Weaning-induced Cardiac Dysfunction

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Introduction

Mechanical ventilation can be beneficial for the cardiovascular system in patients suffering from left heart failure [1]. In this regard, mechanical ventilation is used routinely as a therapy for acute heart failure even using a non-invasive mode [2]. Conversely, the cardiovascular consequences of abrupt transfer from mechanical ventilation to spontaneous breathing could be responsible for weaning failure in patients with left-side heart failure. Accordingly, cardiogenic pulmonary edema and/or myocardial ischemia have been reported to occur abruptly during weaning from mechanical ventilation in patients with preexisting cardiac disease [3–7].

Consequences of the Transfer from Mechanical Ventilation to Spontaneous Breathing on the Cardiovascular System

The two major consequences of transferring a patient from mechanical ventilation to spontaneous breathing are:

- the increase in respiratory muscle activity, which results in increased work of breathing and in decreased intrathoracic pressure, and
- the increase in sympathetic tone.

Increase in Work of Breathing

As a result of respiratory muscle activity, spontaneous breathing causes an increase in global oxygen demand [8, 9]. This results in increases in cardiac work and myocardial oxygen demand that can lead to myocardial ischemia in patients with coronary artery disease. In addition, the increased oxygen demand of the respiratory muscles may lead to blood flow redistribution towards the respiratory muscles with subsequent risks of hypoperfusion of critical organs [10–14].

Negative Intrathoracic Pressure

During weaning from mechanical ventilation, intrathoracic pressure becomes negative [3]. This leads to an increase in the systemic venous return pressure gradient and a decrease in the left ventricular (LV) ejection pressure gradient [1, 15]. The increase in systemic venous return pressure gradient can be responsible for an increase in central blood volume [16] with subsequent risks of pulmonary edema for-

mation. During spontaneous inspiration, the pressure surrounding the left ventricle decreases while the pressure surrounding the extrathoracic arterial compartment remains constant. Consequently, the left ventricle must generate a higher pressure – i.e., transmural pressure – before blood can leave the thorax. This condition is sensed by the left ventricle as an increased afterload [1].

Increase in Sympathetic Tone

The emotional stress due to the abrupt disconnection from the ventilator in patients ventilated for a long time can result in a dramatic adrenergic response. Lemaire et al. [3] measured a two-fold increase in epinephrine and norepinephrine blood levels during weaning of patients with chronic obstructive pulmonary disease (COPD). Acute development of marked hypoxemia and hypercapnia may also contribute to this catecholamine release, which can play a role in the induction of LV dysfunction through several mechanisms. Adrenergic discharge is responsible for:

- the increase in systemic arterial pressure and thus in LV afterload, and
- the increase in myocardial oxygen demand (tachycardia and increased systolic wall stress) that is potentially deleterious in the setting of coronary artery disease.

Main Cardiovascular Causes of Weaning Failure

Myocardial Ischemia

Mechanisms. In a patient with preexisting coronary artery disease, weaning from mechanical ventilation has potential to induce some degree of myocardial ischemia through several mechanisms:

- Myocardial oxygen demand might be potentially increased:
  - As mentioned earlier, the increased work of breathing results in an increased myocardial oxygen demand.
  - As we shall discuss later, the potential increase in LV afterload during weaning-induced loaded inspiration may lead to increased systolic LV wall stress and hence myocardial oxygen demand.
  - The excessive catecholamine release associated with difficult weaning [3, 17] may also result in increased myocardial oxygen demand related to tachycardia.
- Myocardial oxygen delivery might be reduced because of the following mechanisms:
  - Weaning-induced hypoxemia that can be secondary to 1) worsening of ventilation/perfusion ratios heterogeneity, as described during weaning from mechanical ventilation in patients with COPD [18], 2) onset of weaning-induced pulmonary edema as described below, and 3) decrease in PvO_2 related to excessive increase in global oxygen demand [19]. The decreased PaO_2 combined with respiratory acidosis may lead to low values of SaO_2, which may significantly lower the amount of oxygen delivered to the myocardium.
  - Decrease in diastolic arterial pressure related to the decrease in intrathoracic pressure during inspiration that may be significant in patients with marked inspiratory efforts due to difficult weaning. As diastolic arterial pressure is the inflow pressure to coronary perfusion, a decrease in coronary blood flow

could subsequently occur. In addition, tachycardia induced by excessive catecholamine release in difficult weaning is able to shorten the coronary perfusion time by reducing the duration of diastole.

Clinical Correlates. Evidence of development of myocardial ischemia during weaning in patients with preexisting coronary artery disease has been shown in numerous studies. In a series of 12 patients ventilated for acute myocardial infarction (AMI) and pulmonary edema, Rasanen et al. [20] observed five cases of myocardial ischemia during the switch from mechanical ventilation to spontaneous breathing. Lemaire et al. [3] have suggested that weaning-induced LV dysfunction can play a role in preventing successful weaning in patients with COPD and preexisting LV disease. They observed, in 15 patients who were recovering from acute cardiopulmonary decompensation, that weaning was associated with segmental wall motion abnormalities, suggesting the onset of myocardial ischemia [3]. To evaluate the possibility that myocardial ischemia may occur during weaning, Hurford et al. [4] performed Thallium 201 myocardial scintigraphy in 15 ventilator-dependent patients able to breathe spontaneously and comfortably for at least 10 minutes. During spontaneous breathing, eight out of 15 patients exhibited decreased myocardial Thallium uptake at redistribution on delayed images indicating decreased myocardial perfusion during spontaneous ventilation [4]. Chatila et al. [6] examined the rate of occurrence of ST segment abnormalities during weaning in a population of 93 patients (49 had known coronary artery disease). Only 6% of the patients exhibited ST segment abnormalities during the weaning period. This occurrence was associated with the highest rate of weaning failure [20]. Similar results were found by the same group of investigators in 83 patients suffering from coronary artery disease [6].

A case of ischemic LV failure and ischemic mitral insufficiency during weaning from mechanical ventilation was recently reported [21]. Transluminal angioplasty made weaning possible. This suggests that acute ischemic mitral insufficiency may contribute to cardiac failure during weaning and that angioplasty can allow successful weaning [21].

Cardiogenic Pulmonary Edema

A marked increase in pulmonary artery occlusion pressure (PAOP) has been observed during weaning in patients with pre-existing left heart disease [3, 19, 22]. Several mechanisms may explain this abnormality:

Increase in LV Afterload

Effects of Negative Intrathoracic Pressure. As pointed out earlier, a marked decrease in intrathoracic pressure during inspiratory efforts should result in an increased LV afterload [1]. This effect is likely to play a role in the development of acute LV dysfunction that may occur in association with acute exacerbation of COPD [23]. In this regard, increased aortic transmural pressures consistent with increased LV afterload were measured during a Mueller maneuver in normal volunteers [24] and in cardiac surgery patients [15].

In a series of patients with COPD and without pre-existing LV disease, a weaning-induced increase in LV afterload was suggested by a decrease in LV ejection fraction during the transfer from mechanical ventilation to spontaneous breathing [25].

Influence of increased sympathetic tone. Independent of any change in intrathoracic pressure an increase in LV afterload may occur during weaning because of the systemic hypertension related to marked catecholamine discharge [3, 26].

Increase in LV Preload

The fall in intrathoracic pressure during spontaneous inspiration is responsible for the widening of the systemic venous return pressure gradient owing to the decrease in right atrial pressure while the peripheral venous pressure remains unchanged relative to the atmospheric pressure. The resulting increase in right ventricular (RV) preload leads to increased RV stroke volume, pulmonary venous return, and LV preload, provided that the right ventricle is preload dependent. This necessarily

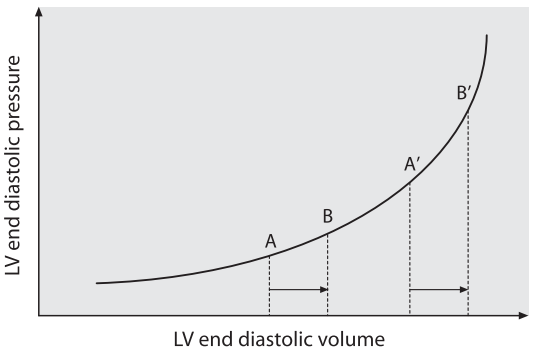

Fig. 1. Left ventricular (LV) end-diastolic pressure/LV end-diastolic volume relationship. Note that the relationship is curvilinear, such that when LV end-diastolic volume increases during weaning, the increase in LV end-diastolic pressure is low if the LV volume is previously normal (from A to B) while the increase in pressure is marked when the LV volume is previously high (from A′ to B′)

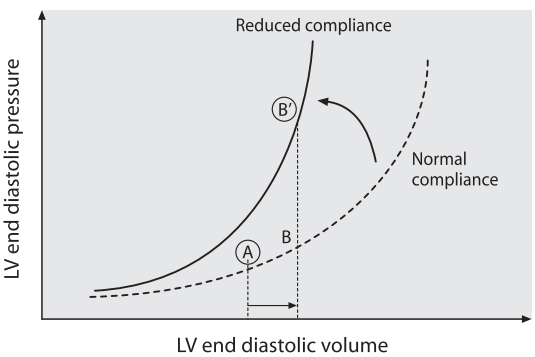

Fig. 2. Left ventricular (LV) end-diastolic pressure/LV end-diastolic volume relationship in normal and reduced LV compliance. Note that when LV end-diastolic volume increases during weaning, the increase in LV end-diastolic pressure remains low if the LV volume and compliance are previously normal (from A to B). By contrast, when the compliance of the left ventricle is either previously low or decreased by the weaning process *per se*, the increase in LV volume induced by weaning results in a marked increase in LV end-diastolic pressure (from A to B′)

induces an increase in LV filling pressures, particularly in the case of preexisting cardiac disease. Indeed, in the presence of a dilated cardiomyopathy, a further increase in LV end-diastolic volume will result in a marked increase in LV filling pressure (Fig. 1). In the presence of a reduced LV ventricular compliance, the increase in LV end-diastolic volume induced by weaning will result in a marked increase in LV filling pressure (Fig. 2). These mechanisms probably explain in part, the rise in PAOP observed during weaning in patients with pre-existing cardiac disease, in whom an increase in LV end-diastolic volume was actually measured during weaning from ventilation [3].

Decrease in LV Compliance

The transfer from mechanical ventilation to spontaneous breathing can reduce LV compliance and induce an increase in PAOP provided that the pulmonary venous return is maintained or increased. This phenomenon may result either from the onset of myocardial ischemia or from biventricular interdependence. This mechanism can occur during weaning especially when RV impedance increases secondary to an increase in pulmonary artery pressure [25]. The latter phenomenon may occur as a consequence of:

- weaning-related worsening of hypoxemia,
- weaning-related respiratory acidosis,
- weaning-induced increase in PAOP,
- weaning-induced alveolar vessel compression related to dynamic pulmonary hyperinflation created by tachypnea.

The resulting increase in RV afterload associated with the simultaneous increase in systemic venous return and RV filling may lead to a marked enlargement of the right ventricle during the transfer from mechanical ventilation to spontaneous breathing. This may decrease the ability of the left ventricle to fill during diastole and hence may result in a marked increase in PAOP. This phenomenon is likely to occur in patients with pre-existing RV disease and has been considered as responsible for weaning-induced pulmonary edema in COPD patients [3].

In summary, numerous mechanisms can contribute to increase PAOP during the transfer from mechanical ventilation to spontaneous breathing. However, in the absence of left heart disease, the increase in PAOP is limited [9, 27]. By contrast, marked increases in PAOP have been reported to occur in patients suffering from left heart disease who failed to wean because of the onset of cardiogenic pulmonary edema [3, 19, 22].

Diagnosis of the Cardiac Origin of the Weaning Failure

The diagnosis of weaning-induced cardiac dysfunction can be evoked in high-risk patients (COPD and chronic left heart disease) after discarding the classical causes of weaning failure. To establish such a diagnosis, it is useful to perform a weaning trial over a one-hour period of spontaneous breathing either using a T-piece or pressure support with low levels of insufflation pressure (7–10 cm H_2O). Detection of weaning-induced myocardial ischemia can be made with ST segment monitoring [5–7] although this method may suffer from a lack of sensitivity [28]. Detection of

weaning-induced pulmonary edema may require pulmonary artery catheterization showing a significant increase in PAOP during the weaning test [3, 19]. The decrease in mixed venous oxygen saturation (SvO_2) during the trial may also detect weaning failure from a cardiovascular origin [19]. Whether monitoring of central venous oxygen saturation ($ScvO_2$) [29] could also be useful remains undetermined. The PiCCO system, by showing an increase in extravascular lung water (EVLW) during weaning, could be helpful for detecting weaning-induced pulmonary edema. However, its clinical utility for that purpose remains to be established.

Treatment of Weaning-induced Cardiac Dysfunction

The treatment must be logically adjusted according to the mechanism that is most likely to have occurred. This requires an individual pathophysiological analysis. Diuretics can be considered when excessive increase in LV preload is assumed to be the predominant mechanism [3]. Treatment by nitrates seems a logical consideration when weaning-induced pulmonary edema is presumed to be related to a marked increase in LV preload and/or occurrence of myocardial ischemia. Vasodilators could be considered when augmentation of LV afterload is presumed to be the predominant mechanism. In this regard, phosphodiesterase inhibitors were demonstrated to allow successful weaning in patients with weaning-induced pulmonary edema [22, 30].

Conclusion

Weaning-induced cardiac dysfunction may occur in some patients suffering from left heart disease, in particular when associated with airway obstruction and/or right heart disease. Among the numerous pathophysiological mechanisms, myocardial ischemia and increase in LV afterload must be underlined. Detecting such phenomena may allow successful weaning after applying the most appropriate treatment.

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Circulatory Shock