Indian J Physiol Pharmacol 2016; 60(4) : 310–314

Review Article

Interactive Physiology in Critical Illness : Pulmonary and Cardiovascular Systems

Dr. Deepak Shrivastava, MD, FACP, FCCP, FAASM

Professor of Pulmonary, Critical Care and Sleep Medicine
Director, Critical Care Services
University of California Davis, CA
San Joaquin General Hospital, California, USA

Introduction

Human physiology is the science of physical, biochemical, and mechanical function of human body. Physiology forms the framework to understand the adaptation of body to everyday stresses, diseases, and critical illness. In the intensive care unit (ICU), knowledge of physiology provides guiding principles of scientific thinking and inquiry. Technological advances have increased the survival of critically ill people. Given the complexity of critical illness, traditional knowledge of organ system based physiology is not enough. The first of the four article series addresses interactive pulmonary and cardiovascular physiology. In future, follow up articles discuss the physiology of other systems during the stress of critical illness.

Heart-Lung interactions occur with each breath. Although their effects are subtle during spontaneous breathing at rest, these interaction become profound during exercise and in critical illness especially with the use of mechanical ventilation. The heart and lungs function together to deliver sufficient oxygen throughout the body to maintain normal organ function and activity. Mechanical ventilation is common in the ICU and it can directly influence the oxygen homeostasis in the body by changes in arterial oxygen content, cardiac output, and total oxygen consumption (Vo_2). Ventilation affects the circulation primarily by altering the preload and after-load conditions of the heart though changes in intrathoracic pressure (ITP) and lung volume. However, the final effect of respiration on systemic oxygen delivery (Do_2) is the product of several distinct yet interrelated heart-lung interactions. A thorough understanding of the factors involved and knowledge of often-simple bedside techniques to detect these physiologic changes is necessary to care for the critically ill patient.

***Corresponding author :**

Dr. Deepak Shrivastava, MD, FACP, FCCP, FAASM
Email: drshrivastava@sjgh.org

(Received on April 12, 2016)

Changes in Intrathoracic pressure

Intrathoracic pressure exerts changes in cardiovascular system. Pleural pressure is an acceptable surrogate marker of intrathoracic pressure. Ventilation alters the pressure between the opposing surfaces of the thorax separated by the visceral and parietal pleura known as pleural pressure. Gravity-dependent difference in regional pleural pressure explains the greater degree of lung distension in the nondependent portions of the chest compared with the dependent portions, because alveolar pressure at end expiration is similar throughout the lungs. The change in pleural pressure

with breathing is also different in different portions of the lung due to local differences in surface forces. With the lung expansion, there is outward movement of the chest wall and diaphragm. However since the heart is confined within cardiac fossa, it is unable to move. Therefore, the pleural pressure is greater around the heart in the juxtacardiac pleural space than it is on the lateral chest-wall surface at the same hydrostatic level.

Since bedside measurement of pleural pressure is cumbersome, the nonspecific ITP is useful because it makes no assumptions as to any specific value and can be interchanged as necessary to discuss transpulmonary, transmural vascular, and transdiaphragmatic pressures. Spontaneous breathing and positive pressure ventilation induce opposite changes in ITP. In addition, the determinants of the changes in ITP during spontaneous ventilation and positive-pressure ventilation are quite different. During spontaneous breathing, the potential space within the thorax expands and decreases ITP based on degree of respiratory muscle activity and lung compliance and resistance. Positive-pressure ventilation increases alveolar pressure by passively distending the lungs and ITP increases based on the degree of lung expansion and chest-wall compliance.

Mean ITP and changes in ITP during ventilation are major determinants of cardiovascular status. Conceptually, circulation has two compartments, one within the chest cavity that is affected by ITP and another outside the chest that is affected by atmospheric pressure. As changes in ITP induced by ventilation and spontaneous ventilatory efforts alter ITP but not atmospheric pressure, a variable pressure gradient is created between these two compartments by ventilation. Increasing ITP, for example will make all the pressures within the thorax relatively greater than in other areas of circulation, whereas decreasing ITP will have the opposite effect. Therefore, changes in ITP affect cardiac function in general by altering the pressure gradients between the vasculature within the thorax and in the rest of the body. Similarly, a decrease in ITP, as occurs with spontaneous ventilatory efforts, will increase these pressure gradients. An increase in the pressure gradient for venous return will cause an acceleration of blood flow back to the right side of the heart that increases the RV end-diastolic volume and an increase in transmural LV ejection pressure that impedes LV ejection and increases LV end-systolic volume. These combined effects will increase both biventricular blood volume and the absolute amount of blood in the thoracic compartment. An increase in ITP will have the opposite effect.

A decrease in intrathoracic pressure caused by spontaneous inspiration affects left ventricular after load. During LV systole, the intraluminal pressures in the LV and aorta are nearly identical. However, the LV and the intrathoracic aorta are surrounded by a lower ITP than the extra- thoracic aorta. Thus, the directionally opposite forces of the ITP impede the inward contraction of the LV during systole. Therefore, the decrease in ITP during spontaneous inspiration causes an increase in LV afterload (1). Cardiovascular decompensation from increases in LV afterload causes difficult weaning from positive-pressure ventilation and is a well-known cause of weaning failure in the ICU.

Changes in mean systemic pressure

Right ventricular end-diastolic volume is a function of the systemic venous return to the right atrium (RA) and RV diastolic compliance. During a spontaneous inspiration, venous return to the right side of the heart increases. The blood drains along a decreasing pressure gradient from the systemic venous reservoirs toward the heart; systemic venous return is roughly proportional to the pressure gradient that drives the blood flow from these systemic veins to the RA. Right atrial pressure usually represents the back pressure against which venous return must flow. Because the RA is an intrathoracic structure, phasic respiratory-induced changes in ITP directly affect the pressure gradient for venous return. By physically decreasing right atrial pressure (Pra), spontaneous inspiration increases the pressure gradient for venous return, thus accelerating venous blood flow toward the right side of the heart (2). Additionally, vascular tone, the blood volume and flow distribution within the venous reservoirs of the systemic circulation determine the upstream pressure

for venous return. The average pressure of all these vascular reservoirs is termed the mean systemic pressure (Pms). The Pms represents the upstream pressure that drives the blood flow from the systemic circulation toward the RA. Pms increases with volume resuscitation or vasoconstrictors, which then increase RV preload.

During spontaneous inspiration, right atrial pressure (Pra) can decrease to sub- atmospheric pressure. Since veins lack the structural integrity to sustain a negative wall pressure, they tend to collapse when transmural pressure falls below zero, increasing their resistance to flow in proportion to the decrease in ITP. This Starling resistor mechanism induces a flow limitation of venous return at some maximal plateau value. Further reductions in ITP, and hence in Pra, will not continue to increase the amount of blood returned to the right side of the heart. This mechanism of flow limitation for venous return avoids overloading the central (thoracic) circulation during conditions associated with exaggerated decrease in ITP, as may occur during spontaneous hyperpnea, increased airway resistance, or decreased respiratory compliance. In subjects with normal cardiovascular function, the cardiac output is preload-dependent and relatively afterload-insensitive. Thus, ventilator-induced changes in RV end-diastolic volume significantly affect cardiac performance. It is considered one of the most common detrimental heart-lung interactions in the intensive-care unit (ICU) in mechanically ventilated patients requiring support. Appropriate management in this setting usually involves adjustment of ventilator settings to reduce mean airway pressures and to prevent over distension of the lungs and restoration or increase of Pms by volume resuscitation. On the other hand, in patients with myocardial dysfunction, cardiac output is relatively insensitive to end-diastolic volume changes and is affected by changes in afterload. In this clinical situation, the institution of positive-pressure ventilation can improve cardiovascular performance through its effects on decreasing LV afterload, despite the obligatory decrease in the pressure gradient for venous return.

Ventricular interdependence

Ventricular interdependence refers to the effect that the filling or ejection of one ventricle has on the function of the opposite ventricle. Until recently it was felt that ventricular interdependence was minimal during normal tidal volume positive-pressure ventilation because the changes in ITP are small, making both the lung inflation-induced pulmonary vascular resistance and venous return changes small (3). However, it was shown in animals that positive-pressure ventilation and altered left ventricular output in a fashion explained by ventricular interdependence. With positive-pressure inspiration, as right ventricular dimensions decreased, the left ventricular dimensions increased and left ventricular stroke volume increased slightly (4).

The LV end-diastolic volume can be altered by changes in RV end-diastolic volume with and without change in LV diastolic compliance. This interaction between the RV and the LV is a parallel interaction because it occurs in phase between the two ventricles, although the changes in end-diastolic volumes are often in opposite direction. This relationship is explained by pericardial pressure changes that occur as lung volume increases or during the strain phase of a valsalva maneuver, directly affect the surrounding pressure of the heart. The change in stroke volume and cardiac output depends on biventricular contractility as can be assessed by the Frank-Starling relationship. This pericardial pressure-dependent decrease in biventricular filling is analogous to tamponade. Second, ventricular interdependence occurs through the interventricular septum. According to this mechanism, as the RV fills during diastole, it pushes on the intraventricular septum altering the diastolic compliance of the opposite ventricle with minimal changes in pericardial pressure (5). Considering the influence of ventricular interdependence, if RV end-diastolic volume decreases due to either a decrease in the pressure gradient from systemic venous return for example during positive-pressure ventilation or compression of the heart by the expanding lungs during spontaneous as well as mechanical ventilation, then LV diastolic compliance will increase. Similarly, if RV end-diastolic volume increases like in spontaneous inspiration, then LV diastolic compliance will decrease. This will cause *pulsus paradoxes* that is a spontaneous inspiration-

associated decrease in LV stroke volume and aortic pulse pressure (6).

Measurement of cardiac output in the critically ill individual

While complex interplay between cardiovascular and respiratory systems effects hemodynamic status of a critically ill individual, it creates challenging situations that can mask the correct measurements of the crucial data. The multidimensional effects of respiratory cycle on the cardiovascular function can directly influence measures of cardiac performance such as the thermodilution techniques to determine cardiac output. The timing of the injectate relative to the respiratory cycle is an important determinant that can account for much of the variability in measurements of thermodilution cardiac output (7). Single thermodilution cardiac output determinations can vary plus or minus 30 percent depending on the timing of the injectate relative to the cardiac cycle (8).

Although new concepts are being developed and techniques are being used with greater frequency and accuracy, information about vascular pressures derived from catheter placed in the central circulation (CVP) and occasionally in pulmonary artery (Pulmonary artery occlusive pressure or PAOP) is still commonplace. These monitoring tools measure the adequacy of circulating volume in critically ill patients (9). Since respiratory-induced changes in ITP are transmitted to intrathoracic blood vessels, fluctuations in intrathoracic vascular pressure, as measured using CVP or PAOP, may reflect changes in ITP rather than actual changes in intravascular pressure. The magnitude of these fluctuations often approximates the actual changes in ITP; therefore, values for measured intrathoracic vascular pressures may vary substantially throughout a single respiratory cycle. The most reproducible estimates of intravascular filling pressures measurements are usually taken at end expiration. During a spontaneous breath, this value is the highest point whereas during a passive positive-pressure breath, end expiration defined as the lowest point on the pressure curve. Measurement of CVP reflect adequacy of intravascular volume. A high CVP virtually excludes hypovolemia as a cause of hemodynamic instability. A low CVP, on the contrary is of little diagnostic value due to its universal possible presence in hypovolemic, normovolemic, and hypervolemic states.

Changes in arterial pressure

Positive-pressure ventilation also can induce changes in arterial pressure. During preload-dependent conditions, systolic arterial pressure shows a biphasic response to a single positive-pressure breath. First, in a patient with increased intrathoracic blood volume, systolic pressure increases because of the transfer of the pulmonary arterial blood volume into the left atrium increasing LV end-diastolic volume, which transiently increases stroke volume for two or three heartbeats. Later, as systemic venous return decreases because of increases in CVP from the positive pressure breath, systolic arterial pressure decreases below baseline apneic values. Conversely, patients with depressed cardiac contractility and pulmonary vascular congestion often exhibit a “reverse pulsus paradoxus,” whereby arterial pressure increases only after a positive pressure breath (10).

Stroke volume variation (SVV)

SVV is a natural phenomenon manifested by fall in arterial pulse pressure during inspiration and rise during expiration. This occurs due to changes in ITP secondary to negative pressure ventilation (spontaneous breathing). Reverse pulsus paradoxus is the same phenomenon with positive pressure breathing (controlled mechanical ventilation), however, in reverse order. Arterial pressure rises during inspiration and falls during expiration due to changes in intra-thoracic pressure secondary to positive pressure ventilation. There are other names in the literature as paradoxical pulsus, respiratory paradox, systolic pressure variation, and pulse pressure variation. SVV and its comparable measurement, pulse pressure variation (PPV), are not indicators of actual preload but of relative preload responsiveness. SVV has been shown to have a very high sensitivity and specificity when compared to traditional indicators of volume status (heart rate, mean arterial pressure, central venous pressure, pulmonary artery diastolic and, pulmonary artery occlusive pressure), and their ability to determine fluid responsiveness (11-12).

Although not in regular clinical use, esophageal and gastric pressure measurements have been extremely helpful in understanding the physiology of the respiratory system during spontaneous breathing and mechanical ventilation. However, it improves the understanding of basic physiologic mechanisms, the technique has been occasionally used in clinical situations to diagnose diaphragm paralysis, assess the work of breathing during mechanical ventilation, and estimate pulmonary compliance (13).

The clinical use of functional hemodynamic parameters that are derived from respiratory-induced variations in the arterial pressure is gaining wider popularity in the hemodynamic monitoring of ventilated patients. In order to correctly measure and interpret these parameters, one must have a basic knowledge of the normal and abnormal physiology of heart– lung interaction during mechanical ventilation. In addition, the inherent limitations, and the associated confounding factors, of these parameters have to be clearly recognized (14).

Many other clinical appilcations can be highlighted in the context of underlying physiological deviations from normal. The reversability of adverse microvascular changes in obstructive sleep apnea patients treated with copntinuous positive airway pressures via non-invasive ventilation is well documented (15).

In the second part of this series, in an effort to expose non-clinicians to the clinical context and clinicians to foundations, the author describes physiologic perspectives of the clinical situations commonly encountered in the intensive care unit.

References

1. Buda AS. Effect of intrathoracic pressure on left ventricular performance. *N Engl J Med* 1979; 301: 453–459.
2. Guyton AC. Venous return at various atrial pressures, and the normal venous return curve. *Am J Physiol* 1957; 189: 609–615.
3. Mitchell JR, et al. RV filling modulates LV function by direct ventricular interaction during mechanical ventilation. *Am J Physiol* 2005; 289: H549–H557.
4. Michael R Pinski. Heart lung interactions, Current Opinion in Critical Care 2007; 13: 528–531.
5. Taylor RR. Dependence of ventricular distensibility on filling the opposite ventricle. *Am J Physiol* 1967; 213: 711–718.
6. Marini JJ, Mechanical effects of lung distention with positive pressure in cardiac function. *Am Rev Respir Dis* 1981; 124: 382–386.
7. Steven JH. Thermodilution cardiac output measurements: effects of respiratory cycle with reproducibility. *JAMA* 1985; 253: 2240–2242.
8. Daper A. Timing of cardiac output measurements during mechanical ventilation. *Acute Care* 1986; 12: 113–116.
9. Goldenheim PD. Cardiopulmonary monitoring of critically ill patients. *N Engl J Med* 1984; 311: 776–780.
10. Szold A. The effect of tidal volume and intravascular volume on systolic pressure variation in ventilated dogs. *Intensive Care Med* 1989; 15: 368–371.
11. Berkenstadt H, et al. Stroke volume variation as a predictor of fluid responsiveness in patients undergoing brain surgery. *Anesth Analg* 2001; 92: 984–989.
12. Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005; 103: 419–428.
13. Joshua O Benditt. Esophageal and Gastric Pressure Measurements. *Respir Care* 2005; 50(1): 68–75.
14. A Perel. The physiological basis of arterial pressure variation during positive-pressure ventilation. *Réanimation* (2005); 14: 162–171.
15. Shrivastava D. Impact of sleep disordered breathing treatment on upper anatomy and physiology. *Sleep Medicine* 2014; 15(07): 733–741.