

Clinical implications of heart-lung interactions during mechanical ventilation: an update

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ABSTRACT

As opposed to spontaneous respiration wherein small cyclic changes in transpulmonary, negative pressure coincide with lung volume changes, positive pressure (mechanical) ventilation results in a simultaneous rise in transpulmonary pressure and lung volumes. The changes may affect biventricular cardiac loading and function in dissimilar ways, depending on baseline cardiopulmonary function. This review is intended to update current knowledge on the pathophysiology of these heart-lung interactions in helping to explain the common circulatory alterations occurring during airway pressure changes and to better understand mechanisms of disease and modes of action of treatments, during spontaneous and mechanical ventilation.

KEYWORDS

Cardiopulmonary interactions, cardiac function, mechanical ventilation, pulsus paradoxus.

INTRODUCTION

Spontaneous respiration as well as mechanical ventilatory support can alter cardiac loading and function and thereby contribute to circulatory alterations. This may particularly occur in some disease states. If severe, as in critically ill patients in the intensive care unit, the changes may be associated with diminished tissue oxygen delivery and distant organ dysfunctions, and thereby contribute to morbidity and mortality. This update is meant to explain these frequently encountered alterations to provide a rationale for treatment. We will summarise current knowledge on the effects of airway pressures on the right and left ventricle separately (*table 1*) and will focus on animal and human studies with major mechanistic or therapeutic implications. We will not discuss the effect

Table 1. Effects of increase in airway pressure and volume

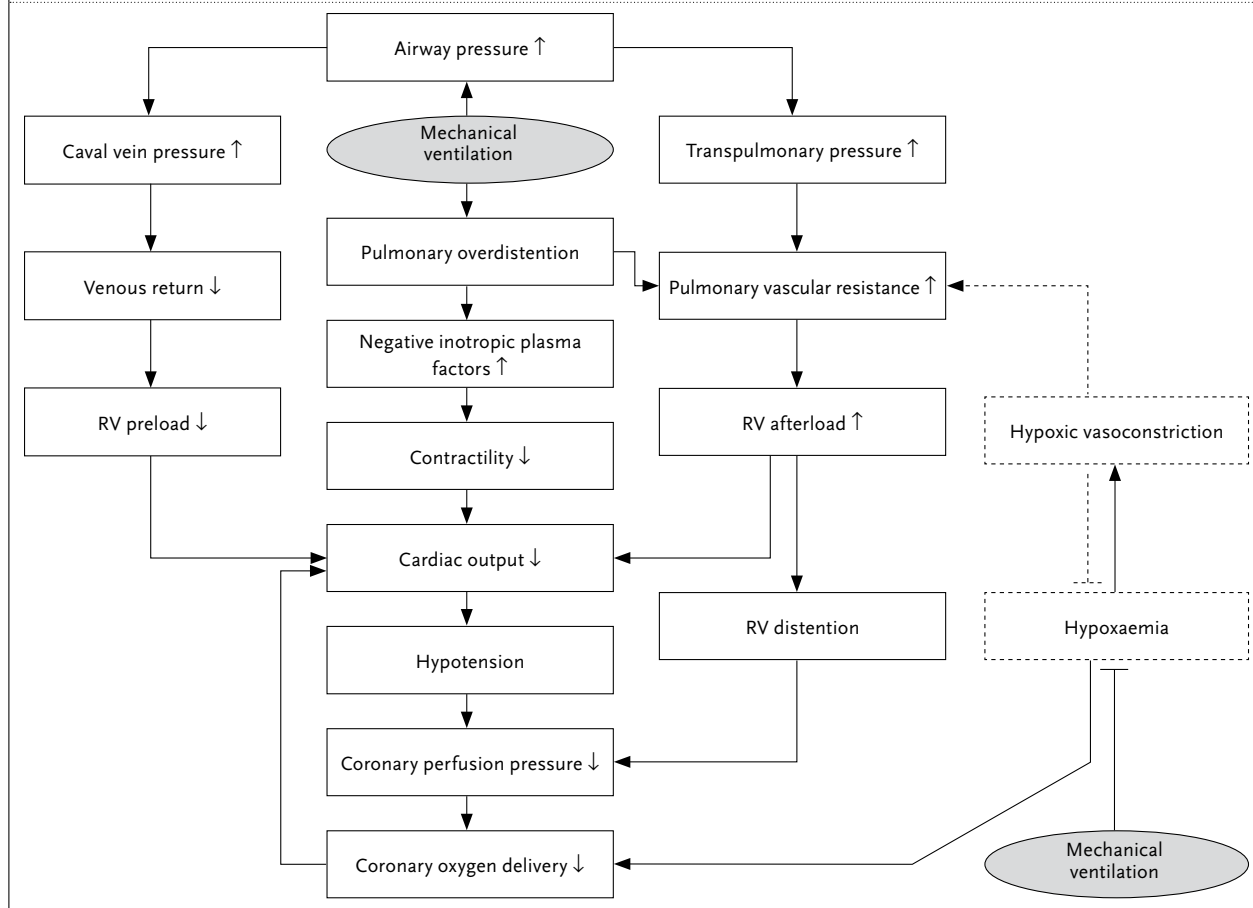
Right ventricle	Left ventricle
Decreased preload	Decreased preload
Increased afterload	Decreased compliance
Reduced contractility	Variable effects on (autonomous nervous system control of) contractility
Compression of heart in cardiac fossa	Decreased afterload
	Compression of heart in cardiac fossa

of airway pressure on the peripheral circulation and for more in-depth physiological reviews the reader is referred to recent publications.¹⁻⁴

THE RIGHT VENTRICLE

After instituting mechanical ventilation for acute respiratory failure, arterial blood pressure is often observed to fall. This can, most commonly and importantly, be attributed, at least in part, to a fall in right ventricular filling following impeded venous return, depending on the transmission of airway to juxtacardiac pressure and on systemic filling (abdominal) pressure (*figure 1*).^{5,6} The difference between transpulmonary and systemic filling pressures is indeed the gradient for venous return. The transmission can be assessed by measuring pleural or pericardial (rather than oesophageal) pressure and is normally about 50% of prevailing airway pressure.⁷ Therefore, right ventricular end-diastolic volume generally falls upon increases in airway pressure as a reflection of a fall in venous return and a resultant fall in right ventricular preload, which largely explains the fall in stroke volume and cardiac output that is dependent on (transmission of) mean airway pressure during the respiratory cycle.^{5,9} Also contributing to a fall in cardiac

Figure 1. Cardiovascular effects of mechanical ventilation and application of PEEP. Mechanical ventilation alters intrathoracic pressures and thereby affects the cardiovascular system, mainly the right ventricle



preload is compression of the heart by the lungs in the cardiac fossa,⁷ so that haemodynamic alterations in response to airway pressure may be greater in closed than in open chest conditions. The latter may be relevant for conditions after sternotomy during cardiac surgery.¹⁰ Airway pressure transmission is expected to decrease with decreasing lung (or increasing chest wall) compliance. If, however, lung (tidal) volume is kept constant in diseased lungs, the atmospheric-pressure referenced pleural, pericardial and thus right atrial pressures will rise, since airway pressure is increased in face of diminished compliance. Then, the effect of altered airway pressure transmission on net right ventricular preload may be negligible. Conversely, open abdomens may be associated with increased chest wall compliance.

In addition to a pressure-related fall in right ventricular preload, a volume-induced rise in pulmonary vascular resistance may, particularly with inspiration, result in a rise in right ventricular afterload. The latter phenomenon may in turn attenuate a fall in right ventricular end-diastolic volume, for instance during inspiration as compared with expiration, but may aggravate a fall in cardiac output. The preload effect may

prevail with rises in mean airway pressure upon altering ventilatory settings, while the rise in inspiratory afterload may further modulate this effect. However, if an increase in right ventricular afterload predominates over the fall in venous return, right ventricular end-diastolic volume may increase with rising airway pressures, and indeed features of acute cor pulmonale may develop in up to 25% of patients with acute lung injury on mechanical ventilation, as supported by echocardiography.¹¹ This may render the right ventricle susceptible to an imbalance in coronary blood supply to demand and may further depress function, particularly in case of arterial hypotension and coronary hypoperfusion (*figure 1*). Occurrence of tricuspid regurgitation may further confound haemodynamics. The acute cor pulmonale is potentially ameliorated or prevented by lung-protective and low (*vs* high) tidal volumes during mechanical ventilation.¹¹ Also, too much positive end-expiratory pressure (PEEP) and presumably resultant overdistention of the lung may liberate plasma factors that may have negative inotropic actions on the heart, possibly by spillover of the inflammatory response to overdistention, at least in experimental animals.¹²

The response of the right ventricle to increasing airway pressure and PEEP may depend on underlying conditions and the effect of lung volume on pulmonary vascular resistance. Pulmonary hypertension is a common complication of chronic lung disease. Exacerbations and resultant hypoxaemia and hypoxic vasoconstriction may further elevate pulmonary artery pressure and thus afterload upon the right ventricle. A component of acute cor pulmonale can then be superimposed upon chronic cor pulmonale during mechanical ventilation.¹¹ Underlying intrinsic (right ventricular) disease, for instance in coronary artery (surgery) patients, may also affect cardiac loading and function alterations caused by elevated airway pressures, increasing the risk for right ventricular ischaemia.⁸ One may also speculate that overdistention by mechanical ventilation will increase vascular resistance and that recruitment of previously collapsed alveoli ('opening the lung') may decrease resistance following amelioration of hypoxic vasoconstriction and improved CO₂ removal.^{11,13,14} Hence, baseline pulmonary pressure/volume relations and effects of altering airway pressures hereon may determine if a right ventricular preload or afterload effect predominates during increases in airway pressure and PEEP. Conversely, the effect of tidal inflation and plateau pressure may depend on baseline PEEP, since PEEP increases plateau airway pressure during pressure-controlled ventilation and may thereby accentuate inspiratory effects. Respiratory compliance-dependent airway pressure transmission may further confound heart-lung interactions. On the other hand, hypovolaemia may aggravate the negative effect of PEEP on cardiac output.¹⁵ Together, the factors may at least explain some of the varying results in the literature on steady state and cyclic changes in right ventricular dimensions during alterations in airway pressures.

THE LEFT VENTRICLE

In patients with severe left ventricular dysfunction that is sensitive to afterload changes, application of positive (end-expiratory) airway pressure, as in a Valsalva manoeuvre, may decrease transmural aortic pressure and thereby afterload. Hence, under these circumstances, PEEP may increase rather than decrease cardiac output, in spite of a reduction in right ventricular preload by the rise in airway pressure.

Increased vagal nerve afferent and efferent activity via lung stretch and stimulation of stretch receptors (by lung volume) may depress biventricular function and lower peripheral vascular resistance, during increments of airway pressure (PEEP), independently of altered loading.¹⁶ Finally, right and left heart function are tied together in ventricular interdependence via a series effect, pericardial constraint,

systolic augmentation, diastolic septal interaction, or combinations.¹⁷ Indeed, right ventricular distention may flatten the septum and decrease left ventricular compliance, thereby contributing to a reduction in left ventricular filling and output.⁹

CLINICAL IMPLICATIONS

Imaging techniques to assess biventricular loading consist of echocardiography, magnetic resonance imaging, radionuclide imaging, and determinations of ventricular volumes by thermodilution, but some of these techniques may not be routinely applicable at the bedside. The imaging techniques can thus be helpful to document cardiac loading alterations, for instance during changes in ventilation modes or settings. Indeed, atmospheric pressure-referenced, end-expiratory right atrial and pulmonary capillary wedge pressures, when measured, do not indicate transmural filling pressure of the right and left ventricle, respectively, in the presence of PEEP. The effect of transmitted airway pressure on these measurements is unpredictable and hard to account for, although bedside methods for adjustment have been described.¹⁸ Indeed, when subtracting transmitted airway pressure from atmospheric pressure-referenced pressures in the thorax, transmural cardiac filling pressures can be calculated that may fall upon increases in airway pressure, i.e. PEEP, when pressures are measured at the end of expiration.¹⁸ Finally, because of cyclic variations within the respiratory cycle, bolus thermodilution measurements of cardiac output are determined by the phase in which the measurements are done.^{19,20} The practical implication is that right-sided bolus thermodilution cardiac output measurements should be done, particularly in mechanically ventilated patients, at three to four equally spaced time intervals or from four to five random injections throughout the respiratory cycle to obtain a true mean value over that cycle.^{19,20}

We will now discuss clinical implications of heart-lung interactions on specific disease manifestations and treatment, during spontaneous and mechanical ventilation.

BRONCHO-OBSTRUCTIVE SYNDROMES AND PERICARDIAL DISEASE

During spontaneous respiration, cyclic changes in pleural pressure occur, which may alter cardiac loading and function and result in the classical pulsus paradoxus, with increases in right ventricular filling upon inspiration (as compared with expiration) while left ventricular filling decreases concomitantly. Pulsus paradoxus refers to an inspiratory fall of 10 mmHg or more of systolic arterial

blood pressure resulting from a fall in left ventricular filling and stroke volume. The inspiratory decrease in left ventricular filling can be attributed, at least in part, to a rise in transmural pressure elevating left ventricular afterload and a fall in compliance by right ventricular distention. These alterations are augmented by positive airway pressures when expiration is impaired, for instance during broncho-obstructive syndromes, and confounded by pre-existent alterations in the pulmonary vasculature that may result in pulmonary hypertension and right ventricular overload. Indeed, the pulsus paradoxus is the clinically most common example of heart lung interactions,²¹ which can occur in patients with (severely exacerbated) broncho-obstructive pulmonary disease or with pericardial tamponade. In the latter, the sign may necessitate further diagnostics and treatment by pericardiocentesis.²¹

The impaired expiration following broncho-obstruction in the course of asthma or chronic obstructive pulmonary disease may result in intrinsic positive end-expiratory pressure (PEEPi) with hyperinflation that may hamper venous return and thereby contribute to arterial hypotension and tachycardia in these patients.²² This may be only partially counteracted by large negative swings in pleural pressure during inspiratory attempts increasing venous return. Treatment of underlying disease and broncho-obstruction to diminish right ventricular overloading remains of crucial importance and can be done by noninvasive ventilation with continuous positive airway pressure (CPAP or bilevel positive airway pressure) counteracting PEEPi, for instance.^{22,27}

SLEEP APNOEA

Noninvasive ventilation is also commonly used in the treatment of sleep apnoea syndromes. Here, nocturnal delivery of CPAP by face mask augments lung volumes and improves gas exchange to combat or prevent hypoxaemia, thereby unloading the heart and increasing cardiac output and tissue oxygenation. Even on the long term, benefits of cardiovascular status have been described that may relate to less sympathetic overstimulation, among others.^{23,24}

CARDIOGENIC PULMONARY OEDEMA

The circulatory effects of noninvasive ventilation (bilevel positive airway pressure and CPAP) in this condition or its nocturnal prevention are generally considered beneficial by unloading the heart, particularly when systolic function is compromised.²⁴⁻²⁷ Unloading of

respiratory muscle may decrease systemic oxygen requirements and unloading of the heart may reduce myocardial oxygen requirements and thus favourably effect coronary oxygen supply to demand ratios. By these cardiopulmonary mechanisms, CPAP decreases morbidity and perhaps mortality.^{25,26} CPAP may also increase cardiac function and output, at high pulmonary capillary wedge pressures and alleviation of myocardial ischaemia. Hence, this noninvasive treatment is considered safe and can particularly be used in congestive heart failure-induced respiration disorders.²⁴

MECHANICAL VENTILATION

Acute respiratory failure may necessitate intubation and mechanical ventilation. The changes in airway pressure during positive pressure ventilation are opposite to those in spontaneous ventilation and, in contrast to the latter, synchronous with lung volume changes. The reversed pulsus paradoxus refers to the inspiratory increase in left ventricular output when right ventricular output falls, and vice versa during expiration.⁹ Obviously, pulmonary blood volume changes contribute to different behaviours of the right and left ventricle through the respiratory cycle. Moreover, left ventricular stroke volume variations (SVV) and thereby pressure variations, induced by mechanical ventilation and measured by noninvasive techniques, increase during a fall in biventricular preload and cardiac output,²⁸ thereby predicting a rise in cardiac output during fluid challenges; this is referred to as fluid responsiveness.²⁹ Hence, these variations may guide fluid treatment of critically ill and mechanically ventilated patients, in the absence of spontaneous respiratory efforts, constant ventilatory rates and volumes, and regular heart rates.²⁹ Finally, weaning from mechanical ventilation can be associated with recurrent pulmonary oedema, particularly in patients with poor left ventricular function.

Acute cor pulmonale evidenced by echocardiography can be treated by adjustment of ventilatory settings and amelioration of arterial hypotension by, for example, the use of vasopressors. Obviously, the modes of ventilatory support may modulate some of the effects described, but further discussion is beyond the scope of this review. It may suffice here to state that ventilatory support modes that alter pressure volume relations in the lungs may favourably affect haemodynamics when lowering mean airway pressure and preventing overdistention. Conversely, recruitment manoeuvres by applying temporary high airway pressures may have negative circulatory effects.^{10,13}

Finally, a fall in cardiac output may partly offset a rise in arterial O₂ saturation by PEEP so that O₂ delivery to

the tissues may not fall even when cardiac output does. Therefore, authors have defined best PEEP as the level with highest O₂ delivery to the tissues.

FLUID THERAPY

Understanding heart-lung interactions is important since fluid loading to compensate for the fall in venous return with mechanical ventilation may only help increasing cardiac output when the right heart is fluid responsive by operating in the steep part of its function curve.⁵ Right ventricular distention is generally believed to limit or preclude a rise in cardiac output upon fluid loading, particularly when right ventricular ischaemia ensues and the ventricle operates in the plateau of its function curve (*figure 1*). Fluid loading is thus usually counterproductive in right ventricular overloading and may worsen right ventricular failure. In contrast, fluid administration is the treatment of choice to enhance venous return and tissue oxygenation, if deemed necessary on clinical grounds, when cardiac dimensions have decreased, but this is often at the expense of a supranormal plasma volume and resultant tissue oedema.⁵ Imaging the heart may thus be helpful in individual treatment decisions.

During broncho-obstructive syndromes, fluid loading may also be counterproductive in the case of concomitant pulmonary hypertension and cor pulmonale, when right ventricular overload precludes an increase in cardiac output with an attempted increase in preload. In contrast, exacerbations of chronic obstructive pulmonary disease may be accompanied by diastolic dysfunction or even overt left ventricular failure and administration of diuretics is often attempted to treat any concomitant pulmonary overhydration. This may in turn aggravate a fall in cardiac output and arterial hypotension. Hence, assessing volaemic status and heart function to guide treatment is important but hard at the bedside of patients with exacerbated chronic obstructive pulmonary disease and hypotension, and may therefore necessitate echocardiography.

CONCLUSIONS

The effect of airway pressures and volumes on cardiac loading and function is complex. The predominance of effects on cardiac output depends on the underlying function of the heart and pulmonary vasculature. Although the preload effect of increasing airway pressures often predominates in patients, a detrimental rise in right ventricular afterload is unpredictable and should be evaluated in case of severe haemodynamic compromise and absence of fluid responsiveness.

This can be done by echocardiography and may have therapeutic implications. Heart-lung interactions may play a role in the manifestations and treatment of a variety of disorders.

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