Cardiovascular Issues in Respiratory Care*

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The hemodynamic effects of ventilation are complex but can be grouped under four clinically relevant concepts. First, spontaneous ventilation is exercise, and critically ill patients may not withstand the increased work of breathing. Initiation of mechanical ventilatory support will improve oxygen delivery to the remainder of the body by decreasing oxygen consumption. To the extent that mixed venous oxygen also increases, Pao_2 will increase without any improvement in gas exchange. Similarly, weaning from mechanical ventilatory support is a cardiovascular stress test. Patients who fail to wean also manifest cardiovascular insufficiency during the failed weaning attempts. Improving cardiovascular reserve or supplementing support with inotropic therapy may allow patients to wean from mechanical ventilation. Second, changes in lung volume alter autonomic tone and pulmonary vascular resistance (PVR), and at high lung volumes compress the heart in the cardiac fossa. Hyperinflation increases PVR and pulmonary artery pressure, impeding right ventricular ejection. Decreases in lung volume induce alveolar collapse and hypoxia, stimulating an increased pulmonary vasomotor tone by the process of hypoxic pulmonary vasoconstriction. Recruitment maneuvers, positive end-expiratory pressure, and continuous positive airway pressure may reverse hypoxic pulmonary vasoconstriction and reduce pulmonary artery pressure. Third, spontaneous inspiration and spontaneous inspiratory efforts decrease intrathoracic pressure (ITP). Since diaphragmatic descent increases intra-abdominal pressure, these combined effects cause right atrial pressure inside the thorax to decrease but venous pressure in the abdomen to increase, markedly increasing the pressure gradient for systemic venous return. Furthermore, the greater the decrease in ITP, the greater the increase in left ventricular (LV) afterload for a constant arterial pressure. Mechanical ventilation, by abolishing the negative swings in ITP, will selectively decrease LV afterload, as long as the increases in lung volume and ITP are small. Finally, positive-pressure ventilation increases ITP. Since diaphragmatic descent increases intra-abdominal pressure, the decrease in the pressure gradient for venous return is less than would otherwise occur if the only change were an increase in right atrial pressure. However, in hypovolemic states, positive-pressure ventilation can induce profound decreases in venous return. Increases in ITP decrease LV afterload and will augment LV ejection. In patients with hypervolemic heart failure, this afterload reducing effect can result in improved LV ejection, increased cardiac output, and reduced myocardial oxygen demand.

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Key words: heart-lung interaction; mechanical ventilation; spontaneous respiration

Abbreviations: CHF = congestive heart failure; CPAP = continuous positive airway pressure; HPV = hypoxic pulmonary vasoconstriction; ITP = intrathoracic pressure; LV = left ventricle/ventricular; PEEP = positive end-expiratory pressure; PVR = pulmonary vascular resistance; RV = right ventricle/ventricular; Svo_2 = mixed venous oxygen saturation

Learning Objectives: 1. To review the complex physiologic interactions between the cardiovascular and respiratory systems as they apply to the critically ill patient. 2. To understand the effects of mechanical ventilation versus spontaneous respiration on cardiorespiratory responses. 3. To describe the impact of ventilator settings and weaning from mechanical ventilation on heart-lung interactions.

Ventilation can profoundly alter cardiovascular function via complex, conflicting, and often opposite processes. These processes reflect the interaction between myocardial reserve, ventricular pump function, circulating blood volume, blood flow distribution, autonomic tone, endocrinologic responses, lung volume, intrathoracic pressure (ITP), and the surrounding pressures for the remainder of the circulation. Clearly, the final response to ventilatory stress is dependent on the baseline cardiovascular state of the subject.

Lung volume increases in a tidal fashion during both spontaneous and positive-pressure inspiration. However, ITP decreases during spontaneous inspiration owing to the contraction of the respiratory muscles, whereas ITP increases during positive-pressure inspiration due to passive lung expansion to increasing airway pressure. Thus, changes in ITP and the metabolic demand needed to create these changes represent the primary determinants of the hemodynamic differences between spontaneous and positive-pressure ventilation.[1]

Spontaneous Ventilation Is Exercise

Although ventilation normally requires < 5% of total oxygen delivery,[2] in lung disease states the work of breathing is increased, such that its metabolic demand for oxygen may reach 25% of total oxygen delivery. If cardiac output also is limited, blood flow to other organs can be compromised, causing tissue hypoperfusion, ischemic dysfunction, and lactic acidosis.[3] Mechanical ventilation will decrease the work of breathing, even if delivered by noninvasive ventilation mask continuous positive airway pressure (CPAP).[4] The resultant cardiovascular effects will be increased oxygen delivery to other organs, decreased serum lactate levels, and increase mixed venous oxygen saturation (Sv_{O_2}). The obligatory increase in Sv_{O_2} will result in an increase in the Pa_{O_2} if fixed right-to-left shunts exist, even if mechanical ventilation does not alter the ratio of shunt blood flow to cardiac output. Finally, if cardiac output is severely limited, respiratory muscle failure develops despite high central neuronal drive, such that many heart failure patients die a respiratory death prior to cardiovascular standstill.[5]

Ventilator-dependent patients who fail to wean from mechanical ventilation may display impaired baseline cardiovascular performance[6] but routinely only have signs of heart failure during weaning. The transition from positive-pressure to spontaneous ventilation can be associated with pulmonary edema,[6] myocardial ischemia,[7,8] tachycardia, and gut ischemia.[9] Jubran et al[10] demonstrated that although all subjects increase their cardiac outputs in response to a weaning trial, consistent with the increased metabolic demand, those who subsequently fail to wean also display a decrease in Sv_{O_2}. Since the increased work of breathing may come from the endotracheal tube flow resistance,[11] failure to wean may reflect ventilator work rather than innate respiratory system resistance. Thus, some patients who fail a t-tube trial pass an extubation trial. Since weaning from mechanical ventilatory support is a cardiovascular stress, it is not surprising that weaning-associated ECG and thallium cardiac blood flow scan-related signs of ischemia have been reported in both subjects with known coronary artery disease[7] and in otherwise normal patients.[8] Similarly, initiating mechanical ventilation in patients with severe heart failure and/or ischemia can reverse myocardial ischemia.[12]

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Inspiration Increases Lung Volume

Autonomic Tone

Inflation induces immediate changes in autonomic output,[13] causing cardiac acceleration otherwise known as respiratory sinus arrhythmia,[14] which implies normal autonomic responsiveness.[15] Loss of respiratory sinus arrhythmia is seen in diabetic peripheral neuropathy, and its reappearance precedes the return of peripheral autonomic control.[16] Lung inflation to larger tidal volumes (> 15 mL/kg) decreases heart rate by sympathetic withdrawal.[17] Reflex arterial vasodilatation can also occur with lung hyperinflation.[13,18] Since patients with ARDS often ventilate a small amount of lung, regional hyperinflation of aerated lung units may develop and lead to reflex cardiovascular depression. Although humoral factors released from pulmonary endothelial cells during lung inflation may also induce this depressor response,[19] these interactions do not appear to be relevant clinically because unilateral lung hyperinflation does not alter systemic hemodynamics.[20]

Humoral Factors

Positive-pressure ventilation and sustained hyperinflation induce fluid retention via right atrial stretch receptors that increase plasma norepinephrine, plasma renin activity,[21] and decrease atrial natriuretic peptide activity.[22] Congestive heart failure (CHF) patients receiving nasal CPAP decrease their plasma atrial natriuretic peptide activity inversely with the associated increase in cardiac output.[23]

Pulmonary Vascular Resistance

Lung inflation primarily affects cardiac function and cardiac output by altering right ventricular (RV) preload and afterload.[24] Changes in ITP that occur without changes in lung volume, as may occur with obstructive inspiratory efforts or a Valsalva maneuver, will not alter pulmonary vascular resistance (PVR). Lung volume must change. The mechanism by which ventilation alters PVR is complex. If regional alveolar P_{O_2} decreases below 60 mm Hg, local

pulmonary vasomotor tone increases, reducing local blood flow[25] by a process known as hypoxic pulmonary vasoconstriction (HPV). Decreases in end-expiratory lung volume promote alveolar collapse stimulating HPV. Patients with acute hypoxemic respiratory failure usually have small lung volumes.[26] Restoration of lung volume to normal values by recruitment maneuvers and positive end-expiratory pressure (PEEP) usually reduces PVR in these patients by reversing HPV.[27]

Hyperinflation passively compresses the alveolar vessels[26] increasing PVR.[28] Hyperinflation can create significant pulmonary hypertension and may precipitate acute RV failure (acute cor pulmonale)[29] and RV ischemia.[30] Thus, PEEP may decrease PVR if it reverses HPV,[31] or it may increase PVR if it only hyperinflates the lungs.[32]

Mechanical Heart-Lung Interactions

Hyperinflation compresses the heart between the expanding lungs,[33] increasing juxtacardiac ITP and pericardial pressure more than lateral chest wall ITP.[34] This decrease in "apparent" left ventricular (LV) diastolic compliance was previously misinterpreted as PEEP-induced impaired LV contractility.[35] However, when patients are fluid resuscitated back to their original LV end-diastolic volume, cardiac output also returns to its original levels[36] despite the continued application of PEEP.[37]

Ventilation Alters ITP

The heart is a pressure chamber within a pressure chamber. Therefore, changes in ITP will affect the pressure gradients for both systemic venous return to the RV and systemic outflow from the LV, independent of the heart. Increases in ITP, by increasing right atrial pressure and decreasing transmural LV systolic pressure, will reduce the pressure gradients for venous return and LV ejection decreasing intrathoracic blood volume. Decreases in ITP will augment venous return and impede LV ejection and increase intrathoracic blood volume.

Systemic Venous Return

Right atrial pressure is the backpressure to systemic venous return.[38] Blood flows back to the heart from the periphery through low-pressure/low-resistance venous conduits. Guyton et al[38] characterized venous flow from the venous reservoirs into the right atrium. Right atrial pressure can change rapidly during the ventilatory cycle because of the concomitant changes in ITP.[39] Positive-pressure inspiration increases ITP and right atrial pressure, decreasing the pressure gradient for venous return, which decreases venous blood flow,[40] RV stroke volume, and consequently cardiac output.[39] This decrease in venous return is minimized by the concomitant increase in intra-abdominal pressure induced by diaphragmatic descent and abdominal wall muscle contraction.[41] We recently documented that increasing CPAP up to 20 cm H_2O would not decrease cardiac output as long as intra-abdominal pressure also increased similarly.[42] Markedly negative swings in ITP, as occur with obstructed inspiratory efforts, do not flood the RV with blood because venous return becomes flow limited as ITP becomes subatmospheric.[38]

LV Preload and Ventricular Interdependence

Changes in venous return must eventually result in directionally similar changes in LV preload after two or three beats, as seen with a Valsalva maneuver.[43] This phase delay in changes in output from the RV to the LV is exaggerated if tidal volume or respiratory rate are increased or in the setting of hypovolemia.[44] Direct ventricular interdependence can also occur and be clinically significant. Increasing RV volume shifts the intraventricular septum into the LV and simultaneously decreases LV diastolic compliance. During positive-pressure ventilation, RV volumes are usually decreased, minimizing ventricular interdependence.[36,44,45] Positive-pressure ventilation-induced increases in lung volume compress the two ventricles into each other, decreasing biventricular volumes.[46] Restoring LV end-diastolic volume with fluids returns cardiac output during PEEP therapy[47] without LV diastolic compliance changes.

However, during spontaneous inspiration, as RV volumes transiently increase, septal shift into the LV lumen is the rule,[48] decreasing LV diastolic compliance and end-diastolic volume.[31,45] This interdependence is the primary cause of inspiration-associated decreases in arterial pulse pressure, otherwise known as pulsus paradoxus.[1]

Left Ventricular Afterload

Maximal LV wall tension, or afterload, normally occurs at the end of isometric contraction. LV afterload normally decreases during ejection because LV volume decreases markedly despite the small increase in ejection pressure. With LV dilation, however, as in CHF, maximal LV wall stress occurs during LV ejection, making the heart more sensitive to changes in ejection pressure. Since arterial pressure with respect to atmosphere is kept constant by baroreceptor feedback,[18] if arterial pressure were to remain constant as ITP increases, then LV ejection pressure must decrease.[49] Similarly, decreases in

ITP with a constant arterial pressure will increase LV ejection pressure.[43,50] Accordingly, any process associated with marked decreases in ITP must also be associated with increased LV afterload and myocardial oxygen consumption. This is part of the reason why weaning induces cardiac stress.

Rapid increases in ITP, as in coughing, will increase arterial pressure but not alter LV ejection pressure[1,51] or aortic blood flow.[33] However, sustained increases in ITP, as seen with a Valsalva maneuver, will eventually decrease aortic blood flow and arterial pressure because venous return decreases.[1] However, if ITP were to increase arterial pressure without changing transmural arterial pressure, then the periphery would reflexively vasodilate to maintain a constant extrathoracic arterial pressure-flow relation,[52] causing a reflex-induced decrease in LV afterload. Although increasing ITP to reduce LV ejection pressure is an impractical clinical strategy because of the associated decrease in venous return, abolishing negative swings in ITP will have the identical effect of reducing LV ejection pressure but without affecting venous return. Negative swings in ITP, as seen with spontaneous inspiratory efforts during airway obstruction or stiff lungs, will selectively increase LV afterload without increasing venous return. Selective increases in LV afterload in these conditions may cause acute LV failure and pulmonary edema,[6,53] especially if contractility is already compromised.[6] Importantly, abolishing such large negative swings in ITP by either removing the inspiratory obstruction (*eg*, intubation) or offsetting the negative ITP swings with positive airway pressure (*eg*, starting mechanical ventilation) usually reduces LV afterload without decreasing cardiac output.[38] Similarly, spontaneous inspiration during weaning must increase LV afterload.[10]

Hemodynamic Effects of Ventilation Depend on Cardiopulmonary Status

A single ventilatory maneuver can have opposite cardiovascular effects in different patients. Importantly, the hemodynamic response to a specific ventilatory state may also be used to identify the cardiovascular reserve of that patient. In patients who are otherwise normal, their cardiovascular state is characterized by preload dependency. Thus, in normal subjects or those patients with hypovolemia (*eg*, hemorrhagic shock, severe vomiting, diarrhea, loss of vasomotor tone, spinal cord shock) and also in subjects who may have RV failure with hyperinflation (severe obstructive lung disease, RV contusion during anterior chest trauma), intubation and positive-pressure ventilation may rapidly induce cardiovascular insufficiency requiring massive volume resuscitation. In patients with CHF, positive-pressure ventilation will not impair cardiac output unless hyperinflation also occurs. Since mechanical ventilation will also decrease global and myocardial oxygen demand, overall organ function may improve as well. Similarly, withdrawal of ventilatory support in patients with limited cardiovascular reserve should be done slowly because the increased load on the heart can precipitate heart failure and pulmonary edema.[6]

The hemodynamic differences between different modes of total mechanical ventilatory support at a constant airway pressure and PEEP can be explained by their differential effects on lung volume and ITP.[54] If two different modes of ventilatory support induce similar changes in ITP and ventilatory effort, their hemodynamic effects will also be similar, despite markedly different airway waveforms. Partial ventilatory support with either intermittent mandatory ventilation or pressure support ventilation give similar hemodynamic responses when matched for similar tidal volumes.[55] Positive-pressure ventilation decreases intrathoracic blood volume[56] and PEEP decreases it even more[57,58] without altering LV systolic performance.[59] However, since lung and chest wall compliance can vary widely over time and among patients with the same diagnosis, increases in airway pressure may not reflect increases in ITP. Increases in lung volume, not airway pressure, define the degree of increase of ITP during positive-pressure ventilation.[60] If the increase in lung volume is held constant among forms of positive-pressure ventilation, the hemodynamic effects are similar,[61] whereas pressure-limited ventilation, if associated with lower tidal volume, will enjoy higher cardiac output.[62] Importantly, during spontaneous ventilation trials, the degree of hyperinflation, not the airway pressure, determines the decrease in cardiac output.[63] Most of the decrease in cardiac output can be reversed by fluid resuscitation.[59,64] If cardiac output does not increase with fluid resuscitation, then other processes, such as cor pulmonale, increased PVR, or cardiac compression, may also be inducing this cardiovascular depression.[63]

The cardiovascular benefits of positive airway pressure can be seen by withdrawing negative swings in ITP. Increasing levels of CPAP improve cardiac function in patients with heart failure but only once the negative swings in ITP are abolished.[65] Nasal CPAP can also accomplish the same results in patients with obstructive sleep apnea and heart failure,[66] although the benefits do not appear to be related to changes in obstructive breathing pattern.[67] Prolonged nighttime nasal CPAP can selectively

improve respiratory muscle strength, as well as LV contractile function if the patient had preexisting heart failure.[68]

Patients with COPD are at an increased risk of hyperinflation, either due to bronchospasm, loss of lung parenchyma or dynamic hyperinflation (inadequate expiratory time). Hyperinflation will compress the heart, increase PVR, and impede RV filling. Intrinsic PEEP (hyperinflation) alters hemodynamic function similar to extrinsic PEEP. Thus, matching intrinsic PEEP with ventilator-derived PEEP does not alter hemodynamics.[69] There is little hemodynamic difference between increasing airway pressure to generate a breath and decreasing extrathoracic pressure (iron lung-negative pressure ventilation).[70]

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