Cardiovascular Effects of Mechanical Ventilation

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ABSTRACT

Objective: *To review the cardiovascular effects of spontaneous breathing and mechanical ventilation in healthy and pathological states.*

Data sources: *A review of articles published in peer-reviewed journals from 1966 to 1998 and identified through a MEDLINE search on cardiopulmonary interaction.*

Summary of review: *Respiration has a hydraulic influence upon cardiovascular function. Pulmonary and cardiac pathology alter this interaction. Spontaneous inspiration increases right ventricular (RV) preload and left ventricular (LV) afterload. Mechanical ventilation with positive pressure (MV) reduces LV preload and afterload. The influence of MV upon the cardiovascular system (CVS), particularly in critically ill patients, depends upon the mode of ventilation and the pre-existing cardiac and respiratory status. The influence of these factors is reviewed. Consideration of these parameters will enable the clinician to predict the likely effect of MV and develop strategies to minimise adverse events.*

Conclusions: *Mechanical ventilation has an adverse effect upon the CVS in healthy subjects and in patients with pulmonary pathology, particularly in the presence of preload-dependent LV dysfunction or afterload-induced RV dysfunction. Mechanical ventilation may benefit cardiac function in patients with respiratory failure and afterload-dependent or exercise-induced LV dysfunction.* (**Critical Care and Resuscitation 1999; 1: 388-399**)

Key Words: Mechanical ventilation, cardiovascular physiology, cardiopulmonary interaction, acute respiratory distress syndrome

Respiration and circulation are complementary physiological processes that interact with each other during spontaneous breathing.[1,2] The introduction of mechanical ventilation (MV), or the presence of pulmonary and cardiac disease, increases the complexity of this interaction. Research in this area is daunting and interpretation of the data is difficult because these and other interrelated variables must be considered.

What is the predominant mechanism underlying this interaction? Explanations have included mechanical (hydraulic),[1] neural,[3] and humoral mechanisms.[4] Phasic variation in cardiac function during respiration is closely linked in time and magnitude to changes in intrathoracic pressure and occurs more rapidly than most neural or humoral processes. Therefore current data support the hydraulic effect of intrathoracic (pleural) pressure (P_{pl}) on cardiac transmural pressure (P_{tm}) as the predominant mechanism.[1-3,5]

To appreciate the complex cardiovascular effects of MV, especially in critically ill patients, it is prudent first to identify the cardio-respiratory interactions of spontaneous breathing in healthy subjects and in those with respiratory and/or cardiac disease, and then consider the influence of MV in each situation. Consideration of cardiovascular and respiratory changes over time is also important. An understanding of these interactions should enable the clinician to predict the likely cardiovascular effect of MV in a given clinical situation.

Thoracic anatomy and transmural pressure

Respiration induces phasic swings in cardiac trans-

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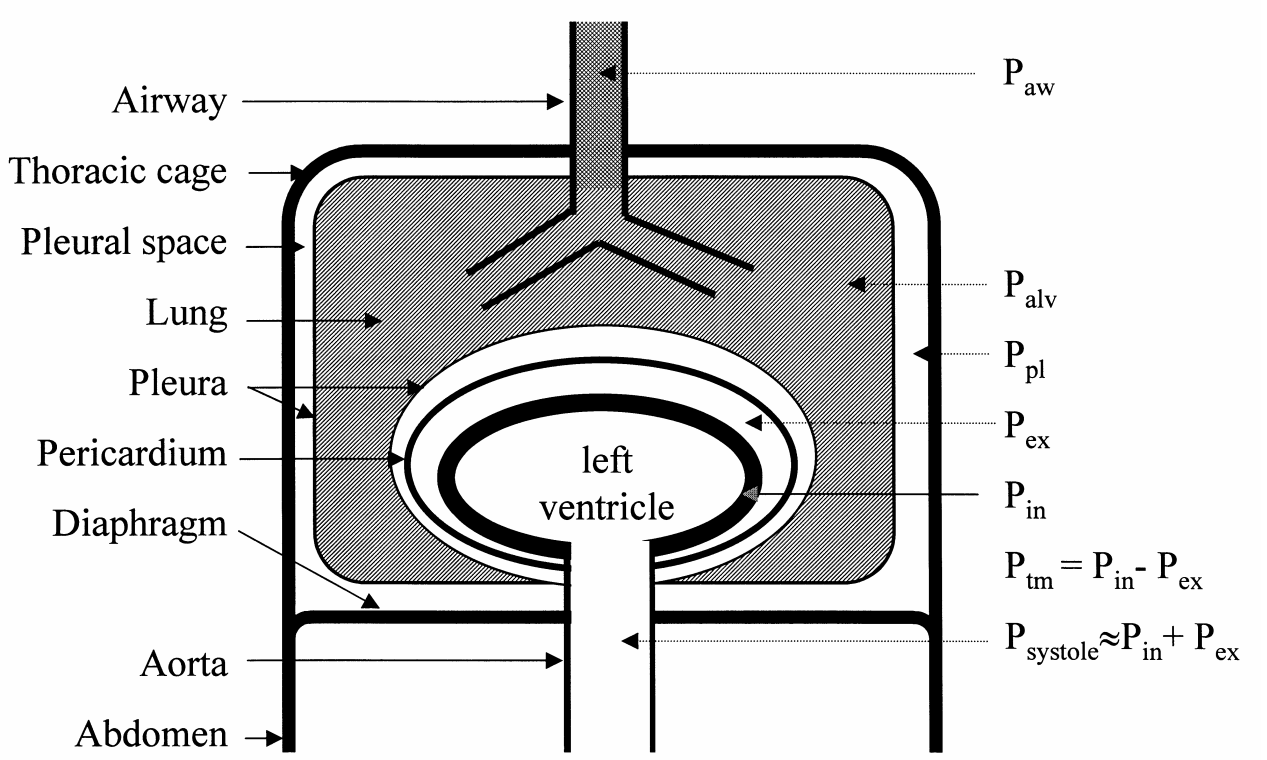

Figure 1. Schematic representation of cardiorespiratory relationship. P_{aw} = airway pressure, P_{alv} = alveolar pressure, P_{pl} = intrathoracic pleural pressure, P_{ex} = extramural stress, P_{in} = intramural stress, P_{tm} = transmural pressure, $P_{systole}$ = aortic blood pressure

mural pressure (P_{tm}) as a result of the anatomical and functional proximity of respiratory and cardiovascular organs. P_{tm} is the difference between intramural stress (P_{in}) and extramural stress (P_{ex}), $P_{tm} = P_{in} - P_{ex}$ (Figure 1).

The thorax contains the lungs and pulmonary vasculature (divided into intra- and extra-alveolar vessels) and the heart and great vessels (i.e. thoracic aorta and great veins). The proximity of these organs within the thorax, together with their dynamic mechanical properties (e.g. volume and elastance) ensures that changes in lung volume and P_{pl} are likely to influence cardiac function even during spontaneous breathing. For example, an increase in lung volume produces a non-uniform compression of the lateral ventricular wall (P_{ex}) and, although low in magnitude does influence ventricular function.[6]

The intra-thoracic cardiovascular system may be described as a dual series of pumps (right and left ventricles) separated from each other by the pulmonary vasculature, and from the systemic circulation by the great veins and thoracic aorta. Since the ventricles are in series, the output of the right ventricle (RV) provides the input (venous return) for the left ventricle (LV) with the intervening pulmonary circulation producing a lag time of (usually) 1-2 beats.

P_{pl} is lowered by the respiratory muscles during spontaneous inspiration and increased during the application of positive pressure MV, and the resultant ΔP_{pl} is seen by the heart as a change in extramural pressure (ΔP_{ex}). P_{pl} has a direct influence on cardiac (epicardial) P_{ex} and thus an influence on LV[7,8] and RV[1,3] volume and function. For example, a fall in P_{pl} will usually result in a fall in P_{ex} (rise in P_{tm}) that will favour ventricular filling but impede ejection.

The cardiovascular effects of respiration appear to be dependent upon both the magnitude of ΔP_{tm} and the sensitivity of the cardiovascular system to ΔP_{tm}. Thus the most important clinical variables in cardio-pulmonary interactions include: 1) the cardiovascular status of the subject; 2) the respiratory status of the subject, and; 3) the mode of respiration.

Accurate measurement of P_{ex}, P_{in} and ventricular volume is important in the assessment of cardio-pulmonary interaction. Cardiac P_{ex} is difficult to measure accurately.[6,9] The use of surrogate measures of P_{ex} such as oesophageal or pleural pressure may significantly underestimate P_{ex} particularly in the presence of pulmonary disease or during positive pressure MV. P_{ex} varies across the surface of the heart, depending upon the volume and compliance of the adjacent lung, pericardium, and cardiac chamber.[9]

Indirect measurement of cardiac P_{in} (e.g. estimation of left ventricular end-diastolic P_{in} by pulmonary artery catheter) may also be misleading.[10-13] More direct measurements of P_{ex} ,P_{in}, and chamber volume are preferred but usually restricted to animal models.

Ventricular interdependence (VI) is another important physiological concept, anatomically based on the adjacent LV and RV sharing a common pericardial sac (with limited volume and compliance) and a common interventricular septum. VI is commonly used to imply that the pressure/volume characteristics of the RV influence those of the LV.[7,14-16]

Cardiovascular effects of spontaneous breathing

To understand the cardiovascular changes resulting from MV it is important to first understand cardio-pulmonary interactions during spontaneous breathing. This topic has been extensively reviewed elsewhere[2,3] and whilst much of the data comes from animal (usually dog) models there is a substantial agreement with available human data.[17]

Spontaneous inspiration in healthy subjects is usually associated with a small fall in systolic blood pressure (< l0 mmHg). Explanations for this observation include: 1) an increase in LV afterload, 2) a decrease in venous return, 3) the influence of VI, and, 4) transmission of reduced intra-thoracic aortic P_{ex} to extrathoracic vessels. Both animal and human data indicate that the first explanation is probably the most important mechanism.[1-3,7]

Inspiration occurs as a result of the reduction in P_{pl} which is transmitted to the intra-thoracic organs. Whilst the primary purpose of this pressure fall is to expand the lungs it is also results in a fall in cardiac P_{ex} (and a rise in P_{tm}). The increase in P_{tm} facilitates right ventricular diastolic filling - the 'thoracic pump' mechanism - until the closing pressure of the extra-thoracic veins is reached[1,3] and the resultant increase in RV end-diastolic volume (RVEDV) increases stroke volume via the Frank-Starling mechanism.[7,16,18] The subsequent rise in pulmonary flow increases left ventricular end diastolic volume (LVEDV) after a delay of 1-2 beats[3,19] - a duration similar to the inspiratory phase of the respiratory cycle. This may partially account for the rise in blood pressure observed during expiration.

Spontaneous inspiration induces an increase in LV afterload that accounts for the observed inspiratory fall in stroke volume and systolic blood pressure. During inspiration left ventricular $P_{ex,}$ falls and $P_{tm,}$ rises. Since this ΔP_{tm} must be 'overcome' during systole it creates, by definition, an increase LV afterload. As a result, LV stroke volume and systolic blood pressure are observed to fall and LV end-systolic volume rises.[1-3,5,6,16] (Figure 2)

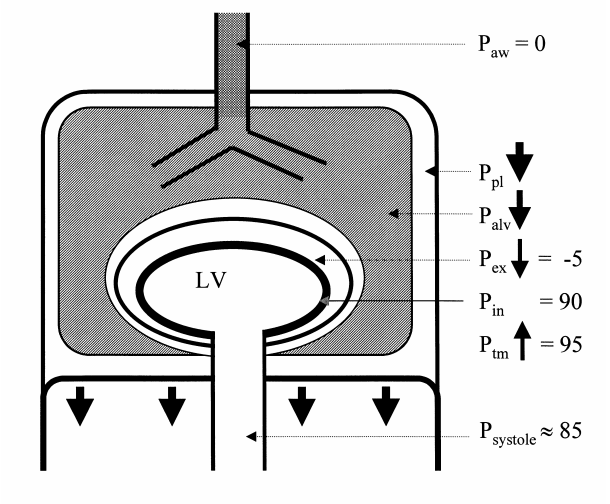

Figure 2. Schematic representation of cardiorespiratory interaction during spontaneous inspiration and cardiac systole. Arrows depict direction of change. Spontaneous inspiration increases P_{tm} and reduces $P_{systole}$. P_{aw} = airway pressure, P_{alv} = alveolar pressure, P_{pl} = intrathoracic pleural pressure, P_{ex} = extramural stress, P_{in} = intramural stress, P_{tm} = transmural pressure, $P_{systole}$ = aortic blood pressure, LV = left ventricle

Under certain pathological states this inspiratory blood pressure fall is exaggerated and referred to as 'pulsus paradoxus'.[3,20,21] This may be found where there is: 1) a greater inspiratory effort and a greater ΔP_{pl} and ΔP_{tm} (e.g. acute asthma[22,23] or pulmonary oedema[24]), or: 2) an increased sensitivity to ΔP_{tm} (e.g. hypovolaemia,[25] tamponade,[3,21] or congestive cardiac failure[26]).

During exhalation systolic blood pressure rises as a result of the return of left ventricular afterload to baseline and aided by the augmentation of LV preload from the (delayed effect of the) inspiratory rise in RV output.

There is little evidence to suggest other mechanisms have a significant influence. The role of VI is equivocal.[1] Although there is little doubt that increasing RV volume can induce leftward septal shift and increase LVEDP, there is little data to support a significant influence during spontaneous breathing[14,15] and disagreement as to its clinical significance even in pathological states.

Spontaneous breathing has little direct effect on the vasculature. Healthy subjects have a low pulmonary vascular resistance (PVR) which does not appreciably alter during tidal breathing.[2,27] There is also little evidence to suggest intra-pulmonary pooling of blood during inspiration. Although the extra-alveolar pulmonary blood volume increases, this is opposed by a fall in intra-alveolar blood volume.[1,28] Whilst inspiratory changes in aortic P_{tm} are transmitted to the extra-

thoracic vessels these are inadequate to explain the observed respiratory swing in systolic blood pressure.

In summary, there are two predominant cardiovascular effects of spontaneous inspiration:
1) a rise in LV afterload and,
2) a rise in RV preload.

An inspiratory fall in systemic blood pressure is produced by the former and limited by the latter. Factors that will potentially accentuate blood pressure fluctuation during spontaneous breathing include:
1) a fall in preload (e.g. hypovolaemia, venodilation), or;
2) a rise in left ventricular afterload as a result of increased inspiratory effort (e.g. bronchospasm[3] or spontaneous breathing through an endotracheal tube[29]).

The cardiovascular effects of mechanical ventilation in healthy subjects

Like spontaneous breathing, MV is associated with an inspiratory fall in aortic flow and systolic blood pressure, but the mechanism is quite different.[2,30] Unlike spontaneous breathing, MV produces a positive ΔP_{pl} during inspiration whose cardiovascular effects are the opposite to those seen with the negative ΔP_{pl} of spontaneous breathing. Proposed mechanisms for the blood pressure fall with MV include:
1) reduced LV preload,
2) reduced RV preload,
3) increased PVR and RV impedance, and
4) ventricular interdependence.

Most of these mechanisms are present in varying degrees but the predominant effect is a reduction in LV preload.[5,31,32]

With the commencement of MV, the positive airway pressure results in a fall in right ventricular P_{tm} and a fall in venous return (or loss of the 'thoracic pump'), causing a reduction in RVEDV (preload).[18,32,33]. Positive airway pressure (P_{aw}) is also transmitted to the pulmonary vasculature inducing a (small) rise in pulmonary artery pressure (P_{pa}) and RV impedance (afterload), and so with time RVEDV returns to the baseline.[32] Although P_{pa} rises, PVR does not - unless intra-thoracic pressure or volume are unusually high.[34,35] Thus MV induces a fall in transpulmonary flow and venous return to the LV, reducing LV preload (Figure 3).

In contrast to the transient changes in RVEDV, MV produces a sustained reduction in LVEDV because both afterload[36,37] and preload[38] are reduced. Both aortic pressure and cardiac output fall progressively during inspiration and can be (partially or wholly) reversed by volume loading,[18,32] suggesting the fall in preload is more influential. Compensatory increases in sympathetic drive induce tachycardia, vasoconstriction, oliguria and retention of sodium and water.

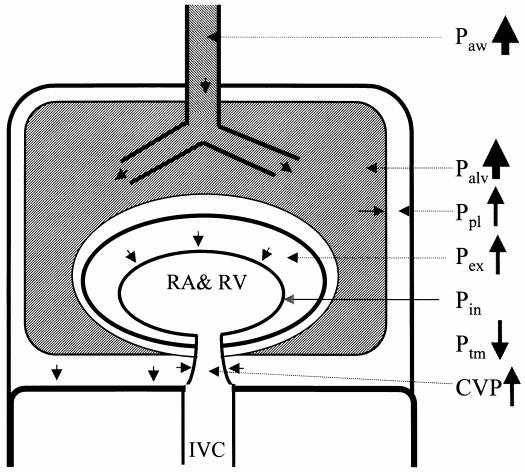

Figure 3. Schematic representation of cardiorespiratory interaction during positive pressure inspiration and diastole. Arrows depict direction of change. Inspiration decreases venous return and RVEDV. P_{aw} = airway pressure, P_{alv} = alveolar pressure, P_{pl} = intrathoracic pleural pressure, P_{ex} = extramural stress, P_{in} = intramural stress, P_{tm} = transmural pressure, CVP = central venous pressure, RA = right atrium, RV = right ventricle, IVC = inferior vena cava

There is little evidence to support a major influence from ventricular interdependence (VI).[9] While a reduction in the LV septal-lateral wall dimension during MV has been reported by early investigators,[14,39] recent investigators have either not demonstrated the presence of VI during MV,[32,34] or found the reduction in LV dimensions were symmetrical, and no greater in the septal-free wall axis.[9] Some even suggest that asymmetrical reduction in the septal-free wall axis would also be consistent with increased lateral wall P_{ex} from the inflation of the adjacent lung and not from VI.[40,41] Finally, a number of researchers have demonstrated preservation of LV pressure-volume relationships during MV implying that any effect from VI is clinically insignificant.[9,42]

By maintaining some spontaneous inspiratory effort, assisted modes of ventilation such as CPAP, PSV, BiPAP and even SIMV, will tend to produce a lower mean P_{aw} and P_{pl} compared with controlled modes of MV for a similar level of minute volume. These modes have been shown to reduce the adverse cardiovascular effects of MV.[18,43] However, assisted modes of respiratory support are unsuitable if the patient has severe lung disease or an inadequate respiratory drive (e.g. from sedation, anaesthesia, or coma) or is at risk from respiratory muscle fatigue (e.g. a high respiratory rate).

Mechanical or extrinsic PEEP ($PEEP_e$) is commonly used to recruit alveoli, defend end-expiratory lung volume (EELV), and improve oxygenation during MV. PEEP increases mean P_{aw} and (usually) P_{pl} and thus the haemodynamic effects are similar to MV. Some data support the potential for humoral and neural mediated effects of PEEP on cardiac function in addition to its hydraulic effects.[4,9] The concept of 'best PEEP' is based upon the balance between the respiratory benefits of PEEP and its adverse cardiovascular (and respiratory) effects.[44]

Factors that may accentuate the haemodynamic effects of MV in healthy subjects include:

1) a decrease in venous return[25,38] (e.g. hypovolaemia, venodilation),
2) an increase in mean intra-thoracic pressure (e.g. the use of large tidal volume or high $PEEP_e$), or
3) blunting of compensatory sympathetic reflexes (e.g. anaesthesia, sedatives).

Strategies to minimise these effects include:

1) the use of volume expansion to restore LV preload,
2) the use of assisted modes of ventilation to reduce ΔP_{pl}, and
3) the avoidance of high mean intra-thoracic pressure (P_{pl}) that may occur with a high minute volume, high inspiratory flow or $PEEP_e$.

Cardio-pulmonary interaction in the presence of pulmonary disease

Pulmonary disease alters lung mechanics in a number of ways which alter the cardio-pulmonary interactions observed during spontaneous breathing. The important changes in lung mechanics include those affecting lung volume, airflow resistance, minute volume (V_e), work of breathing (W_B), and RV impedance.

Reduced lung volume

Many pulmonary diseases are associated with a reduction in lung compliance and volume. This may occur as a result of 1) bronchial obstruction (e.g. inflammation, secretions), 2) an increase in closing volume (e.g. lung disease, elderly), 3) a reduction in functional residual capacity (FRC, e.g. anaesthesia, supine posture, abdominal and thoracic trauma), or 4) an increase in lung elastance (eg. pulmonary oedema, pneumonia, ARDS).

A decrease (or an increase) in lung volume will increase PVR and RV impedance (i.e. afterload).[2,27,30] A pathological increase in lung volume most often occurs in the presence of airflow limitation (see later). A reduction in lung volume increases the resistance in extra-alveolar pulmonary vessels[1,27] due to hypoxic vasoconstriction,[35,45] structural distortion,[1,45] and in some cases vasoconstrictor mediators (e.g. thromboxanes).[30,45,46] PVR has an inverse hyperbolic relationship with the lung volume $(FRC)^2$ so that in severe cases, a marked rise PVR may induce RV systolic dysfunction.[45]

Acute respiratory failure resulting from extensive alveolar collapse (e.g. post-operative respiratory failure) may necessitate the use of MV for respiratory support. In this setting MV may increase both P_{pa} and PVR through hyperinflation of healthy lung units.[9,30,34] The use of $PEEP_e$ to recruit collapsed lung units may exacerbate these effects.[47-49] The adverse haemodynamic effects of MV seen in healthy subjects are thus accentuated in these patients and strategies to recruit and defend EELV tend to oppose those strategies which minimise the adverse cardiovascular effects of MV.[2,9]

MV strategies to defend cardiac output in the face of reduced lung elastance and volume include:

1) attempts to minimise any unnecessary elevation in P_{pl} that may occur with high tidal volume (V_t), V_e, and inspiratory flow rates, and the judicious use of $PEEP_e$,
2) alveolar recruitment and reversal of hypoxia and acidosis in an effort to reduce PVR,
3) careful use of volume expansion to improve LV preload but avoid pulmonary oedema, and,
4) use of inotropic agents to support cardiac output.

In theory, the use of assisted non-invasive modes of ventilation (e.g. CPAP, BiPAP, PSV) to recruit alveoli and provide respiratory support whilst minimising the adverse cardiovascular effects of MV is attractive.[50] However, there is little data to support a successful therapeutic role for this modality in these patients.[43]

Airflow limitation and dynamic hyperinflation

Airflow limitation (e.g. asthma, COPD) prolongs the expiratory time and opposes alveolar deflation resulting in an increase in EELV (i.e. dynamic hyperinflation) and the creation of intrinsic PEEP ($PEEP_i$). Expiratory P_{pl} and P_{ex} will rise as a result of PEEP. These mechanical effects reduce LV (and RV) preload.[22,51]

Dynamic hyperinflation and inspiratory airflow limitation both increase the inspiratory effort to maintain alveolar ventilation. The elevated lung elastance of high lung volume, together with high inspiratory flow resistance, increases work and the ΔP_{pl} required to maintain alveolar ventilation. Thus the LV afterload effect (of inspiratory ΔP_{pl}) is exaggerated in the presence of airflow limitation, producing a greater fall in systolic blood pressure and 'pulsus paradox-us'.[22,51]

A number of other factors may reduce RV output and trans-pulmonary flow in the presence of airflow limitation. Although heightened inspiratory effort will tend to increase RV preload, venous return is limited by

the collapse of the extra-thoracic veins.[2,3] $PEEP_i$ will further decrease venous return. Over-inflation of alveoli during inspiration compresses intra-alveolar vessels and (along with other changes in pulmonary vasculature[51]) increases PVR and RV impedance.[2,23,35]

With severe airflow obstruction the reduction in P_{pl} and P_{ex} may be so severe as to cause pulmonary[23] and aortic flow to fall dramatically, or hydrostatic pulmonary oedema to occur.[52] Alternatively, dynamic hyperinflation and airflow limitation may increase W_B[51] to the extent that respiratory fatigue leads to hypercarbia and a respiratory arrest. These mechanisms may account for unexplained sudden death in some asthmatics.[53]

Great care must be taken when instituting MV in the presence of severe airflow limitation as MV may further increase dynamic hyperinflation and P_{pl}.[54] Even in the presence of mild airflow limitation, the use of MV parameters which inadvertently shorten expiratory time (e.g. large V_t, high frequency, prolonged inspiratory time) may produce dynamic hyperinflation.

Monitoring dynamic hyperinflation during MV is not difficult. With appropriate volume-measuring devices, the trapped volume (V_{ei}) of dynamic hyperinflation can be measured during a prolonged expiratory pause (30-60 seconds). Data from Tuxen and Lane[54] suggests that a V_{ei} < 20 mL/kg should minimise the adverse haemodynamic effects of MV in the presence of severe airflow limitation.

Alternatively, alveolar pressure (P_{alv}) may be measured. In the presence of airflow limitation, P_{alv} cannot be inferred from (upstream) P_{aw} since the later will be higher than P_{alv} during inspiration, and lower during exhalation.[55] By temporarily adding an inspiratory or expiratory pause (0.5-1.0 seconds) P_{aw} will more accurately indicate peak inspiratory P_{alv} and end-expiratory P_{alv} (or $PEEP_i$) respectively.

Strategies to minimise the haemodynamic effects of MV in patients with mild airflow limitation include the use of,

1) assisted modes of ventilation to reduce threshold work, inspiratory effort and improve minute volume,[43,56]
2) MV parameters which reduce the inspiratory to expiratory time (I:E) ratio, and
3) avoidance of $PEEP_e$ in excess of $PEEP_i$.[57,58]

However, in the presence of severe airflow limitation it is often necessary to monitor trapped lung volume (V_{ei}) and $PEEP_i$, and to use a very low I:E ratio with controlled hypoventilation.[54,59,60]

Increased work of breathing (W_B)

Most pulmonary diseases are associated with an increase in minute volume (V_e) and/or an increase in respiratory effort per breath (W_B).[30,61] High V_e demand may result from an elevation in metabolic rate or deterioration in gas exchange. Increased W_B may result from increased lung elastance or airflow limitation.[62] The metabolic (e.g. oxygen) cost of breathing - normally only 1-2% of total body oxygen consumption - may rise to as much as 20% in acute respiratory failure.[61,65]

Respiration may thus be viewed as a form of (cardiac and respiratory) exercise stress.[30] A high level of W_B may produce respiratory muscle fatigue and cause acute respiratory failure.[66-68] Respiratory muscle blood flow may be significantly limited in the presence of cardiac failure, further exacerbating respiratory muscle fatigue, lactic acidosis and respiratory failure.[69] In addition, the increased metabolic demand of respiration may induce myocardial ischaemia.[70,71] In this setting, MV and muscle relaxation may reduce some of the adverse metabolic and cardiovascular stresses of spontaneous breathing and may improve outcome.[65,69,72-75]

Increased right ventricular impedance

Pulmonary hypertension (PHT) is a frequent complication of acute and chronic pulmonary disease. Particular mention is warranted here because severe PHT (mean P_{pa} > 30mmHg) may precipitate acute right heart failure.[2,45,76,77] This may arise in such diverse conditions as pulmonary embolism, acute exacerbation of chronic lung disease, or the acute respiratory distress syndrome (ARDS).

The compliant, thin-walled RV and pulmonary circulation usually operate as a low-pressure flow generator. PHT increases RV impedance (i.e. afterload), induces acute RV dilatation and, when severe, RV failure.[76] This may significantly reduce pulmonary flow (i.e. LV preload) and precipitate systemic hypotension. The initial effects of MV will exacerbate this situation.[49] The transmission of positive P_{alv} via the intra-alveolar vessels will increase mean P_{pa} whilst compression of intra-alveolar vessels will increase PVR. In the long-term, however, MV may beneficially reduce PVR through the recruitment of collapsed lung units and reversal of acidotic and hypoxic pulmonary vasoconstriction.[30,45,77]

The combination of systemic hypotension and pulmonary hypertension has an adverse effect on RV myocardial oxygen supply and demand.[78,79] RV myocardial perfusion pressure (P_{RVM}) is determined by the balance of the driving pressure (i.e. mean arterial pressure) and the opposing mean ventricular pressure ($P_{in,RV}$). The critical level for P_{RVM} is around 25-40mmHg, below which right ventricular ischaemia and acute right heart failure may occur.[79]

$$P_{RVM} = P_{in,RV} - MAP$$

Where

$P_{in,RV}$ = 1/3 ($P_{pa,sys}$ - CVP) + CVP
$P_{pa,sys}$ = systolic pulmonary artery pressure
MAP = mean arterial pressure
CVP = central venous pressure.

Strategies to avoid RV ischaemia include defence of RV preload (with volume loading), defence of MAP (with pressor agents)[79,80] and monitoring of P_{RVM} (e.g. via a pulmonary artery catheter). Unfortunately most inotropic agents also have some pulmonary vasoconstrictor properties, and those with significant vasodilatory properties (e.g. isoprenaline, dobutamine and milrinone) may be best avoided. Noradrenaline appears to have the best profile for the RV by producing less pulmonary vasoconstriction for similar levels of inotropic effect and support of myocardial perfusion.[80,81]

Acute lung injury (ALI), ARDS and MV

Special mention of MV in acute lung injury (ALI) and ARDS is warranted because the complexity of the cardio-respiratory interaction of MV with lung disease is epitomised in a patient with ARDS. The dynamic interaction of pathological processes and pulmonary mechanics demonstrates that care should be taken to identify these variables when interpreting clinical and research data.

The pathological changes in pulmonary and cardiovascular function with ALI and ARDS are documented elsewhere.[46,82] In summary, all the mechanical factors discussed previously are seen in various degrees with ALI and ARDS. For example, increased elastance, alveolar collapse, loss of EELV, airflow limitation, pulmonary hypertension, and elevated metabolic rate and W_B. Humoral inflammatory mediators produce pulmonary vasoconstriction, myocardial depression, and systemic hypotension. Control of oxygen flux, organ blood flow and cellular respiration may also be deranged.

A number of different modes of MV may be utilised depending upon the stage and severity of ALI. These vary from non-invasive modes (e.g. face-mask PSV and CPAP) for ALI, through to assisted modes (e.g. SIMV and PSV) and to the extremes of (pressure or volume) controlled modes with significant levels of $PEEP_e$ being required for ARDS.

ARDS is characterised by markedly increased lung elastance so that during MV, a greater inspiratory airway pressure ($P_{aw,i}$) is required to maintain adequate alveolar ventilation, and high levels of $PEEP_e$ are often utilised to prevent airway collapse and aid recruitment of alveoli. Healthy lung units exposed to high $P_{aw,i}$ will be subject to overdistension. To the extent that P_{aw} is transmitted to P_{pl}, MV will decrease P_{tm} and impair cardiac function (see previously). Counteracting this is the fact that non-distensible (i.e. collapsed or consolidated) lung segments will 'protect' P_{pl} and cardiac P_{tm} from the elevation in P_{aw}.[8,34,83]

Right ventricular dysfunction during MV is unavoidable due to the combined effects of positive P_{aw} and P_{pl} and the presence of PHT (which is often severe) and an elevated PVR.[46] Not surprisingly, the cardiovascular effects of MV for ARDS are predominantly borne by the RV.[82,84] RV dysfunction, elevated PVR and VI (if present), will all reduce LV preload.

The effects of ARDS on LV function are determined by the combined effect of reductions in preload, afterload and contractility.[85] Contractility may be impaired by humoral myocardial depressant factors and myocardial ischaemia.[46] Peripheral vascular failure (systemic vasodilatation) reduces LV afterload and favours a hyperdynamic circulation so that the clinical observation of a warm periphery and a bounding pulse may mask the presence of significant LV dysfunction.

The addition of MV has little cardiovascular benefit in ARDS.[86] Strategies to minimise the haemodynamic effects of MV tend to oppose many of the ventilatory strategies used to overcome the pulmonary dysfunction of ARDS. Where possible MV parameters which minimise mean P_{aw} and total PEEP ($PEEP_e$ plus $PEEP_i$) will favour cardiac function as well as limiting ventilator-induced lung injury. Maintenance of RV preload (volume loading), RV contractility (inotropic agents) and systemic blood pressure (pressor agents), together with frequent clinical and haemodynamic assessment (e.g. pulmonary artery catheter, echocardiography, etc.) are essential. Clinical goals will often need to be guided by response to these therapeutic challenges and will differ for each patient depending on the severity and progression of the disease.

The elusive search for an ideal MV mode for ARDS patients - which supports ventilation without adverse cardiac (and respiratory) side effects - has included the use of high frequency ventilation,[87] inverse ratio ventilation,[89] extra-corporeal oxygenation,[90] partial liquid ventilation,[91] inhaled pulmonary vasodilators (e.g. nitric oxide[92] and prostaglandins[93]), prone ventilation, phasic abdomino-thoracic pressure support,[74] and extra-thoracic negative-pressure ventilators.[94,95] Many of these options are worthy of consideration in the presence of severe cardiovascular dysfunction in response to MV but evidence of improved outcome is lacking.

Cardio-pulmonary interaction in the presence of cardiac disease

Cardiovascular pathology is a common finding in patients who require MV. Some of these factors have

already been mentioned. The effect of MV is particularly dependent upon the type and severity of cardiac dysfunction. When ventricular dysfunction is preload-dependent (e.g. hypovolaemia, ischaemia, restrictive cardiomyopathy, tamponade, and valvular stenoses), MV will generally cause a further reduction in cardiac output. Poor ventricular compliance (resulting from myocardial ischaemia, hypertrophy or fibrosis) is a particular situation that often causes a rise in P_{in} and P_{tm} but not preload (LVEDV). General measures to prevent hypotension include the use of MV parameters that minimise mean P_{aw} together with volume loading and, when necessary, the use of inotropic agents.

When left ventricular dysfunction is afterload-dependent, MV may improve cardiac output. Two important groups are worthy of mention: 1) cardiac-induced acute respiratory failure (e.g. cardiogenic pulmonary oedema), and, 2) respiratory-induced acute cardiac failure in the presence of severe systolic dysfunction.

Acute cardiogenic pulmonary oedema most commonly occurs as a result of ischaemic LV diastolic dysfunction leading to a hydraulic shift of fluid from the intravascular compartment into the lung parenchyma.[96] Increased inspiratory effort (W_B) produces a large negative P_{pl} that increases LV afterload[70] and may lead to respiratory muscle fatigue[68,75] and respiratory acidosis. Myocardial ischaemia and afterload impair LV systolic function and cardiac output, initiating a compensatory sympathetic response. RV dysfunction may also occur as a result of adverse changes in afterload (e.g. hypoxic pulmonary vasoconstriction), preload (e.g. hypovolaemia), and myocardial oxygen supply (e.g. coronary hypoperfusion).

MV is useful in cardiogenic pulmonary oedema because it reverses hypoxia, reduces metabolic demand and improves afterload[72] (Figure 4). Many subjects with acute cardiogenic pulmonary oedema are hypovolaemic and due consideration must be given to the adverse preload effects of MV.[97] Noninvasive modes of assisted breathing (e.g. face-mask CPAP) provide high inspired oxygen, reduce W_B and improve LV afterload and have been shown to be equally effective as MV, with lower a rate of intubation, compared with pharmacological therapy alone.[98]

Respiratory-induced acute cardiac failure occurs in the presence of severe systolic dysfunction (e.g. severe cardiomyopathy or ischaemic heart disease). Since spontaneous breathing is a form of exercise[30] an increase in WB during respiratory failure will increase the metabolic (oxygen) demand of the respiratory muscles by as much as ten-fold.[68,69,75] If myocardial reserve is insufficient to meet this demand acute myocardial ischaemia or systolic failure may occur.

MV may be beneficial in these patients by reducing metabolic demand and W_B[65] and by favourably altering LV mechanics (e.g. decrease the afterload). Consistent with this hypothesis is the observation that patients with stress-induced ischaemia may experience difficulty in weaning from supported (MV) to spontaneous breathing.[71,72,99,100] Even long-term nocturnal CPAP in severe cardiac failure patients (e.g. New York Heart Association class III & IV) has been shown to produce a sustained improvement in LV and respiratory reserve.[101]

In subjects with afterload-induced RV dysfunction (e.g. severe pulmonary hypertension, acute PE, COPD, or RV infarct) MV may also adversely effect the balance of RV oxygen supply and demand. As discussed above, treatment of reversible pulmonary vasoconstriction (e.g. from hypoxia or acidosis) and defence of coronary perfusion pressure with pressor agents may be beneficial.

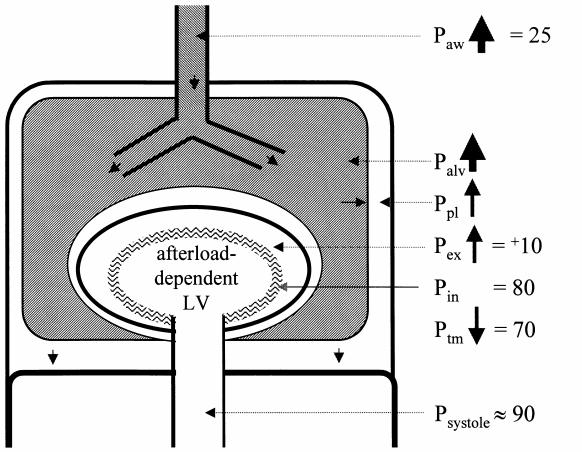

Figure 4. Schematic representation of the effect of positive pressure inspiration in the presence of systolic dysfunction. Arrows depict direction of change. Inspiration decreases afterload (P_{tm}) and increases aortic pressure ($P_{systole}$). P_{aw} = airway pressure, P_{alv} = alveolar pressure, P_{pl} = intrathoracic pleural pressure, P_{ex} = extramural stress, P_{in} = intramural stress, P_{tm} = transmural pressure, LV = left ventricle

Summary

MV has significant haemodynamic side-effects, the nature of which depend upon the cardiac and respiratory status of the subject, the mode of ventilatory support and the ventilatory parameters chosen. In general, MV reduces RV and LV preload and improves LV afterload. MV will increase the risk of adverse cardiovascular effects in the presence of acute or chronic pulmonary disease, especially in association with preload-dependent LV function, or afterload-induced RV

dysfunction. Optimal MV modes and parameters to minimise this will depend upon the pulmonary pathophysiology present, and may change over time in the same subject. Conversely, MV may benefit cardiac function in patients with respiratory failure associated with afterload-dependent or exercise-induced LV dysfunction.

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