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REVIEW ARTICLE

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The hemodynamic consequences of mechanical ventilation: an evolving story

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Introduction

A primary goal of the cardiopulmonary system is to continuously deliver adequate amounts of oxygen (O_2) to meet the metabolic demands of the organism. Persistent tissue hypoperfusion results in end-organ dysfunction and death. Preventing initial tissue dysoxia by optimizing cardio-pulmonary function in post-operative surgical patients at risk for the development of multiple organ failure substantially increases the changes of a successful outcome [1]. Often such optimization requires the use of artificial mechanical ventilation, invasive monitoring and potent pharmacological therapies. Although artificial ventilation, in particular, may improve pulmonary gas exchange and restore arterial blood acid-base balance in those in whom it was previously deranged, it may also disrupt an already fragile hemodynamic balance developed in response to these disturbances. Presently, clinical practice defends a therapeutic approach which favors maintaining a minimal level of systemic O_2 delivery to tissues so as to prevent tissue hypoxia. In practice this is accomplished by maintaining cardiac output and arterial perfusion pressure with the patient in a stable metabolic condition. Ventilation may modify all of these processes. Thus, an understanding of cardiopulmonary interactions is central to the effective implementation of intensive care treatment programs.

Fundamentals of heart-lung interaction

Ventilation and ventilatory maneuvers can have profound cardiovascular effects which can be either beneficial or detrimental. The reader is referred to several recent in-depth reviews on this subject for a fuller discussion of the foundations of heart-lung interactions [2–4]. In this review, we shall first define the known processes involved in clinically-relevant heart-lung interactions, discuss the present-day limitations in applying this knowledge at the bedside and them explore recently described and potential future methods of both assessing heart-lung interactions and using them at the bedside to diagnose cardiovascular insufficiency.

Both spontaneous ventilatory efforts and passive IPPV can support tidal breathing. Both alter lung volume and intrathoracic pressure (ITP). Although lung volume increases above a resting end-expiratory level with both forms of ventilation, the swings in ITP are opposite in the two modes of ventilation. Thus, most hemodynamic differences between spontaneous ventilation and intermittent positive-pressure ventilation (IPPV) reflect differences in ITP and the energy necessary to create these swings. Importantly, since changing lung volume can profoundly alter pulmonary vascular resistance and capacitance and at high lung volumes may compress the heart in the cardiac fossa, its hemodynamic effects can not be dismissed. Accordingly, changes in both lung volume and ITP need to be considered when assessing the hemodynamic effects of either spontaneous ventilation or IPPV [5]. All hemodynamic effects of ventilation can be simply grouped into processes that affect left ventricular (LV) preload, contractility and afterload.

Preload: Clinically, LV preload is synonymous with LV end-diastolic volume (EDV). By the Frank-Starling mechanism, increases in LV EDV should increase cardiac output and vice versa. The two primary mechanisms by which LV EDV may be altered is by varying either systemic venous return or LV diastolic filling. If systemic venous return decreases, for example, then LV EDV must eventually decrease as well. However, changes in systemic venous return may also alter LV diastolic compliance, by modifying the relationship between distending pressure and volume. LV diastolic compliance can be altered by changes in right ventricular (RV) EDV, by the process of ventricular interdependence [6, 7]. Since both ventricles share a common interventricular septum and are housed in a common pericardial sac which limits maximal bi-ventricular volume, increases in RV EDV will make the left ventricle less able to distend. Similarly, decreasing RV EDV will increase LV diastolic compliance.

How then may ventilation alter LV EDV? Since the vena cavae and right atrium are within the thorax, increasing ITP will cause a directionally similar increase in right atrial pressure (Pra) when measured relative to atmospheric pressure. Pra is the back pressure to systemic venous return. However, the downstream pressure for venous return, referred to as mean systemic pressure, senses atmospheric pressure as its background pressure. Selective increases in Pra will reduce the driving pressure for venous return. Thus, the primary effect of IPPV is to increase ITP impeding venous return by increasing Pra. If this fall in venous blood flow is sustained then LV EDV must ultimately be reduced, thus decreasing cardiac output by decreasing LV preload (Fig. 1).

Increases in ITP decrease venous flow by inducing a parallel increase in Pra, decreasing the pressure gradient for venous return. Although some recent data suggest that the pressure gradient for venous return may not decrease as much, because intra-abdominal pressure also rises [8], during IPPV inspiration venous return a decrease is seen. During spontaneous ventilation, when the inspiratory swings in both ITP and Pra become negative, venous return increases. This phenomenon is referred to as the "thoracic pump" and is an important mechanism to maintain maximal venous return under both resting conditions and exercise. However, if Pra becomes very negative, as usually occurs with marked spontaneous inspiratory efforts or in the setting of upper airway obstruction, then venous flow becomes flow-limited because the veins collapse as they pass from extrathoracic to intrathoracic domains [9]. Accordingly, once flow limitation occurs, markedly increasing the fall in ITP should not increase venous return more than less negative swings in ITP (Fig. 1).

Similarly, lung distention above normal resting lung volume will increase pulmonary vascular resistance and

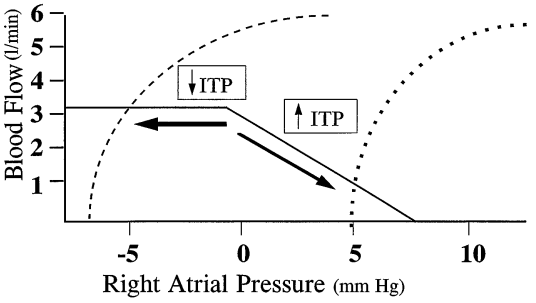

Fig. 1 Effect of changes in intrathoracic pressure (ITP) on the balance between venous return and cardiac output as shown on the cardiac output (venous return) to right atrial pressure relation. Venous return decreases linearly as right atrial pressure increases above 0 mm Hg. However, as right atrial pressure decreases below atmospheric pressure its maximal flow is limited by venous collapse. Left ventricular (LV) output increases progressively as filling pressure increases (Starling's Law of the Heart) whereas changes in ITP shift the LV function curve in a parallel fashion on the venous return curve. Decreases in ITP minimally increase cardiac output while increases in ITP may profoundly decrease cardiac output

at high lung volumes will compress the heart in the cardiac fossa. Both of these processes can reduce LV EDV, but by different mechanisms. As lung volume increases, the small pulmonary vessels become increasingly compressed as they traverse the space between the interstitial compartment and enter the alveolar wall due to the obligatory difference in surrounding pressure between the interstitium, which approximates ITP, and the alveoli, which approximates airway pressure. Since the pressure gradient determining lung distention, or transpulmonary pressure is equal to airway pressure minus ITP, as lung volume increases this extravascular pressure difference between the interstitium and the alveoli increases proportionally. When transpulmonary pressure exceeds pulmonary artery pressure the vasculature will collapse, thus limiting flow. Likewise, decreases in lung volume will also increase pulmonary vasomotor tone, but as a result of nitric oxide-dependent hypoxic pulmonary vasoconstriction.

Interestingly, if LV filling is limited by RV EDV, as may occur in cor pulmonale, then IPPV inspiration by transiently decreasing venous return [9–15], will decrease RV EDV [9–16] and by ventricular interdependence increase LV diastolic compliance. Thus, IPPV inspiration may be associated with a transient increase in LV diastolic compliance and LV EDV increasing LV stroke volume and arterial pulse pressure by the Frank-Starling mechanism, if RV dilation co-exists. This phenomenon is referred to as "Reversed Pulses Paradoxus." Furthermore, as lung volume increases above functional residual capacity, pulmonary vascular resistance increases and may impede RV ejection causing RV ESV to increase. If venous return continues, then RV

EDV will increase on the subsequent beat reducing LV diastolic compliance. Hyperinflation is common in acute respiratory failure associated with airflow obstruction. In acute lung injury states, the opposite change in lung volume occurs. Lung volumes are reduced because of alveolar flooding and increased interstitial recoil increasing pulmonary vasomotor tone by the mechanism of hypoxic pulmonary vasoconstriction. Increased pulmonary vascular resistance is common in ventilator-dependent patients with lung disease. Accordingly, measures of LV filling pressure may not reflect either absolute or directionally similar changes in LV EDV if RV EDV also changes. However, when large swings in both ITP and lung volume are minimized, ventricular interdependence appears to play a minor role in LV performance [16]. Although increasing ITP can increase cardiac output in patients with heart failure, most data suggest that decreases in both LV ESV and LV afterload associated with increased ITP, rather than increases in preload, account for a majority of the observed improvement in cardiac output in these circumstances [17].

Despite these known and documented negative hemodynamic effects of IPPV on instantaneous venous return, numerous studies [18–27] have shown that for the same LV filling pressure, LV EDV and presumably, rate of venous return, increasing ITP can also increase LV stroke volume (SV) and steady state cardiac output by decreasing LV end-systolic volume (ESV). This IPPV-associated cardiac augmentation is usually appreciated when LV contractility is impaired and intravascular volume is expanded. In these conditions, although IPPV decreases LV volumes, ESV decreases more than EDV [17]. Based on the above model, the ultimate hemodynamic effect of ventilation represents the balance of forces which alter LV EDV and ESV.

Contractility and afterload: If LV ejection is a dynamic process wherein contractile elements increase their tension and shorten whenever possible over a predefined interval which encompasses myofibril length, developed tension, rate of shortening and time. If LV outflow pressure were to suddenly increase, the LV would not eject as much of its SV as it might if the ejection pressure were lower. The relationship between varying LV ejection pressure and LV ESV appears to be independent of LV EDV and is called the LV end-systolic pressure-volume relationship (ESPVR). This relationship is important in analyzing the effects of ventilation on cardiac function because it allows the observer to separate out the effects of ventilation on both contractility and afterload. LV contractility varies quantitatively with the slope of the LV ESPVR [28]. Increases in LV contractility increase the LV ESPVR slope, whereas decreases in contractility are associated with a decrease. Similarly, if contractility is unaltered but afterload varied, then both LV ESV and end-systolic pressure will co-vary but along the line described by the ESPVR. Clinically, these concepts play an important role in defining myocardial energetics and risk of developing myocardial ischemia because both absolute LV ESV and the slope of the LV ESPVR have primary importance in determining myocardial O_2 demand (MVO_2). As shown by Suga et al. [28] MVO_2 is not proportional to LV stroke work (the area inside the LV pressure-volume loop of one cardiac cycle) alone, but also includes an internal work characterized by the ESPVR-defined "triangle" subserved by the ESPVR, ESV and diastolic compliance, also known as elastance-defined potential work. These points are described in Fig. 2. The sum of LV stroke work plus the ESPVR-defined potential work triangle, the pressure-volume area, known as (PVA) is proportional to MVO_2. Any process that reduces PVA will reduce MVO_2 and vice versa.

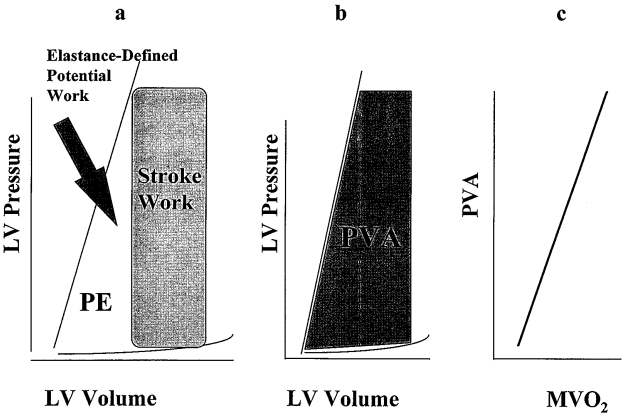

Fig. 2 **a** Inter-relation between left ventricular (LV) pressure and volume during one cardiac cycle (stroke work), and the potential energy (PE) defined by the end-systolic elastance to the left of it. **b** The sum of stroke work and PE being defined as the pressure-volume area (PVA). **c** Relation between PVA from second graph and myocardial O_2 consumption (MVO_2). Note that MVO_2 is linearly related to PVA such that increases in either stroke work or PE will increase MVO_2

How then may ventilation alter LV PVA? Since LV ejection pressure is equal to the pressure gradient from inside the LV wall to the outside, where inside pressure during ejection can be approximated to arterial pressure and outside pressure can be approximated to ITP, isolated changes in ITP will inversely alter LV ejection pressure. Increasing ITP, as may occur during IPPV inspiration will decrease LV ejection pressure. Decreasing LV ejection pressure for a constant LV EDV will decrease both ESV and PVA but not alter the slope of the LV ESPVR, whereas spontaneous ventilation by decreasing ITP increases both PVA and MVO_2. If IPPV increased LV contractility, then it should be reflected by an increase in the slope of the LV ESPVR [28]. Potentially IPPV could increase contractility if by reducing

LV PVA it also reverses myocardial ischemia. However, this scenario has not been frequently documented. More often IPPV merely decreases LV afterload, without changing contractility, such that the slope of the LV ESPVR remains constant while ESV decreases.

In canine models of AVF induced by β-adrenergic blockade [29] and patients with congestive heart failure (CHF) [30], increases in ITP increase cardiac output despite decreasing LV EDV. This is analogous to peripheral vasodilator therapy in heart failure, in which cardiac output increases with a minimal decrease in arterial pressure but with a significant decrease in LV filling pressure [27, 31, 32]. Clinical studies show that in the setting of severe LV dysfunction with an expanded intravascular volume, increasing ITP improves LV performance and increases cardiac output despite decreasing LV volumes [23, 24, 33], and agree with initial studies using high frequency jet ventilation (HFJV) to minimize lung volume changes during IPPV [18]. Thus, when LV function is normal, rises in ITP lowers cardiac output by decreasing LV filling pressure. When LV function is impaired, although rises in ITP lowers LV filling pressure, cardiac output increases because of the decrease in LV afterload predominated as long as LV EDV remains above a minimal value. Clinical studies support the concept of a minimal preload threshold for increased ITP-cardiac augmentation in heart failure [23, 33–35].

Using cardiac cycle-specific increases in ITP, the selective effects of ITP on venous return and LV ejection can be identified. The ventilator-induced increase in ITP can be delivered at specific points within the cardiac cycle and also with each beat. This is referred to as synchronous (sync) HFJV in distinction to conventional HFJV or IPPV delivered at a fixed rate not equal to the HR [18]. The sync HFJV technique is powerful because it allows for selective examination of the effects of increases in ITP on specific parts of the cardiac cycle in a steady state environment. Thus, ventricular function and ESPVR can be assessed during selective steady state increases in ITP at specific points in the cardiac cycle at a constant lung volume. Sync HFJV delivered either late in diastole (following atrial systole) or in systole will not decrease LV SV relative to apneic levels [19], even in hypovolemia [36]. This response can be used to define preload-dependency or normal cardiovascular function in either animals or humans. In heart failure states, systolic sync HFJV increases LV SV and cardiac output to a greater amount than during diastolic sync HFJV or apnea [19]. Sync HFJV delivered during ejection in AVF states increases arterial pulse pressure by selectively increasing SAP equal to the increase in ITP. This form of reversed pulsus paradoxus can be used to define afterload-dependency in either animals or humans. Furthermore, coronary sinus O_2 saturation increased during systolic sync HFJV, consistent with either an increased coronary blood flow, a decreased MVO_2, or both. Subsequent studies from other laboratories have demonstrated that the increased coronary sinus O_2 saturation was due to decreased MVO_2 [25]. These data are also important because they lend support to the concept that increasing ITP will improve LV ejection efficiency by increasing LV stroke work relative to MVO_2 as discussed above.

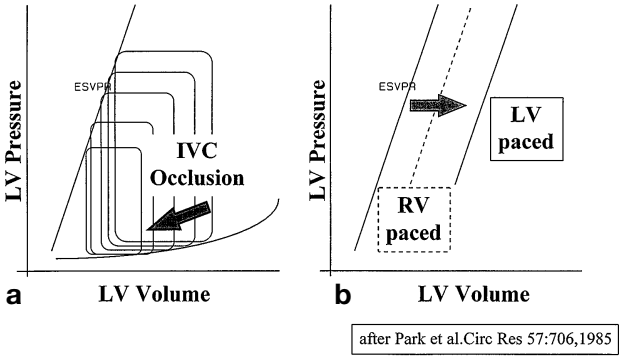

Fig. 3 **a** Schematic demonstration of generation of the left ventricular (LV) end-systolic pressure-volume relationship (ESPVR) by rapid inferior vena caval (IVC) occlusion. Note that as end-diastolic volume decreases, both end-systolic volume and pressure decrease along a pressure-volume domain. **b** Effect of abnormally conducted beats (asynchronous LV contraction) on the LV ESPVR. Note that with progressive asynchronous contractions (LV pacing as compared to RV pacing) the LV ESPVR is shifted further to the right without a change in its slope

However, the mechanism by which increased ITP interacts with LV contractility independent of changes in ejection pressure remains unclear and is probably more complex than the process described above. LV ESV is determined by three interdependent processes: ejection pressure, synchrony of contraction among LV contractile elements, and the slope of the LV ESPVR [37–39]. The slope of the LV ESPVR can be altered by changes in cardiac contractility, coronary blood flow, sympathetic tone, and heart rate [38, 40, 41] all of which may be influenced by ventilation. Furthermore, to the extent that parallel segments of contracting myocardium do not contract synchronously, global LV ejection efficiency will be impaired and the LV ESPVR will be shifted to the right in a parallel fashion with pressure on the *x* axis in a manner analogous to that seen with ventricular paced beats which increase asynchrony of contraction [42]. When LV pacing is done from increasingly asynchronous regions (LV versus RV) the ESPVR shifts further to the right without a measurable change in slope (Fig. 3). This scenario commonly occurs in ischemic heart disease as manifest by regional wall motion abnormalities. To the extent that asynchronous segments are brought into alignment with the remainder of the ejecting heart, LV ESV decreases augmenting LV ejection and decreasing MVO_2. One mechanism by

which delayed segmental contraction can be reversed is by reducing LV ejection pressure. Relevant to this argument, we recently showed that increases in synchrony of contraction among regions of myocardium will induce a parallel shift of the ESPVR to the left [43], thereby decreasing MVO_2.

Since ejection is coupled to arterial pressure through SV and ITP, as described above, the effects of ventilation on LV ejection can be analyzed from the perspective of the circulation by examining the behavior of the systolic arterial pressure (SAP) during ventilation. Specific IPPV-associated changes in systolic arterial pressure may characterize preload or afterload-dependency. The group headed by Perel demonstrated that when compared with an apneic baseline, SAP decreased more during IPPV in hypovolemic dogs than in fluid resuscitated dogs [44]. Presumably due to an associated LV EDV decrease, IPPV increased SAP during fluid-resuscitated AVF analogous to the "reversed pulsus paradoxus" described in patients with CHF [45]. Whether or not LV SV increases during IPPV inspiration is uncertain and its mechanisms unclear. Potentially, LV SV could increase, either from a rise in LV filling (increased end-diastolic volume) or a decrease in LV ejection pressure. LV end-diastolic volume could increase during inspiration by an increase in pulmonary venous blood flow, as alveolar vessels are squeezed by the increasing transpulmonary pressure [46], or by an increase in LV diastolic compliance, as RV EDV decreases owing to the fall in systemic venous return to the right ventricle. Both LV afterload and ESV could decrease, if inspiration-associated increases in ITP decreases transmural LV ejection pressure [29]. However, changes in SAP during IPPV could involve processes independent of changes in LV preload or afterload. SAP could vary during IPPV because of direct transmission of ITP to the aorta, similar to a Valsalva maneuver. Inspiration would increase SAP similar to the initial phase (phase 1) of a Valsalva maneuver [47]. SV would eventually decrease, because of the associated fall in venous return [48], although SAP would remain elevated as long as ITP remained high. Most importantly, however, the increase in SAP would be in phase with inspiration, whereas any decrease would not. Furthermore, SAP could fall during IPPV expiration because of the withdrawal of ITP-supported arterial pressure in the setting of decreased aortic blood volume. Here the fall in SAP would invariably follow inspiration, but need not reflect a decrease in LV SV. Furthermore, these ventilation-associated changes in SAP need not be related to changes in LV volume, nor be influenced by the level of LV contractility, but would reflect only the changes in ITP. Importantly, all these hypotheses, though attractive have never been validated by analysis of IPPV-induced changes in either LV EDV or ESV.

Limitations in our understanding of the effects of ventilation on LV performance

Although ventilation and ventilatory maneuver have profound hemodynamic effects, a practical clinical approach to understanding these interactions still eludes us primarily because of difficulties in estimating LV EDV, uncertainties of the relationship between global and regional myocardial function, and defining the limits of cardiac augmentation or impairment by changing ITP. The primary issues which are unresolved regarding the interaction between ventilation and cardiac ejection performance can be summarized as: 1) the effect of ventilation and ventilatory maneuvers on LV EDV, and 2) the effect of increases in ITP on LV ESPVR and LV ejection synchrony, and 3) the limits of these interactions. The practical problem is to define and measure accurately LV pressure and volume in a non-invasive fashion during ventilation in the clinical setting. From the above discussion at least one thing should be clear: the mechanisms by which LV function is altered during ventilatory maneuvers in any given subject remains controversial [49–57]. Several factors described above may explain the cardiopulmonary dysfunction observed clinically, including hypoxia-induced myocardial dysfunction [54], RV failure with RV chamber enlargement limiting LV filling (ventricular interdependence) [6, 58–61], and ventilation-associated changes in ITP, which by altering the pressure gradient for systemic venous return and transmural LV pressures, change LV preload and afterload [55].

Conceptually, ventilation induces cyclic changes in lung volume and intrathoracic pressure (ITP). Changes in ITP should affect the pressure gradients for both systemic venous return [9–12, 14, 15, 62] and LV ejection [63–65]. The resulting cardiac output will depend on the degree to which LV ejection is dependent on EDV and ejection pressure. Increasing lung volume can increase pulmonary vascular resistance thus impeding right ventricular (RV) ejection and at high lung volumes may compress the heart in a fashion analogous to tamponade. When LV function is normal, increased ITP decreases cardiac output by decreasing LV preload (Fig. 4). When cardiac contractility is reduced, increased ITP may increase cardiac output by decreasing LV afterload despite decreasing LV preload, in a manner similar to systemic vasodilator therapy (Fig. 5). Accordingly, the hemodynamic consequences of ventilation are considered to reflect the combined actions of increasing lung volume and changing ITP on both ventricular filling (EDV), and ejection (ESV). Those actions plus any work cost of breathing define the cardiovascular stress of either spontaneous or positive-pressure ventilation. Unfortunately, this simplistic approach does not accurately model the balance of forces determining heart-lung interactions nor does it explain commonly

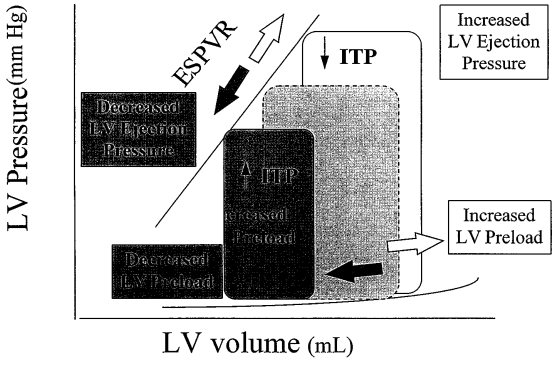

Fig. 4 Relation between left ventricular (LV) pressure and volume as intrathoracic pressure (ITP) increases (*shaded arrows*) or decreases (*open arrows*) when LV contractility is normal, as defined by the LV end-systolic pressure-volume relation (ESPVR). Note that decreases in ITP increase LV end-diastolic volume more than they increase end-systolic volume causing LV stroke volume to rise. Whereas increases in ITP decrease LV end-diastolic volume more than they decrease end-systolic volume causing LV stroke volume to fall

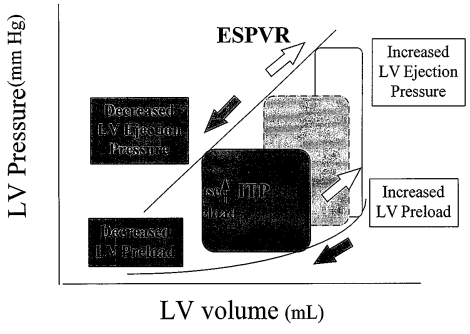

Fig. 5 Relation between left ventricular (LV) pressure and volume as intrathoracic pressure (ITP) increases (*shaded arrows*) or decreases (*open arrows*) when LV contractility is reduced, as defined by the LV end-systolic pressure-volume relation (ESPVR). Note that decreases in ITP increase LV end-diastolic volume less than they decrease end-systolic volume causing LV stroke volume to fall. Whereas increases in ITP decrease LV end-diastolic volume less than they decrease end-systolic volume causing LV stroke volume to rise

seen and clinically relevant hemodynamic effects of ventilation and weaning from ventilation for three important reasons which form the basis of recent and ongoing studies in both animals and humans.

This simple analysis breaks down at several points. First, the hemodynamic effects of positive and negative swings in ITP may not be mirror images of each other. Markedly negative swings in ITP do not increase venous return more than less negative swings in ITP, because venous return becomes flow-limited as ITP becomes more negative by more then – 5 cm H_2O owing to venous vascular collapse [17] (Fig. 1). However, increasingly negative swings in ITP will progressively increase LV ejection pressure and imped LV ejection. Accordingly, abolishing large negative ITP swings should selectively reduce LV afterload without impairing venous return, thus improving LV performance and cardiac output. As shown in Fig. 4 and 5, decreasing ITP (white arrows) will decrease LV SV, and increase PVA and therefore, MVO_2. On the other hand, increases in ITP (gray arrows) should progressively and continually impede venous return to zero, proportionally reducing LV EDV. However, increasing ITP should only improve LV ejection to a limited degree because LV ESV can only decrease so much before it reaches some minimal volume, owing to the relative steepness of the LV ESPVR. It follows that the magnitude of change in LV ejection by increases and decreases in ITP are inversely proportional to contractility. Although unproved, this assumption has important clinical relevance. Increased ITP compromises LV preload by decreasing systemic venous flow [9–13, 18, 66], intrathoracic blood volume [18, 67], and LV EDV [55, 60, 68]. Although sustained increases in ITP must be self-limiting in their ability to augment cardiac function by reducing LV afterload because of associated decreased venous return, therapeutic maneuvers that selectively abolish markedly negative swings in ITP should selectively reduce LV afterload without altering either LV EDV or organ perfusion pressure, even in the setting of hypovolemia. Considering that large negative swings in ITP commonly occur with spontaneous inspiration during severe asthma, restrictive (pulmonary fibrosis, pulmonary edema) and obstructive lung disease, a better ventilatory approach to these problems may lead to a more rational clinical management of patients with lung disease. Similarly, increasing ITP should ony increase cardiac output if venous return is not reduced. This hypothesis, however, remains to be proven.

Second, if changes in venous return and ejection pressure were the only forces determining heart-lung interactions, then the application of 5 cm H_2O positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) would not induce much hemodynamic perturbation because the increases in ITP and lung volume would be small. However, numerous clinical and animal studies consistently demonstrate improvement in cardiac output during heart failure at these low levels of PEEP or CPAP. Furthermore, even when IPPV does significantly increase ITP, the decrease in LV ESV often exceeds amounts predicted solely by the reduction in LV ejection pressure. An attractive theory explaining the beneficial effects of low levels of increased airway pressure in heart failure evokes mechanical compression of the heart by the lungs in the cardiac fossa via two distinct processes. First, compression of an over-distended RV improving LV filling, and second, by compression of bulging surfaces of the LV free wall associated with regional wall motion abnormalities

(RWMA) tending to make asynchronous LV regions ejection more efficient. The former effect would selectively increase LV diastolic compliance, whereas the latter would shift the LV ESPVR, as a marker of contractility, to the left, with volume on the *x* axis, without a change in its slope (no change in contractility). Thus, to the extent that ITP-induced changes in LV ejection pressure summarize or disperse the phase relation of shortening among parallel LV contractile elements, ejection efficiency will increase and LV volumes decrease. Since MVO_2 is proportional to the pressure-volume area (Fig. 2), increased synchrony should increase LV ejection efficiency. Neither of these hypotheses has been proven but both can be easily tested using new measuring techniques.

Third, many patients with otherwise adequate respiratory mechanical reserve fail to wean from mechanical ventilatory support. Since spontaneous ventilation the works muscules it places an increased stress on the cardiovascular system. Thus, such ventilator-dependent patients may have inadequate cardiac reserve which could be corrected by increasing LV function (e.g. increased inotropy, afterload reduction). Thus, we hypothesize that contractile reserve and associated visceral organ perfusion may be useful predictors of which patients need IPPV and which need increased inotropic support to facilitate weaning. Marked negative swings in ITP commonly occur in subjects in acute respiratory distress. Inspiration against a partially or totally occluded airway markedly decreases ITP, raising LV afterload rapidly and leading to acute pulmonary edema [69–77]. During acute asthmatic attacks in children, peak negative ITP can be – 40 cm H_2O and mean tidal ITP maintained between – 24 and – 7 cm H_2O [20] increasing both LV afterload [63] and systemic venous return [10] and promoting the formation of pulmonary edema. Additionally, changing from spontaneous to IPPV during acute myocardial infarction by unloading the LV decreases electrocardiographic (ECG) evidence of myocardial ischemia [49]. Importantly, this beneficial effect occurs only after the negative swings in ITP are abolished [34, 35]. In fact, as shown by Lemaire et al., ITP-induced LV failure can occur immediately (< 5 min) upon cessation of ventilatory support in patients with LV dysfunction [78]. In that study, mean esophageal pressure, as a surrogate for ITP, decreased from 5 ± 3 to -2 ± 3 mm Hg and acute LV failure rapidly developed as evidenced by a rise in pulmonary artery occlusion pressure from 8 ± 5 to 25 ± 13 mm Hg. Thus, severe life threatening LV dysfunction can rapidly develop, unmasking occult LV failure during the initiation of spontaneous breathing. Furthermore, spontaneous ventilation can be thought of as an exercise stress test. Those with limited cardiovascular reserve may not be able to sustain spontaneous ventilation. Mohsenifar et al. [79] assessed the effect of weaning on gastric pHi, as a marker of splanchnic blood flow, in 29 ventilated patients deemed ready for weaning. Patients who could not be weaned had a substantially reduced gastric intramucosal pH (pHi) from 7.36 during IPPV to 7.09 during weaning. Patients who were successfully weaned showed no change in pHi (7.45 to 7.46). Thus, occult cardiovascular insufficiency may play a major role in the development of failure to wean in critically ill patients. If cardiovascular insufficiency is a major determinant of weaning success, then it would explain the poor predictive value of traditional weaning parameters. Considering cardiovascular status in the assessment of ventilator-dependent patients may improve predictive power and suggest specific therapeutic interventions.

Clinical implications of these frontiers of research: The supposition that removing large negative swings in ITP should selectively decrease LV ejection pressure without altering LV preload is relevant to many disease states, such as asthma, ARDS and upper airway obstruction, all of which are associated with profoundly negative swings in ITP during spontaneous ventilation. Unlike other forms of afterload reduction therapy, since arterial pressure should not be decreased by removing negative swings in ITP, organ perfusion pressure should be not be reduced. Improving LV ejection effectiveness by increasing airway pressure by reducing asynchrony of myocardial contraction should reduce ischemic myocardial dysfunction. Regional wall motion abnormalities are the most common cardiac abnormality and some degree of asynchrony occurs in normal hearts. Thus, increasing the synchrony of myocardial contraction would represent a novel mechanism by which LV ejection could be improved without increasing MVO_2. Finally, spontaneous ventilation is an exercise stress test, and weaning to spontaneous ventilation will induce LV dysfunction in patients with minimal LV contractile reserve. Many patients presently unable to be weaned from mechanical ventilation may have a primary cardiovascular etiology to their ventilator dependency.

Future studies

Clearly, a major limitation in the investigations of heart-lung interactions in both animal models and man is the inability to accurately measure changes in LV volumes not between steady-state apneic systole and diastole, but throughout the entire ventilatory cycle, and cardiac cycle and from one region of the heart to another. Accordingly, several workers have focused on defining and validating novel monitoring techniques which can assess LV volumes across a variety of conditions [80–83]. These methodologies include on-line analysis of two-dimensional echocardiographic images, conduc-

tance catheter-derived signals and complex ventricular mechanical modeling.

However, methods of assessing LV volumes and performance have their limitations. Cineangiography dye alters LV contractility [84] and both intramyocardial markers [63] and ultrasonic crystals [43] represent highly invasive procedures which may alter heart-lung interactions and baseline cardiac function. Conductance catheter technology [82] and echocardiographic methods [80] are relatively new techniques which represent an apparent compromise between invasion and power in assessing LV function.

Conductance catheter: The conductance catheter accurately reflects volumes [85, 86] and when interfaced with a LV pressure signal allows construction of LV pressure-volume loops and LV ESPVR [86]. Recently, it has been used to measure both RV and LV pressure-volume relationships simultaneously in rabbits and piglets [82, 87]. This technique relies on the conductivity of blood in a closed space. Briefly, the volume of blood measured between two sensing electrodes can be considered to be a cylinder bounded by the endothelial surfaces, and change in conductance over time reflects change in volume through a relation which includes ratios of conductances, electrode spacing and empirical coefficients for each catheter type.

Several factors independent of actual changes in LV blood volume may alter the conductance volume signal. If they are to be used to assess heart-lung interactions, the relative independence of the catheter from this confounding variable must be documented. Variances in the sensed volume may arise from parallel conductance attributable to the surrounding myocardium, right ventricular blood pool and lung structure. Since lung tissue is primarily air-filled and low in conductivity, changes in lung volume probably do not alter LV conductance. Unpublished data from our laboratory documents this by demonstrating no change in volume signal in an asystolic dog during mechanical ventilation. Furthermore, IPPV inspiration appears to selectively reduce RV EDV and minimally affect LV volumes [88]. The presence or absence of the pericardium does not alter this effect, suggesting that IPPV decreases RV EDV by increasing ITP and not by stretching the pericardium [89].

Data gained from conductance catheters can be analyzed in novel ways that may extent its usefulness in assessing heart-lung interactions based on the above theoretical constructs. The LV is modeled by the catheter as a series of parallel discs stacked upon each other such that their inphase regional ejections are summarized to derive overall LV volume. Preliminary data in dogs shows that different LV regions display a small degree of asynchrony, such that they do not all reach minimal volume at the same time. This is illustrated for a canine model in figure 6 a. Interestingly, when this animal was

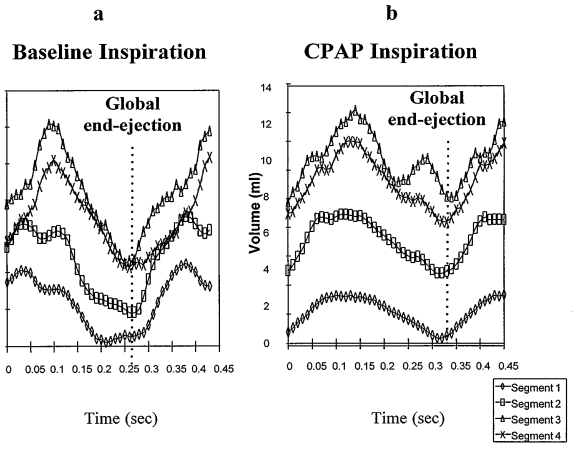

Fig. 6 Effect of lung expansion (end-inspiration) on the synchrony of contraction of different regions (segments) of the left ventricle in a acute closed-chested canine model. Segment 1 is in the apex and segment 4 is in the base. Note that without hyperinflation (baseline) *(panel a)* segment 1 reaches minimal volume prior to the remainder of the heart, whereas during 5 cm H_2O CPAP *(panel b)* all segments reach minimal volume at the same time. Thus, asynchrony of contraction may be minimized by lung expansion

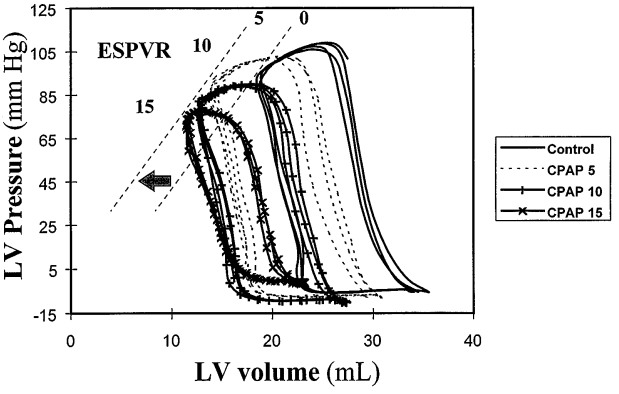

Fig. 7 Effect of progressive increases in CPAP on the left ventricular (LV) pressure-volume relation during inferior vena caval occlusion to define the end-systolic pressure volume relation (ESPVR). Note that increasing CPAP from 0 to 5 cm H_2O shifts the ESPVR to the left without changing stroke volume, whereas further increases in CPAP do not alter the position of the LV ESPVR but decrease LV volumes

given 5 cm H_2O CPAP the asynchrony was eliminated. If asynchrony impairs LV ejection, its removal should improve LV ejection efficiency. Based on the data described previously in figure 3, one would expect the LV ESPVR to shift to the left with the addition of CPAP. Indeed, as shown in figure 7, the addition of 5 cm H_2O CPAP shifts the ESPVR to the left of the zero CPAP relation. Note that apneic LV SV is preserved, which based on the PVA data shown in figure 1 represents an increase in LV ejection efficiency. This analysis also demonstrates why higher levels of CPAP in normal con-

ditions may decrease cardiac output. Higher levels of CPAP decrease EDV more than ESV decreases SV, without any further ESPVR shift. Since regions of the myocardium that reach minimal volume before LV end-systole eject too early, and those that reach it after global end-systole eject too late, their effective contribution to LV SV is less than their maximal regional volume change.

Echocardiography: Gorcsan et al. validated a novel automated border detection (ABD, acoustic quantification) algorithm for transesophageal echocardiography (TEE) to measure on-line LV areas in both dogs [90] and humans [80]. Briefly, acoustic quantification for TEE ABD uses the radio-frequency signals received which are analyzed separately from the standard 2D processing and converted to a power signal. This signal is smoothed, integrated and submitted to an edge detection algorithm by comparing it to an operator-adjusted threshold level, displayed on the video monitor and digitized for continuous on-line measures of LV area [90].

TEE ABD reflects LV volumes and can be used to assess contractility on-line in both dogs and humans in a highly sensitive and specific fashion [80, 91, 92]. Furthermore, one need only measure arterial pressure and LV area to accurately assess contractility and systolic function in humans since systolic LV and arterial pressure vary in a similar fashion during ejection [90]. Using TEE ABD, Gorcsan et al. [93] addressed the issue of parallel conductance and measurement reliability. They found that conductance catheter and TEE ABD-derived LV volumes varied similarly during both inferior vena caval occlusion, when RV volumes were low, and caval release, when RV volumes were high. It will be interesting to see if TEE ABD as a non-invasive monitor of LV volume, when coupled with arterial pressure recording, will permit the near total non-invasive analysis of heart-lung interactions at the bedside. Clearly, the development of this and other novel techniques will extend both our understanding of ventricular function and heart-lung interactions clinically beyond that defined by highly invasive techniques in the artificial environment of the operating room or animal laboratory.

The three limitations of our application of heart-lung interaction at the bedside are becoming smaller, but still exist. Once these more complex and perhaps subtler interactions are better delineated, a more rational approach to the management of the clinically ill ventilator-dependent patient may occur. Finally, to the extent that changes in SV or SAP during IPPV and spontaneous ventilation can identify preload or afterload dependency, rapid and repetitive techniques can be developed for the bedside assessment of the functional cardiovascular status of the critically ill patient.

References

1. Boyd O, Grounds RM, Bennett ED (1993) A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. JAMA 270: 2699–2707
2. Pinsky MR (1995) Hemodynamic Effects of Artificial Ventilation. In: Shoemaker, Ayres, Grenvik et al (eds) Textbook of critical care. W. B. Saunders & Co., Philadelphia, 3rd edition, pp 911–922
3. Miro AM, Pinsky MR (1994) Heart-lung interactions. In: Tobin MJ (ed) Principles and practice of mechanical ventilation. McGraw-Hill, Inc., New York, pp 647–671
4. Pinsky MR (1993) Heart-lung interactions. In: Pinsky MR, Dhainaut JF (eds) Pathophysiologic foundations of critical care. Williams and Wilkins, Baltimore, pp 472–490
5. Robotham JL, Rabson J, Permutt S, Bromberger-Barnea B (1979) Left ventricular hemodynamics during respiration. J Appl Physiol 47: 1295–1303
6. Taylor RR, Covell JW, Sonnenblick EH, Ross J Jr (1967) Dependence of ventricular distensibility on filling of the opposite ventricle. Am J Physiol 213: 711–718
7. Lloyd TC Jr (1982) Mechanical cardiopulmonary interdependence. J Appl Physiol 52: 333–339
8. Takata M, Robotham JL (1992) Effects of inspiratory diaphragmatic descent on inferior vena caval venous return. J Appl Physiol 72: 597–607
9. Guyton AC, Lindsey AW, Abernathy B, Richardson T (1957) Venous return at various right atrial pressures and the normal venous return curve. Am J Physiol 189: 609–615
10. Pinsky MR (1984) Determinants of pulmonary arterial flow variation during respiration. J Appl Physiol 56: 1237–1245
11. Morgan BC, Abel FL, Mullins GL, Guntheroth GW (1966) Flow patterns in cavae, pulmonary artery, pulmonary vein, and aorta in intact dogs. Am J Physiol 20: 865–877
12. Brecker GA, Hubay CA (1995) Pulmonary blood flow and venous return during spontaneous respiration. Circ Res 3: 210–214
13. Guyton AC (1963) Effect of cardiac output by respiration, opening the chest, and cardiac tamponade. In: Guyton AC, Jones CE, Coleman CE (eds) Circulatory physiology: cardiac output and its regulation. Philadelphia, W. B. Saunders, pp 378–386
14. Pinsky MR (1984) Instantaneous venous return curves in an intact canine preparation. J Appl Physiol 56: 765–771
15. Vesprille A, Jansen JRC (1985) Mean systemic filling pressure as a characteristic pressure for venous return. Pflügers Arch 405: 226–233
16. Bell RC, Robotham JL, Badke FR, Little WC, Kindred MK (1987) Left ventricular geometry during intermittent positive pressure ventilation in dogs. J Crit Care 2: 230–244

17. Naughton MT, Rahman MA, Hara K, Flora JS, Bradley TD (1995) Effect of continuous positive airway pressure on intrathoracic and left ventricular transmural pressures in patients with congestive heart failure. Circulation 91: 1725–1731
18. Pinsky MR, Matuschak GM, Klain M (1985) Determinants of cardiac augmentation by elevations in intrathoracic pressure. J Appl Physiol 58: 1189–1198
19. Pinsky MR, Matuschak GM, Bernardi L, Klain M (1986) Hemodynamic effects of cardiac cycle-specific increases in intrathoracic pressure. J Appl Physiol 60: 604–612
20. Pinsky MR, Marquez J, Martin D, Klain M (1987) Ventricular assist by cardiac cycle-specific increases in intrathoracic pressure. Chest 91: 709–715
21. Guimond J-G, Pinsky MR, Matuschak GM (1990) Effect of synchronous increase in intrathoracic pressure on cardiac performance during endotoxemia. J Appl Physiol 4: 1502–1508
22. Stein KL, Kramer DJ, Killian A, Pinsky MR (1990) Hemodynamic effects of synchronous high-frequency jet ventilation in mitral regurgitation. J Appl Physiol 69: 2120–2125
23. Grace MP, Greenbaum DM (1982) Cardiac performance in response to PEEP in patients with cardiac dysfunction. Crit Care Med 10: 358–360
24. Mathru M, Rao TLK, El-etr AA, Pifarre R (1982) Hemodynamic response to changes in ventilatory patterns in patients with normal and poor left ventricular reserve. Crit Care Med 10: 423–426
25. Fessler HE, Brower RG, Wise RA, Permutt S (1988) Mechanism of reduced LV afterload by systolic and diastolic positive pleural pressure. J Appl Physiol 65: 1244–1250
26. Beyar R, Halperin HR, Tsitlik JE, Guerci AD, Kass D, Weisfeldt ML, Chandra NC (1989) Circulatory assistance by intrathoracic pressure variations: optimization and mechanisms studied by a mathematical model in relation to experimental data. Circ Res 64: 703–720
27. Chatterjee K, Parmley WW, Ganz W, Forrester J, Walinsky P, Crexells CC, Swan HJC (1973) Hemodynamic and metabolic responses to vasodilator therapy in acute myocardial infarction. Circulation 48: 1183–1192
28. Suga H, Hayashi T, Shirahata M (1981) Ventricular systolic pressure-volume area as predictor of cardiac oxygen consumption. Am J Physiol 240: H39–H44
29. Pinsky MR, Summer WR, Wise RA, Permutt S, Bromberger-Barnea B (1983) Augmentation of cardiac function by elevation of intrathoracic pressure. J Appl Physiol 54: 950–955
30. Pinsky MR, Summer WR (1983) Cardiac augmentation by phasic high intrathoracic pressure support in man. Chest 84: 370–375
31. Pouleur H, Covell JW, Ross J Jr (1980) Effects of nitroprusside on venous return and central blood volume in the absence and presence of acute heart failure. Circulation 61: 328–337
32. Pagani M, Vatner SF, Braunwald E (1978) Hemodynamic effects of intravenous sodium nitroprusside in the conscious dog. Circulation 57: 144–151
33. Calvin JE, Driedger AA, Sibbald WJ (1981) Positive end-expiratory pressure (PEEP) does not depress left ventricular function in patients with pulmonary edema. Am Rev Respir Dis 124: 121–128
34. Rasanen J, Vaisanen IT, Heikkila J, Nikki P (1985) Acute myocardial infarction complicated by left ventricular dysfunction and respiratory failure. Chest 87: 158–162
35. Rasanen J, Heikkila J, Downs J, Nikki P, Vaisanen I, Vitanen A (1985) Continuous positive airway pressure by face mask in acute cardiogenic pulmonary edema. Am J Cardiol 55: 296–300
36. Matuschak GM, Pinsky MR, Klain M (1986) Hemodynamic effects of synchronous high-frequency jet ventilation during acute hypovolemia. J Appl Physiol 61: 44–53
37. Suga H, Sagawa K (1974) Instantaneous pressure-volume relationships and their ratio in the excised supported canine left ventricle. Circ Res 35: 117–134
38. Sagawa K, Suga H, Shoukas AA et al (1978) End-systolic pressure-volume ratio: A new index of contractility. Am J Cardiol 40: 748–756
39. Grossman W, Braunwald E, Mann T et al (1977) Contractile state of the left ventricle in man as evaluated from end-systolic pressure-volume relations. Circulation 56: 845–856
40. Kass DA, Maughan WL (1988) From "Emax" to pressure-volume relations: a broader view. Circulation 77: 1203–1212
41. Maughan WL, Sunagawa K, Burkhoff D, Sagawa K (1984) Effect of arterial impedance on end-systolic pressure-volume relation. Circ Res 54: 585–602
42. Park RC, Little WC, O'Rourke RA (1985) Effect of alteration of left ventricular activation sequence on the left ventricular end-systolic pressure-volume relation in closed-chest dogs. Circ Res 57: 706–717
43. Strum DP, Pinsky MR, Melick JA, Lutz JW (1995) The definition of regional systole matters: effective vs. maximal SV. FASEB J 9: A559
44. Perel A, Pizov R, Cotev S (1987) Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to grade hemorrhage. Anesthesiology 67: 498–502
45. Massumi RA, Mason DT, Vera Z, Zelis R, Otero J, Amsterdam EA (1973) Reversed pulsus paradoxus. N Engl J Med 289: 1272–1275
46. Brower R, Wise RA, Hassapoyannes C, Bromberger-Barnea B, Permutt S (1985) Effect of lung inflation on lung blood volume and pulmonary venous flow. J Appl Physiol 58: 954–963
47. Nishimura RA, Tajik AJ (1986) The Valsalva maneuver and response revisited. Mayo Clin Proc 61: 211–217
48. Robertson D, Stevens RM, Friesinger GC, Oates JA (1977) The effect of Valsalva maneuver on echocardiographic dimensions in man. Circulation 55: 596–602
49. Rasanen J, Nikki P, Heikkila J (1984) Acute myocardial infarction complicated by respiratory failure. The effects of mechanical ventilation. Chest 85: 21–28
50. Polianski JM, Huchon GJ, Gaudebout CC, Newth CJL, Murray JF (1986) Pulmonary and systemic effects of increased negative inspiratory intrathoracic pressure in dogs. Am Rev Respir Dis 133: 49–54
51. Michelson N (1960) Bilateral ventricular hypertrophy due to chronic pulmonary disease. Chest 38: 435–446
52. Fluck DC, Chandraseker RG, Gardner RV (1966) Left ventricular hypertrophy in chronic bronchitis. Br Heart J 28: 92–97
53. Rao BS, Cohn KE, Eldridge FL (1968) Left ventricular failure secondary to pulmonary disease. Am J Med 45: 229–241
54. Fishman AP (1971) The left ventricle, in "chronic bronchitis and emphysema". N Engl J Med 285: 402–404
55. Permutt S (1973) Physiologic changes in the acute asthmatic attack. In: Austen KF, Lichtenstein LM (eds) Asthma: physiology immunology and treatment. New York, Academic Press, pp 15–24

56. Stalcup SA, Mellins RB (1977) Mechanical forces producing pulmonary edema in acute asthma. N Engl J Med 297: 592–596
57. Luke MJ, Mehrizi A, Folger GM Jr, Rowe RD (1966) Chronic nasopharyngeal obstruction as a cause of cardiomegaly, cor pulmonale, and pulmonary edema. Pediatrics 37: 762–768
58. Brinker JA, Weiss JL, Lappe DL, Rabson JL, Summer WR, Permutt S, Weisfeldt ML (1980) Leftward septal displacement during right ventricular loading in man. Circulation 61: 626–633
59. Scharf SM, Brown R (1982) Influence of the right ventricle on canine left ventricular function with PEEP. J Appl Physiol 52: 254–259
60. Olsen CO, Tyson GS, Maier GW, Spratt JA, Davis JW, Rankin JS (1983) Dynamic ventricular interaction in the conscious dog. Circ Res 52: 85–104
61. Santamore WP, Heckman JL, Bove AA (1986) Right and left ventricular pressure-volume response to elevated pericardial pressure. Am Rev Resp Dis 134: 101–107
62. Cournand A, Motley HL, Werko L, Richards DW Jr (1948) Physiological studies of the effects of intermittent positive-pressure breathing on cardiac output in man. Am J Physiol 152: 162–174
63. Buda AJ, Pinsky MR, Ingels NB, Daughters GT, Stinson EB, Alderman EL (1979) Effect of intrathoracic pressure on left ventricular performance. New Engl J Med 301: 453–459
64. Robotham JL, Stuart RS, Borkon AM, Doherty K, Baumgartner W (1988) Effects of changes in left ventricular loading and pleural pressure on mitral flow. J Appl Physiol 65: 1662–1675
65. Scharf SM, Brown R, Saunders N, Green LH (1979) Effects of normal and loaded spontaneous inspiration on cardiovascular function. J Appl Physiol 47: 582–590
66. Scharf SM, Caldini P, Ingram RH Jr (1977) Cardiovascular effects of increasing airway pressure in the dog. Am J Physiol 232: H35–H43
67. Braunwald E, Binion JT, Morgan WL, Sarnoff SJ (1957) Alterations in central blood volume and cardiac output induced by positive-pressure breathing and counteracted by metaraminol (Aramine). Circ Res 5: 670–675
68. Dhainaut JF, Devaux JY, Monsallier JF, Brunet F, Villemant D, Huyghebaert MF (1986) Mechanisms of decreased left ventricular preload during continuous positive-pressure ventilation in ARDS. Chest 90: 74–80
69. Conzanitis DA, Leijala M, Pesoner E, Saki HA (1982) Acute pulmonary edema due to laryngeal spasm. Anesthesia 37: 1198–1199
70. Jackson FN, Rowland V, Corssen G (1980) Laryngospasm-induced pulmonary edema. Chest 78: 819–824
71. Leatherman JW, Schwartz S (1983) Pulmonary edema due to upper airway obstruction. South Med J 76: 1058–1060
72. Lee KWT, Downes JJ (1983) Pulmonary edema secondary to laryngospasm in children. Anesthesiology 59: 347–349
73. Oswalt CE, Gates GA, Holstrom FMG (1977) Pulmonary edema as a complication of acute upper airway obstruction. JAMA 238: 1833–1835
74. Poulton TJ (1981) Laryngospasm-induced pulmonary edema. Chest 80: 762–763
75. Stradling JR, Bolton P (1982) Upper airways obstruction as cause of pulmonary edema. Lancet I: 1353–1354
76. Sofer S, Bar-Ziv J, Scharf SM (1984) Pulmonary edema following relief of upper airway obstruction. Chest 86: 401–403
77. Travis KW, Todrea ID, Shannon DC (1977) Pulmonary edema associated with croup and epiglottis. Pediatrics 59: 695–698
78. Lemaire F, Teboul JL, Cinotti L, Giotto G, Abrouk F, Steg G, Macquin-Mavier I, Zapol WM (1988) Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. Anesthesiology 69: 171–179
79. Mohsenifar Z, Hay A, Hay J, Lewis MI, Koerner SK (1993) Gastric intramural pH as a predictor of success or failure in weaning patients from mechanical ventilation. Ann Intern Med 119: 794–798
80. Gorcsan J, Gasior T, Mandarino WA, Deneault LG, Hattler BG, Pinsky MR (1994) Assessment of the immediate effects of cardiopulmonary bypass on left ventricular performance by on-line pressure-area relations. Circulation 89: 180–190
81. Gorcsan J, Denault AY, Gasior TA, Mandarino WA, Kancel MJ, Deneault LG, Hattler BG, Pinsky MR (1994) Rapid estimation of left ventricular contractility from end-systolic relations by echocardiographic automated border detection and femoral arterial pressure. Anesthesiology 81: 553–562
82. Solda P, Pantaleo P, Perlini S, Calciati A, Finardi G, Pinsky MR, Bernardi L (1992) Continuous monitoring of right ventricular volume changes using a conductance catheter in the rabbit. J Appl Physiol 73: 1770–1775
83. Pinsky MR, Gorcsan J, Gasior T, Mandarino WA, Deneault LG, Hattler BG, Kunig H (1995) Changes in electrocardiographic morphology reflect instantaneous changes in left ventricular output in cardiac surgery patients. Am J Cardiol 76: 667–674
84. Ingles NB, Daughters GT, Stinson EB, Alderman EL (1975) Measurement of mid-wall myocardial dynamics in intact man by radiography of surgically implanted markers. Circulation 52: 859–867
85. Baan J, Long TTA, Kerkhof PLM et al (1981) Continuous SV and cardiac output from intraventricular dimensions obtained with an impedance catheter. Cardiovasc Res 15: 328–334
86. McKay R, Spears JR, Aroesty J et al (1984) Continuous measurement of left and right ventricular SV and pressure-volume relationships with an impedance catheter. Circulation 69: 703–710
87. Pinsky MR, Perlini S, Solda PL, Pantaleo P, Calciati A, Bernardi L (1996) Dynamic evaluation of ventricular interactions in the rabbit: simultaneous measurement of bi-ventricular pressure-volume loops. J Crit Care 11: 65–76
88. Shi W, Lutz JW, Ondulick BW, Pinsky MR (1995) Positive-pressure ventilation selectively reduces right ventricular end-diastolic volume. FASEB J 9: A329
89. Schertz C, Pinsky MR (1993) Effect of the Pericardium on Systolic Ventricular Interdependence in the Dog. J Crit Care 8: 17–23
90. Gorcsan J, Romand JA, Mandarino WA, Deneault LG, Pinsky MR (1994) Assessment of Left Ventricular Performance By on-line Pressure-Area Relationships Using Echocardiographic Automated Border Detection. J Am Coll Cardiol 23: 242–252
91. Gorcsan J, Morita S, Mandarino WA, et al (1993) Two-dimensional echocardiographic automated border detection accurately reflects changes in left ventricular volume. J Am Soc Echocardiogr 6: 482–489
92. Gorcsan J, Lazar JM, Romand JA, Pinsky MR (1993) On-line estimation of SV by means of echocardiographic automated border detection in the canine left ventricle. Am Heart J 125: 1316–1323
93. Gorcsan J III, Denault A, Mandarino WA, Pinsky MR (1996) Left ventricular pressure-volume relations with transesophageal echocardiographic automated border detection: comparison with conductance-catheter technique. Am Heart J 131: 544–552