Original articles

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CLINICAL APPLICATIONS OF CARDIOPULMONARY INTERACTIONS

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The hemodynamic consequences of both spontaneous and positive-pressure ventilation may be profound and may have opposite effects on cardiovascular stability in differing patient populations. Thus, no firm rules apply as to the specific response that will be seen in all patients and under all conditions. Some generalities, however, are probably reasonable. In patients with markedly increased work of breathing, hypervolemia, or impaired LV pump function, the institution of mechanical ventilatory support can be lifesaving because of its ability to support the cardiovascular system, independent of any beneficial effects that mechanical ventilation may have on gas exchange. In patients with decreased pulmonary elastic recoil, increased pulmonary vascular resistance, hypovolemia, or airflow obstruction, the institution of mechanical ventilatory support may induce cardiovascular instability, which, if not corrected, can lead to total cardiovascular collapse. Similarly, withdrawal of ventilatory support invariably increases intrathoracic blood volume and LV afterload and can be thought of as a type of cardiovascular stress test. Patients who pass this test easily can usually be successfully weaned from mechanical ventilatory support, whereas those who fail often are not ready to be weaned. Some patients who fail weaning trials do so because of the cardiovascular effects of spontaneous ventilation, not because the work of breathing is too great. Identification of such patients early on may improve their treatment by directing supportive therapies toward cardiovascular rather than ventilatory endpoints. However, in many situations, it will be difficult to single out a primary process determining cardiovascular instability, because multiple factors are compounded to create the observed situation and the patient's response to initiation of ventilatory support or weaning. Thus, the clinician is left with a series of therapeutic options, which if depending on the patient's response, suggest specific origins of the ventilatory and cardiovascular dysfunction. In that regard, the initiation and withdrawal of ventilatory support can be seen as a ventilatory probe into the determinants of cardiovascular homeostasis in the ventilator-dependent patient.

K e y   w o r d s: *afterload, hemodynamics, interdependence, preload, ventricular function*

INTRODUCTION

Although, positive-pressure ventilation can be life saving in the setting of acute respiratory failure, it also results in complex cardiovascular interactions that may alter blood flow in unexpected ways, thus potentially modulating O_2 delivery to the body independent of its effects on arterial O_2 content. The primary function of the cardiovascular-respiratory system is to deliver adequate amounts of O_2 to meet the metabolic demands of the body. Oxygen delivery is equal to the product of arterial O_2 content and cardiac output. Thus, if either decreases far enough, O_2 delivery to the tissues will become compromised. The treatment of critically ill patients requires an understanding of cardiopulmonary interactions associated with both mechanical ventilation and the use of positive end-expiratory pressure (PEEP).

Clinically, hemodynamic instability or a change associated with artificial ventilation usually occurs when ventilatory support is either added or withdrawn, rather than when ventilatory support is constant. This observation seems obvious since when things are stable there is little cause for change. However, it is with initiation of mechanical ventilatory support and its withdrawal that most of the attention is placed on the critically ill patient. The following discussion will attempt to clarify how cardiovascular function is altered by starting or stopping various ventilatory maneuvers.

Clinically relevant heart-lung interactions can be conveniently grouped into four basic concepts which can be considered separately, though they often coexist in the same clinical situation. These concepts are: (a) ventilation is exercise, requiring increased organ blood flow, oxygen consumption and CO_2 production; (b) inspiration increases lung volume above end-expiratory values increasing transpulmonary pressure and compressing the heart in the cardiac fossa; (c) spontaneous inspiration decreases pleural pressure, the pressure surrounding the heart; and (d) positive-pressure ventilation increases pleural pressure.

VENTILATION AS EXERCISE

Obviously, spontaneous ventilatory efforts require contraction of the diaphragm and intercostal muscles. Maximal blood flow to these muscles is potentially unlimited if cardiac output increases enough, making limitation of muscle performance primarily determined by muscle stamina and actual maximal cardiac output (1). Thus, under conditions of normal cardiovascular function blood flow is not the limiting factor determining maximal ventilatory effort. Although ventilation normally requires less than 5% of total O_2 delivery to meet its demand (1), in lung disease states where the work of breathing is increased, such as pulmonary edema or bronchospasm, the requirements for O_2 may increase to 25% or 30% of total O_2 delivery (1-3). Similarly, if cardiac

output is limited, either by hypovolemia, tamponade or heart failure, then blood flow to other organs and to the respiratory muscles may be compromised, inducing both tissue hypoperfusion and lactic acidosis. The institution of mechanical ventilation for ventilatory and hypoxemic respiratory failure will reduce work of breathing decreasing global metabolic demand on the stressed cardiovascular system. Intubation and mechanical ventilation, when adjusted to the metabolic demands of the patient, may dramatically decrease the work of breathing, resulting in increased O_2 delivery to other vital organs and decreased serum lactic acid levels. Under conditions in which fixed right-to-left shunts exist, the obligatory increase in venous O_2 saturation will result in an increase in the partial pressure of O_2 in arterial blood, despite no change in the ratio of shunt blood flow to cardiac output.

Inspiration increases lung volume refreshing alveolar gas with the tidal breath. Except during conditions of high frequency ventilation all forms of breathing require lung volume to increase above a resting end-expiratory value. During both spontaneous and positive-pressure ventilation lung volume increases; however, the change in pleural pressure during inspiration between the two forms of ventilation is in opposite directions. Pleural pressure (Ppl) decreases with spontaneous inspiration and increases with positive-pressure inspiration. Thus, changes in Ppl represent the primary difference between spontaneous and positive-pressure ventilation (4,5). However, to better understand the complex interactions between ventilation and cardiovascular function, we will first consider the effects of changes in lung volume on cardiovascular performance and then the effects of changes in Ppl as summarized in *Fig. 1*.

Fig. 1. This diagram schematically highlights the salient factors determining heart-lung interactions. (1) Changes in Ppl by modulating right atrial pressure alter the pressure gradient for venous return; (2) the common interventricular septum and limiting pericardium directly affect perceived biventricular diastolic compliance by the effect that one ventricle's end-diastolic volume exerts on the other; (3) changing lung volume directly affects resistance to pulmonary blood flow and alters systolic pulmonary arterial pressure; (4) changes in Ppl, by altering transmural aortic pressure, affect the LV systolic pressure load. (Reproduced with permission from **Cardiopulmonary Critical Care**, Dantzker, ed., 2nd edition, W.B. Saunders Co., 1991)
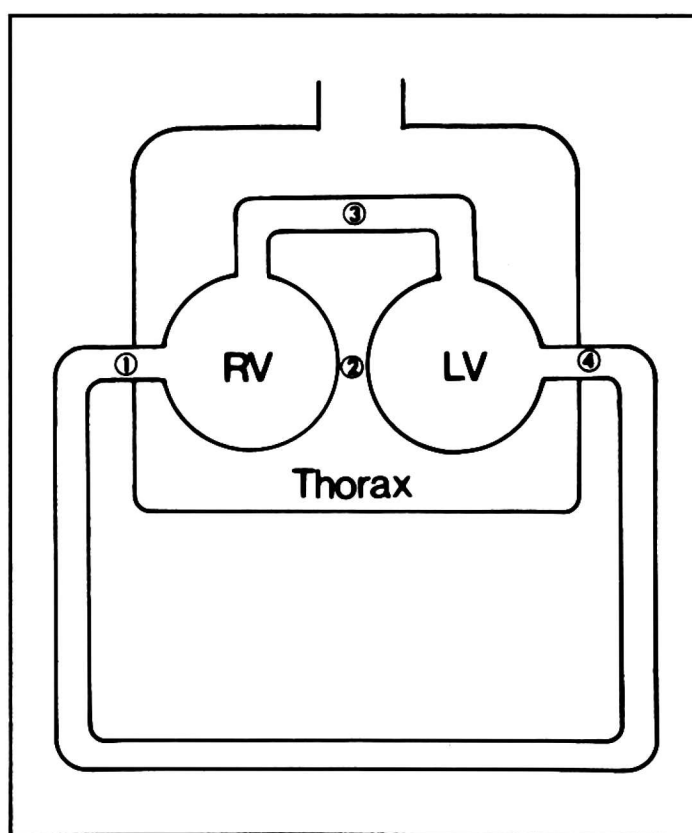
HEMODYNAMIC EFFECTS OF CHANGES IN LUNG VOLUME

Lung inflation alters autonomic tone and pulmonary vascular resistance and, at high lung volumes, interacts mechanically with the heart in the cardiac fossa to limit absolute cardiac volumes. Each of these processes is important in determining the hemodynamic response to mechanical ventilation.

Autonomic tone

The lungs are innervated with autonomic fibers that mediate several homeostatic processes. For example, lung inflation decreases heart rate *via* vagally-mediated reflex arcs (6, 7). Reflex arterial vasodilation can also occur with lung inflation (6, 8—12). This inflation-vasodilation response appears to be mediated by afferent vagal fibers and is abolished by selective vagotomy. Blocking sympathetic afferent fibers also blocks this reflex (10, 13), presumably by withdrawing central sympathetic tone. However, this inflation-vasodilation response does not appear to result in significant cardiovascular depression, except during high-frequency ventilation (6, 10). Although humoral factors, including compounds blocked by cyclooxygenase inhibition (14), released from pulmonary endothelial cells during lung inflation may also induce this depressor response (15—17), these interactions appear not to grossly alter cardiovascular status.

Pulmonary vascular resistance

The major determinants of the hemodynamic response to increases in lung volume are mechanical in nature (4, 18—22). Lung inflation, independent of changes in Ppl, primarily affects cardiac function and cardiac output because of the changes in right ventricular (RV) afterload and both RV and left ventricular (LV) preload (23).

Right ventricular afterload can be estimated as maximal RV systolic wall stress (24), which, by the LaPlace equation, is maximum at end-diastolic volume (maximal volume) and systolic RV pressure (maximal pressure) which occurs immediately prior to opening of the pulmonic value (25). Because both the RV and pulmonary arteries are within the thorax whose pressure, Ppl, may vary but will not alter the pressure gradients between intrathoracic compartments, systolic RV pressure can be defined as pulmonary arterial pressure (Ppa) minus Ppl (transmural Ppa). Increases in transmural Ppa increase RV afterload, thus impeding RV emptying (26). If the RV does not empty as much as before, then RV stroke volume will decrease (27), resulting in an increase in RV end-systolic volume (24). This will cause both an immediate increase in RV end-diastolic volume, and, if right atrial pressure (Pra) increases, a decrease in systemic venous return (28), because Pra is the back pressure for

systemic blood flow back to the heart from the periphery. For RV stroke volume, and thus cardiac output, to remain constant, RV end-diastolic volume must increase further (25, 29). This can be accomplished by increasing either the circulating blood volume (fluid retention or intravascular volume infusion) or the peripheral vasomotor tone (30). Transmural Ppa may increase during ventilation because of an increase in either LV filling pressure, as in acute LV dysfunction, or pulmonary vascular resistance. If transmural Ppa increases during mechanical ventilation, it is usually caused by increases in pulmonary vascular resistance, because mechanical ventilation does not impair LV contractile function.

Mechanical ventilation can modify pulmonary vascular resistance by any of several mechanisms. It may reduce pulmonary vascular resistance by increasing alveolar O_2 tension (P_AO_2) (31—34), reexpanding collapsed alveolar units (35-39), reversing acute respiratory acidosis (34), or decreasing the central sympathetic tone (40, 41). Mechanical ventilation can also increase pulmonary vascular resistance by overdistending lung units. If regional P_AO_2 decreases below 60 mm Hg, local pulmonary vasomotor tone will increase, reducing local blood flow. This process is called hypoxic pulmonary vasoconstriction is mediated in part by local synthesis and release of nitric oxide by pulmonary vascular endothelium. Hypoxic pulmonary vasoconstriction is an important process to optimize matching of ventilation to perfusion, when regional impairments in ventilation exist. However, if alveolar hypoxia occurs throughout the lungs, then overall pulmonary vasomotor tone increases, increasing pulmonary vascular resistance and impeding RV ejection (24). At low lung volumes, alveoli spontaneously collapse as a result of loss of interstitial traction. Acute hypoxemic respiratory failure is often associated with both a decreased functional residual capacity (FRC) and alveolar instability (36, 42). Therefore, pulmonary vascular resistance is often increased in these patients owing to alveolar collapse and the resultant hypoxic pulmonary vasoconstriction.

The primary effect of PEEP is to increase end-expiratory lung volume by increasing end-expiratory transpulmonary pressure. Thus, with acute hypoxemic respiratory failure, if positive-pressure inspiration and PEEP open collapsed lung units and replenish the alveolar gas with inspired O_2, then hypoxic pulmonary vasoconstriction will be reduced, pulmonary vascular resistance will decrease, and RV ejection will improve. Presumably this beneficial effect of PEEP on pulmonary vascular resistance would be greatest in the neonate whose ability to respond to hypoxia is accentuated.

Changes in lung volume also affect pulmonary vascular resistance, independent of the effect of lung volume on alveolar stability (35-38). The pulmonary circulation can be considered to consist of two populations of vessels that depend on the pressure that surrounds them (37). The small pulmonary arterioles, venules, and capillaries that reside in the alveolar septa

sense alveolar pressure as their surrounding pressure and can be referred to as alveolar vessels. The remaining large pulmonary arteries, veins, and their tributaries sense interstitial pressure as their surrounding pressure and can be called extraalveolar vessels. Interstitial pressure is usually similar to Ppl. Extraalveolar vessels, like airways, are acted upon by the interstitial forces of the lung that keep them patent (35, 43, 44). As lung volume decreases, the radial interstitial traction decreases, and extraalveolar vessels decrease their cross-sectional diameter, thereby increasing pulmonary vascular resistance (32, 35). Thus, at small lung volumes pulmonary vascular resistance is increased owing to the combined effect of hypoxic pulmonary vasoconstriction and extraalveolar vessel collapse.

Increases in lung volume above FRC also increase pulmonary vascular resistance. The increased resistance occurs in the alveolar vessels (32, 44). The cause of this increase in alveolar vessel resistance is two fold. First, transpulmonary pressure (alveolar pressure minus Ppl) increases as lung volume increases. Because the heart and extraalveolar vessels sense Ppl as their surrounding pressure, whereas the alveolar vessels sense alveolar pressure as their surrounding pressure, a transpulmonary extralumenal pressure gradient exists between the extraalveolar and alveolar vessels. The intralumenal pressure in the pulmonary arteries is generated by RV ejection relative to Ppl. Thus, if transpulmonary pressure increases enough to exceed intralumenal pressure, the pulmonary vasculature will collapse as this increased pressure passes from extraalveolar to alveolar loci. As the vasculature is compressed, its cross-sectional area is reduced, increasing pulmonary vascular resistance. Similarly, increasing lung volume by stretching and distending the alveolar septa may also compress alveolar capillaries. Thus, hyperinflation must increase pulmonary vascular resistance. If the cross-sectional area of the pulmonary capillaries is already reduced, as occurs in the setting of severe COPD, then the additional hyperinflation can create significant pulmonary hypertension and may precipitate acute RV failure (acute cor pulmonale) (45, 46).

Ventricular interdependence

Since the two ventricles pump in series, LV preload can also be indirectly altered by changes RV end-diastolic volume. The RV and LV share a common intraventricular septum; if RV end-diastolic volume increases, the septum shifts into the LV, thereby decreasing LV diastolic compliance (47-49). Hyperinflation may induce RV dilation, and if inspiration-associated RV dilation does occur, it can be partially mitigated by volume resuscitation (50) or vasopressor infusion (51). Accordingly, in the fluid-resuscitated patient, RV volumes can and will be increased during pulmonary hypertension (29) and thus decrease with LV diastolic compliance.

Mechanical heart-lung interactions

If lung volumes increase greatly, then the heart will be compressed between the two expanding lungs (52), which increases juxtacardiac Ppl more than lateral chest wall Ppl (53). This decrease in "apparent" LV diastolic compliance was previously misinterpreted as impaired LV contractility, because LV stroke work for a given LV end-diastolic pressure or pulmonary artery occlusion pressure is decreased during hyperinflation (54,55). However, when patients are fluid resuscitated to return LV end-diastolic volume to its original level, then both LV stroke work and cardiac output also returned to their original levels (20,50) despite the continued application of PEEP.

HEMODYNAMIC EFFECTS OF CHANGES IN INTRATHORACIC PRESSURE

The heart within the thorax is a pressure chamber within a pressure chamber. Therefore, changes in Ppl will affect the pressure gradients for both systemic venous return to the RV and systemic outflow from the LV, independent of the heart itself. Increases in Ppl, by both increasing Pra and decreasing transmural LV systolic pressure, will reduce these pressure gradients, thereby decreasing intrathoracic blood volume. However, decreases in Ppl, using the same argument, will augment venous return and impede LV ejection, thus increasing intrathoracic blood volume.

Although the hemodynamic effects of Ppl are important, it is difficult to accurately measure Ppl. Many clinicians associate changes in airway pressure (Paw) with changes in Ppl, assuming that Paw approximates alveolar pressure and is therefore transmitted *via* alveolar pressure to the pleural surface. However, the relation between Paw and Ppl during ventilation is complex and is determined by both pulmonary mechanics, the method of ventilation, and the presence or absence of spontaneous ventilatory efforts. If pulmonary compliance is reduced or airway resistance is increased, then the percentage increase in mean or peak Paw transferred during positive-pressure ventilation to the pleural space will be reduced. Thus, Ppl will increase less for the same increase in Paw when the lungs are stiff. Conversely, during spontaneous ventilation, Ppl must decrease more in patients with stiff lungs, owing to the need for a greater transpulmonary pressure to generate a given tidal volume.

Because acute lung injury is usually nonhomogeneous, with aerated areas of the lung displaying normal specific compliance, large increases in Paw often seen during mechanical ventilation in such patients should overdistend these aerated lung units (56). Despite this nonhomogeneous alveolar distention, if tidal volume is kept constant, then Ppl will increase equally, independent of the mechanical properties of the lung (57, 58). Thus, under conditions in which

tidal volume is kept constant, changes in peak and mean Paw will reflect changes in the mechanical properties of the lungs and patient cooperation, but will not reflect changes in Ppl, nor should these changes alter global dynamics of the cardiovascular system. Unfortunately, as was recently demonstrated with progressive levels of PEEP, one can not predict the percentage of Paw which will be transmitted to the pleural surface in post-operative patients (59). Accordingly, assuming some constant fraction of Paw transmission to the pleural surface as a means of calculating the effect of increasing Paw on Ppl is inaccurate and potentially dangerous to patient management.

Systemic venous return

Blood flows back to the heart from the periphery through low pressure-low resistance conduits. Systemic venous flow from the venous reservoirs into the right atrium can be defined by the ratio of the pressure gradient between those systemic venous reservoirs and the right atrium and the summed resistance to venous return (60). The pressure in the venous reservoirs, called mean systemic pressure, is a function of blood volume, peripheral vasomotor tone, and the distribution of blood within the vasculature (61). Mean systemic pressure does not change rapidly during the ventilatory cycle, whereas Pra does owing to concomitant changes in Ppl. Accordingly, variations in Pra represent the major factor determining the fluctuation in pressure gradient for systemic venous return during ventilation (28). With increases in Ppl, as seen with positive-pressure ventilation or hyperinflation during spontaneous ventilation, Pra relative to atmosphere increases. This decreases the pressure gradient for systemic venous return, decelerating venous blood flow (27) and decreasing RV filling and, consequently, RV stroke volume (27, 28, 62—69). During normal spontaneous inspiration, Ppl decreases, decreasing Pra, accelerating venous blood flow and increasing RV filling and RV stroke volume (5, 27, 51, 64—67, 70).

Recent studies in animal models have suggested that the decrease in venous return during positive-pressure ventilation may be less than one would predict based on the above scenario. PEEP increases intraabdominal pressure by causing the diaphragm to descend, thereby increasing the pressure surrounding the intraabdominal vasculature. Because a large proportion of venous blood is in the abdomen, the net effect of PEEP is to increase mean systemic pressure, as well as increasing Pra (71—73). Accordingly, the pressure gradient for venous return may not be reduced by PEEP, especially in patients with hypervolemia. Furthermore, although PEEP decreased blood flow to the liver in proportion to the induced decrease cardiac output in normovolemic dogs, the liver's ability to clear hepatocytic-specific compounds, such as indocyanine green, was unaltered (74). Finally, when cardiac output was restored to pre-PEEP levels by fluid resuscitation while PEEP was maintained, liver

clearance mechanisms increased above pre-PEEP levels. These data are consistent with a PEEP-induced alteration in intrahepatic blood flow distribution. Thus, the effects of ventilation on venous return may be less than we originally postulated but more complicated than we imagined.

Right ventricular filling

The physiology of RV filling pressure is far from being understood to the level to which we understand LV filling. For example, RV filling pressure is insignificantly altered by acute volume loading. Although Pra increases with volume loading, pericardial pressure increases equally, such that RV filling pressure remains unchanged (75). This suggests that under normal conditions, RV diastolic compliance is greater than pericardial compliance. Thus, with RV filling, right heart sarcomere length probably remains constant. Presumably, conformational changes in the RV more than wall stretch are responsible for RV enlargement. In support of this hypothesis, Pinsky *et al.* (76) demonstrated that when RV end-diastolic volume was reduced in post-operative surgical patients by the aplication of PEEP, both Pra and pericardial pressure increased but RV filling pressure remained constant. Accordingly, changes in Pra do not follow changes in RV end-diastolic volume (49, 73). When cardiac contractility is reduced and intravascular volume is expanded, RV end-diastolic volume can become very large. Under these conditions, RV filling pressure increases as a result of either decreased diastolic compliance, increased pericardial compliance, increased end-diastolic volume, or a combination of all three. The relation between RV filling pressure and volume in isolated hearts is curvilinear, such that as RV end-diastolic volume increased above a threshold level, RV filling pressure increased greatly (75). Furthermore, in dogs with acute ventricular failure, volume loading increases pericardial pressure more than Ppl, consistent with pericardial restraint (77). However, with the application of PEEP in this setting, Ppl selectively increased until it equals pericardial pressure, then both increased equally as PEEP was progressively increase. We (59) subsequently demonstrated similar phenomena in post-operative patients. Thus, PEEP, and by extension, lung expansion, compresses the heart within the cardiac fossa in a fashion analogous to pericardial tamponade, but in this setting it is the expanding lungs that increases PPL and not pericardial restraint, which limits ventricular filling.

The conclusion that, under normal conditions, RV filling occurs at or below RV unstressed volume has important clinical implications. Since under normal conditions, cardiac output is primarily dependent on venous return (61), the small changes in heart rate and LV afterload induced by ventilation are insignificant (10, 69, 70). In this environment, cardiac output would be maximized if Pra was kept as low as possible, so as to minimize the back

pressure to venous blood flow (60, 65). A RV functioning below its unstressed volume could accommodate changes in venous blood flow without decreasing the pressure gradient for venous return. For this mechanism to operate efficiently, however, RV output in the steady state must equal venous return, so that sustained increases in venous blood flow do not overdistend the RV, increasing Pra. Under normal conditions, the RV ejects a stroke volume proportional to its instantaneous venous blood flow, independent of either the amount of that flow or the phase of the respiratory cycle (28). This accommodation occurs primarily because the pulmonary circulation can accept large changes in blood flow without undergoing large changes in pressure (27). If RV diastolic compliance decreased or if Pra increased independent of changes in RV end-diastolic volume, then cardiac output would decrease. Examples of the latter include tamponade and positive-pressure ventilation. Thus, positive-pressure ventilation, by dissociating Pra from RV filling pressure, may prevent the normal adaptive processes operative in RV hemodynamics seen with spontaneous ventilation. Furthermore, even if one restores "normal" interactions by allowing spontaneous ventilatory efforts to occur cardiac output will only increase if the RV can transduce the associated increase in venous return to forward blood flow. Thus, failure to improve forward blood flow in a hemodynamically unstable patient, when transiting from positive-pressure to spontaneous ventilation, may potentially reflect isolated RV failure.

The primary effect of changes in lung volume and Ppl on cardiovascular function, therefore, is to alter RV preload via altering venous blood flow. This detrimental hemodynamic effect of increasing Ppl on cardiac output can be minimized by keeping mean Ppl as low as possible. Therefore, increasing the mean inspiratory flow rate so as to increase expiratory time, decreasing tidal volume, and avoiding PEEP all minimize this decrease in systemic venous return to the RV (2, 28, 64-68, 78, 79). Regrettably, most ventilatory strategies used to minimize lung injury and recruit collapsed alveolar units in subjects with acute lung injury use the ventilatory approaches most associated with impairment in hemodynamic stability. To compensate for this, intravascular fluid infusion or increased autonomic tone, by increasing upstream venous pressure (60), will also maintain venous blood flow and cardiac output, despite the addition of increased Ppl (51).

Spontaneous inspiration decreases both Ppl and Pra and accelerates blood flow into the RV (5, 18, 65—67). However, this augmentation of venous return is limited. As Pra decreases below atmospheric pressure, the systemic veins collapse as they enter the thorax, limiting flow (60). This "flow-limitation" is useful, because Ppl can decrease greatly with obstructive inspiratory efforts (11). If the increase in venous blood flow were unlimited, the RV would easily be overloaded with volume and may fail.

Left ventricular preload and ventricular interdependence

Any change in venous return must eventually result in a change in LV preload. Sustained increases in Ppl, as occur during a Valsalva maneuver, initially reduce RV filling but do not alter LV preload (80). However, after two to three beats, the decreased RV output is reflected by a decrease in both LV preload and output (52, 81). This interaction has also been used to explain both the decrease in LV output seen during positive-pressure ventilation and its phase relation to the ventilatory cycle (2, 21, 22, 50, 54, 55, 69, 78, 82—86). Because RV volumes are reduced by increases in Ppl, ventricular interdependence plays a decreasing role in the subsequent hemodynamic responses (47, 87, 88). In intact dog models minimal LV deformity occurs with the application of 15 cm H_2O PEEP (84, 85, 89). Similarly, during PEEP therapy, there is no change in LV compliance when pericardial pressure is considered the surrounding pressure of the LV (50). In humans PEEP does result in some degree of right-to-left intraventricular septal shift, but this shift was small (20, 21). Although positive-pressure ventilation can markedly alter both end-diastolic and end-systolic volumes in humans, it does not change the LV pressure-volume relation (90).

Right ventricular end-diastolic volume increases during spontaneous inspiration, and this increase results in a transient shift of the intraventricular septum from its neutral position into the LV (48). As the RV dilates, LV diastolic compliance is reduced (47, 87, 88), reducing LV end-diastolic volume. This mechanism probably causes the spontaneous ventilation-associated change in arterial pulse pressure that is characteristic of pulsus paradoxus (5). Taken together, these data suggest that the lungs, by compressing the heart within the cardiac fossa, effectively limit LV filling during positive-pressure ventilation, whereas septal shift impedes LV filling only transiently, and then primarily filling during spontaneous inspiration. Because spontaneous inspiration can occur during positive-pressure ventilation, and is the method of ventilation used during continuous positive airway pressure therapy, the hemodynamic effects of spontaneous ventilation can be seen in the mechanically ventilated patient.

Left ventricular afterload

Left ventricular afterload or systolic wall tension, like RV afterload, is proportional to the product of transmural LV pressure and the radius of curvature of the LV. Maximal LV afterload normally occurs at the end of isometric contraction immediately prior to opening of the aortic valve. Arterial pressure can be used to approximate LV intralumenal pressure. Accordingly, if arterial pressure were to remain constant as Ppl increased, then LV wall

tension would decrease as well because transmural arterial pressure (arterial pressure minus Ppl) would decrease. Similarly, if transmural arterial pressure were to remain constant as Ppl increased but LV end-diastolic volume decreased owing to the decrease in systemic venous return usually seen with increases in Ppl, then LV wall tension would also decrease because LV volumes would be less. Thus, increasing Ppl will decrease LV afterload. As a reciprocal argument, decreases in Ppl with a constant arterial pressure result in an increase in LV transmural pressure and, consequently, an increase in LV wall tension (afterload) impeding LV ejection (80). Thus, decreases in Ppl increase LV afterload.

Rapid changes in Ppl will directly alter arterial pressure without altering arterial pressure relative to Ppl (transmural arterial pressure) (80). Rapidly increasing Ppl, as may occur with coughing, increases arterial pressure to an amount equal to the increase in Ppl without changing aortic blood flow (52). If the increase in Ppl is sustained then the Ppl-induced decrease in systemic venous return will eventually decrease LV output, thus decreasing arterial pressure (80). Changes in Ppl that result in altered cardiac output must eventually alter peripheral vasomotor tone owing to baroreceptor mechanisms (10). Baroreceptor reflexes tend to keep systemic pressure (arterial pressure) constant (83).

The afterload-reducing augmentation of LV ejection by increasing Ppl is limited because increasing Ppl, by reducing LV ejection pressure, can only decrease LV end-systolic volume. Normally, LV end-systolic volume is already small and cannot decrease much more except in conditions associated with cardiac dilation. However, the decrease in venous return associated with the increase in Ppl can totally arrest venous blood flow. Mechanistically speaking, not only do increases in Ppl unload the LV, but stopping decreases in Ppl will also reduce LV afterload.

Although increasing Ppl may not augment flow much, preventing negative swings in Ppl can markedly improve cardiac function. This is clinically relevant for many reasons. First, many pulmonary disease states are associated with exaggerated decreases in Ppl during inspiration. In restrictive lung disease states, such as interstitial fibrosis or acute hypoxemic respiratory failure, Ppl must decrease greatly to generate a large enough transpulmonary pressure to ventilate the alveoli. Similarly, in obstructive diseases, such as upper airway obstruction or asthma, large decreases in Ppl occur owing to increased resistance to inspiratory airflow (3, 4, 11). Second, exaggerated decreases in Ppl require increased respiratory efforts that increase the work of breathing, taxing a potentially stressed circulation. Finally, the exaggerated decreases in Ppl can only increase venous blood flow so much before venous collapse limits blood flow. This flow-limiting Ppl is different in different states but occurs in all patients below a pressure of 10 cm H_2O (60). Thus, further decreases in Ppl will further increase only LV afterload. Accordingly, abolishing these decreases

in Ppl should result in a disproportional reduction in LV afterload more so than venous return. By endotracheally intubating and ventilating such patients, marked decreases in Ppl can be abolished without an obligatory proportional increase in Ppl. Left ventricular performance often improves after the institution of positive-pressure ventilation in patients with heart failure and lung disease (51, 82, 91—93). Also, weaning patients from positive-pressure ventilation, by allowing the return of decreases in Ppl, may precipitate acute LV failure and pulmonary edema in patients with borderline LV function (94, 95). Weaning can be seen as a form of cardiac stress testing, because LV loading invariably occurs in the transition from positive-pressure to spontaneous ventilation. Finally, the institution of PEEP in patients with heart failure may further augment LV output by reducing LV afterload, despite the obligatory decrease in LV preload (51, 82, 91—93, 96).

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