Cardiopulmonary interactions in patients with heart failure

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Purpose of review

The purpose of this review was to summarize recent findings concerning the consequences of cardiopulmonary interactions in acute cardiogenic pulmonary edema, weaning from mechanical ventilation and fluid-responsiveness assessment by respiratory variations of stroke volume.

Recent findings

The efficacy of continuous or bilevel positive airway pressure in patients with acute cardiogenic pulmonary edema was strongly suggested by two recent meta-analyses. There is growing evidence to suggest that weaning-induced cardiac dysfunction and acute cardiogenic pulmonary edema could explain a large amount of liberation failure from mechanical ventilation. Despite a potential role for echocardiography and plasma measurements of B-type natriuretic peptide in demonstrating a cardiac origin to weaning failure, the demonstration of a significant increase in pulmonary-artery occlusion pressure during the weaning trial remains the gold standard for this purpose. In patients with heart failure there is no evidence for revisiting the reliability of the respiratory variation of stroke-volume surrogates to predict fluid responsiveness.

Summary

For clinical practice, the knowledge of cardiopulmonary interactions is of paramount importance in understanding the crucial role of mechanical ventilation for treating patients with heart failure and, by contrast, the deleterious cardiovascular effects of weaning in patients with overt or hidden cardiac failure.

Keywords

cardiogenic pulmonary edema, cardiopulmonary interactions, fluid responsiveness, weaning from mechanical ventilation

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Abbreviations

ACPE	acute cardiogenic pulmonary edema
AHF	acute heart failure
BiPAP	bilevel positive airway pressure
BNP	B-type natriuretic peptide
CPAP	continuous positive airway pressure
NIPPV	noninvasive positive-pressure ventilation
PAOP	pulmonary-artery occlusion pressure

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Introduction

Cardiovascular and respiratory systems are working with different pressure regimens in the thorax. This generates hemodynamic consequences commonly called cardiopulmonary interactions that may be negligible in spontaneously breathing healthy subjects but that may be of major concern when positive-pressure ventilation is applied or withdrawn in critically ill patients. Depending on the underlying pathological condition, heart–lung interactions can be either harmful or beneficial. In this review, we focus on the beneficial effects of applying positive-pressure ventilation in patients with acute heart failure (AHF) and on the potential deleterious consequences of withdrawing mechanical ventilation, which may result in weaning failure.

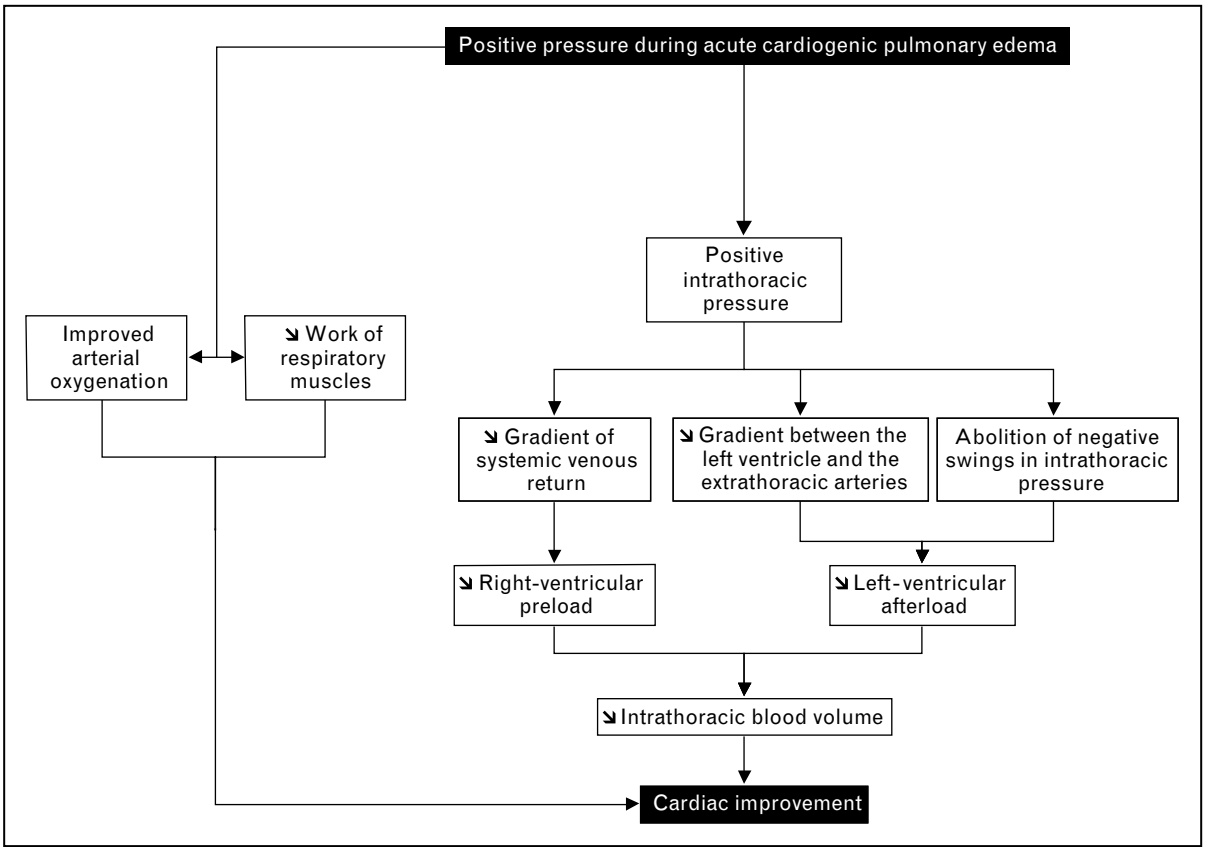
Beneficial effects of cardiopulmonary interactions: mechanical ventilation in acute cardiogenic pulmonary edema

The major cardiovascular changes induced by application of positive-pressure ventilation may be highly beneficial in patients suffering from AHF in contrast to what may occur in those with normal cardiac function. Accordingly, noninvasive positive-pressure ventilation (NIPPV) is becoming one of the first-line therapies of patients with acute cardiogenic pulmonary edema (ACPE).

Pathophysiological issues

The increase of intrathoracic pressure produced by mechanical ventilation exerts significant effects on cardiac preload and afterload, two important components of the cardiac performance. Indeed, by increasing the pressure in the right atrium and in the left ventricle with respect to extrathoracic vascular beds, positive-pressure ventilation affects the pressure gradients for both systemic venous return (decrease) and left-ventricular ejection (increase; Fig. 1). The combination of these phenomena must lead to a decrease in intrathoracic blood volume, an effect which is expected to be beneficial in

Figure 1 Schematic pathophysiological effects of positive-pressure ventilation in a case of acute cardiogenic pulmonary edema



patients suffering from ACPE. Moreover, the effect of increased intrathoracic pressure on the left-ventricular ejection-pressure gradient, which is equivalent to a decreased left-ventricular afterload, could be particularly beneficial in a patient with congestive AHF whose stroke volume is sensitive to changes in left-ventricular afterload and relatively insensitive to changes in preload. In this regard, in response to incremental increase in intrathoracic pressure, stroke volume was shown to progressively increase in patients with congestive heart failure and to progressively decrease in patients with normal heart function and in those with cardiac dysfunction and low filling pressures [1]. In patients with AHF, application of mechanical ventilation can improve hemodynamics not only through increase in mean intrathoracic pressure but also through abolition of large negative swings in intrathoracic pressure [2], which are assumed to impede markedly left-ventricular afterload during severe episodes of ACPE (Fig. 1).

In addition to its effects related to intrathoracic pressure, mechanical ventilation (even with a noninvasive mode) exerts beneficial effects on peripheral oxygenation through reduction in work of breathing and in respiratory-muscle oxygen demand [3] and through improvement in blood gas exchange and arterial oxygenation [4].

Clinical evidence

NIPPV has received a great deal of interest in the management of ACPE. Two techniques of NIPPV can be used: continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP). CPAP was investigated in several studies [1–9]. In patients with AHF, CPAP was demonstrated to increase cardiac output [1,7,8] and left-ventricular ejection fraction [10] and to decrease left-ventricular transmural filling pressure [2,3,11]. A first meta-analysis performed in 1998 addressed CPAP efficacy for treating ACPE [12]. Based on only three randomized studies, it was concluded that CPAP may decrease the need for intubation but does not exhibit any effect on mortality compared with standard therapy alone.

As compared to CPAP, BiPAP provides a more sophisticated ventilatory support since it combines inspiratory assistance with positive end-expiratory pressure. In the context of ACPE, BiPAP was found to be more effective than CPAP at unloading the respiratory muscles but both

ventilation modalities exerted comparable hemodynamic effects [11]. However, in a randomized double-blind trial comparing BiPAP and CPAP in ACPE, a higher rate of myocardial infarctions was reported with BiPAP, although a more rapid improvement in ventilation and vital signs was produced by this ventilatory mode [13]. Although further small studies did not confirm the association between the onset of myocardial infarction and the use of BiPAP [14,15], some doubts have been raised about the respective efficacy and safety of CPAP and BiPAP in ACPE.

Numerous randomized trials concerning the use of CPAP [6,9] or BiPAP [14–19] in ACPE have been recently published. All were taken into account by three recent meta-analyses comparing CPAP and BiPAP with conventional therapy alone and with each other [20••,21••,22]. The three meta-analyses have found quite similar results. The first major one is that the use of CPAP was associated with a reduction in mortality compared with standard therapy alone. In the three meta-analyses, there was a trend toward reduced mortality when BiPAP was added to standard treatment but the effects of BiPAP on mortality did not reach statistical significance, likely because of a limited number of patients included in BiPAP studies. Second, all three meta-analyses confirmed the results of the previous studies in reducing the need for intubation when NIPPV of either mode was compared with standard therapy. In all systematic reviews there was no difference between CPAP and BiPAP concerning the effects on mortality and the need for intubation [20••]. This was also confirmed by another recent meta-analysis that specifically addressed the comparison of CPAP and BiPAP in patients with ACPE [23•]. Finally, the meta-analyses [20••,21••,22] showed a potential excess of the occurrence rate of myocardial infarction with BiPAP but the trend did not reach significance. To explain this effect, Peter *et al.* [21••] hypothesized that BiPAP may induce a more rapid correction of P_aCO_2 with a potential coronary vasoconstriction and that there could be more asynchrony between patients and ventilator under BiPAP than under CPAP. It seems reasonable to state that there is no advantage of using one mode of noninvasive ventilation rather than the other in the setting of ACPE. Due to these results and since bilevel devices need sophisticated apparatus the British Thoracic Society guidelines recommended the use of CPAP in ACPE [24]. It could be reasonably advised that CPAP should be used in first intention in cardiology departments or emergency rooms because it does not require advanced experience for appropriate use. Either mode could be chosen in intensive care units. Finally, although no statistically significant argument could be found in the literature, caution should be taken for patients with suspected myocardial ischemia regarding the potential risk of BiPAP in these patients.

The proportion of patients presenting with ACPE who require NIPPV has been estimated to be 10% [23•]. It remains uncertain which subgroup of patients may preferentially benefit from this support. Although previous studies found that the benefit of NIPPV was more evident in patients with hypercapnia [5,25–27], the presence of hypercapnia at admission did not influence the comparison of BiPAP with CPAP in the meta-analyses of either Ho and Wong [23•] or Winck *et al.* [20••]. These meta-analyses did not confirm the potential superiority of BiPAP over CPAP due to a greater respiratory muscles unloading. Peter *et al.* [21••] found no specific clinical variable to be associated with the effect of any ventilation mode over standard therapy so that criteria for defining a target population who may benefit from these specific therapies are lacking. From a practical point of view, the use of NIPPV should be considered in the most severe forms of ACPE, once contraindications for using CPAP and BiPAP, or a face mask, have been excluded (such as coma and vomiting). Finally, studies are needed to define the exact level of positive end-expiratory pressure and its role on outcome and the place for BiPAP in hypercapnic ACPE, particularly when patients suffer from both chronic obstructive pulmonary disease and left-cardiac dysfunction.

Deleterious effect of cardiopulmonary interactions: acute cardiogenic pulmonary edema during weaning from mechanical ventilation

Abrupt transfer from mechanical ventilation to spontaneous breathing may result in ACPE in patients with previous heart disease. Among the pathophysiological mechanisms, the sudden shift from a positive to a negative intrathoracic pressure plays an important role since it results on the one hand in an increased pressure gradient for systemic venous return and in cardiac preload and on the other hand in a decreased pressure gradient for left-ventricular ejection and an increase in left-ventricular afterload [28]. In patients with previously impaired left-cardiac function, both mechanisms have the potential for increasing central blood volume and eventually lung filtration pressure. In some conditions, weaning may result in a marked increase in right-ventricular afterload and in right-ventricular enlargement, and hence in left-ventricular end-diastolic pressure through diastolic biventricular interdependence [29]. Finally, disconnecting the patient from the ventilator could result in a marked increase in work of breathing and in adrenergic state and hence in increased cardiac work and myocardial oxygen demand with the potential risk of myocardial ischemia in patients with prior coronary artery disease. Accordingly, ACPE and/or myocardial ischemia were reported to suddenly occur during weaning in patients with preexisting cardiac disease [30–34].

The certain diagnosis of weaning-induced ACPE often requires pulmonary-artery catheterization [35] since it is usually made by the demonstration of a marked increase in pulmonary-artery occlusion pressure (PAOP) during spontaneous breathing trial [30]. To date, no studies have tested the value of echocardiographic estimates of PAOP for diagnosing weaning-induced pulmonary edema [35]. Measuring the changes of plasma B-type natriuretic peptide (BNP) during weaning can be of particular value since it represents an hormonal sensor of left-ventricular distension. Mekontso-Dessap *et al.* [36•] measured plasma BNP concentration in patients undergoing a 1-h weaning trial on a T-tube. The changes in BNP concentration (measured before and at the end of the weaning trial) were not significant in patients who succeeded or in those who failed the spontaneous-breathing trial. These disappointing results may be explained by too short time elapsed between the two BNP dosages with regard to de-novo secretion of the hormone. Whether a later BNP dosage would allow diagnosis of weaning-induced ACPE remains to be proved. In a preliminary study [37] we suggested a simple but accurate method for this purpose by hypothesizing that ACPE is characterized by the transfer of a low-concentration fluid toward the interstitium that should result in hemoconcentration. In 29 patients we found that a weaning-induced increase in plasma protein concentration by more than 5% allowed detection of a weaning-induced increase in PAOP above 18 mmHg with high sensitivity and specificity. This approach could represent a simple way to diagnose ACPE during weaning provided that confirmation of these preliminary results is brought. Once the cardiac origin of weaning failure is clearly shown, a specific treatment based on diuretics and vasodilators should be proposed [29], although no recent study has addressed this question specifically. It remains to be investigated whether an inotropic drug like levosimendan, also able to exert systemic and pulmonary vasodilating effects [38], could be beneficial in this context.

Whatever the cause of weaning failure the analysis of cardiovascular and tissue-oxygenation variables before and during weaning has been proposed for characterizing weaning-outcome profiles. Jubran *et al.* [39] showed an increased oxygen transport sufficient to meet the increased oxygen demand in patients who succeeded in weaning during a spontaneous-breathing trial, so that mixed venous oxygen saturation (S_vO_2), a variable which can be easily monitored, did not change. On the other hand, in patients who failed to wean, S_vO_2 decreased during weaning since oxygen transport did not increase enough in the face of the increased oxygen demand due to the increased work of breathing [39]. A recent study re-examined tissue oxygenation variables during weaning [40]. Although debatable [34], the results of this study emphasized that the cardiovascular response to a spontaneous breathing trial was quite heterogeneous regardless of the weaning outcome. Accordingly, decrease in S_vO_2 was not always observed in patients who failed to wean, maybe because of respiratory-center depression or sepsis and hence because of no increase in oxygen consumption.

Another recently addressed question was to determine whether hemodynamic variables measured while a patient is still receiving mechanical ventilation could help to predict weaning failure. Interestingly, in the study by Mekontso-Dessap *et al.* [36•], the plasma BNP concentration measured before a spontaneous-breathing trial was significantly different between patients who succeeded in weaning and patients who failed to wean. A high baseline plasma BNP concentration was an independent risk factor for weaning failure and the best threshold BNP value to predict weaning failure was 275 pg/ml [37]. Such results are in agreement with those of the study by Upadya *et al.* [41•], who showed a link between positive cumulative fluid balance and weaning failure. Despite the findings of these two studies [37,41•], there is to date no evidence that systematic administration of diuretics aimed at reducing preweaning plasma BNP concentration and/or generating negative fluid balance can significantly increase the rate of weaning success.

Respiratory variation of hemodynamic signals in patients with cardiac failure

Another clinical implication of the cardiopulmonary interactions is the prediction of fluid responsiveness. Numerous studies have brought the evidence that the magnitude of respiratory variation of surrogates of stroke volume, like arterial pulse pressure [42], subaortic blood flow [43], pulse contour-derived stroke volume [44] or descending aortic blood flow [45], is able to reliably predict fluid responsiveness. The underlying hypothesis is that respiratory variation in stroke volume is related to respiratory variation in cardiac preload and thus would occur only in the case of preload reserve and hence in the case of volume responsiveness [46]. Whether these predictors remain valuable in the case of cardiac failure could be questioned since the meaning of respiratory variation of stroke volume could be different. Indeed, in such a case, as detailed above, stroke volume may increase rather than decrease with each insufflation because of the beneficial unloading effect of increased intrathoracic pressure. In addition, in the case of congestive heart failure, mechanical insufflation, by compressing overfilled capillaries, has the potential to flush blood towards the left ventricle, increasing its preload. Combination of both mechanisms might result in a respiratory variation of stroke volume unrelated to volume responsiveness that is assumed to be reflected by the Δup component of the arterial systolic pressure [47]. In this regard, induction of

experimental ventricular failure in animals was demonstrated to result in a predominant Δup component since the Δdown component, reflecting the preload-dependency, became negligible (rightward shift of the Frank–Starling relationship) [47]. However, the magnitude of the arterial systolic pressure variation (sum of Δup and Δdown) was lower after induction of ventricular failure than before. This suggests that a great arterial pressure variation in patients with left-heart disease is unlikely to reflect a high Δup component. Therefore, in our opinion, the presence of a high stroke volume or pulse-pressure variation in patients with left-cardiac dysfunction should still indicate some degree of volume responsiveness and in most cases some degree of hypovolemia. In this regard, in patients with reduced cardiac function after cardiac surgery, Reuter *et al.* [48] demonstrated the usefulness of left-stroke-volume variation to assess fluid responsiveness. Using the PiCCO system, they demonstrated that regardless of the left-ventricular ejection fraction (higher or lower than 35%), the same close relationship was observed between stroke-volume variation determined by the PiCCO system before fluid infusion and the increase in stroke volume following volume expansion [48].

If some doubt persists about the meaning of a high respiratory variation of stroke volume or of pulse pressure, we recommend following response to passive leg raising, a simple method able to detect volume responsiveness [49]: a decrease in the magnitude of stroke-volume variation or pulse-pressure variation would mean that volume responsiveness was actually present before passive leg raising had been performed.

Conclusion

There is now a large body of evidence to support the use of NIPPV for treating the most severe forms of ACPE. By contrast, weaning from mechanical ventilation may induce cardiac impairment and ACPE, particularly in patients with previous cardiac disease. This cause of weaning failure may be underdiagnosed if PAOP is not adequately measured. Finally, indices of heart–lung interaction, like pulse-pressure variation, remain valuable predictors of volume responsiveness in patients with left-heart dysfunction receiving mechanical ventilation.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 99–100).

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