Cardiopulmonary Interactions in Children with Heart Failure

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Abstract: Cardiopulmonary interactions are present but inconsequential in humans with normal cardiac and respiratory function; however, in the presence of significant impairment in either system, the importance of the interplay between cardiovascular and pulmonary systems cannot be overstated. This review will discuss the physiologic underpinnings and consequences of these interactions in patients with heart failure.

Keywords: Cardiopulmonary interactions, heart failure, mean systemic pressure, pediatrics, transmural pressure, ventricular afterload.

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INTRODUCTION

The importance of cardiopulmonary interactions in the pathophysiology and treatment of acute and chronic heart failure cannot be overstated. In subjects with normal underlying cardiopulmonary function these interactions are present but inconsequential. However, in patients with significant underlying pulmonary and or cardiovascular disease these interactions between the pulmonary and cardiovascular systems play a prominent role in the evolution and treatment of acute and chronic cardiovascular disease. In this review we will discuss the physiologic underpinnings of these interactions; demonstrate the impact of respiration on cardiovascular function; and review the evidence for respiratory interventions in the management of acute and chronic heart failure.

VOLUME - PRESSURE AND PRESSURE - FLOW RELATIONSHIPS

The volume - pressure and pressure - flow principles that govern the movement of fluid through a distensible structure provide much of the physiologic underpinnings for understanding the interplay between the cardiovascular and pulmonary systems. There are numerous elastic structures in the body that undergo deformation in response to a force. The extent to which an elastic structure undergoes a change in volume is determined by its transmural pressure (P_{tm}) and compliance. The P_{tm} is the difference between inside and surrounding pressures. A positive P_{tm} causes the chamber to distend while a negative P_{tm} causes the chamber to reduce in volume. For example, for a given internal pressure as the surrounding pressure increases the P_{tm} decreases and as a result chamber volume decreases producing an increase in

internal pressure. The resulting increase in internal pressure drives fluid out of that compartment. The extent to which a chamber undergoes deformation in response to a P_{tm} also depends on its compliance. For a given P_{tm}, the more compliant chamber experiences a greater change in volume than a less compliant structure.

THE DETERMINANTS OF SYSTEMIC VENOUS RETURN

A discussion of systemic venous return and its determinants is germane to any discussion of how respiration impacts cardiovascular function, particularly in patients with heart failure. The determinants of systemic venous return are the difference in pressure between the systemic venous reservoirs and right atrium and the resistance to venous return [1]. The resistance to venous return changes little even in the face of large adrenergic activation [2]. The pressure within the venous reservoirs is the mean systemic pressure, which is a function of intravascular volume and vascular capacitance, the vast majority of which reside within and with the systemic venous reservoirs [3]. The most important venous reservoirs are located within the abdominal compartment and include the liver, spleen and mesentery.

An increase in intravascular volume or decrease in venous capacitance increases the mean systemic pressure. Venoconstricting agents such as dopamine, epinephrine, and norepinephrine decrease venous capacitance and therefore the volume of these reservoirs, as a result the pressure within rises driving systemic venous return from the periphery to the right atrium. A decrease in intravascular volume or increase in venous capacitance, which occurs with venodilators such as the nitric oxide donors nitroglycerin and nitroprusside and furosemide and the combined inodilators dobutamine and milrinone, decrease systemic venous return.

Changes in intrathoracic pressure also impact the gradient for venous return by altering right atrial pressure. As intrathoracic pressure becomes negative during spontaneous

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respiration, the Ptm for the right atrium increases. As a result, right atrial volume increases and the pressure within falls, promoting systemic venous return. The converse occurs with positive pressure ventilation. The extent to which positive pressure ventilation decreases systemic venous return depends on the adequacy of compensatory circulatory reflexes and their effect on intravascular volume and venomotor tone [4]. Acutely, neurohormonal activation induces venoconstriction and a compensatory increase in the mean systemic pressure. Over time, neurohormonal activation leads to fluid retention and an increase in intravascular volume, contributing to a compensatory increase in the mean systemic pressure.

Any strategy that decreases the mean systemic pressure decreases the congested state by reducing systemic venous return and pulmonary venous pressure; stroke volume and cardiac output do not change unless the operating point for the ventricle shifts from the plateau portion to the ascending portion of its pressure stroke volume curve at which point stroke volume begins to decrease [5].

THE IMPACT OF RESPIRATION ON LEFT VENTRICULAR AFTERLOAD

Changes in respiration impact cardiovascular function by altering intrathoracic pressure and therefore the Ptm of the thoracic systemic arterial vessels relative to the extrathoracic arterial vessels [6]. Because the pulmonary circulation is contained entirely within the chest changes in intrathoracic pressure do not create a pressure gradient and therefore do not impact right ventricular afterload. With exaggerated negative pressure breathing, as occurs with pulmonary edema for example, intrathoracic pressure falls dramatically, increasing the Ptm for the thoracic arterial vessels. As a result the volume of these structures increase, the pressure within falls creating a pressure gradient between thoracic and extrathoracic arterial vessels. With positive pressure ventilation the opposite occurs. The Ptm for the thoracic arterial vessels decreases, the volume within decreases, and as a result the pressure within rises, creating a waterfall-like effect between thoracic and extrathoracic arterial structures.

This same phenomenon may be demonstrated by assessing the impact of changes in the left ventricular systolic Ptm with manipulation of aortic and intrathoracic pressures. Take for example a patient with systolic heart failure and cardiogenic pulmonary edema who is tachypneic, labored and agitated. For these reasons, the systolic blood pressure has risen from 90 to 110 mmHg. Meanwhile intrathoracic pressure during inspiration decreases to -30 mmHg (intrathoracic pressure during normal inspiration ranges from -5 to -10 mmHg) due to a decrease in lung compliance. As a result of all of these factors, the Ptm has risen from 95 (90 - -5) during quiet breathing to 140 during exaggerated negative pressure breathing (110 - -30) for a nearly 50% increase in afterload for a ventricle that is sensitive to changes in afterload. With the implementation of continuous positive airway pressure of 5 mmHg the Ptm decreases substantially from 140 to 105 mmHg (110 - +5). With improved oxygenation and respiratory mechanics sympathetic discharge is partially withdrawn causing the systolic blood pressure to return to baseline levels and the Ptm to fall even further to 85 (90 - +5).

COMPETITION FOR A LIMITED CARDIAC OUTPUT

Another important so-called cardiopulmonary interaction that is present in patients with heart failure occurs when there is a competition amongst viscera for a limited cardiac output. This is exemplified in some patients with chronic heart failure who demonstrate a marked increase in the cerebral oxygen extraction ratio at rest, indicative of limited cerebral blood flow. The competition becomes more remarkable as the load imposed on the respiratory muscles increases, as with cardiogenic pulmonary edema, which necessitates a compensatory increase in respiratory muscle perfusion to maintain respiratory function.

Under normal conditions, the diaphragm consumes less than 3% of global oxygen consumption and receives less than 5% of cardiac output. However, when the respiratory load is elevated diaphragmatic metabolic demand increases and respiratory muscle oxygen consumption may increase to values over 50% of the total oxygen consumption [7]. To meet these demands either cardiac output must increase or if cardiac output is limited blood flow must be redistributed to the respiratory pump from other vital organs to meet the increase in oxygen demand otherwise respiratory failure ensues [7]. Viires and colleagues used an animal of cardiogenic shock and demonstrated a significant increase in respiratory muscle perfusion in spontaneously breathing animals compared to those animals receiving mechanical ventilation [8]. With unloading of the respiratory muscles with mechanical ventilation blood flow to other vital organs was significantly greater, including the brain [8]. It is clear from several lines of investigation that cerebral perfusion does not occur at the expense of other organs but rather the brain is in competition for blood flow with other viscera when cardiac output is limited. Further, as described above, the use of positive pressure ventilation eliminates exaggerated negative pressure breathing and in doing so markedly reduces left ventricular afterload substantially improving stroke volume and cardiac output.

SYSTOLIC HEART FAILURE

In patients with systolic heart failure ventricular operating volumes and filling pressures are elevated throughout the cardiac cycle, increasing the diastolic and systolic load and metabolic demand of the myocardium. Positive pressure ventilation limits systemic venous return and ventricular preload while reducing afterload, increasing stroke volume and output [9, 10]. And, as described above, unloading of the respiratory pump allows for a redistribution of a limited cardiac output to other vital organs, including the myocardium. The net effect of all these changes is a marked improvement in the oxygen supply and demand relationship on a global scale as well for the myocardium [11]. The benefits of mechanically unloading the myocardium are in sharp contrast to the impact of inotropic agents on global and myocardial energetics.

Several clinical studies have demonstrated the profoundly beneficial impact of invasive and non-invasive continuous positive airway pressure and positive pressure ventilation on acute and chronic cardiovascular function. Meta-analyses of adults with decompensated heart failure and car-

diogenic pulmonary edema have found that non-invasive continuous airway pressure and non-invasive positive pressure ventilation significantly decrease the need for intubation and mortality [12, 13].

The benefits of continuous positive airway pressure and positive pressure ventilation have also been demonstrated in adults with chronic heart failure. Haruki and colleagues evaluated the impact of chronic non-invasive positive pressure ventilation on ventricular function in adults with chronic heart failure [14]. Patients agreed to therapy for at least four hours per day. Chronic positive pressure ventilation significantly reduced left ventricular and left atrial volumes, mitral regurgitation and significantly improved left ventricular systolic function. Multivariate regression analysis showed that chronic positive airway pressure ventilation was an independent predictor for left ventricular remodeling.

Sleep disordered breathing is prevalent in chronic heart failure and adversely impacts outcomes. Obstructive breathing leads to exaggerated negative pressure ventilation, which as discussed above increases systemic venous return and left ventricular filling as well as left ventricular afterload. This leads to an increase in myocardial oxygen demand at a time when cardiac output is falling from a depressed baseline. The presence of central apnea and decreases in oxygen content further compromise the myocardial oxygen supply demand relationship. A poignant example of the adverse impact of sleep disordered breathing on cardiovascular function was provided by Kuniyoshi and colleagues who found that the nocturnal onset of myocardial infarction was significantly associated with the presence of sleep disordered breathing [15]. Several studies have demonstrated that not only does sleep disordered breathing contribute to the evolution of heart failure but that intervention with non-invasive continuous positive airway pressure and positive pressure ventilation reverses ventricular remodeling and leads to improved cardiac function [16, 17].

CONCLUSION

The interaction between the cardiovascular and respiratory systems plays an important role in the evolution and treatment of acute and chronic heart failure. A thorough understanding of these interactions is essential for optimizing the care of these patients, impacting both the acute and chronic phases of this illness.

LIST OF ABBREVIATIONS

P_{tm} = transmural pressure
mm Hg = pressure in millimeters of mercury

CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.

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