopulmonary interactions refer to the relationship between airway pressures, lung volumes, and CO.³

The heart and lungs share the same intrathoracic space, essentially it resembles having a pump within a pump. Hence the ITP and volume changes in the lungs during respiration affect the performance of the heart.² There are also neural and humoral mediated phenomena that act on the heart and lungs, this together with direct mechanical effects constitute heart-lung interactions.² To understand how breathing affects CO, it is necessary to understand the normal factors that regulate CO.⁷ This is governed by the equation:⁴

$$\text{CO} = \text{stroke volume} \times \text{heart rate}$$

The determinants of stroke volume are preload, afterload, and contractility. This article will examine how the lungs affects the heart. It is important to consider each ventricle separately, as changes in intrathoracic pressure during spontaneous ventilation and PPV have differing effects on the ventricles.¹

Right ventricular (RV) preload

The preload is essentially the end-diastolic volume (EDV). It depends on the VR, which in turn depends on the driving pressure between the extrathoracic great veins (EGV) and the

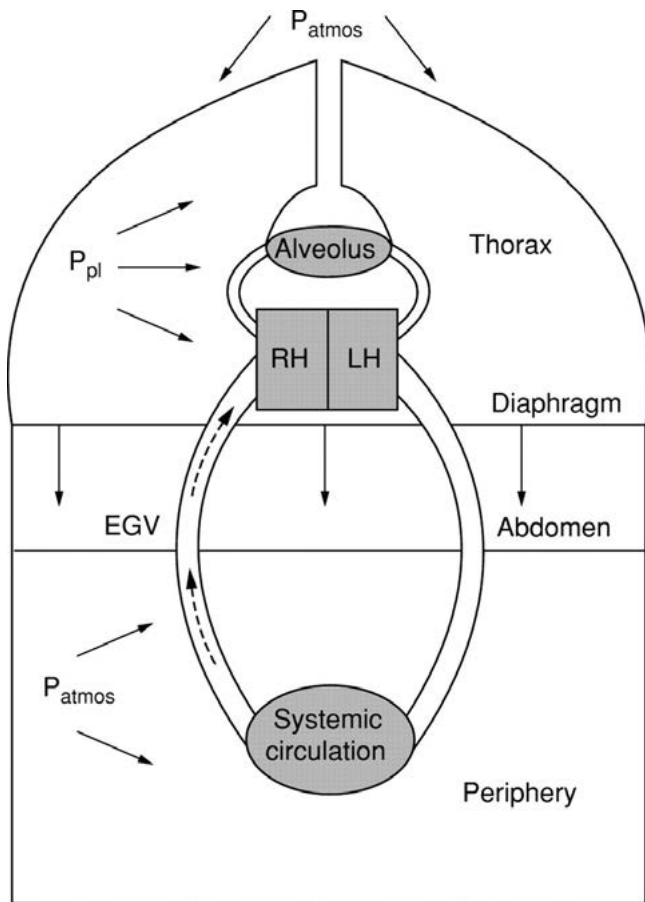


Figure 1: Model of the circulation showing factors that influence systemic venous drainage.⁶

$$\text{Flow} = \frac{\text{Driving pressure}}{\text{Resistance}} \text{ therefore, VR (dotted line)} = \frac{\text{EGV-Right arterial pressure}}{\text{Resistance}}$$

pressure in the right atrium. There is also the resistance to VR to consider, as determined by Ohm's law: $\text{Flow} = \frac{\Delta P}{R}$. The gradient for VR is equal to the difference between the mean systemic venous pressure (Msvp), or EGV, and the right atrial pressure (Rap) as seen in figure 1.² The right heart (RH), and intrathoracic great veins are subjected to pleural pressure (P_{pl}). Therefore, during spontaneous ventilation, also known as negative pressure ventilation, the ITP decreases, and this is transmitted to the right atrium. This increases the driving pressure and thus makes it easier for blood to return.

Additionally, as you breathe in your diaphragm moves down, and the intra-abdominal pressure increases, resulting in an increased pressure in the EGV, this normalises to atmospheric (P_{atmos}) with expiration. The combined benefit of increased upstream pressure and decreased downstream pressure works to increase VR in the right atrium.⁴ The opposite occurs when PPV is introduced. The increased ITP is transmitted to the right atrium, this reduces the gradient for the driving pressure, and thus the preload. At the initiation of PPV, there is a drop in CO because there is not as much VR.

LV preload

LV preload is equal to RV output. Therefore, a decreased RV stroke volume, regardless of the cause, translates to reduced LV

preload. There is a slight lag in time as the blood must traverse the pulmonary circulation. LV preload cannot be discussed without mentioning RV afterload as this influences the blood going to the left atrium. It is governed by the equation:⁴

$$\text{Pulmonary venous return} = \frac{P_{mv} - P_{la}}{R_{pv}}$$

Where: P_{mv} = mean pulmonary pressure, P_{la} = left atrial pressure, R_{pv} = pulmonary venous resistance

RV afterload

RV afterload is the load the RV cardiac myocytes have to overcome to contract, as determined by the PVR.³ In other words, the RV afterload is known as the RV systolic wall tension. RV wall tension is approximately described by Laplace's equation for a spherical chamber:⁸

$$\text{Wall tension} = \frac{P_{tm} \times r}{2 \times h}$$

Where: P_{tm} = RV transmural pressure, r = radius, h = wall thickness

The systolic RV pressure is the transmural pressure. Transmural pressure is the pulmonary artery pressure minus the ITP.⁸ The right ventricle output flows through the pulmonary vasculature, generally a low-pressure system that will ultimately determine the left ventricle preload. RV output is dependent upon RV preload, contractility, and afterload, and afterload is proportional to PVR. PVR is influenced by changes in the lungs' volumes during inflation and deflation. The alveolar oxygen tension, pH, and partial pressure of carbon dioxide (pCO_2) may also alter the PVR to an extent.⁸

The PVR is a function of the extra-alveolar and intra-alveolar vessels. The pulmonary vasculature can be divided into extra-alveolar vessels and intra-alveolar vessels. The extra alveolar vessels are large capacitance vessels and run along the lung interstitium, they are kept open by increased lung volumes as radial traction pulls them open. Therefore, at high lung volumes, they cause a decrease in the PVR.^{2,8} At low lung volumes the interstitial traction decreases, reducing the cross-sectional diameter, thereby causing an increase in PVR.

In the intra-alveolar vessels, the reverse happens. At high lung volumes, the intra-alveolar vessels which are surrounded by alveoli are squashed and their cross-sectional diameter decreases, leading to an increase in PVR. At low lung volumes the intra-alveolar diameter is at its largest and PVR is minimal. These PVR changes are illustrated in Figure 2.⁹ The net PVR is a result of the additive effect of the two forces. At functional residual capacity (FRC) the overall PVR is minimal. Therefore, the goal is to ventilate to FRC. Alveolar hypoxia, hypoventilation, and resorption atelectasis may occur at volumes below FRC. This may lead to hypoxic pulmonary vasoconstriction (HPV), which further increases PVR.¹ Alveolar hypoxia can increase PVR, and hypocapnia can reduce PVR.³

It is worth mentioning that when positive end-expiratory pressure (PEEP) is applied to the alveolar for recruitment purposes and the alveoli are open to receive oxygen, HPV will be diminished,

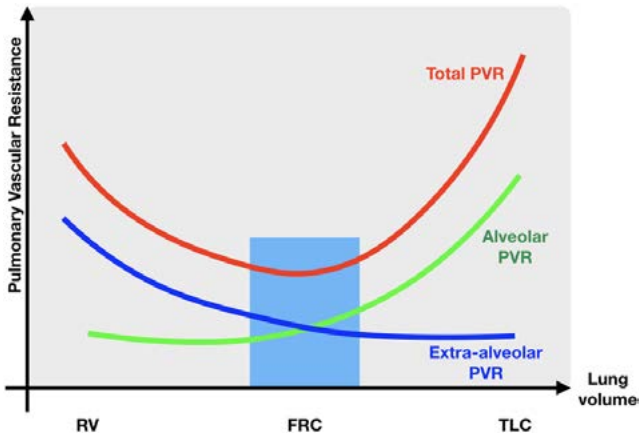


Figure 2: Relationship between PVR and lung volume
RV = residual volume, TLC = total lung capacity⁹

thus decreasing their contribution to an increased PVR. The recruitment of previously closed capillaries occurs when the lungs are opened by exposure to higher upstream pressures, this recruitment increases the total volume available for RV CO and reduces resistance to flow.⁹ The caveat is significantly increased tidal volumes, such that the lung is overdistended, results in an increase in PVR and ultimately leads to a decrease in CO. This effect is exacerbated with excessive use of PEEP.¹

Distribution of pulmonary blood flow

Gravity and HPV are the major determinants of pulmonary blood flow. Perfusion to an alveolus is dependent on the relationship between the pulmonary alveolus pressure (P_A), the pulmonary arteriolar pressure (P_a), and the pulmonary venous pressure (P_v).¹

- In west zone I, $P_A > P_a > P_v$ resulting in compression of the vessels and dead space ventilation. This does not normally occur in healthy individuals.
- In west zone II, $P_a > P_A > P_v$ there is pulmonary blood flow mainly in systole.
- In west zone III, $P_a > P_v > P_A$, there is blood flow in systole and diastole.

During mechanical ventilation, positive pressure can create more zone I and zone II areas and alter zone III areas. This creates more resistance and RV afterload dead space ventilation and potential increased shunt flow.¹⁰

LV afterload

This is the pressure the heart must overcome to be able to eject blood during systole. It is also referred to as ventricular wall stress. The pressure is significantly greater than the pressure generated by the right ventricle. This wall stress is governed by the law of Laplace as seen in Figure 3.^{2,4} It is proportional to the pressure within the cavity and the radius, and inversely proportional to the width of the chamber.

$$T_a = \frac{P \times r}{u}$$

Transmural pressure is the “actual working” pressure that the wall heart chambers have to generate (Figure 4).² The immediate pressure around the heart is the pericardial pressure; however, in

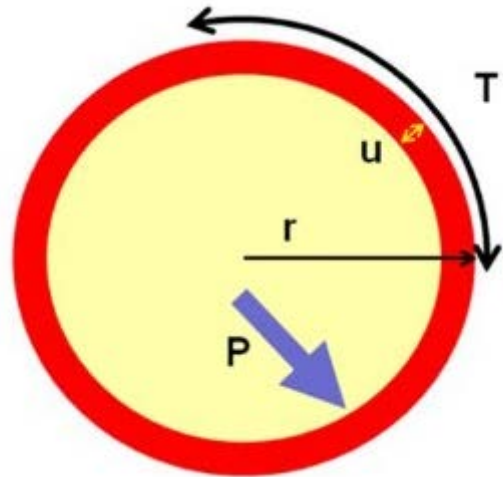


Figure 3: Demonstration of factors influencing LV afterload¹¹
T – wall stress, P – transmural pressure, r – radius, u – wall thickness

the absence of pericardial disease, pericardial pressure is equal to the pleural pressure. Pleural pressure varies cyclically with inspiration and expiration.

Transmural pressure = intracavitary pressure - surrounding pressure

During spontaneous negative breathing, the thorax exerts an outward negative pressure, this creates extra pressure on the ventricle that is trying to contract. The opposite occurs with PPV; the surrounding pressure on the heart pushes inwards and thus decreases the wall stress on the LV and allows the LV to contract better. In a way, the positive ventilation acts as an LV assist device. As seen below in Figure 5a, if the ITP is -20 mmHg, to generate 80 mmHg in the aorta, the ventricle must contract strongly to overcome the -20 mmHg. It will have to generate 100 mmHg effectively and thus work harder. If the pleural pressure is +20 mmHg (Figure 5b), the ventricle will have to generate 60 mmHg to measure a pressure of 80 mmHg in the aorta.

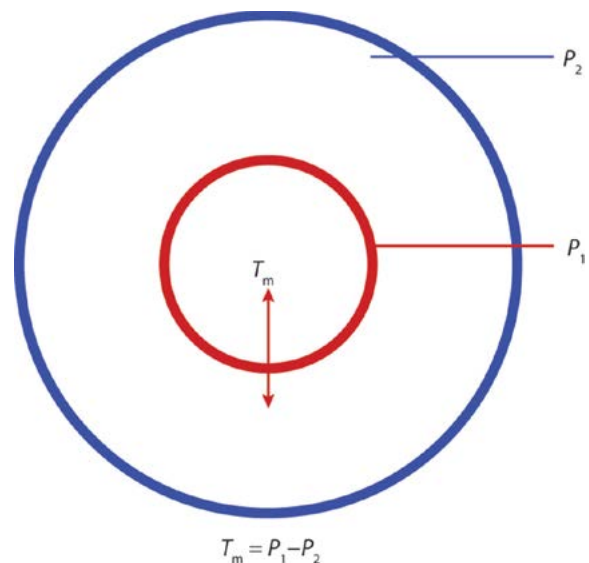


Figure 4: Transmural pressure is the net pressure experienced by the inner chamber walls.
 T_m = transmural pressure, P_1 = pressure in the inner chamber, P_2 = pressure in the outer chamber

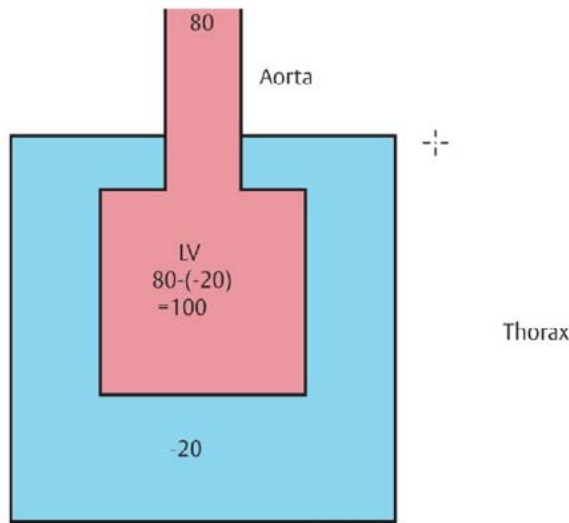


Figure 5a (left): Spontaneous negative pressure;

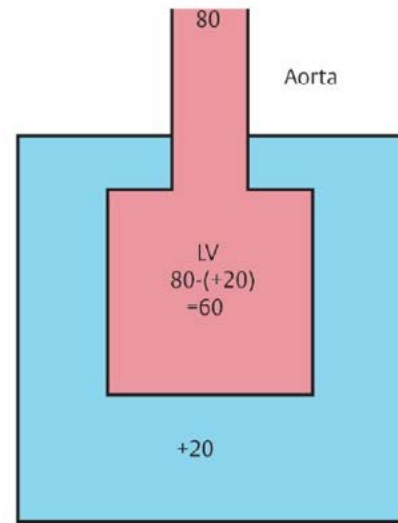


Figure 5b (right): PPV.

The afterload is determined by transmural pressure and systemic vascular resistance (SVR). The SVR is largely unaltered by respiration; it is the transmural pressure during breathing that influences the afterload. In diseased states, such as acute bronchospasm, LV afterload is exacerbated by excessive negative ITP, which may potentially precipitate acute LV dysfunction.⁴

Ventricular interdependence

The right and left ventricles share a pericardial space. Therefore, volumes and pressures on one side will ultimately affect volumes and pressures on the other side, this phenomenon is known as ventricular interdependence.² During normal spontaneous respiration, there is an increase in VR and RV filling and pressure, causing a slight shift of the interventricular septum to the left, as seen in Figure 6.⁵ This leads to less space for the LV to fill, thus the LV output decreases and leads to a normal fall in systolic blood pressure on inspiration. On expiration, the opposite happens where there is an increase in ITP, less RV preload, and RV filling, the LV can fill better, and the systolic blood pressure goes back to normal.

In normal, healthy individuals with normal spontaneous ventilation, this is not an issue. However, in a case of acute

obstruction, where one takes large negative breaths, the RV preload increases significantly and the right-sided EDV increases, ultimately affecting the filling of the LV, due to the bowing of the interventricular septum.⁴ This phenomenon of drop in blood pressure is known as pulsus paradoxus.⁴ During excessive ventilation, the lungs can expand significantly, and the PVR will increase and result in an increased right-sided EDV, which can impair LV filling and CO.

Lung volumes and ventricular contractility

Ventricular contractility is determined by preload-dependent and preload-independent variables. Preload-dependent variables include the Frank-Starling mechanism whereby an increase in preload results in an increase in stroke volume up to a point. PEEP affects these preload-dependent variables.³ Preload-independent mechanisms will not be affected by PEEP but by the tidal volumes and ITP by their activation of lung stretch receptors, which affects chronotropic, inotropy, and systemic vasodilation. Consequently, a response known as "lung-inflation vasodepressor reflex" is activated, resulting in dilation of systemic vessels and negative inotropy.³

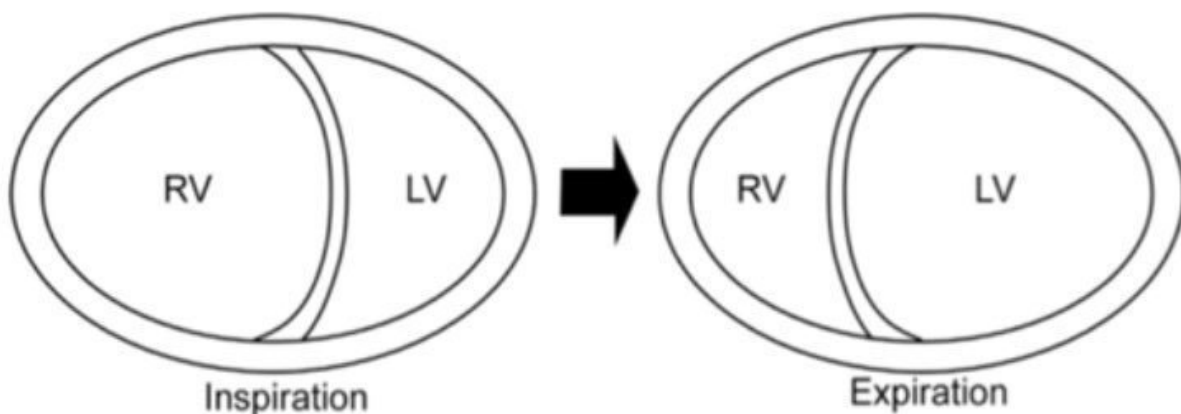


Figure 6: Cyclical respiratory variation of LV filling

Consolidated effect of spontaneous ventilation

- As ITP ↓ there is ↑ VR to the RH.
- RV afterload ↓ due to fall in PVR (secondary to lung inflation to FRC).
- The combined effect leads to ↑ RV output; however, takes time to traverse pulmonary circulation.
- Simultaneously LV preload decreases due to immediate pooling of blood in pulmonary circulation on inspiration.
- LV afterload and transmural pressure ↑ due to negative ITP.
- Leads to ↓ LV stroke volume seen as ↓ systolic and pulse pressure on arterial pressure waveform.
- At expiration, the increased portion of RV output generated from inspiration reaches the LV, this manifests as ↑ LV stroke volume and ↑ systolic and pulse pressure on the arterial trace.

Consolidated effect of mechanical ventilation

- With PPV the ITP ↑ results in a ↓ VR.
- RV afterload ↑ due to a rise in PVR (occurs with lung overinflation).
- Thus, RV output ↓; however, takes time to traverse the pulmonary circulation before it becomes LV preload.
- Simultaneously LV preload ↑ due to squeezing of blood out of the pulmonary circulation by ↑ ITP.
- LV afterload and transmural pressure ↓ leading to ↑ systolic and ↑ pulse pressure on the arterial trace.
- At expiration, the ↓ RV output produced during inspiration reaches the LV and manifests as ↓ LV stroke volume and ↓ systolic and pulse pressure on the arterial pressure trace.

Clinical implications of cardiopulmonary interactions

In a patient with LV failure, which may manifest as pulmonary rales, low blood pressure, and low arterial oxygen content, PPV assists the LV by lowering the LV afterload. PPV may also help to recruit closed alveoli and thus mitigate the effects of hypoxic pulmonary vasoconstriction. PPV on the PVR is the sum of vasodilation caused by alveolar reoxygenation and vasoconstriction mediated by pulmonary vasculature stretch at volumes greater than FRC. PPV reduces the respiratory work of patients, which reduces their metabolic demands, and in turn, reduces the required cardiopulmonary interactions.

In patients with obstructive lung disease who are breathing spontaneously, they must generate large negative ITP during

respiration. In the patient with a compromised LV function, this may be detrimental as their LV has a much larger LV afterload to overcome.

Pulse pressure variation can be used as a surrogate for stroke volume variation (SVV). A pulse pressure variation > 12% is strongly associated with fluid responsiveness. SVV is based on the same principle as pulse pressure variation, thus SVV > 10% is associated with fluid responsiveness.

Conclusion

The heart and lungs are inextricably linked as they share a common space. Lung volumes and ITP affect CO and the determinants of stroke volume. A good understanding of how the pressures in the thorax affect the CO in a healthy individual is important as these effects are exaggerated in disease. This will have an important bearing on how one can ventilate and manage critically ill patients in the intensive care unit setting and mitigate the adverse effects of cardiopulmonary interactions.

ORCID

M Ngwenya  <https://orcid.org/0000-0003-1129-6647>

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