Cardiopulmonary Interactions: Physiologic Basis and Clinical Applications

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Abstract

The hemodynamic effects of ventilation can be grouped into three concepts: *1*) Spontaneous ventilation is exercise; *2*) changes in lung volume alter autonomic tone and pulmonary vascular resistance and can compress the heart in the cardiac fossa; and *3*) spontaneous inspiratory efforts decrease intrathoracic pressure, increasing venous return and impeding left ventricular ejection, whereas positive-pressure ventilation decreases venous return and unloads left ventricular ejection. Spontaneous inspiratory efforts may induce acute left ventricular failure and cardiogenic pulmonary edema. Reversing the associated negative intrathoracic pressure swings by using noninvasive continuous positive airway pressure rapidly reverses acute cardiogenic pulmonary edema and improves survival. Additionally, in congestive heart failure, states increasing intrathoracic pressure may augment left ventricular ejection and improve cardiac output. Using the obligatory changes in venous return induced by positive pressure breathing, one can quantify the magnitude of associated decreases in venous flow and left ventricular ejection using various parameters, including vena caval diameter changes, left ventricular stroke volume variation, and arterial pulse pressure variation. These parameters vary in proportion to the level of cardiac preload reserve present, thus accurately predicting which critically ill patients will increase their cardiac output in response to fluid infusions and which will not. Common parameters include arterial pulse pressure variation and left ventricular stroke volume variation. This functional hemodynamic monitoring approach reflects a practical clinical application of heart–lung interactions.

Keywords: functional hemodynamic monitoring; heart–lung interactions; left ventricular afterload; mechanical ventilation; spontaneous ventilation

(Received in original form April 26, 2017; accepted in final form July 10, 2017)

Supported in part by National Institutes of Health grants HL074316, HL120877, HL07820, and NR013912.

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Ann Am Thorac Soc Vol 15, Supplement 1, pp S45–S48, Feb 2018

DOI: 10.1513/AnnalsATS.201704-339FR
Internet address: www.atsjournals.org

As we mark the 60th anniversary of the awarding of the Nobel Prize for the fundamental work on heart–lung interactions, we need to reflect that all the accomplishments came about because of the introduction of invasive measures of cardiac filling pressures and blood flow over 60 years ago by Andre Cournand and his coworkers at Bellevue Hospital in New York (1). By asking basic questions about the nature of heart–lung interactions, they opened the door to the physiologic foundations of modern cardiovascular resuscitation physiology of the critically ill. Heart–lung interactions can be grouped into interactions that involve three basic concepts that usually coexist (2, 3). First, spontaneous ventilation is exercise, requiring O_2 and blood flow, thus placing demands on cardiac output and producing CO_2, adding additional ventilatory stress on gas exchange. Second, inspiration increases lung volume above resting end-expiratory volume. Thus, some of the hemodynamic effects of ventilation are due to changes in lung volume and chest wall expansion. Third, spontaneous inspiration decreases intrathoracic pressure (ITP), whereas positive-pressure ventilation increases ITP (3). Thus, the differences between spontaneous ventilation and positive-pressure ventilation primarily reflect the differences in ITP swings and the energy necessary to produce them. This review is focused on the third interaction, the effects of changes in ITP.

Ventilation can profoundly alter cardiovascular function. Although changes in lung volume and hyperinflation can profoundly alter right ventricular function, this review is focused on left-sided effects because these are the ones that emerged from the initial work of Cournand and colleagues (3). The specific response seen is dependent on myocardial reserve, circulating blood volume, blood flow

distribution, lung volume, ITP, and the surrounding pressures for the extrathoracic circulation (3, 4). Relevant to this issue is the relationship between airway pressure and ITP: the transpulmonary pressure. Airway pressure is relatively easy to measure (5, 6), but ITP is not. Positive-pressure ventilation–induced increases in airway pressure do not necessarily equate to proportional increases in ITP. Only lung and thoracic compliance determine the relationship between end-expiratory airway pressure and lung volume in the sedated and paralyzed patient. However, with spontaneous ventilatory activity, ITP can vary widely compared with airway pressure.

Effect of Intrathoracic Pressure on Cardiac Function

The heart, being within the thorax, is a pressure chamber within a pressure chamber. Therefore, changes in ITP affect the pressure gradients for both systemic venous return to the right ventricle and systemic outflow from the left ventricle, independently of the heart itself. Increases in ITP, by increasing right atrial pressure and decreasing transmural left ventricular (LV) systolic pressure, reduce the pressure gradients for venous return and LV ejection, decreasing intrathoracic blood volume. Decreases in ITP augment venous return and impede LV ejection, increasing intrathoracic blood volume.

Blood flows back from the systemic venous reservoirs into the right atrium through low-pressure–low-resistance venous conduits (7). Right atrial pressure is the back pressure for venous return; ventilation alters both right atrial pressure and venous reservoir pressure. Changes in right atrial pressure and venous capacitance vessel pressure create most of the observed cardiovascular effects of ventilation. Pressure in the upstream venous reservoirs is the mean systemic pressure. Mean systemic pressure is a function of blood volume, peripheral vasomotor tone, and blood flow distribution (8). Because mean systemic pressure is usually constant over a breath, variations in right atrial pressure represent the major factor determining the fluctuation in pressure gradient for systemic venous return during ventilation (9), causing cyclic changes in venous return. The positive-pressure inspiration increases right atrial pressure and causes venous return to decrease during inspiration (10), whereas spontaneous ventilation has the opposite effect (10).

Spontaneous inspiratory efforts usually increase venous return because of the combined decrease in right atrial pressure (2, 5) and increase in intraabdominal pressure (11, 12), due to diaphragmatic descent. However, this augmentation of venous return is limited (13) because as ITP decreases below atmospheric pressure, central venous pressure also becomes subatmospheric, collapsing the great veins as they enter the thorax and creating a flow-limiting segment (7).

The detrimental effect of positive-pressure ventilation on cardiac output can be minimized either by fluid resuscitation to increase mean systemic pressure (6, 14, 15) or by keeping both mean ITP and swings in lung volume as low as possible. Accordingly, prolonging expiratory time, decreasing tidal volume (V_T), and avoiding positive end-expiratory pressure all minimize this decrease in systemic venous return (3, 9, 16). However, if positive-pressure ventilation increases lung volumes, the diaphragm descends, compressing the abdominal compartment and increasing intraabdominal pressure (11, 12). Because a large proportion of venous blood exists in the intraabdominal vasculature, it is pressurized as well, increasing mean systemic pressure, mitigating much of the otherwise large falls in cardiac output that would occur if right atrial pressure alone increased (17).

Changes in ITP alter LV afterload by altering both LV end-diastolic volume and ejection pressure. LV ejection pressure is arterial pressure relative to ITP. If arterial pressure remained constant as ITP increased, transmural LV pressure and thus LV afterload would decrease. Similarly, if arterial pressure remained constant as ITP decreased, then LV wall tension would increase (18). Thus, under steady-state conditions, increases in ITP decrease LV afterload, and decreases in ITP increase LV afterload (19, 20). The spontaneous inspiration-associated decrease in ITP-induced increase in LV afterload is one of the major mechanisms thought to be operative in the weaning-induced LV ischemia because increased LV afterload increases myocardial O_2 consumption. Thus, spontaneous ventilation increases not only global O_2 demand by its exercise component (21) but also myocardial O_2 consumption.

Profoundly negative swings in ITP commonly occur during forced spontaneous inspiratory efforts in patients with bronchospasm and obstructive breathing. This condition may rapidly deteriorate into acute heart failure and pulmonary edema (22), as seen in patients with airway obstruction (asthma, upper airway obstruction, vocal cord paralysis) or stiff lungs (interstitial lung disease, pulmonary edema, and acute lung injury). The negative ITP swings may selectively increase LV afterload, causing LV failure and pulmonary edema (1, 22, 23), especially if LV systolic function is already impaired (24). Thus, weaning from mechanical ventilation is a selective LV stress test (18).

The improvement in LV function seen with positive-pressure ventilation in subjects with LV failure is self-limited because venous return also decreases, limiting intrathoracic blood volume. However, the effect of removing large negative swings of ITP on LV performance also acts to reduce LV afterload but is not associated with a change in venous return, because until ITP becomes positive, venous return remains constant. Accordingly, removing negative ITP swings selectively reduces LV afterload without impeding venous return (6, 7, 24). This process improves LV function in patients with heart failure treated with continuous positive airway pressure for obstructive sleep apnea (25), even at low continuous positive airway pressure levels, if it inhibits obstructive airway breathing (26). Prolonged nighttime nasal continuous positive airway pressure can selectively improve respiratory muscle strength, as well as LV contractile function if the patients have preexistent heart failure (27); these benefits are associated with reductions of serum catecholamine levels (28). Furthermore, continuous positive airway pressure therapy now forms the fundamental first step in the management of acute cardiogenic pulmonary edema because it both abolishes the negative swings in ITP during inspiration and sustains alveolar oxygenation, and it does this from the very first breath it delivers (29).

Using Heart–Lung Interactions to Diagnose Cardiovascular Reserve

Clinically, the dynamic changes in venous return and LV afterload can be used as a cyclic forcing function to plumb cardiovascular reserve. Because the cardiovascular response to positive-pressure breathing is determined by the baseline cardiovascular state, ventilation-associated changes in arterial pulse pressure and stroke volume should be inferential for dynamic

changes in venous return and the responsiveness of the heart to these transient and cyclic changes in preload (30). Both arterial pulse pressure and systolic pressure variations (PPV and SPV, respectively) during positive-pressure ventilation describe preload responsiveness, with threshold values greater than 10 to 15% being highly predictive of volume responsiveness if patients are on V_T greater than or equal to 8 ml/kg, adapted to the ventilation and without dysrhythmias (31, 32). Both PPV and SPV are calculated in the same manner from sequential pulse pressure or stroke volume data points over a minimum of three to four breaths. The ratio of difference between the maximal and minimal pulse pressure or stroke volume values, independent of which breaths they occur in relative to the mean pulse pressure or stroke volume, defines PPV and SPV, respectively. Because a primary cardiovascular management decision in shock is whether to give intravascular fluids to increase blood flow (33), knowing if a patient is volume responsive before giving fluids both prevents overhydration of nonresponsive patients and aids in monitoring the response to fluid resuscitation in responsive ones. This approach has been termed *functional hemodynamic monitoring* because it uses a repetitive, known physiologic perturbation to drive a readout physiologic signal defining cardiovascular reserve. This functional hemodynamic monitoring approach of using heart–lung interactions was verified across many studies by metaanalysis (34). If chest wall compliance were to decrease owing to increased intraabdominal pressure limiting diaphragmatic descent, then the accuracy of PPV and SPV to predict volume responsiveness would decline.

Two primary caveats limit the universal application of SPV- and PPV-driven resuscitation across patient groups. First, the patient must be adapted to the ventilator with minimal spontaneous breathing (35). Although not a limiting factor in intraoperative volume management and potentially also not an issue early in the resuscitation of the recently intubated patient in profound shock, this issue becomes relevant after the initial "rescue" phase is completed. However, another major limiting factor in the use of SPV and PPV thresholds to define volume responders and nonresponders is the need to create enough of a dynamic change in ITP to induce the obligatory variation in venous return, upon which these parameters hinge (31, 32). The most common cause of inadequate variations in ITP is the use of low V_T ventilation. In the original studies, my colleagues and I used 8 ml/kg V_T to derive threshold SPV and PPV values of 10 and 13%, respectively (32). Such "larger" V_T values, if sustained, may cause ventilator-induced lung injury. Large V_T ventilation increases mortality in both patients with acute respiratory distress syndrome (36) and those with normal lungs ventilated for only short periods of time (9). Thus, the negative predictive value of SPV and PPV degrades as V_T is constrained to 6 ml/kg or less. To address this issue, it was demonstrated in one recent study that changes in SPV and PPV during a 1-minute 8 ml/kg "V_T challenge" showed excellent discrimination between volume responders and nonresponders (37). The threshold values for the change in SPV and PPV that provide good prediction of volume responders and volume nonresponders when ventilation was transiently increased from 6 to 8 ml/kg were 2.5% and 3.5%, respectively. Importantly, volume responsiveness does not equate to the need for fluids; it only identifies the ability of the heart to increase stroke volume if given fluids. The decision to give fluids needs to be based on the presumption that cardiac output is inadequate to meet the metabolic demands of the body, not just on the fact that the cardiovascular system is volume responsive.

Many functional hemodynamic monitoring approaches use these dynamic transients to measure volume responsiveness (38). Both spontaneous and positive-pressure breathing, by altering the pressure gradients for venous return to the right ventricle, assess both right ventricular and LV preload reserve (39). For dynamic changes in venous return to alter LV stroke volume or arterial pulse pressure, both right ventricular and LV preload reserve need to be present. Dynamic venous flow changes during spontaneous and positive-pressure ventilation identify right ventricular preload reserve indirectly by the dynamic changes in inferior vena caval (40), superior vena caval (41), and internal jugular venous diameters (42). Threshold values above a 10 to 15% change in diameter define volume responsiveness. Healthy subjects demonstrate spontaneous inspiratory inferior vena caval collapse, and when reflex hyperpnea of shock exaggerates the inspiratory efforts, this inferior vena caval collapse becomes a cardinal sign of hypovolemic volume responsiveness, though only a greater manifestation of the normal inferior vena caval diameter changes seen in normally volume-responsive individuals.

Because both SPV and PPV sensitivity degrade during spontaneous ventilation, low V_T ventilation, severe cor pulmonale, and other extremes of physiology (43), alterative functional hemodynamic monitoring tests are used. Specifically, performing passive leg-raising maneuvers that transiently increase venous return while concomitantly monitoring LV output is a very sensitive and specific predictor of volume responsiveness under most conditions (44).

In summary, understanding heart–lung interactions has led to the use of continuous positive airway pressure as primary therapy for acute cardiogenic pulmonary edema to support a failing left ventricle in patients with obstructive sleep apnea and for positive-pressure breathing–induced changes in ITP to identify volume responsiveness in critically ill patients in need of resuscitative efforts. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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