EFFECT OF MECHANICAL VENTILATION ON HEART–LUNG INTERACTIONS

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CLINICAL RELEVANCE

The heart and lungs are intimately coupled by their anatomic proximity within the thorax and, more importantly, by their responsibility to deliver the O₂ requirements of individual cells and organs while excreting the CO₂ by-product of metabolism. During critical illness, if these two organ systems fail, either alone or in combination, the end result is an inadequate O₂ delivery to the body with inevitable tissue ischemia, progressive organ dysfunction, and if untreated, death. Thus, restoration and maintenance of normalized cardiopulmonary function is an essential and primary goal in the management of critically ill patients. Heart failure can impair gas exchange by inducing pulmonary edema and limiting blood flow to the respiratory muscles. Ventilation can alter cardiovascular function by altering lung volume, and intrathoracic pressure (ITP), and by increasing metabolic demands. These processes are discussed from the perspective of the impact that ventilation has on the cardiovascular system.

Acute Respiratory Distress Syndrome and Acute Lung Injury
Congestive Heart Failure
Intraoperative State

STEPS TO LIMIT OR OVERCOME DETRIMENTAL HEART–LUNG INTERACTIONS

Minimize Work of Breathing
Minimize Negative Swings in Intrathoracic Pressure
Prevent Hyperinflation
Fluid Resuscitation during Initiation of Positive-Pressure Ventilation
Prevent Volume Overload during Weaning
Augment Cardiac Contractility

IMPORTANT UNKNOWNS

THE FUTURE

SUMMARY AND CONCLUSIONS

The ventilatory apparatus and the cardiovascular system have profound effects on each other. Acute hypoxia impairs cardiac contractility and vascular smooth muscle tone, promoting cardiovascular collapse. Hypercarbia causes vasodilation and increases pulmonary vascular resistance. Hyperinflation increases pulmonary vascular resistance, which impedes right-ventricular (RV) ejection and also compresses the heart inside the cardiac fossa in a fashion analogous to tamponade. Lung collapse also increases pulmonary vascular resistance, impeding RV ejection. Acute RV failure, or cor pulmonale, is not only difficult to treat, but it can induce immediate cardiovascular collapse and death.

Ventilator technologies and numerous vasoactive drugs have been developed as means to improve oxygenation of arterial blood. These advances are the subjects of other chapters in this volume. The complex interactions, however,
between the heart, circulation, and lungs often leads to a paradoxical worsening of one organ system function while the function of the other is either maintained or even improved by the use of these technologies and drugs. To minimize these deleterious events, and in the hope of more efficiently and effectively treating critical ill patients with cardiorespiratory failure, a better knowledge and understanding of the integrated behavior of the cardiopulmonary system, during both health and critical illness is essential. Based on this perspective, the health care provider can more appropriately manage this complex and challenging group of patients.

Respiratory function alters cardiovascular function and cardiovascular function alters respiratory function. A useful way to consider the cardiovascular effects of ventilation is to group them by their impact on the determinants of cardiac performance. The determinants of cardiac function can be grouped into four interrelated processes: heart rate, preload, contractility, and afterload. Phasic changes in lung volume and ITP can simultaneously change all four of these hemodynamic determinants for both ventricles. Our current understanding of cardiovascular function also emphasizes both the independence and interdependence of RV and left-ventricular (LV) performance on each other and to external stresses. Complicating these matters further, the direction of interdependence, from right to left or left to right, can be similar or opposite in direction, depending on the baseline cardiovascular state. It is clear, therefore, that a comprehensive understanding of the specific cardiopulmonary interactions and their relative importance in defining a specific cardiovascular state is a nearly impossible goal to achieve in most patients. By understanding the components of this process, however, one can come to a better realization of its determinants, and, to a greater or lesser degree for any individual patient, predict the limits of these interactions and how the patient may respond to stresses imposed by either adding or removing artificial ventilatory support.

PHYSIOLOGY OF HEART–LUNG INTERACTIONS

Both spontaneous and positive-pressure ventilation increase lung volume above an end-expiratory baseline. Many of the hemodynamic effects of all forms of ventilation are similar despite differences in the mode of ventilation. ITP, however, decreases during spontaneous inspiration and increases during positive-pressure ventilation. Thus, the primary reasons for different hemodynamic responses seen during spontaneous and positive-pressure breathing are related to the changes in ITP and the energy necessary to produce those changes.

Effect of Lung Volume

Changing lung volume phasically alters autonomic tone and pulmonary vascular resistance. At very high lung volumes, the expanding lungs compress the heart in the cardiac fossa, limiting absolute cardiac volumes analogous to cardiac tamponade, except that with hyperinflation both pericardial pressure and ITP increase by a similar amount.

AUTONOMIC TONE

Although neurohumoral processes define a few immediate effects of ventilation on the heart, these neurohumoral processes probably play a primary role in all the long-term effects of ventilation on the cardiovascular system. Most of the immediate effects of ventilation of the heart are secondary to changes in autonomic tone. The lungs are richly enervated with somatic and autonomic fibers that originate, traverse through, and end in the thorax. These networks mediate multiple homeostatic processes through the autonomic nervous system altering instantaneous cardiovascular function. The most commonly known of these are the vagally mediated heart rate changes during ventilation. Inflation of the lung to normal tidal volumes (<10 mL/kg) induces vagal-tone withdrawal, accelerating heart rate. This phenomenon is known as respiratory sinus arrhythmia and can be used to document normal autonomic control, especially in patients with diabetes who are at risk for peripheral neuropathy. Inflation to larger tidal volumes (>15 mL/kg), however, decreases heart rate by a combination of both increased vagal tone and sympathetic withdrawal. Sympathetic withdrawal also creates arterial vasodilation. This inflation–vasodilation response can reduce LV contractility in healthy volunteers and in ventilator-dependent patients with the initiation of high-frequency ventilation or hyperinflation. This inflation–vasodilation response is presumed to be the cause of the initial hypotension seen when infants are placed on mechanical ventilation. It appears to be mediated at least partially by afferent vagal fibers, because it is abolished by selective vagotomy. Hexamethonium, guanethidine, and bretylium, however, also block this reflex. These data suggest that lung inflation mediates its reflex cardiovascular effects by modulating central autonomic tone. Interestingly, the almost total lack of measurable hemodynamic effects of unilateral hyperinflation in subjects with normal lungs receiving split-lung ventilation suggests that these autonomic cardiovascular effects require a general increase in lung volume to be realized. This is not a minor point because selective hyperinflation within lung units commonly occurs in patients with acute lung injury (ALI) and chronic obstructive pulmonary disease (COPD). If localized hyperinflation were able to induce cardiovascular impairment, these subjects would be profoundly compromised.

Humoral factors, including compounds blocked by cyclooxygenase inhibition, released from pulmonary endothelial cells during lung inflation may also induce this depressor response within a short (15 seconds) time frame. These interactions, however, do not appear to grossly alter cardiovascular status. Ventilation also alters the more chronic control of intravascular fluid balance via hormonal release. The right atrium functions as the body’s effective circulating blood-volume.
sensor. Circulating levels of a family of natriuretic peptides increase in heart failure states secondary to right-atrial stretch. These hormones promote sodium and water diuresis. The levels of these hormones vary directly with the degree of heart failure. Both positive-pressure ventilation and sustained hyperinflation decrease right-atrial stretch mimicking hypovolemia. During positive-pressure ventilation, plasma norepinephrine and renin increase, whereas atrial natriuretic peptide decreases. This humoral response is the primary reason why ventilator-dependent patients gain weight early in the course of respiratory failure, because protein catabolism is also usually seen. Interestingly, when patients with congestive heart failure (CHF) are given nasal continuous positive airway pressure (CPAP), plasma atrial natriuretic peptide activity decreases in parallel with improvements in blood flow. This finding suggests that some of the observed benefit of CPAP therapy in heart failure is mediated in part through humoral mechanisms, owing to the mechanical effects of CPAP on cardiac function.

**PULMONARY VASCULAR RESISTANCE**

Changing lung volume alters pulmonary vascular resistance. Marked increases in pulmonary vascular resistance, as may occur with hyperinflation, can induce acute cor pulmonale and cardiovascular collapse. The reasons for these changes are multifactorial. They can reflect conflicting cardiovascular processes and almost always reflect both humoral and mechanical interactions.

Lung volume can only increase if its distending pressure increases. Lung-distending pressure, called the **transpulmonary pressure**, equals the pressure difference between alveolar pressure (Palv) and ITP. If lung volume does not change, then transpulmonary pressure does not change. Thus, occluded inspiratory efforts (Mueller maneuver) and expiratory efforts (Valsalva maneuver) cause ITP to vary by an amount equal to Palv, but do not change pulmonary vascular resistance. Although obstructive inspiratory efforts, as occur during obstructive sleep apnea, are usually associated with increased RV afterload, the increased afterload is caused primarily by either increased vasomotor tone (hypoxic pulmonary vasoconstriction) or backward LV failure. By law of Laplace, wall stress equals the product of the radius of curvature of a structure and its transmural pressure. Systolic RV pressure equals transmural pulmonary artery pressure. Increases in transmural pulmonary artery pressure increases RV afterload, impeding RV ejection, decreasing RV stroke volume, inducing RV dilation, and passively causing venous return to decrease. If such acute increases in transmural pulmonary artery pressure are not reduced, or if RV contractility is not increased by artificial means, then acute cor pulmonale rapidly develops. If RV dilation and RV pressure overload persist, RV free-wall ischemia and infarction can develop. These concepts are of profound clinical relevance because rapid fluid challenges in the setting of acute cor pulmonale can precipitate profound cardiovascular collapse secondary to excessive RV dilation, RV ischemia, and compromised LV filling. Ventilation can alter pulmonary vascular resistance by either altering pulmonary vasomotor tone, via a process known as **hypoxic pulmonary vasoconstriction**, or mechanically altering vessel cross-sectional area, by changing transpulmonary pressure.

**Hypoxic Pulmonary Vasoconstriction.** Unlike systemic vessels that dilate under hypoxic conditions, the pulmonary vasculature constricts. Once alveolar partial pressure of oxygen decreases below 60 mm Hg, or acidemia develops, pulmonary vasomotor tone increases. Hypoxic pulmonary vasoconstriction is mediated, in part, by variations in the synthesis and release of nitric oxide by endothelial nitric oxide synthase localized on pulmonary vascular endothelial cells, and in part by changes in intracellular calcium fluxes in the pulmonary vascular smooth muscle cells. The pulmonary endothelium normally synthesizes a low basal amount of nitric oxide, keeping the pulmonary vasculature actively vasodilated. Loss of nitric oxide allows the smooth muscle to return to its normal resting vasomotor tone. Nitric oxide synthesis is dependent on adequate amounts of O₂ and is inhibited by both hypoxia and acidosis. Presumably, hypoxic pulmonary vasoconstriction developed to minimize ventilation–perfusion mismatches caused by local alveolar hypoventilation. Generalized alveolar hypoxia, however, increases global pulmonary vasomotor tone, impeding RV ejection. At low lung volumes, terminal bronchioles collapse, trapping gas in the terminal alveoli. With continued blood flow, these alveoli lose their O₂ and also may collapse. Patients with acute hypoxemic respiratory failure have small lung volumes and are prone to both alveolar hypoxia and spontaneous alveolar collapse. This is one of the main reasons why pulmonary vascular resistance is increased in patients with acute hypoxemic respiratory failure.

Based on the above considerations, mechanical ventilation may reduce pulmonary vasomotor tone by a variety of mechanisms. First, hypoxic pulmonary vasoconstriction can be inhibited if the patient is ventilated with gas enriched with O₂ increasing alveolar partial pressure of oxygen. Second, mechanical breaths and positive end-expiratory pressure (PEEP) can refresh hypoventilated lung units and recruit collapsed alveolar units, causing local increases in alveolar partial pressure of oxygen especially if small lung volumes are returned to resting functional residual capacity (FRC) from an initial smaller lung volume. Third, mechanical ventilation often reverses respiratory acidosis by increasing alveolar ventilation. Fourth, decreasing central sympathetic output, by sedation or decreased stress of breathing against high-input impedance during mechanical ventilation, also reduces vasomotor tone. Importantly, these effects do not require endotracheal intubation to occur; they occur with mere reexpansion of collapsed alveoli. Thus, PEEP, CPAP, recruitment maneuvers, and noninvasive ventilation may all reverse hypoxic pulmonary vasoconstriction and may all improve cardiovascular function.
Volume-Dependent Changes in Pulmonary Vascular Resistance. Changes in lung volume directly alter pulmonary vasomotor tone by compressing the alveolar vessels.\textsuperscript{39,46,47} The actual mechanisms by which this occurs have not been completely resolved, but appear to reflect vascular compression induced by a differential extraluminal pressure gradient. The pulmonary circulation lives in two environments, separated from each other by the pressure that surrounds them.\textsuperscript{46} The small pulmonary arterioles, venules, and alveolar capillaries sense Palv as their surrounding pressure, and are called alveolar vessels. The large pulmonary arteries and veins, as well as the heart and intrathoracic great vessels of the systemic circulation, sense interstitial pressure or ITP as their surrounding pressure, and are called extraalveolar vessels. Because the pressure difference between Palv and ITP is transpulmonary pressure, increasing lung volume increases this extraluminal pressure gradient. Increases in lung volume progressively increase alveolar vessel resistance by increasing this pressure difference once lung volumes increase much above FRC (Fig. 36-1).\textsuperscript{42,53} Similarly, increasing lung volume, by stretching and distending the alveolar septa, may also compress alveolar capillaries, although this mechanism is less well substantiated. Hyperinflation can create significant pulmonary hypertension and may precipitate acute RV failure (acute cor pulmonale)\textsuperscript{54} and RV ischemia.\textsuperscript{37} Thus, PEEP may increase pulmonary vascular resistance if it induces overdistension of the lung above its normal FRC.\textsuperscript{55}

Extraalveolar vessels are also influenced by changes in transpulmonary pressure. Normally, radial interstitial forces of the lung, which keep the airways patent, only make the large vessels more distended as lung volume increases,\textsuperscript{43,56,57} just as increasing lung volume increases airway diameter. These radial forces also act upon the extraalveolar vessels, causing them to remain dilated, increasing their capacitance.\textsuperscript{58} This tethering is reversed with lung deflation, thereby increasing extraalveolar vascular resistance.\textsuperscript{32,40} Thus, pulmonary vascular resistance is increased at small lung volumes owing to the combined effect of hypoxic pulmonary vasoconstriction and extraalveolar vessel collapse, and at high lung volumes by alveolar compression.

Right-Ventricular Afterload. The right ventricle, as opposed to the left ventricle, ejects blood into a low-pressure, high-compliance system: the pulmonary circulation. The pulmonary circulation is capable of accommodating high volumes of blood without generating high pressure, which is beneficial for the right ventricle. Despite being compliant, this circuit does pose resistance to the ejecting right ventricle as quantified by pulmonary artery pressure, which is the pressure limit the right ventricle has to overcome to open the pulmonary valve. RV afterload is conceptually similar to LV afterload and is determined by the wall tension of the right ventricle. RV afterload is highly dependent on the distribution of blood flow in the lung, namely, the proportion of West zones 1 and 2, as compared to zone 3, as originally described by Permutt et al.\textsuperscript{59} Zones 1 and 2 exist whenever the intraluminal pressure of juxtaalveolar capillaries is lower than the Palv during the respiratory cycle, thus collapsing vessels and increasing pulmonary vascular resistance. In contrast, zone 3 occurs when intraluminal capillary pressure is higher than Palv, decreasing pulmonary resistance. Importantly, intraluminal pressure of alveolar capillaries tracks changes in ITP,\textsuperscript{60} and thus decreases less than Palv during spontaneous inspiration, and increases less than Palv during positive-pressure inspiration. Consequently, both spontaneous and positive-pressure inspiration above FRC increase the afterload to the right ventricle as opposed to the LV afterload, which is reduced by increased ITP.

VENTRICULAR INTERDEPENDENCE

Because right ventricle output is linked to left ventricle output serially, if right ventricle output decreases, left ventricle output must eventually decrease. The two ventricles, however, are also linked in parallel through their common septum, circumferential fibers, and pericardium, which limits total cardiac volume. For this reason, the diastolic filling of the RV has a direct influence on the shape and compliance of the LV, and vice versa. This phenomenon is known as ventricular diastolic interdependence.\textsuperscript{62} The most common manifestation of ventricular interdependence is pulsus paradoxus. Changes in RV end-diastolic volume inversely alter LV diastolic compliance.\textsuperscript{62} Because venous return can and often does vary by as much as 200% between inspiration and expiration, owing to associated changes in the pressure gradient for venous return (infra vide), right ventricle filling also changes in parallel.
FIGURE 36-2  Schematic of the effect of increasing right-ventricular (RV) volumes on the relationship between left-ventricular (LV) diastolic pressure and left ventricle volume (filling). Increases in right ventricle volumes decrease LV diastolic compliance, such that a higher filling pressure is required to generate a constant end-diastolic volume. (Adapted, with permission, from Taylor RR, Covell JW, Sonnenblick EH, Ross J Jr. Dependence of ventricular distensibility on filling the opposite ventricle. Am J Physiol. 1967;213:711–718.)

as occurs during spontaneous inspiration and spontaneous inspiratory efforts, will reduce LV diastolic compliance, immediately decreasing LV end-diastolic volume. Positive-pressure ventilation may decrease venous return causing RV volumes to decrease, increasing LV diastolic compliance. Except in acute cor pulmonale or biventricular overloaded states, however, the impact of positive-pressure ventilation on LV end-diastolic volume is minimal.

Ventricular interdependence functions through two separate processes. First, increasing RV end-diastolic volume induces an intraventricular septal shift into the LV, thereby decreasing LV diastolic compliance (Fig. 36-2). Because left ventricle wall stress is unaltered, any change in LV output does not reflect a change in LV preload. Because spontaneous inspiration increases venous return, causing right ventricle dilation, LV end-diastolic compliance decreases during spontaneous inspiration. Whereas right ventricle volumes usually do not increase during positive-pressure inspiration, ventricular interdependence usually has less impact on the patient's hemodynamic status. Second, if pericardial restraint or absolute cardiac fossa volume restraint limits absolute biventricular filling, then right ventricle dilation will increase pericardial pressure, with minimal to no septal shift because the pressure outside of both ventricles will increase similarly.

Positive-pressure ventilation, however, can still display right ventricle dilation-associated ventricular interdependence. If positive-pressure inspiration overdistends alveoli, as for example during lung recruitment maneuvers, pulmonary vascular resistance will increase. Despite the fact that hemodynamic changes elicited by recruitment maneuvers do not cause persistent cardiovascular insufficiency, transient right ventricle dilation and left ventricle collapse can occur during recruitment maneuvers. This is an important concept when treating patients with borderline RV failure. Thus, recruitment maneuvers should be used with caution and be restricted to 10 seconds or less of an end-inspiratory hold to avoid significant hemodynamic derangements.

The presence of ventricular interdependence can be assessed in mechanically ventilated patients based on heart-lung interactions. Using echocardiographic techniques, Mitchell et al and Jardin et al showed that positive-pressure breaths decrease RV dimensions, whereas both LV dimensions and LV flows increase. Still, the changes in RV output generated by positive-pressure inspiration are much less than the changes in LV output. If ventricular interdependence was the primary process driving hemodynamic interactions during a positive-pressure breath, then a phasic increase in LV stroke volume would occur during inspiration. If the primary process was a phasic decrease in venous return, however, a phasic decrease in LV stroke volume would be observed two to three beats later, usually during the expiratory phase, suggesting the right ventricle is preload responsive. These points underscore the use of LV stroke volume variation during positive-pressure ventilation to identify volume responsiveness.

**MECHANICAL HEART–LUNG INTERACTIONS BECAUSE OF LUNG VOLUME**

With inspiration, the expanding lungs compress the heart in the cardiac fossa, increasing juxtacardiac ITP. Because the chest wall and diaphragm can move away from the expanding lungs, whereas the heart is trapped within this cardiac fossa, juxtacardiac ITP usually increases more than these external ITPs. This effect is a result of increasing lung volume. It is not affected by the means whereby lung volume is increased. Both spontaneous and positive-pressure-induced hyperinflation induce similar compressive effects on cardiac filling. If one measured only intraluminal LV pressure, then it would appear as if LV diastolic compliance was reduced, because the associated increase in pericardial pressure and ITP would not be seen. When LV function, however, is assessed as the relationship between end-diastolic volume and output, no evidence for impaired LV contractile function is seen despite the continued application of PEEP. These compressive effects can be considered as analogous to cardiac tamponade and are discussed further in the next section.

**Effect of Intrathoracic Pressure**

The heart lives within the thorax, a pressure chamber inside a pressure chamber. Thus, changes in ITP affect the pressure gradients for both systemic venous return to the right ventricle and systemic outflow from the left ventricle, independent of the heart itself (Fig. 36-3). Increases in ITP, by increasing right-atrial pressure (Pra) and decreasing transmural
LV systolic pressure, will reduce the pressure gradients for venous return and LV ejection decreasing intrathoracic blood volume. Using the same argument, decreases in ITP will augment venous return and impede LV ejection, increasing intrathoracic blood volume. The increases in ITP during positive-pressure ventilation show marked regional differences; juxtaocular ITP increases more than lateral chest wall ITP as inspiratory flow rate and tidal volume increase. Interestingly, lung compliance plays a minimal role in defining the positive-pressure-induced increase in ITP. For the same increase in tidal volume, ITP usually increases similarly if tidal volume is kept constant. If, however, chest wall compliance decreases, then ITP will increase for a fixed tidal volume.

SYSTEMIC VENOUS RETURN

Guyton et al described the determinants of venous return more than 50 years ago. Blood flows back from the systemic venous reservoirs into the right atrium through low-pressure, low-resistance venous conduits. PrA is the backpressure, or downstream pressure, for venous return. Pressure in the upstream venous reservoirs is called mean systemic pressure, and, itself, is a function of blood volume, peripheral vasomotor tone, and the distribution of blood within the vasculature. Ventilation alters both PrA and mean systemic pressure. Many of the observed ventilation-induced changes in cardiac performance can be explained by these changes. Mean systemic pressure does not change rapidly during positive-pressure ventilation, whereas PrA does, owing to parallel changes in ITP (Fig. 36-4). Positive-pressure inspiration increases both ITP and PrA, decreasing venous blood flow, RV filling, and consequently, RV stroke volume. During normal spontaneous inspiration, the opposite effects occur. Spontaneous inspiration decreases ITP and PrA, accelerating venous blood flow, and increasing RV filling and RV stroke volume. 

If changes in PrA were the only process that altered venous return, then positive-pressure ventilation would induce profound hemodynamic insufficiency in most patients. The decrease in venous return during positive-pressure ventilation, however, is often lower than one might expect based on the increase in PrA.

The reasons for this preload-sparing effect seen during positive-pressure ventilation are twofold. First, when cardiac output does decrease, increased sympathetic tone decreases venous capacitance, increasing mean systemic pressure, which tends to restore the pressure gradient for venous return, even in the face of an elevated PrA. Increases in sympathetic tone, however, would increase steady-state cardiac output and would not alter the phasic changes in venous return seen during positive-pressure ventilation. The decreased phasic reductions in venous return are caused by associated increases in mean systemic pressure during inspiration. Diaphragmatic descent and abdominal-muscle contraction increase intraabdominal pressure, decreasing intraabdominal vascular capacitance. Because a large proportion of venous blood is in the abdomen, the net effect of both inspiration and PEEP is to increase mean systemic pressure and PrA in a parallel but unequal fashion. Accordingly, the pressure gradient for venous return may not be reduced as much as predicted as predicted from a pure increase in PrA. This is an important adaptive response by the body to positive-pressure ventilation and PEEP, both of which produce this effect secondary to the associated increase in lung volume, which promotes diaphragmatic descent. This preload-sparing effect is especially well demonstrated in
patients with hypervolemia. In fact, both the translocation of blood from the pulmonary to the systemic capacitance vessels, as well as abdominal pressurization secondary to diaphragmatic descent, may be the major mechanisms by which the decrease in venous return is minimized during positive-pressure ventilation. In fact, van den Berg et al documented that up to 20 cm H₂O CPAP did not significantly decrease cardiac output, as measured 30 seconds into an inspiratory-hold maneuver, in fluid-resuscitated, postoperative cardiac surgery patients. Although CPAP induced an increase in Pra, intraabdominal pressure also increased, preventing a significant change in RV volumes (Fig. 36-5). Interest in inverse-ratio ventilation has raised questions as to its hemodynamic effect, because its application includes a large component of hyperinflation.

Current data clearly show that detrimental effects of increased ITP and PEEP on venous return are far more complex than an effect on the pressure gradient between mean systemic pressure and Pra, and that geometric deformation of the venous vasculature and its flow distribution, which alter the resistance to flow, may be a better explanation. Animal data suggest that compression and deformation of capacitance vessels at the entrance of the thorax and compression of the portal circulation by diaphragmatic descent may account for these increments in venous resistance and thus decreased venous return.

Relevance of Intrathoracic Pressure on Venous Return. It is axiomatic that the heart can only pump out that amount of blood that it receives and no more. Thus, venous return is the primary determinant of cardiac output and the two must be the same. Because Pra is the backpressure to venous return and because Pra is normally close to zero relative to atmospheric pressure, venous return is maintained near maximal levels at rest, because right ventricle filling occurs with minimal changes in filling pressure.

Spontaneous inspiratory efforts usually increase venous return because of the combined decrease in Pra and increase in intraabdominal pressure. For Pra to remain very low, however, RV diastolic compliance must be high and RV output must equal venous return. Otherwise, sustained increases in venous blood flow would distend the RV and increase Pra. During normal spontaneous inspiration, although venous return increases, ITP decreases at the same time, minimizing any potential increase in Pra, which might otherwise occur if ITP were not to decrease. Aiding in this process of minimizing RV workload, the pulmonary arterial inflow circuit is highly compliant and can accept large increases in RV stroke volume without changing pressure. Thus, increases in venous return proportionally increase pulmonary arterial inflow without significant changes in RV filling or ejection pressures. Accordingly, this compensatory system fails if RV diastolic compliance decreases or if Pra increases independent of changes in RV end-diastolic volume. Figure 36-6 illustrates these differential effects of negative (spontaneous inspiration) and positive (positive-pressure inspiration) swings in ITP on dynamic RV and LV performance. In RV failure states, spontaneous inspiration does not decrease Pra and Pra actually increases. This results in the physical sign of increased jugular venous distension during spontaneous inspiration.

Note further in Figure 36-6 that not only does RV stroke volume increase with spontaneous inspiration and decrease with positive-pressure inspiration, but also that LV stroke volume decreases only during spontaneous inspiration (ventricular interdependence); during positive-pressure inspiration, however, any change in LV stroke volume occurs late, as the decrease in RV output finally reaches the left ventricle. RV diastolic compliance can acutely decrease in the setting of
Part IX  Physiologic Effect of Mechanical Ventilation

Finally, with exaggerated negative swings in ITP, as occur with obstructed inspiratory efforts, venous return behaves as if abdominal pressure is additive to mean systemic pressure in augmenting venous blood flow.\textsuperscript{118-121} These findings have some investigators to suggest that obstructive breathing may be a therapeutic strategy in sustaining cardiac output in patients in hemorrhagic shock.\textsuperscript{122} Interestingly, negative pressure ventilation, by augmenting venous return, increases cardiac output by 39% in children following repair of tetralogy of Fallot.\textsuperscript{122} In this condition, impaired RV filling secondary to

Acute RV dilation or cor pulmonale (pulmonary embolism, hyperinflation, and RV infarction). Importantly, acute RV dilation and acute cor pulmonale can not only induce rapid cardiovascular collapse, but they are singularly not responsive to fluid resuscitation. Because spontaneous inspiration and inspiratory efforts cause both ITP and Pra to decrease, RV dilation may occur in patients with occult heart failure. Accordingly, some patients who were previously stable and ventilator-dependent can develop acute RV failure during weaning trials.

FIGURE 36-6 Strip chart recording of right and left-ventricular stroke volumes (SV\textsubscript{rv} and SV\textsubscript{lv}, respectively), aortic pressure (Pa\textsubscript{o}), left-atrial, pulmonary arterial, and right-atrial transmural pressures (Pla\textsubscript{tm}, Ppa\textsubscript{tm}, and Pra\textsubscript{tm}, respectively), airway pressure (Paw), pleural pressure (Ppl), and right-atrial pressure (Pra). During spontaneous ventilation (left) and similar tidal volume positive-pressure ventilation (right) in an anesthetized, intact canine model. (Used, with permission, from Pinsky MR, Matuschak GM, Klain M. Determinants of cardiac augmentation by elevations in intrathoracic pressure. J Appl Physiol. 1985;58:1189–1198.)
RV hypertrophy and reduced RV chamber size are the primary factors limiting cardiac output. This augmentation of venous return by spontaneous inspiration, however, is limited, because as ITP decreases below atmospheric pressure, venous return becomes flow-limited because the large systemic veins collapse as they enter the thorax. This vascular flow limitation is a safety valve for the heart, because ITP can decrease greatly with obstructive inspiratory efforts, and if not flow-limited, the RV could become overdistended and fail. Finally, having subjects breathe through an airway that selectively impedes inspiration will result in exaggerated negative swings in both ITP and Pra, and associated greater increases in intraabdominal pressure secondary to recruitment of accessory muscles of respiration (to sustain a normal tidal volume).

Positive-pressure ventilation tends to create the opposite effect: increase in ITP increases Pra, thus decreasing venous return, RV volumes, and ultimately LV output. The detrimental effect of positive-pressure ventilation on cardiac output can be minimized by either fluid resuscitation, to increase mean systemic pressure, or by keeping both mean ITP and swings in lung volume as low as possible. Accordingly, prolonging expiratory time, decreasing tidal volume, and avoiding PEEP all minimize this decrease in systemic venous return to the right ventricle. Increases in lung volume during positive-pressure ventilation primarily compress the two ventricles into each other, decreasing biventricular volumes. The decrease in cardiac output commonly seen during PEEP is caused by a decrease in LV end-diastolic volume, because both LV end-diastolic volume and cardiac output are restored by fluid resuscitation without any measurable change in LV diastolic compliance.

A common respiratory maneuver, called a Valsalva maneuver, which is forced expiration against an occluded airway, such as one may do while straining at stool, displays most of the hemodynamic effects commonly seen in various disease states and with different types of positive-pressure ventilation.

During a Valsalva maneuver, airway pressure (Paw) and ITP increase equally, and pulmonary vascular resistance remains constant. During the first phase of the Valsalva maneuver, right ventricle filling decreases because venous return decreases with no change in left ventricle filling. LV stroke volume, or arterial pulse pressure. Although LV stroke volume does not change, LV peak ejection pressure increases equal to the amount of the increase in ITP. As the strain is sustained, both LV filling and cardiac output both decrease owing to the decrease in venous return, which results in the second phase of the Valsalva maneuver, both RV and LV output are decreased; arterial pulse pressure is reduced, but peak systolic pressure sustained at an elevated level owing to the sustained increase in ITP.

This phase delay in LV output decrease compared to RV output decrease is also seen during positive-pressure ventilation; it is exaggerated if tidal volumes increase or if the pressure gradient for venous return was already low, as is the case in hypovolemia.

With release of the strain in phase three of the Valsalva maneuver, arterial pressure abruptly declines as the low LV stroke volume cannot sustain an adequate ejection pressure on its own. Furthermore, with the release of the increased ITP, venous return increases, increasing RV volume, and, through the process of ventricular interdependence, decreases LV diastolic compliance, making LV end-diastolic volume even less. Conceptually, then ventricular interdependence usually becomes apparent with sudden increases in RV volume from apneic baseline, as would occur during spontaneous inspiration, but less so when RV volumes decrease below these volumes. As described above, because RV volumes are usually decreased during positive-pressure ventilation, ventricular interdependence is not a prominent feature of this form of breathing (see Fig. 36-6). Although PEEP results in some degree of right-to-left intraventricular septal shift, echocardiographic studies demonstrate that the shift is small. It follows that positive-pressure ventilation decreases intrathoracic blood volume and PEEP decreases it even more without altering LV diastolic or contractile function.

During spontaneous inspiration, however, RV volumes increase transiently shifting the intraventricular septum into the LV, decreasing LV diastolic compliance and LV end-diastolic volume. This transient RV dilation-induced septal shift is the primary cause of inspiration-associated decreases in arterial pulse pressure, which, if greater than 10 mm Hg or 10% of the mean pulse pressure, is referred to as pulsus paradoxus (see Fig. 36-6).

**Left-Ventricular Preload and Ventricular Interdependence.**

Ventricular interdependence does not induce steady-state changes in left ventricle performance, only phasic ones. Thus, the associated rapid changes in right ventricle filling induced by phasic changes in ITP cause marked changes in LV output, which are a hallmark of ventilation-induced hemodynamic changes as described above.

**LEFT-VENTRICULAR AFTERLOAD**

LV afterload is defined as the maximal LV systolic wall tension, which equals the maximal product of LV volume and transmural LV pressure. Under normal conditions, maximal LV wall tension occurs at the end of isometric contraction, with the opening of the aortic valve. During LV ejection, as LV volumes rapidly decrease, LV afterload also decreases despite an associated increase in ejection pressure. Importantly, when LV dilation exists, as in CHF, maximal LV wall stress occurs during LV ejection because the maximal product of pressure and volume occurs at that time. LV ejection pressure is the transmural LV systolic pressure. This is the main reason why subjects with dilated cardiomyopathies are very sensitive to changes in ejection pressure, whereas patients with primarily diastolic dysfunction are not. Normal baroreceptor mechanisms, located in the extrathoracic carotid body, function to maintain arterial pressure constant with respect to atmosphere. Accordingly, if arterial pressure were to remain constant as ITP increased, then transmural LV pressure would decrease. Similarly, if transmural arterial pressure were to remain constant as ITP increased,
then LV wall tension would decrease. Thus, increases in ITP decrease LV afterload, and decreases in ITP increase LV afterload. These two opposing effects of changes in ITP on LV afterload have important clinical implications.

The concept that increases in ITP decrease both LV preload and LV afterload can be clearly illustrated with the use of high-frequency jet ventilation, which can increase ITP but does not result in large swings in lung volume. When high-frequency jet ventilation is delivered in synchrony with the cardiac cycle, such that heart rate and ventilatory frequency are identical, one can dissect out the effects of ITP on preload and afterload. Under hypovolemic and normovolemic conditions with intact cardiovascular reserve, positive-pressure ventilation usually decreases steady-state cardiac output by decreasing the pressure gradient for venous return. When one compares the hemodynamic effects of high-frequency jet ventilation synchronized to occur during diastole (when ventricular filling occurs), cardiac output decreases to levels seen during end-inspiration for normal-to-large tidal-volume (10 mL/kg) ventilation. In the same subject, however, if the increases in ITP occur during systole, the detrimental effects of the same mean Paw, mean ITP, and tidal volume do not impede venous return (Fig. 36-7). Furthermore, in heart failure states, positive-pressure ventilation does not impede cardiac output because the same decreases in venous return do not alter LV preload. If these increases in ITP, however, reduce LV afterload, then cardiac output will also increase. These points are illustrated in Figure 36-8, wherein synchronous high-frequency jet ventilation is delivered either during pre-ejection systole (pre-systolic) or ejection (systolic). The only difference between the two ventilatory states is that arterial pulse pressure does not change despite increases in LV stroke volume with pre-systolic increases in Paw, consistent with a decreased LV afterload, whereas with systolic increases in Paw, arterial pulse pressure increases, and peak arterial pressure increases by an amount equal to the increase in ITP, consistent with mechanically augmented LV ejection.

Relevance of Intrathoracic Pressure on Myocardial Oxygen Consumption. Decreases in ITP increase both LV afterload and myocardial O₂ consumption. Accordingly, spontaneous ventilation not only increases global O₂ demand by its exercise component, but also increases myocardial O₂ consumption. Profound decreases in ITP commonly occur during spontaneous inspiratory efforts with bronchospasm, obstructive breathing, and acute hypoxemic respiratory failure. Under these conditions, the cardiovascular burden can be great and may induce acute heart failure and pulmonary edema. Because weaning from positive-pressure ventilation to spontaneous ventilation may reflect dramatic changes in ITP swings, from positive to negative, independent of the energy requirements of the respiratory muscles, weaning is a selective LV stress test. Similarly, improved LV systolic function is observed in patients with severe LV failure placed on mechanical ventilation. Very negative swings in ITP, as seen with vigorous inspiratory efforts in the setting of airway obstruction (asthma, upper airway obstruction, or vocal cord paralysis) or stiff lungs (interstitial lung disease, pulmonary edema, or ALI), selectively increase LV afterload, and may be the cause of LV failure and pulmonary edema, especially if LV systolic function is already compromised.

Pulsus paradoxus seen during spontaneous inspiration under conditions of marked pericardial restraint reflecting primarily ventricular interdependence. The negative swings in ITP, however, also increase LV ejection pressure, increasing LV end-systolic volume. Other systemic factors may influence LV systolic function during loaded inspiratory efforts. These associated factors also contribute to a greater or lesser degree to the inhibition of normal LV systolic function, including increased in aortic input impedance, altered synchrony of contraction of the global LV myocardium, and hypoxemia-induced decreased global myocardial contractility. Hypoxia also directly reduces LV diastolic compliance. Experimental repetitive periodic airway obstructions induce pulmonary edema in normal animals. Furthermore, removing the negative swings in ITP by applying nasal CPAP results in improved global LV performance in patients with combined obstructive sleep apnea and CHF.

Relevance of Intrathoracic Pressure on Left-Ventricular Afterload. If arterial pressure remains constant, then increases in ITP decrease transmural LV ejection pressure, decreasing LV afterload. These points are easily demonstrated in a subject with an indwelling arterial pressure catheter during cough or Valsalva maneuvers. During a cough, ITP increases rapidly without changes in intrathoracic blood volume. Arterial pressure also increases by a similar amount, as described above for phase I of the Valsalva maneuver. Thus, transmural LV pressure (LV pressure relative to ITP) and aortic blood flow would remain constant. Sustained increases in ITP, however, must eventually decrease aortic blood flow and arterial pressure secondary to the associated decrease in venous return. If ITP increased arterial pressure without changing transmural arterial pressure, then baroreceptor-mediated vasodilation would induce arterial vasodilatation to maintain extrathoracic arterial pressure-flow relations constant. Because coronary perfusion pressure reflects the ITP gradient for blood flow and is not increased by ITP-induced increases in arterial pressure, such sustained increases in ITP can cause decreased coronary perfusion pressure-induced myocardial ischemia.

SPONTANEOUS BREATHING VERSUS MECHANICAL POSITIVE-PRESSURE VENTILATION

Both spontaneous and mechanical ventilation increase lung volume above resting end-expiratory lung volume or FRC. During both spontaneous and positive-pressure ventilation, end-expiratory lung volume can be artificially increased by the addition of PEEP. Thus, the primary hemodynamic
Comparison of synchronous high-frequency jet ventilation to intermittent positive-pressure breathing in the control (normal) state

FIGURE 36-7 Strip chart recording of right- and left-ventricular stroke volumes ($SV_{rv}$ and $SV_{lv}$, respectively), aortic pressure ($Pa_{oa}$), left atrial, pulmonary arterial, and right atrial transmural pressures ($Pla_{tm}$, $Ppa_{tm}$, and $Pra_{tm}$, respectively), airway pressure ($Paw$), and pleural pressure ($Ppl$) during apnea (left), and both systolic (systole) and diastolic (diastole) high-frequency jet ventilation (HFJV) (middle), and intermittent positive-pressure ventilation with similar mean $Paw$ (right) in an anesthetized, intact canine model with normal cardiovascular function. Note that the cardiac cycle-specific increases in $Paw$ created by systole HFJV minimally impede cardiac output, whereas diastole HFJV markedly decreases venous return ($SV_{rv}$ decreases first, then $SV_{lv}$ decreases). The rapid strip chart speed shown on the left is to illustrate the exact timing of synchronous HFJV. (Used, with permission, from Pinsky MR, Matuschak GM, Bernardi L, Klain M. Hemodynamic effects of cardiac cycle-specific increases in intrathoracic pressure. J Appl Physiol. 1986;60:604–612.)
Comparison of synchronous high-frequency jet ventilation to intermittent positive-pressure breathing in acute ventricular failure

![Graph showing the comparison of synchronous high-frequency jet ventilation to intermittent positive-pressure breathing in acute ventricular failure](image)

**FIGURE 36-8** Continuous strip chart recording of right- and left-ventricular stroke volumes (SVrv and SVlv, respectively), aortic pressure (PaO2), left atrial, pulmonary arterial, and right-atrial transmural pressures (PLa, PPa, and Pra, respectively), airway pressure (Paw), pleural pressure (Ppl), and right-atrial pressure (Pra) during intermittent positive-pressure ventilation (tidal volume \( V_T \) 10 mL/kg), apnea (left), and then both presystolic systole (presystolic) and LV ejection (systolic) synchronous high-frequency jet ventilation (HFJV) (middle), and then intermittent positive-pressure ventilation again (right) in an anesthetized, intact canine model with fluid-resuscitated acute ventricular failure. Note that the cardiac cycle–specific increases in Paw created by both presystolic and systolic HFJV increase steady-state SVrv and SVlv (i.e., cardiac output), but affect PaO2 differently. Presystolic HFJV does not change PaO2, pulse pressure despite an increase in SVlv (reduced afterload), whereas systolic HFJV increases PaO2, pulse pressure for a similar increase in SVlv. (Used, with permission, from Pinsky MR, Matuschak GM, Bernardi L, Klain M. Hemodynamic effects of cardiac cycle-specific increases in intrathoracic pressure. *J Appl Physiol.* 1986;60:604–612.)
differences between spontaneous ventilation and positive-pressure ventilation are caused by the changes in ITP and the muscular contraction needed to create these changes. Importantly, even if a patient is receiving ventilator support, spontaneous respiratory efforts can persist and may result in marked increases in metabolic load, and contribute to sustained respiratory muscle fatigue.144,145 Still, a primary reason for instituting mechanical ventilation is to decrease the work of breathing. Normal spontaneous ventilation augments venous return and vigorous inspiratory efforts account for most of the increased blood flow seen in exercise. Conversely, positive-pressure ventilation may impair ventricular filling and induce hypovolemic cardiac dysfunction in normal or hypovolemic subjects while augmenting LV function in patients with heart failure. Finally, heart failure, whether primary or induced by ventilation, may induce acute respiratory muscle fatigue causing respiratory failure or failure to wean from mechanical ventilation, and overtax the ability of the circulation to deliver O₂ to the rest of the body.

Fundamental to this concept is the realization that spontaneous ventilation is exercise. Spontaneous ventilatory efforts are induced by contraction of the respiratory muscles, mainly the diaphragm and intercostal muscles.148 Although ventilation normally requires less than 5% of total O₂ delivery to meet its demand148 (and is difficult to measure at the bedside even when using calibrated metabolic measuring devices), in lung disease states in which work of breathing is increased, the metabolic demand for O₂ can increase to 30% of total O₂ delivery.80,125,148,149 With marked hyperpnea, muscles of the abdominal wall and shoulder girdle function as accessory muscles. Blood flow to these muscles is derived from several arterial circuits, whose absolute flow exceeds the highest metabolic demand of maximally exercising skeletal muscle under normal conditions.148,170,171 Thus, blood flow is usually not the limiting factor determining maximal ventilatory effort. In severe heart failure states, however, blood flow constraints may limit ventilation because blood flow to other organs and to the respiratory muscles may be compromised, inducing both tissue hypoperfusion and lactic acidosis.170–172 Aubier et al demonstrated that if cardiac output is severely limited by the artificial induction of tamponade in a canine model that respiratory muscle failure develops despite high central neuronal drive.171 The animals die a respiratory death before cardiovascular standstill. The institution of mechanical ventilation for ventilatory and hypoxicemic respiratory failure may reduce metabolic demand on the stressed cardiovascular system increasing mixed venous oxygen saturation (SVO₂) for a constant cardiac output and arterial oxygen content (CaO₂).122 Intubation and mechanical ventilation, when adjusted to the metabolic demands of the patient, may dramatically decrease the work of breathing, resulting in increased O₂ 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 SVO₂ will result in an increase in the partial pressure of arterial oxygen (Pao₂), despite no change in the ratio of shunt blood flow to cardiac output.

DETECTION AND MONITORING

Weaning Failure

Ventilator-dependent patients who fail to wean often have impaired baseline cardiovascular performance that is readily apparent,153 but commonly patients develop overt signs of heart failure during weaning, such as pulmonary edema,153,174 myocardial ischemia,175–178 tachycardia, and gut ischemia.179 Pulmonary artery occlusion pressure may rise rapidly to nonphysiologic levels within 5 minutes of instituting weaning.153 Although all patients increase their cardiac outputs in response to a weaning trial, those that subsequently fail to wean demonstrate a reduction in mixed venous O₂ saturation, consistent with a failing cardiovascular response to an increased metabolic demand.180 Weaning from mechanical ventilation can be considered a cardiovascular stress test. Again, investigators have documented weaning-associated electrocardiogram and thallium cardiac blood flow scan-related signs of ischemia in both patients with known coronary artery disease175 and in otherwise normal patients.177,178 Using this same logic, placing patients with severe heart failure and/or ischemia on ventilator support, by either intubation and ventilation141 or noninvasive CPAP182 can reverse myocardial ischemia. Importantly, the increased work of breathing may come from the endotracheal tube flow resistance.183 Thus, some patients who fail a spontaneous breathing trial may actually be able to breathe on their own if extubated. There is, however, no known method of identifying this subgroup.

Using Ventilation to Define Cardiovascular Performance

Because the cardiovascular response to positive-pressure breathing is determined by the baseline cardiovascular state, these responses can be used to define such cardiovascular states. Sustained increases in airway pressure will reduce venous return, allowing one to assess LV ejection over a range of end-diastolic volumes. If echocardiographic measures of LV volumes are simultaneously made, then one can use an inspiratory-hold maneuver to measure cardiac contractility, as defined by the end-systolic pressure-volume relationship,184 which is similar to those created by transient inferior vena-caval occlusion.185,186 Furthermore, these measures can be made during the ventilatory cycle to define dynamic interactions.186 Patients with relative hypervolemia, a condition often associated with CHF, are at less risk of developing impaired venous return during inititation of mechanical ventilation, whereas hypovolemic patients are at increased risk. If positive airway pressure augments LV ejection in heart failure states by reducing LV afterload, then systolic arterial pressure should not decrease but actually increase during inspiration, so-called reverse pulsus paradoxus. This was what Abel et al.187 saw in ten postcardiac surgery patients. Perel et al.188–190 suggested that the relationship between ventilatory efforts
and systolic arterial pressure may be used to identify which patients may benefit from cardiac-assist maneuvers. Patients who increase their systolic arterial pressure during ventilation, relative to an apneic baseline, tend to have a greater degree of volume overload and heart failure, whereas patients who decrease systolic arterial pressure tend to be volume responsive. Perhaps more relevant to usual clinical practice is the identification of patients whose cardiac output will increase if given a volume challenge. The identification of preload responsiveness is important because only half of the hemodynamically unstable patients studied in several clinical series were actually preload-responsive. Thus, nonspecific fluid loading will not only be ineffective at restoring cardiovascular stability in half the subjects, it will also both delay definitive therapy and may promote cor pulmonale or pulmonary edema. Finally, Michard et al found, in a series of ventilator-dependent septic patients, that the greater the degree of arterial pulse-pressure variation during positive-pressure ventilation, the greater the subsequent increase in cardiac output in response to volume-expansion therapy. The recent literature has documented that both arterial pulse-pressure and LV stroke-volume variations induced by positive-pressure ventilation are sensitive and specific markers of preload responsiveness. This literature was recently reviewed. The greater the degree of flow or pressure variation over the course of the respiratory cycle for a fixed tidal volume, the more likely a patient is to increase cardiac output in response to a volume challenge, and the greater that increase. The overarching principles of this clinical tool have only recently been described. There are several important caveats and limitations to this approach that need to be considered before the clinician proceeds to monitoring arterial pulse pressure or stroke volume variation during ventilation as a routine assessment of preload responsiveness.

First, and perhaps most importantly, being preload-responsive does not mean that the patient should be given volume. Otherwise healthy subjects under general anesthesia without evidence of cardiovascular insufficiency are also preload-responsive, but do not need a volume challenge. The presence of positive-pressure-induced changes in aortic flow or arterial pulse pressure does not itself define therapy. Independent documentation of cardiovascular insufficiency needs to be sought before the clinician attempts fluid resuscitation based on these measures. Second, these indices, which quantify the variation in aortic flow, stroke volume, and arterial systolic and pulse pressures, have routinely been demonstrated to outperform more traditional measures of LV preload, such as pulmonary occlusion pressure, Pra, total thoracic blood volume, RV end-diastolic volume, and LV end-diastolic area. There appears to be little relation between ventricular preload and preload responsiveness. Ventricular filling pressures poorly reflect ventricular volumes, and measures of absolute ventricular volumes do not define diastolic compliance. Patients with small left ventricles that are also stiff, as may occur with acute cor pulmonale, tamponade, LV hypertrophy, and myocardial fibrosis, will show poor volume responsiveness. Conversely, patients with large LV volumes, as often occurs with CHF and afterload reduction, may be quite volume responsive. Thus, preload does not equal preload responsiveness. Third, all the reported studies used positive-pressure ventilation to vary venous return. For such changes in venous return, however, to induce LV output changes, the changes must be of sufficient enough magnitude to cause measurable changes in preload. If the increase in lung volume with each tidal breath is either not great enough to induce changes in pulmonary venous flow, or if the positive-pressure breath is associated with spontaneous inspiratory efforts that minimize the changes in venous return, then the cyclic perturbations to cardiac filling may not be great enough to induce the cyclic variations in LV filling needed to identify preload responsiveness. Furthermore, the degree of pressure or flow variation will be proportional to tidal volume, with greater tidal volumes inducing greater changes for the same cardiovascular state. Thus, the means by which cyclic changes in lung volume and ITP are induced will affect the magnitude of arterial pressure and flow variations. Fourth, although the primary determinant of arterial pulse-pressure variation over a single breath is LV stroke-volume variation, because changes in aortic impedance and arterial tone cannot change that rapidly over time, this limitation no longer applies. As arterial tone decreases, for example, then for the same aortic flow and stroke volume both mean arterial pressure and pulse pressure will be less. Accordingly, flow variation becomes more sensitive than pulse pressure variation as hemorrhage progresses.

**CLINICAL SCENARIOS**

**Initiating Mechanical Ventilation**

**NORMOVOLEMIC AND HYPOVOLEMIC PATIENTS**

The process of initiating mechanical ventilation is a complex physiologic process for a variety of reasons. First, pharmacologic factors needed to allow for endotracheal intubation also blunt sympathetic responses, exaggerating the hemodynamic effects induced by increasing airway pressure and defining tidal volume and ventilatory frequency. This point is clearly demonstrated by comparing the relative benign impact that reinstituting ventilator support in a patient with a preexistent tracheotomy, with the impact of the initial intubation and ventilation of the same patient a few days or weeks earlier. As noted above, positive-pressure ventilation increases ITP, which must alter venous return. If the patient has reduced vasomotor tone, as commonly exists during induction of anesthesia, the associated increase in Pra will induce a proportional decrease in venous return, pulmonary blood flow and subsequently cardiac output. If the associated tidal volumes are excessive for the duration of expiratory time available to allow for passive deflation, then dynamic hyperinflation will occur, increasing pulmonary vascular resistance and compressing the heart in the cardiac fossa, further decreasing further biventricular volumes. If one were to examine the dynamic effects of ventilation on...
Effect of Mechanical Ventilation on Heart–Lung Interactions

Chapter 36

LV performance, as described in the first part of this chapter, is overly simplified by this assumption that breathing alters only LV preload. Clearly, other factors also function simultaneously. The preload-reducing effects of tidal volume, however, are best described during hypovolemic states, as illustrated in the right panel of Figure 36-10. Note that the LV pressure-volume relation over the course of a single breath, one would see a more complex effect, characterized by alterations in LV diastolic compliance, end-diastolic volume, stroke volume, and LV afterload (as exemplified by the leftward shift of the end-systolic pressure-volume relations; Fig. 36-9). Importantly, the impact of ventilation on LV performance, as described in the first part of this chapter, is overly simplified by this assumption that breathing alters only LV preload. Clearly, other factors also function simultaneously. The preload-reducing effects of tidal volume, however, are best described during hypovolemic states, as illustrated in the right panel of Figure 36-10. Note that

FIGURE 36-9 Dynamic effect of positive-pressure ventilation on the LV pressure-volume relation from end-expiration through a ventilatory cycle. Note the changes in LV filling (maximal end-diastolic volume), diastolic compliance (the slope of the LV pressure-volume relation as LV volume increases during filling: lower horizontal line), stroke volume (difference between maximal or end-diastolic volume and minimal or end-systolic volume for a given beat), and the end-systolic pressure-volume relation all change during the course of a single breath. Figure 36-10 shows how changes in tidal volume and intravascular volume alter these changes differently. IPPV, intermittent positive-pressure ventilation.

FIGURE 36-10 Effect of increasing tidal volume (VT) on the LV pressure-volume relationship during normovolemic (left) and hypovolemic (right) conditions in an intact anesthetized canine model. Under normovolemic conditions, the preload-reducing effects of positive-pressure inspiration become more pronounced at end-inspiration as tidal volume increases. Under hypovolemic conditions, similar increases in tidal volume also tend to decrease the overall size and performance of the heart along lines consistent with pure reductions in LV preload (end-diastolic volume); that is, steady-state LV end-diastolic and end-systolic volumes decrease, end-systolic pressure decreases, and stroke volume decreases with increasing tidal volumes and airway pressures. IPPV, intermittent positive-pressure ventilation.
Comparing Different Ventilator Modes

Any hemodynamic differences between different modes of total mechanical ventilation at a constant airway pressure and PEEP are a result of differential effects on lung volume and ITP. When two different modes of total or partial ventilator support have similar changes on ITP and respiratory effort, their hemodynamic effects are also similar, despite markedly different airway waveforms. Partial ventilator support with either intermittent mandatory ventilation or pressure-support ventilation give similar hemodynamic responses when matched for similar tidal volumes. Similar tissue oxygenation occurred in ventilator-dependent patients when switched from assist-control, intermittent mandatory ventilation, and pressure-support ventilation with matched tidal volumes. Numerous studies document cardiovascular equivalence when different ventilator modes are matched for tidal volume and level of PEEP. Different ventilator modes will affect cardiac output to a similar extent for similar increases in lung volume.

When pressure-controlled ventilation with a smaller tidal volume was compared to volume-controlled ventilation, however, pressure-controlled ventilation was associated with a higher cardiac output. Davis et al studied the hemodynamic effects of volume-controlled ventilation versus pressure-controlled ventilation in twenty-five patients with ALI. When matched for the same mean Paw, both modes gave the same cardiac outputs. When Paw, however, was increased during volume-controlled ventilation from a sine-wave to a square-wave flow pattern, cardiac output fell. Furthermore, Kiehl et al found that cardiac output was better during biphasic positive-airway pressure than during volume-controlled ventilation, leading to an increased \( \text{SPO}_2 \) and indirectly increasing \( \text{PaO}_2 \). In eighteen ventilator-dependent but hemodynamically stable patients, Singer et al showed that the degree of hyperinflation, not the Paw, determined the decrease in cardiac output. Finally, in an animal model of ALI, Mang et al demonstrated that if total PEEP (intrinsic PEEP plus additional extrinsic PEEP) was similar, no hemodynamic differences were observed between conventional ventilation and inverse-ratio ventilation.

Upper Airway Obstruction

The cardiovascular effects of upper airway obstruction have been reviewed. To understand the effects, it is useful to examine the effect of spontaneous inspiratory efforts against an occluded airway, referred to as a Mueller maneuver. This maneuver is easy to create in a graded fashion in the laboratory by having a subject inspire against an occluded airway connected to a manometer; the negative swings in Paw can be controlled by the subject. Based on the above physiologic discussion, it is clear that a Mueller maneuver will result in an increase in both venous return and LV afterload. The hemodynamic effects, however, of positive and negative swings in ITP may not be mirrored oppositely of each other; the interactions are nonlinear. As ITP becomes more negative, venous return becomes flow limited as the veins collapse because their transmural pressure becomes negative. LV afterload, however, increases progressively and linearly. Figure 36-4 illustrates these nonlinear effects. Changes in ITP will appear to shift the LV Frank-Starling curve to the left or right, with Pra on the x axis, equal to the change in ITP; because the heart is in the chest and acted upon by ITP, whereas venous return is from the body, which is outside of this pressure chamber. Accordingly, large negative swings in ITP will selectively increase LV ejection pressure without greatly increasing RV preload or LV diastolic compliance. This concept is important. Removing large negative swings in ITP without inducing positive swings in ITP, as would occur by endotracheal intubation or tracheotomy to bypass any upper airway obstruction, should selectively reduce LV ejection pressure (LV afterload) and not reduce venous return (LV preload).

Large negative swings in ITP commonly occur in critically ill patients. Upper airway obstruction is a medical emergency. The most common cause of upper airway obstruction is pharyngeal obstruction secondary to loss of muscle tone, which is manifest as snoring or obstructive sleep apnea. Laryngeal edema or vocal cord paralysis following extubation commonly present as acute upper airway obstruction immediately following extubation. Other causes of upper airway obstruction include epiglottis, retropharyngeal hematomas, tumors of the neck and vocal cords, and foreign-body aspiration. Because the site of obstruction is in the extrathoracic airway, increasing inspiratory efforts only cause the obstruction to become more pronounced. By markedly increasing LV afterload, inspiration against an occluded airway rapidly leads to acute pulmonary edema. During an acute asthmatic attack in a child, peak negative ITP can be −40 cm H₂O and mean tidal ITP
maintained between ~24 and ~7 cm H₂O, increasing both LV afterload and promoting pulmonary edema. Chronic Obstructive Pulmonary Disease

The hemodynamic consequences of COPD reflect complex issues related to hyperinflation, a propensity to further dynamic hyperinflation and increased airway resistance. Hyperinflation within the context of preexisting reduced pulmonary vascular cross-sectional area and increased pulmonary vasomotor tone, are the primary reasons for ventilation-induced pulmonary hypertension and RV failure. RV afterload is often increased owing to loss of pulmonary parenchyma and hyperinflation. Ventilation–perfusion mismatch can promote further increases in pulmonary vasomotor tone through hypoxic pulmonary vasoconstriction. The ultimate effects of this process are to impede RV ejection and induce by RV dilation, and, if pulmonary hypertension persists, induce RV hypertrophy. An immediate increase in lung volume may decrease RV end-diastolic volume because of cardiac compression and an associated increase in Pra. Neurohumoral reflex mechanisms, however, acting through right atrial stretch receptors cause salt and water retention, causing blood volume and Pra to increase. The goal of this exercise is to restore venous return to its baseline level. Accordingly, the elevated Pra commonly seen in COPD patients reflects a survival strategy analogous to LV dilation in heart failure.

During exacerbations of COPD, hypoxemia, respiratory acidosis, increased intrinsic sympathetic tone, and increased, but inefficient, respiratory efforts combine to increase the work of breathing. The net result is often unpredictable, but certain scenarios often present themselves, which suggests the dominance of one process over the others. These differences are relevant because these identify specific, and often opposite, therapeutic strategies that are used to reverse the associated cardiovascular insufficiency. On a global level, however, any treatments that can reduce airway obstruction and bronchospasm will reduce work of breathing, minimize hyperinflation, and reverse respiratory acidosis and hypoxemia, decreasing RV afterload. Accordingly, the aggressive use of supplemental O₂, bronchodilating agents, and antibiotics to reduce airway infection and the volume and viscosity of secretion will all improve cardiovascular function. If mechanical ventilation can reverse hyperinflation and alveolar hypoxia, one will see reductions in Pra, increases in cardiac output, and less radical arterial pressure swings during ventilation. If, however, hyperinflation persists or is exaggerated by mechanical ventilation, then acute RV failure may occur.

ACUTE COR PULMONALE

Hyperinflation, in the setting of preexisting pulmonary hypertension or decreased pulmonary vessel cross-sectional area, can induce profound increases in pulmonary arterial pressure, promoting acute cor pulmonale. With the initiation of mechanical ventilation, it is easy to set tidal volume too large and inspiratory time too long, promoting dynamic hyperinflation. Every effort should be made to minimize this life-threatening complication. Importantly, the cardiovascular management of this life-threatening process is to reduce RV wall strain and maintain or improve RV coronary perfusion. These considerations are briefly summarized. First, one almost always sees acute elevations of Pra, often accompanied by acute tricuspid regurgitation at end-inspiration. If a pulmonary arterial catheter is present, Pra equal or exceed pulmonary artery occlusion pressure. Furthermore, if the catheter has the ability to measure RV ejection fraction, it almost always reduced (<40%). Importantly, acute volume infusions will only compromise the dilated right ventricle further, such that both stroke volume and RV ejection fraction are decreased. These are clear signs of impending or existing cardiovascular collapse secondary to acute cor pulmonale. Because most of RV myocardial blood flow occurs in systole, maintaining aortic pressure higher than pulmonary arterial pressure to sustain RV myocardial perfusion is an essential aspect of the initial cardiovascular management.

LEFT-VENTRICULAR FAILURE

Although COPD is usually characterized by right-sided dysfunction owing to the alterations in pulmonary vascular biology, these subjects also tend to be smokers, elderly, and male, three demographic qualities that place them at high risk of coronary artery disease. With the exception of intubation-induced hypotension and reactive tachycardia, the risk of LV ischemia during intubation and sustained mechanical ventilation is relatively low in these patients. Because they are usually volume overloaded and have a reduced cardiac reserve before intubation, these patients usually benefit from a reduction in metabolic demands and reduced ventilatory interdependence owing to the smaller RV volumes. Patients with COPD may fail weaning attempts because their work of breathing exceeds their cardiovascular reserve. Just as these patients cannot climb two flights of stairs, they may wean because of impaired cardiovascular reserve. The combination of occult impaired cardiovascular reserve and the stress of spontaneous ventilation, with associated negative swings in ITP and positive swings intraabdominal pressure, which augment venous return, provide a primary reason for cases of weaning failure characterized by hypoxemia or transient pulmonary edema. Beach et al demonstrated many years ago that heart-failure patients who are ventilator-dependent may be weaned if pharmacologic support of the heart is subsequently introduced.

Auto–Positive End-Expiratory Pressure

The hemodynamic effects of positive-pressure ventilation are caused by changes in ITP, not airway pressure. This concept greatly influences the analysis of heart–lung interactions in patients with lung disease. As discussed above, the primary...
determinants of the hemodynamic responses to ventilation are secondary to changes in ITP and lung volume, not Paw. The relation between Paw, ITP, pericardial pressure, and lung volume varies with spontaneous ventilatory effort, lung compliance, and chest wall compliance. Lung and thoracic compliance determine the relation between end-expiratory Paw and lung volume in the sedated paralyzed patient. If a ventilated patient, however, actively resists lung inflation or sustains expiratory muscle activity at end-inspiration, then end-inspiratory Paw will exceed resting Paw for that lung volume. Similarly, if the patient activity prevents full exhalation by expiratory braking, then for the same end-expiratory Paw, lung volume may be much higher than predicted from end-expiratory Paw values alone. Finally, even if inspiration is passive and no increased airway resistance is present, Paw may rapidly increase over minutes as chest wall compliance decreases. During inspiration, positive-pressure Paw increases as a function of both total thoracic compliance and airway resistance. Patients with marked bronchospasm will display a peak Paw greater than end-inspiratory (plateau) Paw. The difference between measured Paw and Palv is called auto-PEEP. Changes in transpulmonary pressure and total thoracic compliance alter FRC, and FRC is the primary volume about which all hemodynamic interactions revolve. FRC is a nefarious value. When one reclines from a standing position, FRC may decrease by as much as 500 mL in a 70-kg healthy male. PEEP and CPAP increase FRC by offsetting Palv. If a subject does not have sufficient time to exhale completely to FRC, however, then the next breath will stack upon the extra lung volume present. Bergman described this concept of dynamic hyperinflation many years ago. Pepe and Marini coined the term “auto-PEEP” to connote the similarities between dynamic hyperinflation (also called occult PEEP) and extrinsically applied PEEP. Auto-PEEP is not measured by the ventilator, as part of its usual parameters, and may go unappreciated. Yet, if functions identically to extrinsic PEEP in altering pulmonary vascular resistance and recruiting alveoli. The hemodynamic effect of this hyperinflation is to increase ITP and pulmonary vascular resistance, and compress the heart within the cardiac fossa. Thus, one may see Pra and pulmonary artery occlusion pressure progressively increase as arterial pulse pressure and urine output decrease. One may then make the erroneous diagnosis of acute heart failure, when all that is occurring is hyperinflation and the unaccounted increase in ITP. If one adds extrinsic PEEP to the ventilator circuit of patients with auto-PEEP, no measurable hemodynamic effects are seen until extrinsic PEEP exceeds auto-PEEP levels. These data suggest that auto-PEEP and extrinsic PEEP have identical hemodynamic effects during controlled mechanical ventilation.

During assisted ventilator support, however, or spontaneous breathing, auto-PEEP adds an additional elastic workload on the respiratory muscles. This increased workload is often the cause of failure to wean because spontaneous breathing trials are often associated with tachypnea, which prevents adequate time for complete exhalation. Clinical signs and symptoms suggestive of hemodynamically significant auto-PEEP include increased anxiety and agitation during spontaneous breathing associated with a marked increase in respiratory efforts and paradoxical chest wall motion. Because changes in ITP are occurring even though no air movement initially takes place, an arterial pressure recording will show immediate decreases in diastolic arterial pressure without changes in pulse pressure until the inspiratory breath finally occurs. Finally, by adding progressive increases in extrinsic PEEP to the ventilator circuit during a spontaneous breathing trial, changes in arterial diastolic pressure and pulse pressure will start to occur in unison as ventilatory efforts recouple with the ability to cause airflow.

Acute Respiratory Distress Syndrome and Acute Lung Injury

Patients with ALI have decreased aerated lung volumes owing to alveolar collapse and flooding. Because lung expansion during positive-pressure inspiration pushes on the surrounding structures, distorting them, this expansion causes thoracic surface pressures to increase. The degree of lateral chest wall, diaphragmatic or juxtacardiac ITP increase, relative to each other as lung volume increases, will be a function of the compliance and inerterance of their opposing structures. Changes in pleural pressure (Ppl) induced by positive-pressure inflation are different among differing lung regions (Fig. 36-11). Pleural pressure close to the diaphragm increases least during inspiration, and juxtacardiac Ppl increases most, presumably because the diaphragm is very compliant whereas the mediastinal contents are not. If abdominal distension develops, however, then the diaphragm will become relatively noncompliant and ITP will increase similarly across the entire thorax. Increasing Paw to overcome chest wall stiffness (abdominal distension) in secondary acute respiratory distress syndrome should produce a greater increase in ITP, with greater hemodynamic consequences, but it should not improve gas exchange, because the alveoli are not damaged. Conversely, if lung compliance is reduced, as in primary acute respiratory distress syndrome, then for a similar increase in Paw, ITP will increase less, creating fewer hemodynamic effects, but also recruiting more collapsed and injured alveolar units, improving gas exchange. If lung injury induces alveolar flooding or increased pulmonary parenchyma stiffness, then greater increases in Paw will be required to distend the lungs to a constant end-inspiratory volume. Romand et al demonstrated that although Paw increased more during ALI than under control conditions for a constant tidal volume, the increases in lateral chest wall Ppl and pericardial pressure were equivalent for both conditions if tidal volume was held constant (see Fig. 36-11). The primary determinant of the increase in Ppl and pericardial pressure during positive-pressure ventilation is lung volume change, not Paw change.

The distribution of alveolar collapse and lung compliance in ALI is nonhomogeneous. Accordingly, lung distension during positive-pressure ventilation must reflect...
overdistension of some regions at the expense of poorly compliant regions because aerated lung units display a normal specific compliance.\textsuperscript{85} Accordingly, Paw will reflect distension of lung units that were aerated before inspiration, but may not reflect the degree of lung inflation of nonaerated lung units. Pressure-limited ventilation assumes that this is the case and aims to limit Paw in ALI states so as to prevent overdistension of aerated lung units, with the understanding that tidal volume, and thus minute ventilation, must decrease. Thus, pressure-limited ventilation will hypoventilate the lungs, leading to “permissive” hypercapnia. In an animal model of ALI, when tidal volume was either kept constant at preinjury levels or reduced to match preinjury plateau pressure, both Ppl and pericardial pressure increased less as compared with either the pre–lung injury states or the ALI state, but with tidal volume set at the preinjury levels.\textsuperscript{82} These points underlie the fundamental hemodynamic differences seen when different ventilator modes are compared to each other. Important for the hemodynamic effects of ventilation in ALI, vascular structures that are distended will have a greater increase in their surrounding pressure than collapsible structures that do not distend.\textsuperscript{829} However, both Romand et al\textsuperscript{82} and Scharf and Ingram\textsuperscript{83} demonstrated that, despite this nonhomogeneous alveolar distension, if tidal volume is kept constant, then Ppl increases equally, independently of the mechanical properties of the lung. Thus, under constant tidal volume conditions, changes in peak and mean Paw will reflect changes in the mechanical properties of the

**FIGURE 36-11** Effect of increasing ventilatory frequency on regional pleural pressure (Ppl) changes in the lung of an intact dog. Ppl (mean ± standard error [SE]) for six pleural regions of the right hemothorax of an intact supine canine model. Paw, airway pressure; V\textsubscript{T}, tidal volume. (Used, with permission, from Novak R, Matuschak GM, Pinsky MR. Effect of positive-pressure ventilatory frequency on regional pleural pressure. J Appl Physiol. 1988;65:1314–1323.)
Congestive Heart Failure

Patients with CHF are difficult to wean from the ventilator because the increases in work of breathing, venous return, and intrathoracic blood volume during the transition from assisted to spontaneous ventilation may cause acute pulmonary edema. Rasanseri et al documented that decreasing levels of ventilator support in patients with myocardial ischemia and acute LV failure worsened ischemia and promoted the development of pulmonary edema. 231,232 These effects could be minimized by preventing effort-induced negative swings in ITP by the use of CPAP while allowing the patient to continue to breathe spontaneously. 232 Thus, in these patients, it is not the work-cost of breathing that is inducing heart failure, but the negative swings in ITP. Presumably, the ability of CPAP to decrease ventricular explains the beneficial effects of CPAP during weaning trials.

If increases in ITP during positive-pressure ventilation decrease LV afterload, why then does positive-pressure ventilation not induce an increase in cardiac output in patients with CHF? The answer is that it does. Increases in cardiac output with Paw increases suggest the presence of CHF. 231,232 Grace and Greenbaum 232 noted that adding PEEP in patients with heart failure did not decrease cardiac output; cardiac output actually increased if pulmonary artery occlusion pressure exceeded 18 mm Hg. Similarly, Calvin et al 233 noted that patients with cardiogenic pulmonary edema had no decrease in cardiac output when given PEEP. 234 Finally, Pinsky et al demonstrated that ventilator-induced increases in ITP, using ventilatory frequencies of 12 to 20 breaths/min (phasic high intrathoracic pressure support; see Fig. 36-11) and increases in ITP synchronized to occur with each cardiac systole (cardiac cycle-specific where ventilator frequency equals heart rate; Fig. 36-12) greatly increased cardiac output in cardiomyopathy. 235,236 Note the similarities in the increase in mean cardiac output seen with systolic synchronized ventilation with the cardiovascular responses to similar systolic synchronized ventilation (see Fig. 36-8), which was derived in an acute animal model, wherein many more hemodynamic measures were made.

These beneficial effects do not required endotracheal intubation. They are realized with the use of mask CPAP. In fact, CPAP levels as low as 5 cm H2O can increase cardiac output in patients with CHF. Cardiac output, however, decreases with similar levels of CPAP in both normal subjects and in patients with heart failure who are not volume overloaded. Nasal CPAP can also accomplish the same results in patients with obstructive sleep apnea and heart failure, 237 although the benefits do not appear to be related to changes in obstructive breathing pattern. 238 Prolonged nighttime nasal CPAP can selectively improve respiratory muscle strength and LV contractile function in the patients who have preexisting heart failure. 239,240 These benefits are associated with reductions of serum catecholamine levels. 241 There is no special effect of nonintubated CPAP on cardiac performance. In patients with hypovolemic CHF, as manifested by a pulmonary artery occlusion pressure equal to or less than 12 mm Hg, CPAP and biphasic positive airway pressure, at the same mean airway pressure, decrease cardiac output equally. 242
If noninvasive ventilation improves LV performance in patients with both obstructive sleep apnea and CHF, can noninvasive ventilation then be useful in treating acute cardiogenic pulmonary edema? Several workers have asked this question. Rasen et al. used mask CPAP to treat patients with acute coronary insufficiency and cardiogenic pulmonary edema. They demonstrated that myocardial ischemia was reversed by CPAP, but only after the level of CPAP was adjusted to prevent negative swings in ITP. CPAP levels below this threshold did not improve LV performance. The amount of CPAP needed to abolish negative swings in ITP, however, varied among patients. This is important, because subsequent clinical trials of CPAP to treat cardiogenic pulmonary edema used only fixed levels of CPAP, not CPAP levels titrated to abolish negative swings in ITP. Several early studies demonstrated that mask CPAP improved gas exchange and reduced the need for endotracheal intubation. Mortality and hospital length of stay, however, were usually similar among patients on CPAP and conventional O2, suggesting that prevention of intubation is not a determinant of outcome from cardiogenic pulmonary edema. Consistent with an afterload-sparing effect of blocking negative swings in ITP, both CPAP and biphasic positive airway pressure, which decrease equally the negative swings in ITP, demonstrated similar improvement in oxygenation without changing long-term outcome. The lack of long-term benefit from CPAP in acute cardiogenic pulmonary edema underscores the importance of separating outcome from acute processes characterized by symptoms (cardiogenic pulmonary edema) from underlying pathology (CHF). In fact, it would be surprising if mask CPAP had improved outcome as long as endotracheal intubation remained the default option for CHF. Still, abolishing negative swings in ITP acutely improves cardiac function in heart-failure patients.

One cannot, however, readily apply increasing ITP to augment LV performance because the effect rapidly becomes self-limited as venous return declines. This is analogous to phase 3 of the Valsalva maneuver. The effect of removing large negative levels of ITP, however, does not have the same effect on venous return as does increasing ITP. Because venous return if flow-limited below an ITP of zero, removing large negative swings in ITP will not alter venous return. The effect, however, of removing negative ITP swings on LV afterload will be identical millimeter of mercury for millimeter of mercury, as created by using increasing levels of CPAP.

**Intraoperative State**

Most elective surgery patients are kept relatively hypovolemic before surgery because of the risk of aspiration pneumonia during induction. They are not allowed food for 8 to 12 hours, nor anything by mouth for 6 hours before surgery, and they rarely are given intravenous fluids before coming into the operating room. Moreover, with the induction of general anesthesia, basal sympathetic tone is markedly reduced. Thus, it is amazing how little cardiovascular compromise occurs in this setting. Two factors may explain the lack of significant cardiovascular compromise. First, almost all patients are supine, and do not have to perform work; thus, venous return is maximized, and metabolic demand reduced. Second, almost all anesthesiologists insert an intravenous catheter to infuse anesthetic agents; usually they use this port to rapidly infuse large volumes of saline solutions as part of the induction. Nevertheless, to the extent that vasomotor tone is compromised, venous return will decrease, causing cardiac output to become a limiting cardiovascular variable.

Independent of these initial blood volume and vasomotor tone effects, other events can profoundly alter cardiovascular status. Both laparotomies and thoracotomies cause cardiac output to decrease by altering heart–lung interactions. Recall that the primary determinant of venous return is the pressure gradient between the venous reservoirs and Pra (see Fig. 36–4). Because a little over half of the venous blood resides in the abdomen, intraabdominal pressure represents a significant determinant of mean systemic pressure. This point was illustrated earlier, when it was shown that diaphragmatic descent during positive-pressure inspiration pressurized the intraabdominal compartment, minimizing the decrease in venous return predicted by the associated increase in Pra (see Fig. 36–5). During abdominal surgery, however, the act of opening the abdomen and keeping it open abolishes the effect of diaphragmatic descent on intraabdominal pressure. Accordingly, an open laparotomy induces a fall in cardiac output by making the pressure gradient for venous return dependent only on changes in Pra. From the opposite side of the venous return curve, changes in Pra are dependent on changes in ITP. Thus, an open thoracotomy, by abolishing the end-expiratory negative ITP, induces an immediate increase in Pra, causing cardiac output to decrease.

During general anesthesia, most intubated patients have their ventilation completely controlled by the ventilator. Under these conditions, assuming that tidal volume and PEEP remain constant, the hemodynamic effects of ventilation remain remarkably constant. One can use this phasic-forcing function to assess preload responsiveness, as discussed above. Specifically, positive-pressure ventilation induces a cyclic change in LV end-diastolic volume, owing to complex and often different processes. But these ventilation phase-specific changes in LV end-diastolic occur anyway. Thus, in patients whose global cardiovascular system is preload-responsive, they will also manifest ventilation-induced changes in LV stroke volume and arterial pulse pressure.
When quantified as a pressure-induced stroke-volume variation or pulse-pressure variation, numerous studies show that these measures reflect robust and profoundly simple means to assess preload responsiveness. 192–194,200,212,213

**STEPS TO LIMIT OR OVERCOME DETRIMENTAL HEART-LUNG INTERACTIONS**

Two major approaches can be used to minimize deleterious cardiovascular interactions while augmenting the beneficial ones: those focusing on ventilation and those focusing on cardiovascular status. All these approaches, however, are relative.

**Minimize Work of Breathing**

The most obvious technique for minimizing work of breathing during spontaneous ventilation is to decrease airway resistance and recruit collapsed alveolar units. Because ventilation is exercise, minimizing the metabolic load on the respiratory muscles allows blood flow to be diverted to other organ systems in need of O₂. Bronchodilator therapy and recruitment maneuvers accomplish these effects.

**Minimize Negative Swings in Intrathoracic Pressure**

It is important to minimize the negative swings in ITP during spontaneous breathing because these swings account for the increased intrathoracic blood volume and increased LV afterload, and can induce acute LV failure and pulmonary edema. Still, allowing normal negative swings in ITP at end-expiration promotes normal venous return and maintains cardiac output higher than during positive-pressure ventilation in patients with hemorrhagic shock. Although promoting inspiratory strain to augment cardiac output is the logical extension of this concept,122 this logic is self-limiting because the associated increase in metabolic demand exceeds the associated increase in blood flow. Numerous studies, cited above, document the improvements in myocardial O₂ demand, ischemia, and cardiovascular reserve achieved by this strategy. All these effects can be realized in nonintubated patients using noninvasive mask CPAP and biphasic positive airway pressure (Figs. 36-13 and 36-14).

**Prevent Hyperinflation**

Third, by preventing overdistension of the lungs, pulmonary vascular resistance will not increase, cardiac filling will not be impeded, and venous return will remain at or near maximal levels. Several important caveats, however, need to be listed. First, hyperinflation is not PEEP. Recruitment of collapsed alveoli and stabilization of injured alveoli in an

![FIGURE 36-13](image1)  
*FIGURE 36-13 Effect of phasic high intrathoracic pressure support (PHIPS) on cardiac output in ventilator-dependent patients. (Used, with permission, from Pinsky MR, Summer WR. Cardiac augmentation by phasic high intrathoracic pressure support (PHIPS) in man. Chest. 1983;84:370–375.)*

![FIGURE 36-14](image2)  
*FIGURE 36-14 Effect of cardiac cycle-specific increases in airway pressure, delivered by a synchronized high-frequency jet ventilator in intraoperative patients with congestive heart failure. Note that for the same mean airway pressure, tidal volume, and ventilatory frequency, the placement of the inspiratory pulse within the cardiac cycle has profoundly different effects. (Used, with permission, from Pinsky et al. Ventricular assist by cardiac cycle-specific increases in intrathoracic pressure. Chest. 1987,91:709–715.)*
aerated state often requires the use of PEEP, which itself may reduce pulmonary vascular resistance. Although overdistension of aerated alveoli will improve gas exchange further, it will also increase pulmonary vascular resistance. Thus, one should use the lowest level of PEEP required to create adequate oxygenation. Second, in CHF, lung inflation improves LV ejection effectiveness and may itself reflect a type of ventricular support.

**Fluid Resuscitation during Initiation of Positive-Pressure Ventilation**

The act of endotracheal intubation is often accompanied by complex manipulations, including the use of anesthetic and analgesic agents, and institution of positive-pressure ventilation. The consequent reduction in sympathetic tone and increase in Pra act synergistically to reduce venous return. These combined effects can be lifesaving in patients with cardiogenic pulmonary edema. In otherwise healthy subjects or in patients with hypovolemia (e.g., trauma), however, these additive effects can induce hypovolemic cardiovascular collapse. Thus, the bedside caregiver should be prepared to rapidly infuse intravascular volume to potentially hypovolemic patients during the act of endotracheal intubation.

**Prevent Volume Overload during Weaning**

The transition from positive-pressure to spontaneous ventilation must reduce ITP and increase oxygen consumption. Thus, patients are at risk of developing or worsening pulmonary edema, myocardial ischemia, and acute LV failure during weaning trials. Before initiating a spontaneous breathing trial, it is important to ensure that a patient is not volume overloaded. Steps to minimize volume overload include limiting fluids before weaning trials, forced diuresis in the setting of overt volume overload and pleural effusion, and gradual reduction in the level of positive-pressure through the use of partial support modes, so as to allow fluid shifts to be excreted in urine. Furthermore, in patients with markedly increased total-body water, fluid resorption often accelerates as Pra decreases. Thus, attention to subsequent fluid overload over the days following extubation and the use of limited intravascular fluids or forced diuresis is often needed to prevent reintubation. A clinician cannot presume that a patient with clear evidence of increased extravascular water has been successfully extubated when an endotracheal tube has been removed or even several hours later. Although detailed studies on the pathophysiology of extubation failure have not been conducted, and while failure may be multifactorial, cardiovascular compromise secondary to subsequent volume overload from either fluid resorption or intravascular volume loading (often manifested by increased secretions, wheezing, and hypoxemia) is likely to be one important cause.

**Augment Cardiac Contractility**

Because spontaneous breathing trial is exercise, it may precipitate acute coronary insufficiency, even in patients who are successfully weaned. Almost 40 years ago, Beach et al demonstrated that many ventilator-dependent patients can be successfully weaned if they are simultaneously given a positive inotropic agent, such as dobutamine. Although no prospective clinical trial has ever been done to address this issue, many physicians support such patients with dobutamine infusions for 12 to 24 hours before a spontaneous breathing trial. If one were to use this approach, then the inotropic agent may still be needed following extubation and weaned thereafter, because the work of breathing may remain high even if the endotracheal tube is not contributing to the increase in airway resistance.

**IMPORTANT UNKNOWNS**

Perhaps the most important unknown in assessing the hemodynamic effect of ventilation is the assessment of cardiovascular reserve and the effects of breathing on hyperinflation and the swings in ITP. To date, no set of physiologic variables derived from measures of respiratory performance or ventilatory reserve have proven reliable in predicting weaning outcome in the setting of acute ventricular failure. In large part, we believe, this failure reflects an underappreciation of the role that cardiovascular responsiveness plays in weaning and the inadequate methods for assessing cardiovascular reserve. In essence, physicians have chosen an oversimplistic approach, and now institute blind daily spontaneous breathing trials to define when a patient is capable of weaning. Although this approach is commendable in its simplicity, it still places patients who would obviously fail such trials at risk of coronary ischemia, ongoing respiratory muscle fatigue, and impaired gas exchange secondary to LV failure and hydrostatic pulmonary edema. Because the breathing pattern can change in just one breath, and physiologically significant hyperinflation can occur in a single breath, it is probably impossible to predict with accuracy whether one can wean or not from mechanical ventilatory trials using static measures.

**THE FUTURE**

The future of heart–lung interactions is wedded to both new and evolving methods of mechanical ventilation and our increasing reliance on clinical techniques, like the spontaneous breathing trial, to predict weaning success and the need for supplemental cardiovascular support. To the extent that new techniques of ventilator support follow the principle of proportional assist ventilation, they will limit the detrimental effects of positive-pressure ventilation and patient–ventilator dyssynchrony, minimizing the work of breathing. Mask CPAP will need to be titrated to minimize negative swings in...
ITP. To the extent that mask CPAP abolishes swings in ITP, it promotes LV ejection efficiency and minimizes LV failure. The use of pressure-limited ventilation in patients with ALI has resulted in decreases delivered tidal volume. Because increases in ITP are linked to changes in lung volume, these newer ventilatory strategies must result in less cardiovascular dysfunction than were seen with use of higher tidal volumes and peak airway pressures used in the past.

Acute care medicine is evolving from a static treatment and monitoring center into a proactive diagnostic and treatment center. We now use pulse pressure and stroke volume variation during positive-pressure ventilation to identify those hemodynamically unstable patients who are likely to respond to a volume challenge with an increase in cardiac output, and by how much. In the future, patients would be better served if clinicians were to examine the immediate hemodynamic effects of spontaneous breathing trials before patients progressed to ventilatory and cardiovascular deterioration. Invasive and noninvasive measures of tissue oxygenation using data derived from pulmonary artery catheters, central venous catheters, pulse oximetry, and newer evolving noninvasive technologies will result in a dynamic assessment of impending respiratory failure and its causes. The future is upon us, and will be led by the firms that are developing newer noninvasive technologies that address these specific issues.235

SUMMARY AND CONCLUSIONS

Our understanding of clinically relevant cardiopulmonary interactions has advanced far over the past 50 years. What was once cloaked with much mystery, now seems obvious. Still, complacency in the application of these principles at the bedside should be avoided. Just as we thought we knew all there was to know about COPD 20 years ago, the entire management scheme was altered with a better understanding of dynamic hyperinflation and auto-PEEP.234,235 Similarly, the exact nature by which heart–lung interactions define myocardial ejection efficiency and myocardial O₂ requirements in both ALI states and severe airflow obstruction remain to be defined.

The hemodynamic effects of ventilation are multiple and complex, but can be grouped into four clinically relevant concepts. First, spontaneous ventilation is exercise. In patients’ increased work of breathing, initiation of mechanical ventilation improves O₂ delivery to the remainder of the body by decreasing O₂ consumption. To the extent that mixed venous PₓO₂ increases, arterial PᵧO₂ will also increase without any improvement in gas exchange. Similarly, weaning from mechanical ventilatory support is a cardiovascular stress test. Patients who fail weaning exhibit cardiovascular insufficiency during the failed weaning attempts. Improving cardiovascular reserve or supplementing support with inotropic therapy may allow patients to wean.

Second, changes in lung volume alter autonomic tone and pulmonary vascular resistance, and high lung volumes compress the heart in the cardiac fossa, similarly to cardiac tamponade. As lung volume increases, so does the pressure difference between airway and Ppl. When this pressure difference exceeds pulmonary artery pressure, pulmonary vessels collapse as they pass from the pulmonary arteries into the alveolar space, increasing pulmonary vascular resistance. Thus, hyperinflation increases pulmonary vascular resistance and pulmonary artery pressure, which impede RV ejection. Decreases in lung volume below FRC, as occurs in ALI and alveolar collapse, also increase pulmonary vasoconstrictor tone by the process of hypoxic pulmonary vasoconstriction. Recruitment maneuvers, PEEP, and CPAP may reverse hypoxic pulmonary vasoconstriction and reduce pulmonary artery pressure.

Third, spontaneous inspiratory efforts decrease intrathoracic pressure. Because diaphragmatic descent increases intraabdominal pressure, these combined effects cause PRA inside the thorax to decrease but venous pressure in the abdomen to increase, which markedly increases the pressure gradient for systemic venous return. Furthermore, the greater the decrease in intrathoracic pressure, the greater the increase in LV afterload for a constant arterial pressure. Mechanical ventilation, by abolishing the negative swings in intrathoracic pressure, selectively decreases LV afterload, as long as the increases in lung volume and intrathoracic pressure are small.

Finally, positive-pressure ventilation increases ITP. Because diaphragmatic descent increases intraabdominal pressure, the decrease in the pressure gradient for venous return is less than would otherwise occur if the only change were an increase in PRA. In hypovolemic states, however, positive-pressure ventilation can induce profound decreases in venous return. Increases in intrathoracic pressure decreases 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 O₂ demand.

REFERENCES

Chapter 36 Effect of Mechanical Ventilation on Heart–Lung Interactions


Chapter 36
Effect of Mechanical Ventilation on Heart-Lung Interactions


Part IX Physiologic Effect of Mechanical Ventilation


Chapter 36 Effect of Mechanical Ventilation on Heart–Lung Interactions


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AQ1: Figure 36-1, 2, 3, 4, 5, 6, 12 and 13 are redrawn. Please check.
AQ2: Please identify where by section title.
AQ3: By “next section” do you mean “Effect of Intrathoracic Pressure” or the next major section, Spontaneous Breathing Versus Mechanical Ventilation”? Please replace “in the next section” with “in “XYZ”” replacing XYZ with the section title.
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