Complex Heart–Lung Ventilator Emergencies in the CICU

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KEYWORDS

• Cardiopulmonary interactions • Mechanical ventilation • Hemodynamics • Cardiogenic shock

KEY POINTS

- Understanding the complex interplay between the cardiovascular and respiratory systems is essential for clinicians to provide optimal management and improve patient outcomes across diverse scenarios in the critically ill cardiac patient.
- Mechanical ventilation effects can be beneficial or detrimental, depending on the specific patient's physiology, cardiopulmonary reserve, hemodynamics, right and left ventricular function, and loading conditions.
- Monitoring and management of cardiopulmonary function during mechanical ventilation is critical in optimizing gas exchange and hemodynamics in the critically ill cardiac patient.

INTRODUCTION

The complexity and morbidity of patients admitted to the cardiac intensive care unit (CICU) has increased over the last few decades,[1,2] with respiratory failure complicating CICU admissions in 23% to 37% of the cases and representing one of the most common indications for admission to the CICU.[3–5] The presence of respiratory failure in the CICU patients represents a higher risk of adverse effects and mortality, particularly when requiring respiratory support with invasive mechanical ventilation,[4] underscoring the importance of proper coordination between cardiovascular and pulmonary systems.

This review summarizes the cardiopulmonary interactions during the use of invasive mechanical ventilation (IMV) in different clinical scenarios and provides insights for practical management of patients in these situations.

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PATHOPHYSIOLOGY IN HEART–LUNG INTERACTIONS

Effect of Spontaneous Respiration on Cardiac Function

The heart and lungs have a complex, tightly coupled relationship such that intrathoracic pressures modulate cardiac hemodynamics while cardiac pathology can adversely impact respiratory function. Breathing involves pressure–volume work, consuming oxygen and producing carbon dioxide.[6,7] The elastic and resistive components of work of breathing (WOB) can increase with states of decreased respiratory compliance, increased airway resistance, and increased gas flow demands. During spontaneous respiration, inspiration is an active process, and expiration is typically passive. However, a patient in respiratory distress will not only have increased inspiratory WOB but may also involve active inspiratory or expiratory efforts, increasing overall metabolic demand, resulting in profound pleural pressure swings as well as increased oxygen consumption, carbon dioxide production, and alterations in acid–base balance. Thus, states of respiratory distress can strain the myocardium, with specific detrimental effects to the right ventricle (RV) and left ventricle (LV), which is poorly tolerant of hypoxia, hypercarbia, and acidosis.

Flow through the pulmonary circuit is determined by the gradient between the RV intracavitary and left atrial pressures as well as by the pulmonary vasculature resistance (PVR), which in turn is affected by both lung volume and fluctuation in pleural pressure.[8] At low lung volumes, extra-alveolar vessels collapse, while alveolar vessels dilate; however, at high lung volumes, alveolar vessels compress, while extra-alveolar vasculature is tethered open.[9] Therefore, the relationship between lung volume and PVR is U-shaped, with PVR being minimized at functional residual lung capacity. For patients in respiratory distress, profoundly negative pleural pressures are transmitted to the heart so that the left atrial pressure may drop below alveolar pressure and the pulmonary vessels collapse. If so, the flow through the pulmonary circuit is now driven by the gradient between RV intracavitary and alveolar pressures, rather than the left atrial pressures, establishing a Starling Resistor effect.[5] Furthermore, as pericardial pressure drops and is transmitted to the RV, the RV intracavitary pressure becomes closer to alveolar pressure and there is less of a pressure gradient driving blood forward.

During inspiration, inferior diaphragmatic displacement decreases the pleural pressure which is transmitted to the pericardium and subsequently the right atrium while increasing the intra-abdominal pressure which is transmitted to the inferior vena cava (IVC). This pressure gradient established between the more negative atrial pressure and more positive pressures in the IVC favors blood return to the right heart. However, this augmentation of venous return to the right heart only occurs up to a point. For example, during states of respiratory distress, wide excursions of the diaphragm inferiorly can create intensely negative inspiratory pleural pressures which keeps the intrathoracic venous channels patent while raising the intra-abdominal pressure and collapsing the extrathoracic IVC, impairing right heart preload, and increasing left ventricular afterload.[10]

As estimated by Laplace's law, the wall stress of the left ventricle (LV) increases with increasing transmural pressure difference (LV end-diastolic pressure—pericardial pressure) and the chamber size (radius[2]) and decreases with the wall thickness (*h*). Pleural pressure changes that occur with spontaneous inspiration also increase LV afterload by increasing the transmural pressure gradient between the intracavitary pressure and pericardial pressure, which mirrors the pleural pressure. Thus, wide swings in pleural pressure increase the pressure gradient between intracavitary and pericardial pressure, increasing wall stress and LV afterload.[11]

Basics of Ventilator Modes

Mechanical ventilation can profoundly alter cardiopulmonary relationships that characterize normal physiologic breathing. Of the numerous modes of mechanical ventilation available (**Box 1**), we will focus on common types. Depending on the chosen mode, clinicians are generally able to prescribe the fraction of inspired oxygen (Fio_2), the positive end-expiratory pressure (PEEP), the minimum respiratory rate, and either a set volume (volume control) or inspiratory pressure (pressure control). In all modes, expiration is normally a passive process dictated by resistance and compliance of the respiratory system.[12] A variant of pressure control ventilation allows clinician to set a targeted volume (volume target) where the ventilator uses the minimal pressure above PEEP necessary to achieve the prescribed tidal volume. This breath type is known by various names such as pressure regulated volume control or volume control plus depending on the ventilator manufacturer. With this breath type, if the resulting tidal volume exceeds the volume targeted by the clinician, the ventilator will automatically deliver a lower pressure for subsequent breaths and vice versa. While this self-adjusting pressure mechanism

Box 1
Modes of mechanical ventilation

Ventilator Modes by Taxonomy

- Control Variable
  - Pressure control ventilation
  - Volume control ventilation
- Breath Sequence
  - Continuous spontaneous ventilation
  - Continuous mandatory ventilation (CMV)
  - Intermittent mandatory ventilation
- Targeting Scheme
  - Set point
  - Adaptive
  - Dual
  - Optimal
  - Bio-variable
  - Intelligent
  - Servo

Examples of Conventional Ventilator Modes

- CMV or assist/control
  - Volume control CMV
  - Pressure control CMV
- Synchronous intermittent mandatory ventilation
- Spontaneous ventilatory modes
  - Continuous positive airway pressure
  - Pressure support ventilation
  - Volume support

Examples of Other Ventilatory Modes

- CMV
- Airway pressure release ventilation
- Mandatory minute ventilation
- Inverse ratio ventilation
- Pressure-regulated volume control
- Proportional assist ventilation
- Adaptive support ventilation
- Adaptive pressure control
- Volume-assured pressure support
- Neurally adjusted ventilatory assist
- Automatic tube compensation
- High-frequency oscillatory ventilation

clearly has advantages, an important caution is warranted for patients with strong spontaneous inspiratory efforts, as the ventilator may gradually withdraw inspiratory pressure until the patient assumes the entire WOB, potentially leading to fatigue, despite ventilation support.

In assist control (AC) mode, patients trigger breaths if they meet the trigger threshold. If no trigger attempts are detected, the ventilator will deliver controlled breaths at the set rate with the prescribed volume or pressure. Further successful triggers above the set rate result in assisted breaths identical to the controlled ones. Synchronized IMV (SIMV) allows patient-triggered breaths, delivering controlled breaths if no triggers are detected.[13] Spontaneous inspiratory efforts beyond the set rate are managed similarly to pressure support or continuous positive airway pressure (CPAP): the patient must use their respiratory muscles to entrain gas and is allowed to determine their own inspiratory time and flow. Frequently, this mode is modified to provide pressure support above PEEP during these spontaneous breaths, potentially increasing WOB compared to assist-controlled ventilation and the unsupported breaths can lead intrathoracic pressure swings resulting in adverse hemodynamic consequences, such as increasing LV afterload.[14] For AC or SIMV modes, ventilators allow manipulation of inspiratory time or gas flow rate and pattern. During spontaneous ventilation, the patient must initiate all breaths as respiratory rate or inspiratory time is not prescribed by the clinician. The most common spontaneous mode is pressure support ventilation, where a clinician sets the Fio_2, PEEP, and an inspiratory pressure above PEEP. CPAP represents a variant of pressure support where clinicians do not prescribe any pressure above PEEP and instead rely entirely on patient muscular effort to assume the totality of the WOB.

According to the equation of motion ($P_{aw} - P_{mus} = F^*R + V/C + PEEP_{total}$; **Fig. 1**), alveolar pressure (P_{alv}) measured at the end-inspiration represents plateau pressure (P_{plat}) and is equivalent to the highest P_{alv} in the respiratory cycle, reflecting the total volume and the static compliance of the lung and the chest wall. This parameter (P_{plat}) should be routinely monitored to minimize ventilator-associated lung injury. The set PEEP ($PEEP_{set}$), also known as extrinsic PEEP, is provided throughout the respiratory cycle. The sum of $PEEP_{set}$ and autoPEEP ($PEEP_i$) is the total PEEP ($PEEP_{total}$). For a sedated passive patient on pressure control ventilation, P_{mus} which refers to the pressure caused by respiratory muscles during active patient efforts, is zero, while P_{aw} and $PEEP_{set}$ are determined by the clinician. Then, the

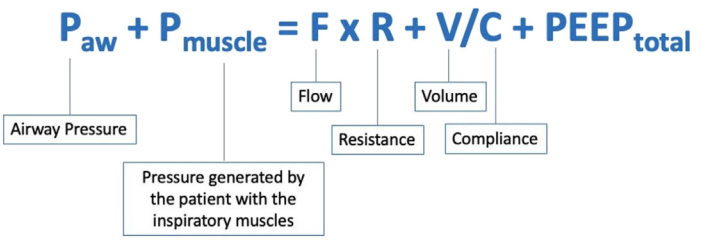

Fig. 1. The equation of motion of mechanical ventilation.

resistance (R) and compliance (C) of the respiratory system will ultimately determine the flow (F), the delivered tidal volume (V), and the P_{plat}. On the other hand, for a sedated passive patient on volume control ventilation, F, TV, and $PEEP_{set}$ are determined by the clinician, and the patient's R and C will determine P_{aw} and P_{plat}. If a patient is actively inspiring on the ventilator, P_{mus} will be negative (<0). For an actively inspiring patient on pressure control ventilation, F and V increase further due to the additional effects of P_{mus}, with a consequent increase in P_{plat} due to higher volumes (V). Conversely, for an actively inspiring patient on volume control ventilation, P_{aw} will decrease, but P_{plat} will remain the same as V, and $PEEP_{set}$ is set by the clinician.

CARDIOPULMONARY INTERACTIONS DURING MECHANICAL VENTILATION

Effect of Positive Pressure and Mechanical Ventilation on Cardiovascular Function

Under positive pressure ventilation (PPV), when positive pressure is applied to the airways, it causes the pleural pressure to become positive. In general terms, PPV leads to a decrease in LV afterload, an increase in RV afterload, and a decrease in both LV and RV preload[15] (**Fig. 2**). PPV also improves myocardial mechanics of the LV by reducing wall tension and modulating afterload via elevation in aortic pressure that activates peripheral baroreceptors.[16] This phenomenon leads to a reduction in systemic vascular resistance (SVR) and LV afterload. Additionally, PPV increases transmural pressure in the LV, which, in combination with the decreased afterload, elevates cardiac output (CO).[17,18] PPV also promotes improved coronary blood flow by enhancing the pressure gradient between the aorta and coronary arteries.[19]

Changes in PPV can significantly impact RV preload, afterload, and myocardial perfusion. Systemic venous return to the right atrium is passive, with blood flow occurring as a result of a pressure gradient between the superior/IVC and right atrium. When PPV is applied, it increases the pressure within the right atrium, which in turn reduces the gradient between the extrathoracic and

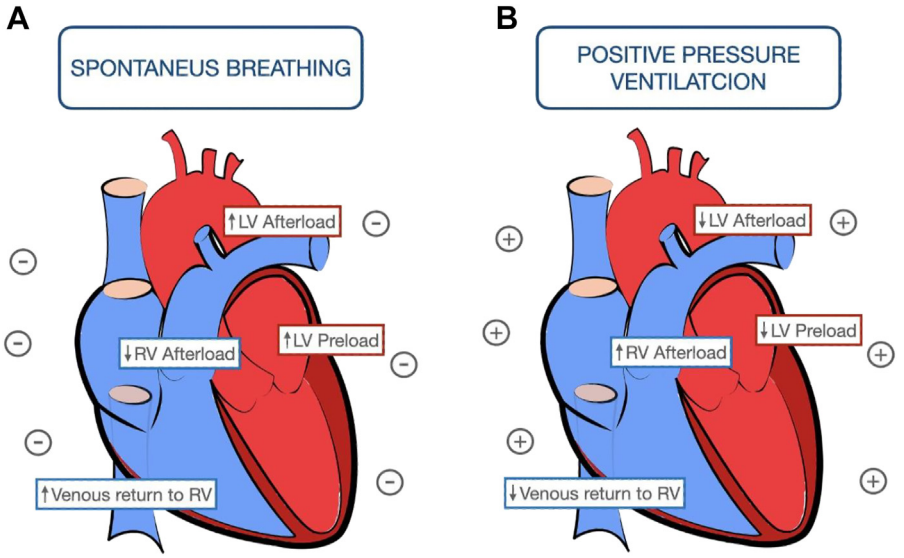

Fig. 2. Effect of pleural pressure on hemodynamics of the right ventricle (RV) and left ventricle (LV). (*A*) During spontaneous respiration, a negative pleural pressure occurs during inspiration. (*B*) Under positive pressure ventilation, the pleural pressure becomes positive.

intrathoracic circulation, leading to a decrease in venous return to the RV.[15] As explained previously, PVR is affected according to the lung volume in a U-shaped pattern.[16] In cases of atelectasis, where there is an increase in PVR due to hypoxia, an increase in PEEP can open alveoli and reverse this effect, thereby reducing the afterload on the RV. However, excessive PEEP can cause alveolar overdistension, compressing the extra-alveolar vessels and elevating PVR. This may redirect blood flow to poorly ventilated areas and creates a mismatch between ventilation and perfusion, resulting in hypoxemia and hypercapnia. High levels of PEEP tend to decrease the RV CO by reducing venous return and increasing afterload.[20] RV afterload can also be increased by increases on volume tidal and driving pressure.[21] Additionally, PPV leads to a decrease in preload on the LV due to reduced CO from the RV; consequently, ventricular interdependence can be potentiated, with RV overdistension and displacement of the interventricular septum toward the LV, subsequently diminishing CO.[22] Of note, the specific PEEP level to balance the concomitant prevention of atelectasis and optimization of pulmonary artery resistance (PVR) in patients with RV dysfunction should be individualized, as it is highly dependent on patients' pulmonary and chest wall compliance, body habitus, and loading conditions.

Hemodynamic Effects During Liberation from Mechanical Ventilation

In general, it is considered that a patient has approached "readiness for liberation from IMV" once minimal ventilator settings are achieved (eg, PEEP $\leq$8 cmH_2O and Fio_2 $\leq$50%), the patient has a mental status that would allow him to participate in the liberation process, and the etiology of their respiratory failure has improved or resolved. In a patient with cardiovascular disease, it is important to consider electrical and hemodynamic instability and integrate patient's individual physiology (eg, LV and RV function) into the approach to liberation. Similarly, patient–ventilator cardiopulmonary interactions should be optimized, ensuring that volume status, synchrony, and vasoactive support, if any, are improved. Removal of PPV has the potential to put incredible stress on the cardiovascular system, especially for those with ongoing ischemia and/or ventricular dysfunction, particularly as removal of PPV can lead to high LV afterload.[23–25] In order to test whether the patient can tolerate such stress, removal of IMV is evaluated with a spontaneous breathing trial (SBT). There are several ways to approach SBT, providing varying degrees of support,[26] which depending on the level of support may reverse many of the potentially favorable effects of PPV detailed earlier.

Withdrawal of positive pressure will increase RV preload and reduce RV afterload, which may be helpful in those with right ventricular failure or pulmonary hypertension (PH). In comparison, LV afterload and preload can abruptly increase once positive pressure is discontinued.[27] Compared to full ventricular support, transition to unassisted spontaneous breathing (eg, T-piece) can increase the pulmonary capillary wedge pressure (PCWP) by upward of 41%.[28] Therefore, optimization of ventricular filling pressures with diuretics and extubation to noninvasive positive pressure will allow for a more successful liberation from IMV. Removal of positive pressure may also unmask worsening mitral regurgitation, a common etiology of weaning and extubation failure, by increasing LV afterload.[29] Alternatively, the increase in afterload may be potentially beneficial for certain pathologies, such as patients with left ventricular outflow tract obstructions, by reducing dynamic outflow tract obstruction, in such scenarios the opposite approach should take place, with avoidance of diuretics and inotropes, while preventing tachycardia and extubating to nasal cannula rather than to noninvasive mechanical ventilation.

MONITORING IN PATIENTS WITH RESPIRATORY FAILURE AND CARDIOVASCULAR DISEASE

Invasive Hemodynamic Monitoring

Invasive hemodynamic monitoring with pulmonary artery catheter (PAC) can be a very useful tool to guide therapeutic interventions in patients with cardiovascular disease undergoing IMV,[30] particularly when monitoring RV function.[31] Elevated RV filling pressures can lead to significantly compromised organ perfusion, attributed to a diminished gradient between mean arterial pressure (MAP) and central venous pressure (CVP), a key determinant of venous return.[32] In instances where RV failure coincides with or stems from LV failure, PCWP may exhibit an increase, which can be further exacerbated by displacement of the interventricular septum to the left.[33] The CVP waveform might display a prominent v-wave due to tricuspid regurgitation (TR) resulting from RV dilation, and in cases of restrictive RV physiology, such as constriction or significant right ventricular failure with ventricular interdependence, a "deep and plateau" waveform can be observed. Similarly, other important parameters of right ventricular dysfunction include a low right ventricular stroke work index, an elevated CVP to PCWP ratio, and

a low pulmonary artery pulsatility index (PAPi). This last parameter, which is calculated as (systolic pulmonary artery pressure [PAP]—diastolic PAP)/CVP, has been validated to diagnose RV failure and RV shock in several conditions, including cardiogenic shock, inferior myocardial infarction, postventricular assist device implantation, and PH.[34] Notably, normal CO or PAP does not necessarily exclude the possibility of RV dysfunction.[22]

Another important application of the PAC relies on its ability to assist in PEEP titration in patients with RV dysfunction, especially when combined with echocardiographic assessment. For instance, in patients with severe hypoxia, slow increase in PEEP can be performed while closely monitoring CVP, pulmonary arterial diastolic pressures, and pulse pressure of the pulmonary artery and PAPi, along with septal positioning with real-time echocardiography. The objective would be to achieve an ideal balance between lung recruitment and hypoxia resolution and avoidance of worsening right heart hemodynamics. Furthermore, PAC can also assist in evaluating fluid responsiveness and filling pressures, not only by measuring CVP and PCWP values[35] but also by dynamic maneuvers. For instance, a rise in CVP following a fluid challenge, without a concurrent change in CO, suggests inadequate fluid responsiveness and should concern clinicians as a potential presence of RV dysfunction.[36]

Point-of-care Ultrasound in Respiratory Failure and Cardiovascular Disease

Echocardiographic assessment is a routine diagnostic modality part of the standard of care of patients admitted to the CICU, as it provides a detail and comprehensive assessment of biventricular and valvular function, as well as filling pressures and diastology. In the recent decades, the use of cardiac and noncardiac point-of-care ultrasound (POCUS) has become a key strategy to guide management in the critically ill patient, including patients with both cardiogenic and noncardiogenic pulmonary edema. Notably, in patients with acute lung injury, the concurrent inflammatory cascade can increase pulmonary vascular resistance, and may be further complicated by the application of PPV,[37] which has the potential of resulting in acute cor pulmonale.[38]

Bedside POCUS offers valuable insights into cardiopulmonary interactions. Evaluation of RV size to assess ventriculo-ventricular interaction and longitudinal function by the tricuspid annular plane systolic excursion (TAPSE) in case of dilatation is important to estimate the potential impact of PPV. Systolic pulmonary arterial pressure (sPAP) estimation using the tricuspid peak velocity is simple and practical; however, it may be limited by patient positioning and lung interpositions yielding suboptimal windows affecting Doppler acquisition. Additionally, sPAP may be largely underestimated in case of RV failure, related to the reduced force of contraction and therefore gradient creation. The ratio TAPSE/sPAP has been established as a marker of RV dysfunction in chronic PH[39]; however, its application in the acute settings has not been yet established. Similarly, the presence of a presystolic a-wave (pulmonary forward flow in correspondence of atrial contraction) is reflective of RV restrictive compliance and increased end-diastolic pressure, serving as a marker of diastolic dysfunction, and it has been described to be associated with higher $Paco_2$, PEEP, and inspiratory peak pressure.[40] However, its role in acute settings has not been systematically evaluated.

In terms of lung POCUS, the identification and quantification of B-lines with lung ultrasound (LUS) holds extremely high accuracy in defining the deaeration of the lung parenchyma and allows the clinician to estimate the extent of congestion in heart failure and myocardial infarction patients.[41–43] Additionally, the balance between lung recruitment and overdistension can also be assessed by LUS,[44] through the characterization of lung morphology,[45] which integrated with assessment of ventricular interdependence can provide useful information when pursuing PEEP titration. Lastly, diaphragmatic ultrasound allows the evaluation of diaphragmatic thickness and thickening fraction. Their alteration has been associated with total ventilation time and rate of weaning failure reflecting the ability of the diaphragmatic muscle mass to cope with the increased WOB due to the sudden cessation of PPV.[46] However, its role has been best characterized in medical intensive care units and less in the CICU. In summary, an ultrasound-integrated approach with POCUS, invasive hemodynamics, and ventilatory parameters (blood gas analysis and ventilation mechanics) is extremely useful for a comprehensive assessment or respiratory failure and hemodynamic response to PPV.[38,47]

Noninvasive Blood Pressure Monitoring

There is a growing field of hemodynamic monitoring technology designed to minimize invasiveness and maximize access to hemodynamic data at the bedside. The available studies evaluating the accuracy of measuring hemodynamic parameters in critically ill, intubated patients are limited.[48–51] Pulse contour analysis, both noninvasive or minimally

invasive, uses proprietary algorithms to reconstruct arterial wave forms from peripheral arteries to calculate the MAP and CO utilizing the area under the systolic curve. This is ideally performed in patients who are completely passive on the ventilator in order to minimize wide variations in stroke volume measurements related to large changes in intrathoracic pressure with patient's respiratory efforts, especially if dyssynchrony is also present. Pulse contour analysis has not demonstrated interchangeability with gold standard thermodilution methods in critically ill patients by neither peripheral arterial nor finger cuff measurements.[48,52–54] Another major consideration when considering the use of minimally invasive devices is the pathophysiology of cardiogenic shock, which is highly variable and multifactorial, along with the limitations of these devices in such clinical scenarios. The physiologic responses in early circulatory failure include an increase in both SVR and venous congestion, which leads to the clinical findings of cool, mottled extremities, along with the evidence of increased extravascular lung water, and peripheral edema. Consequently, noninvasive methods to estimate CO have limited validity valid in situations requiring vasoactive medications, high SVR, and significant peripheral edema.

The value of these devices in the CICU patient population may be for the evaluation of fluid responsiveness and extravascular lung water by either thoracic bioimpedance or bioreactance or by transpulmonary thermodilution when using Pulse Index Continous Cardiac Output (PiCCO).[55–57] Of note, elevations in extravascular lung water will limit hemodynamic assessment by thoracic bioimpedance but can predict weaning failure from mechanical ventilation in patients with left ventricular ejection fraction (LVEF) less than 40%.[58] Similarly, thoracic bioreactance utilizes electrodes also placed on the chest wall to measure the phase shift of oscillating signals transmitted across the thorax. Although this technology has not been validated in patients with CS, it may not be limited by the elevations in extravascular lung water. While it is not directly interchangeable with invasive hemodynamics as the gold standard in CS, there is evidence to support its use in the evaluation of fluid responsiveness.[57] Another modality is transpulmonary thermodilution, which uses both thermodilution with a central venous line and a thermistor, along with a central arterial pulse waveform analysis. While this device provides a fairly accurate estimation of the CO, with a percent error of approximately 27%, it can be interchangeable with the PAC in patients with CS for assessment of the CO.[59] Similarly, this technology also offers the ability to measure extravascular lung water and correlated with B-lines on lung ultrasound,[60] but as with any other noninvasive monitors, it does not provide an accurate and specific assessment of the filling pressures for the LV or the RV. In summary, some of the noninvasive monitoring technologies can assist in assessing CO and extravascular lung water; however, their role in patients with cardiovascular disease undergoing IMV is limited, given their inability to assess intracardiac filling pressures and right ventricular function.

CARDIOPULMONARY INTERACTIONS DURING VENTILATION IN SPECIFIC SITUATIONS

Cardiogenic Shock

The incidence of respiratory failure and the need for PPV in patients with CS rages between 50% and 88%,[61,62] and based on substudies of the TRI-UMPH and CULPRIT-SHOCK trials, delays in initiation of invasive mechanical (IM) PPV in patients with CS are associated with increased mortality.[63,64] In terms of modes of IMV, no differences have been observed between volume-controlled continuous mechanical ventilation (VC-CMV) and pressure-controlled continuous mechanical ventilation (PC-CMV), however as mentioned in prior sections of this article, SIMV mode is not recommended as it can lead to swings in intrathoracic pressure, increased afterload, and ventilator dyssynchrony, thereby increasing myocardial oxygen consumption and worsening myocardial mechanics.[64]

PEEP titration should be individualized based on the hemodynamic profile and oxygen saturation of each patient. Observational studies suggest that PEEP can have a beneficial effect in patients with left ventricular dysfunction, improving CO,[65–68] decreasing PCWP, and mitigating mitral regurgitation.[69,70] Therefore, initiating PEEP at 5 cmH_2O and titrating it for optimal hemodynamics, gas exchange, and bedside ultrasound are recommended. However, in preload-sensitive states such as RV dysfunction, pericardial tamponade, pulmonary embolism with cor pulmonale, hypovolemia, or obstructive hypertrophic cardiomyopathy, higher levels of PEEP may have a negative hemodynamic impact.[71] In these cases, starting with a PEEP range of 3 to 5 cmH_2O and titrating to oxygen saturation greater than 92% with closely hemodynamic and POCUS monitoring are preferred to maintain adequate oxygenation and prevent atelectasis. In regard to tidal volume, as opposed to the acute respiratory distress syndrome (ARDS) literature, there are limited data assessing the impact of low tidal volume ventilation in patients with cardiovascular disease. A small nonrandomized study demonstrated higher mortality with TV above 9.3 mL/kg of ideal body weight[72];

however, the small sample size makes this study was underpowered for hard clinical outcomes and therefore it is difficult to draw conclusions from it. Therefore, tidal volume should be maintained between 6 and 10 mL/kg and titration along with respiratory rate to P_{CO_2} levels while preventing plateau pressures over 30 mmH_2O. Fi_{O_2} should be titrated to ensure proper gas exchange, with a target oxygen saturation greater than 92% and prevention of hyperoxemia (Pa_{O_2} <120 mm Hg; Table 1).

Mechanical Ventilation in the Patient Undergoing Venoarterial Extracorporeal Membrane Oxygenation

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) provides oxygenation by removing deoxygenated blood from the patient's venous system, passing it through an oxygenator in the ECMO circuit, and returning oxygenated blood back into the arterial system. The oxygenator also facilitates gas exchange by removing carbon dioxide (CO_2) and adding oxygen to the blood. Thus, during VA-ECMO support, the impact of mechanical ventilation parameters on oxygenation and CO_2 removal is limited.[73] Additionally, there is a decrease in pulmonary arterial flow, leading to an alteration in the ventilation–perfusion ratio. As a result, maintaining normal alveolar ventilation in this context may result in overventilation of the lungs. The Extracorporeal Life Support Organization (ELSO) guidelines aim to rest the lung in patients supported with VA-ECMO.[74] In order to minimize ventilator-induced lung injury, the ventilation strategy often involves using lung-protective ventilation strategies. These strategies include limiting tidal volumes, maintaining PEEP to prevent alveolar collapse, and avoiding high inspiratory pressures.[75,76] However, mechanical ventilation data in VA-ECMO are limited, with randomized studies primarily focusing on venovenous ECMO with severe respiratory failure. Observational studies have shown that the use of lung-protective ventilation during the first 24 hours is associated with improved survival in CS patients requiring VA-ECMO.[77,78] Higher PEEP (recommended between 5 and 15 cmH_2O) may have a beneficial effect on hemodynamics by unloading the LV.[62,74] It is reasonable to maintain the lowest tolerable Fi_{O_2} to target SaO_2 greater than 90% while avoiding hyperoxemia (Pa_{O_2} > 300 mm Hg) as it has been associated with increased mortality.[79,80] Extubation during VA-ECMO circulatory

Table 1
Proposal for adjusting initial parameters of mechanical ventilation in patients with cardiogenic shock

Ventilator Parameters	Initial Ventilator Settings	Monitoring
Ventilatory mode	PC-CMV or VC-CMV (avoid modes that require patient effort)	Maintain synchrony
Tidal volume	6–10 mL/kg of IBW	• Plateau pressure <28–30 mm Hg • Driving pressure <15 mm Hg • Adjust to Pa_{CO_2}
Respiratory rate	12–16 breaths/min	• Adjust to Pa_{CO_2} • Avoid autoPEEP
PEEP	LV dysfunction: • Start PEEP 5 cmH_2O (8–10 cmH_2O if PCWP > 18 mm Hg) "Preload dependent" states[a]: • Start PEEP 3–5 cmH_2O	• Title according to hemodynamic response (preferably invasive), gas exchange, and bedside ultrasound. • In LVAD or ECMO monitor LV unloading • Control plateau pressure <28–30 mm Hg • Avoid autoPEEP
Fi_{O_2}	Start at 100%, but adjusts rapidly according to SaO_2	• SaO_2 > 92% • Avoid hyperoxia (especially after cardiac arrest)

Abbreviations: ECMO, extracorporeal membrane oxygenation; IBW, ideal body weight; LV, left ventricle; LVAD, left ventricular assist device; PC-CMV, pressure-controlled mechanical ventilation; PEEP, positive end-expiratory pressure; VC-CMV, volume-controlled mechanical ventilation.

[a] Right ventricle dysfunction, cardiac tamponade, constrictive pericarditis, hypovolemia, obstructive hypertrophic cardiomyopathy.

support has been associated with reduced incidence of ventilator-associated pneumonia and mortality.[81] Patients eligible for liberation from mechanical ventilation while on VA-ECMO should be carefully selected due to the risk of sudden changes in blood pressure and blood flow resulting from the cessation of PPV.

Right Ventricular Failure and Pulmonary Hypertension

PH is common in the CICU and independently associated with a higher risk of death.[82] Thus, caring for these patients, it is important to understand cardiopulmonary interactions, particularly as it relates to sedation, intubation, and PPV. PPV is often discouraged in patients with PH and RV failure due to the potential for hemodynamic worsening when intrathoracic pressure is increased. The RV adapts to chronically elevated afterload with RV hypertrophy resulting in increased myocardial oxygen demand and simultaneous reduction in RV myocardial coronary blood flow. Patients with progressive PH often present to the CICU with worsening RV failure characterized by right atrial, RV and tricuspid annular dilation, reduced RV stroke volume, and advanced TR. The overloaded right heart and ventricular interdependence further compromises LV filling and stroke volume, causing systemic hypoperfusion and hypotension, RV ischemia and worsening RV failure. Severe RV failure often occurs in group 1 PH, though it may result from PH of any cause.[83]

In severe RV failure, rapid hemodynamic deterioration may be precipitated by small increases in RV afterload brought on by PPV-mediated compression of pulmonary vasculature. Additionally, PEEP can worsen hypoxemia and hypercapnia if compression of extra-alveolar vessels causes shunting of blood to poorly ventilated areas. The presence of atelectasis, hypoxemia, hypercapnia, and acidosis (both respiratory and metabolic) can increase pulmonary vascular resistance and afterload but can be improved or resolved with the use of PPV, potentially improving hemodynamics.[15] Additionally, reduction in preload and LV afterload with PPV may improve hemodynamics especially when PH is caused by left heart disease. A comprehensive understanding of the severity of RV abnormalities and the cause of PH is helpful to predict the response to PPV (Fig. 3).

In patients with severe RV dysfunction, sedation, endotracheal intubation, and initiation of PPV is particularly hazardous. Preload and MAP should be optimized prior to sedation for intubation. A technique of awake, spontaneously breathing, semirecumbent positioned intubation over a bronchoscope to minimize risks of hemodynamic decompensation has been described.[84]

Cardiopulmonary Resuscitation

Cardiopulmonary resuscitation (CPR) often includes chest compression and ventilation; however, when comparing compressions with and without ventilation yields mixed data.[85–91] Compression-only CPR increases bystander willingness to begin CPR[92–94]; thus, it is an acceptable strategy to encourage early compressions.[95] Given the likely benefits of pairing CPR with ventilation, it is recommended for willing bystanders and health care providers[88,95] because longer duration of CPR without ventilation eventually depletes arterial oxygen stores.[96] When ventilation is attempted, there are equivalent outcomes for continuous asynchronous breaths compared to pausing compressions for breaths.[97] It is thus a 2b recommendation to deliver breaths in an asynchronous manner.[95] Notably, it has been observed that overventilation during CPR is common[98–100] and can lead to decreased coronary perfusion, gastric inflation with aspiration, increased intrathoracic pressure, decreased

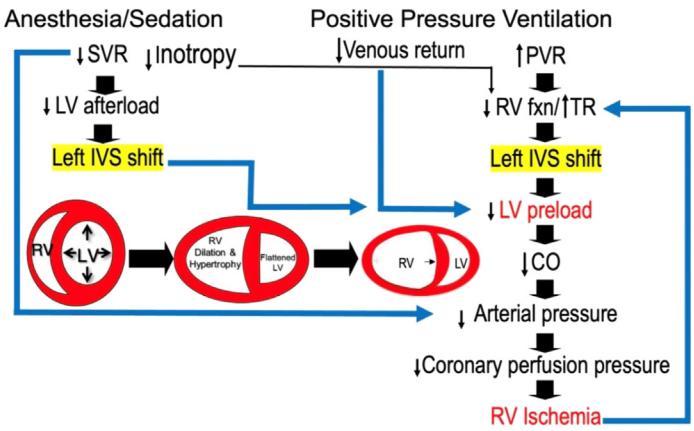

Fig. 3. Mechanism of worsening right ventricle (RV) failure in positive pressure ventilation (PPV). CO, cardiac output; IVS, interventricular septum; LV, left ventricle; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; TR, tricuspid regurgitation. (*Courtesy of* and *adapted from* Teresa De Marco, MD, San Francisco, California.)

venous return, and ultimately decreased survival.[98,99] Therefore, providers in charge of ventilatory efforts during CPR should be mindful about maintaining slow and sustained breaths mimicking physiologic breathing.

Management of oxygenation and ventilation after return of spontaneous circulation varies depending on the etiology of the arrest and underlying comorbid conditions. For example, an arrhythmogenic cardiac arrest may be managed with basic ventilation immediately postarrest, whereas cardiac arrest secondary to respiratory failure may require advanced ventilation strategies, bronchoscopy, other procedural interventions, or additional imaging. There are some data that mild hypoventilation with increased $Paco_2$ may increase cerebral blood flow[101,102] in the postarrest period[103,104]; however, recent data from a randomized controlled trial in cardiac arrest patient showed no difference in neurologic outcomes between patients managed with normocapnia ($Paco_2$ 34–45 mm Hg) and mild therapeutic hypercapnia ($Paco_2$ 50–55 mmHg) goals.[105] Thus, ventilation targeting normal $Paco_2$ is recommended in most cases by the American Heart Association postarrest care guidelines.[106] The use of hyperventilation to correct metabolic acidosis should be avoided as it may induce cerebral vasoconstriction and therefore affect cerebral perfusion.[107–110] In regard of oxygenation targets, it is well established that hypoxia (Pao_2 usually <60 mm Hg) is deleterious[27–29] but optimal targets for Pao_2 are remain nebulous. In terms of hyperoxia, there are variable data, but nonrandomized studies have demonstrated that severe hyperoxia, particularly if Pao_2 greater than 300 mm Hg, is associated with worse outcomes cardiac arrest patients, particularly in terms of neurosurvival.[109–114] The 2015 postcardiac arrest guidelines suggest maintaining an arterial saturation over 94%.[106] The more recent BOX trial suggests that no difference between a restrictive versus liberal oxygenation target, however, the liberal oxygenation group targeted a Pao_2 98 to 105 mm Hg,[115] but this study did not assess the effect of hyperoxemia (usually defined as Pao_2 > 120 mm Hg) in cardiac arrest outcomes.

BEDSIDE TROUBLESHOOTING AND CLINICAL SCENARIOS

Airway Management in the Patient with Cardiovascular Disease

The decision to perform endotracheal intubation in a patient with cardiovascular disease should incorporate a careful assessment of the risk and benefits of intubation and the effects of PPV. The preintubation assessment should consider the underlying cardiac condition, hemodynamic status, right and left ventricular function, baseline pulmonary function, and other therapies such as mechanical circulatory support.[62] As such, the clinician should integrate such elements to decide on the timing of intubation, intubation approach, choice of induction agents, neuromuscular blockade, and selection of analgosedation postintubation. For instance, in patients with CS, early intubation and early initiation of mechanical ventilation are associated with better survival when compared to delayed initiation of IMV.[63,64] However, in patients with severe preload-sensitive conditions, such as PH, severe RV failure, or cardiac tamponade, the preference is to delay or avoid intubation and initiation of IMV.[15,83] If avoiding intubation is not possible, it is recommended to pursue awake intubation with minimal or no sedation by a clinician with expertise in such an approach.[15,84]

Regarding sedative selection, clinicians should consider agents with minimal impact on sympathetic tone and hemodynamics. Most induction agents will decrease the sympathetic tone and a decrease in preload, leading to hypotension. Etomidate at a lower dose may decrease the hemodynamic effects. Ketamine can be considered, recognizing that it may lead to severe hypertension (not a good choice in aortic dissection, acute pulmonary edema, or cardiac dysfunction). These agents are followed by the neuromuscular agent of choice to improve intubation conditions. The technique used will depend on the expertise of the center, although recent evidence may favor the use of video-assisted laryngoscope to minimize timing and intubation attempts.[116]

In patients who are already hypotensive at baseline, premedication with vasopressors can allow the clinician to improve hemodynamic parameters in preparation for intubation, targeting a MAP above 65 mm Hg before induction.[15,62] Correcting acidosis and hypoxia as much as possible before intubation and having readily invasive blood pressure monitoring and POCUS available to perform a comprehensive evaluation if hemodynamic instability ensues quickly should also be considered.

Autopositive End-Expiratory Pressure in the Cardiac Intensive Care Unit

An important parameter to monitor in patients undergoing IM-PPV is autoPEEP,[117] particularly in the presence of cardiovascular conditions given its potential for significant hemodynamic instability.[15,16] At the beginning of exhalation, P_{alv} starts at P_{plat} but gradually decreases exponentially toward set PEEP. Expiratory flow then results due

to a pressure gradient between P_{alv} and P_{aw}, with P_{aw} being simply the set PEEP during exhalation. For passive exhalation, the amount of air remaining in the lungs depends on the expiratory time constant, a combination of resistance, and compliance (Fig. 4) of the respiratory system. In certain patients, incomplete exhalation of the inspired volume can progressively lead to air trapping with each subsequent breath, resulting in autoPEEP (also known as intrinsic PEEP).[12] Notably, patients with high resistance, high compliance, or both (eg, chronic obstructive pulmonary disease) need longer exhalation time and are therefore more prone to developing autoPEEP. Since autoPEEP can cause barotrauma or hemodynamic collapse, it should be carefully monitored in all patients but especially in those with obstructive lung disease, particularly if there is concomitant tachypnea or increased WOB.

If autoPEEP is not detected and addressed in a timely fashion, it has the potential to cause catastrophic hemodynamic consequences. The equation of motion dictates the potential impact of autoPEEP on pressure control versus volume control ventilation. If autoPEEP develops for a patient on pressure control ventilation, according to the equation, the F and TV must decrease since P_{aw} and $PEEP_{set}$ will remain constant, which are set by the clinician in pressure control. Thus, the consequence of autoPEEP for a patient on pressure control ventilation could be worsening respiratory acidosis caused by a decrease in tidal volume and flow. The worsening respiratory acidosis could, in turn, result in hemodynamic compromise. In contrast, if autoPEEP increases for a patient on volume control ventilation, according to the same equation, the P_{aw} and P_{plat} must increase since frequency (F), tidal volume (TV), and $PEEP_{set}$ will remain constant, which are set by the clinician in volume control. Thus, the consequence of autoPEEP for a patient on volume control ventilation, in contrast to pressure control, could be hyperinflation and increased intrathoracic pressures. In turn, the increase in intrathoracic pressure may lead to a decrease in venous return and subsequently, hemodynamic compromise[118] (Fig. 5). Moreover, as more air is trapped and autoPEEP increases, patient will need to work more vigorously to trigger each breath, which can lead to triggering asynchrony, increased WOB, agitation, tachypnea, and tachycardia, which in turn, may further increase autoPEEP in a vicious cycle (Fig. 6). For these reasons, clinicians should be proactively vigilant about autoPEEP.[12]

Identifying and managing autopositive end-expiratory pressure

As opposed to other IM-PPV settings and parameters, such as peak pressures or minute ventilation, the mechanical ventilator does not have a specific alarm for autoPEEP. Moreover, patients with autoPEEP may not have evident hypoxemia or hypercarbia, and its only manifestation may be hemodynamic instability along with respiratory distress and patient–ventilator asynchrony due to air trapping. In cooperative patients, autoPEEP may be assessed by performing an end-expiratory hold. However, many patients who are not sufficiently sedated may not cooperate with the breath hold. If so, active patient efforts (P_{mus}) may interfere with this technique for assessing autoPEEP. An esophageal balloon can estimate autoPEEP in patients who are not cooperative with the end-expiratory pause maneuver. If patient does not cooperate with this maneuver and an esophageal balloon is not available, the clinician should look for indirect signs of autoPEEP such as ineffective triggering, as evidenced by failed inspiratory efforts to initiate a breath or a persistent end expiratory flow and a lack of return to the baseline of the expiratory limb of the flow curve (Fig. 7). Similarly, asymmetric areas under the flow time curves can be seen, particularly as a

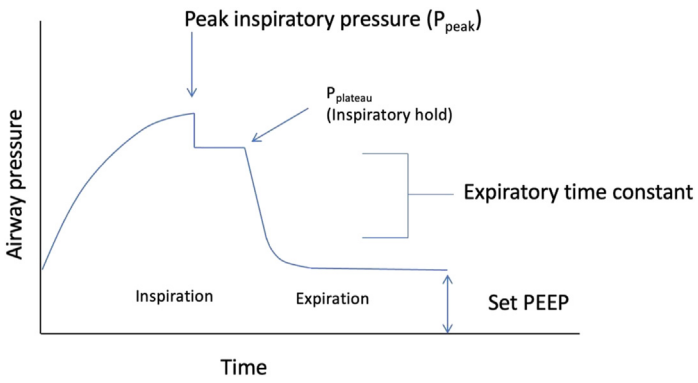

Fig. 4. Pressure–time curve demonstrating the relationship between peak pressure (P_{peak}), plateau pressure ($P_{plateau}$), and positive end-expiratory pressure (PEEP) as well as the expiratory time constant as an exponential decay in pressure during passive exhalation due to recoil from thoracic wall and lung parenchyma.

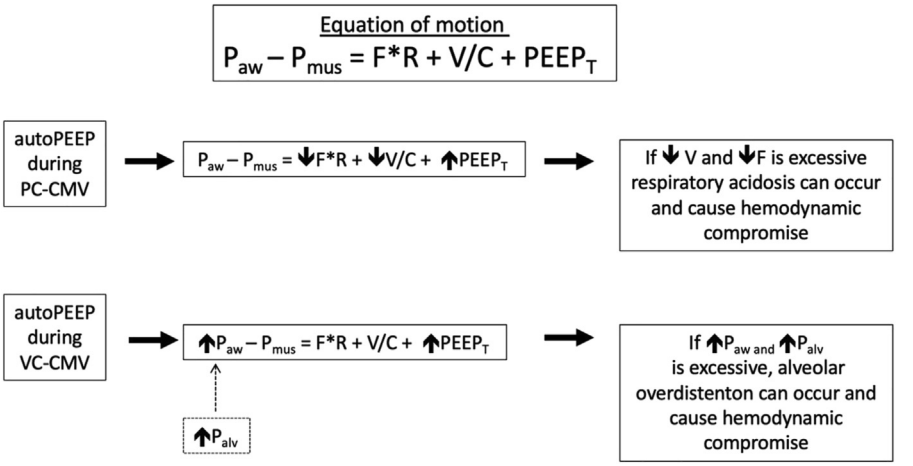

Fig. 5. Effect of autoPEEP on volume control ventilation (VC-CMV) and pressure control ventilation (PC-CMV). As autoPEEP increases, a compensatory effect will occur on F, V, P_{airway} and P_{alv}. If autoPEEP is not addressed hemodynamic compromise will ultimately occur by respiratory acidosis (if PC-CMV) or alveolar overdistension (if VC-CMV). C = compliance; F = flow; P_{airway} = airway pressure; P_{alv} = alveolar pressure; V = volume.

sign of obstructive airway disease, which should alert the clinician that the patient may be prone to developing autoPEEP. If autoPEEP is detected, it should be promptly addressed, and the strategies suggested in **Box 2** should be employed.

Decrease Lung Compliance in Cardiovascular Disease

Few data exist on the pathophysiological mechanisms of reduced lung compliance in cardiovascular

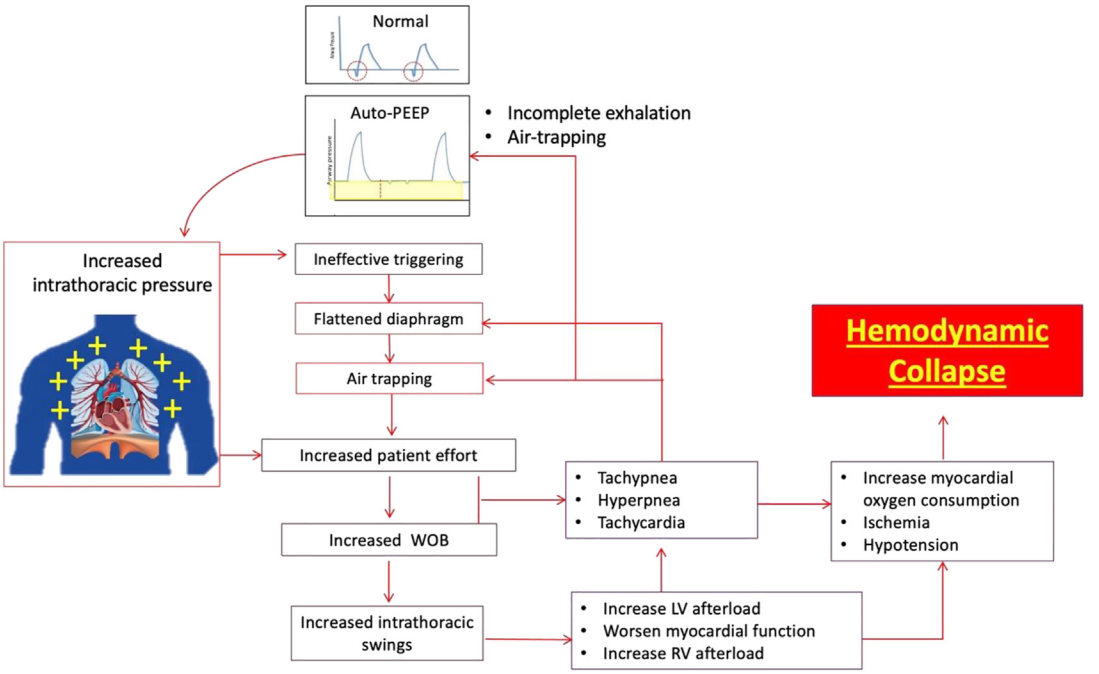

Fig. 6. Pathophysiology of autoPEEP leading to hemodynamic collapse in patients with cardiovascular disease. Note how the increase baseline dictated by autoPEEP (yellow area) represents a higher pressure to overcome by the patient to trigger breaths. As work of breathing increases and the patient becomes more dyssynchronous and tachypneic, autoPEEP will worsen with the potential of leading to hemodynamic collapse. LV, left ventricle; RV, right ventricle; WOB, work of breathing.

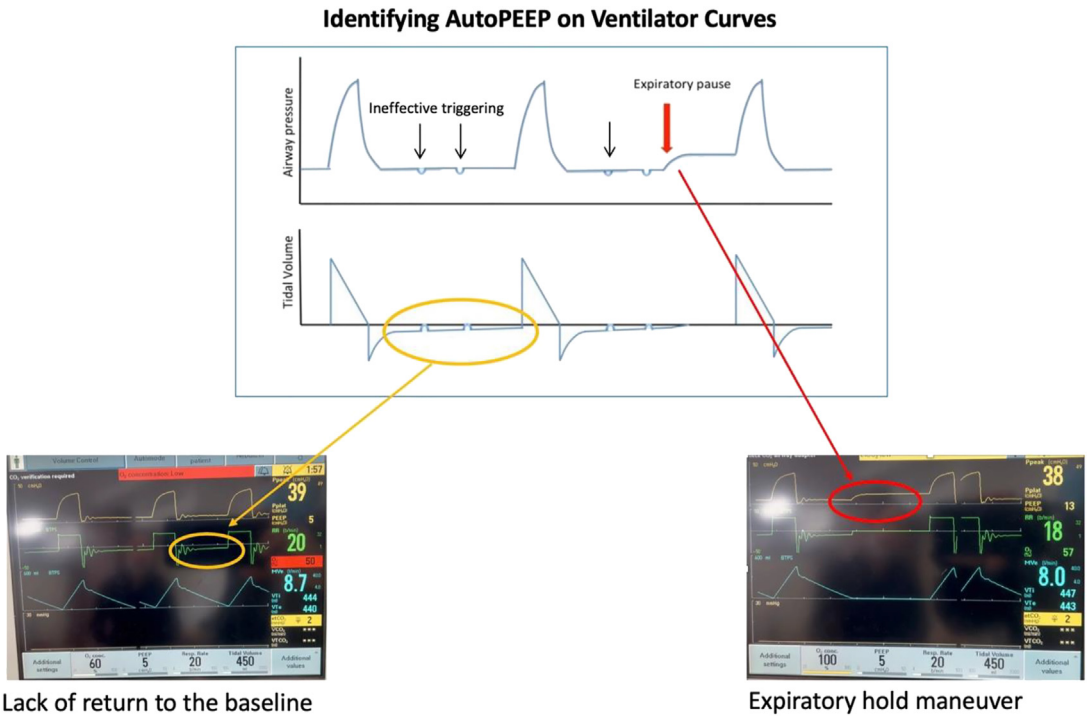

Fig. 7. Detection of autoPEEP on volume control ventilation by assessing ventilator curves. Note the ineffective triggering efforts by the patient (*black arrows*) as well as the lack of return to the baseline in the volume/time curve (*yellow circle*). An expiratory hold maneuver is applied allowing to quantify total PEEP, from which subtracting set PEEP will provide you with the amount of autoPEEP.

disease, probably due to the difficulty in its noninvasive assessment. Impaired lung compliance is associated with several pulmonary alterations in cardiac disease, including impaired alveolar gas diffusion and worsening of ventilation–perfusion match,[119] contributing to exertional dyspnea. This has been reported, for example, in heart failure with preserved ejection fraction,[120,121] where patients may be more likely to cease exercising because pulmonary limitation and not because of impaired CO reserve, as happens in heart failure with reduced ejection fraction.[122]

Many factors causing reduced lung compliance have been hypothesized, with potentially different contributions according to distinct cardiovascular conditions: increased PCWP, increased PVR, and alteration in surface forces in alveoli. The pathophysiologic alteration most strictly linked to this phenomenon is pulmonary edema; in this context, liquid-filled alveoli induce mechanical stress on air-filled alveoli, hence reducing overall lung compliance.[123] Assessing lung compliance is more feasible in ventilated patients, where monitoring tidal volume and airway pressures aids its calculation, and it is not uncommon to observe elevated plateau pressures in pulmonary edema that significantly improved as volume status and CO is optimized.

Esophageal Pressure Monitoring in Cardiovascular Patient

Esophageal pressure (P_{es}) monitoring is valuable for assessing heart–lung interactions and gaining insights into the cardiopulmonary system. It involves inserting a catheter into the esophagus to obtain the esophageal pressure, which is a surrogate of the pleural pressure. Measuring P_{es} allows evaluation of intrathoracic pressure, transpulmonary, and transvascular pressures.[124] The main use of P_{es} is calculating trans-structural pressure. That is the difference in pressure between the inside and outside of a structure. For the critical care patient, the 2 main uses are to calculate the transpulmonary pressure (P_{TP}) and the transvascular pressure.

The P_{TP} is calculated by subtracting P_{es} from the airway pressure (P_{AW}), $P_{TP} = P_{AW} - P_{es}$. This allows partitioning of the pressure required to distend the lung versus the one to distend the chest wall and abdomen. Thus, P_{TP} is the pressure required to distend the lung parenchyma. In patients with ARDS and low lung compliance,[125,126] clinicians calculating P_{TP} can make a more precise adjustment of mechanical ventilation parameters (eg, PEEP), which may lead to improving oxygenation,

Box 2
Strategies to manage autopositive end-expiratory pressure

1. Maximize expiratory time by lowering respiratory rate: This will have a direct effect in the inspiration to expiration time relationship (I:E time), which can also be directly adjusted in the ventilator but that would ultimately depend on respiratory rate. Other maneuvers such as increasing inspiratory flow or decreasing the set inspiratory time (eg, changing the flow pattern from a descending ramp to rectangular) may also increase the expiratory time, but to a lesser degree compared to decreasing the respiratory rate.
2. Optimize sedation: This may help mitigate potential patient discomfort due to auto-PEEP and also slow the patient's respiratory rate to avoid patient overbreathing the ventilator.
3. Optimize resistance: A decrease in the resistance will facilitate expiratory flow and thereby mitigate air trapping and autoPEEP. This can be potentially achieved with bronchodilators, corticosteroids, antibiotics, and secretion management.
4. Increase the set PEEP: This maneuver can facilitate patient triggering of assisted or spontaneous breaths by decreasing the pressure gradient that needs to be overcome by the inspiratory efforts to trigger a breath. However, the set PEEP should not be more than 75% to 85% of the total PEEP.[128,129]
5. Lastly, if none of the aforementioned maneuvers are effective or if the patient is rapidly decompensating with impending hemodynamic collapse, disconnecting the patient from the ventilator and compressing on their chest will relieve air trapping and resolve autoPEEP. However, the risk of alveolar derecruitment with this maneuver needs to be considered within the clinical context.

by recruiting alveoli and preventing barotrauma. This is often used in patients with obesity or restrictive chest disorders where chest wall compliance is reduced, and a significantly elevated plateau pressure is observed. In these patients, the plateau pressure may be elevated, but the P_{TP} is not; thus, an esophageal pressure measurement may allow increasing ventilator settings beyond usual thresholds.

P_{es} provides valuable insights into variations in transmural pressure across pulmonary vascular structures and cardiac chambers during the respiratory cycle. This aids in diagnosing and managing conditions like PH, cardiac tamponade, or right ventricular dysfunction.[127] Additionally, P_{es} enables assessment of ventricular interdependence, revealing complex interactions between heart chambers.[117] However, limitations exist in esophageal pressure measurement due to factors such as patient positioning, respiratory effort, and lung disease affecting accuracy. Interpreting esophageal pressure requires expertise in cardiovascular and respiratory system interactions.[124–127] Consequently, routine use is not recommended; it is reserved for specific cases where the accurate assessment of lung distending pressures is crucial, such as in obesity, abdominal compartment syndrome, chest wall deformities, or large pleural effusion.

CLINICS CARE POINTS

- Positive pressure ventilation produces hemodynamic changes: a decrease in LV afterload, an increase in RV afterload, and a decrease in both LV and RV preload.
- In patients with severe preload-sensitive conditions, such as pulmonary hypertension, severe RV failure, or cardiac tamponade, the preference is to delay or avoid intubation and the initiation of invasive mechanical ventilation. If intubation is necessary, high levels of PEEP should be avoided as they may have a negative hemodynamic impact.
- During induction for sedation, consider agents with minimal impact on sympathetic tone and hemodynamics. In patients who are already hypotensive at baseline, premedication with vasopressors can allow the clinician to improve hemodynamic parameters in preparation for intubation, targeting a mean arterial pressure above 65 mm Hg before induction and optimizing preload should be considered.
- An important parameter to monitor in patients undergoing invasive mechanical positive pressure ventilation is autoPEEP, particularly in the presence of cardiovascular conditions, given its potential for significant hemodynamic instability.
- During the removal of positive pressure, be cautious of the increase in afterload to the left ventricle, which can lead to elevated filling pressures, especially in patients with ventricular dysfunction, or may also unmask worsening mitral regurgitation, a common etiology of extubation failure.

DISCLOSURE

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REFERENCES

1. Morrow DA, Fang JC, Fintel DJ, et al. Evolution of critical care cardiology: transformation of the cardiovascular intensive care unit and the emerging need for new medical staffing and training models: a scientific statement from the American Heart Association. Circulation 2012;126(11):1408–28.
2. Katz JN, Shah BR, Volz EM, et al. Evolution of the coronary care unit: clinical characteristics and temporal trends in healthcare delivery and outcomes. Crit Care Med 2010;38(2):375–81.
3. Bohula EA, Katz JN, Van Diepen S, et al. Demographics, care patterns, and outcomes of patients admitted to cardiac intensive care units: the critical care cardiology trials network prospective North American Multicenter Registry of cardiac critical Illness. JAMA Cardiol 2019;4(9):928–35.
4. Metkus TS, Miller PE, Alviar CL, et al. Advanced respiratory support in the contemporary cardiac ICU. Crit Care Explor 2020;2(9):e0182.
5. Jentzer JC, van Diepen S, Barsness GW, et al. Changes in comorbidities, diagnoses, therapies and outcomes in a contemporary cardiac intensive care unit population. Am Heart J 2019;215:12–9.
6. Banner MJ. Respiratory muscle loading and the work of breathing. J Cardiothorac Vasc Anesth 1995;9(2):192–204.
7. Cabello B, Mancebo J. Work of breathing. Intensive Care Med 2006;32(9):1311–4.
8. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. J Appl Physiol 1964;19(4):713–24.
9. Disselkamp M, Adkins D, Pandey S, et al. Physiologic approach to mechanical ventilation in right ventricular failure. Ann Am Thorac Soc 2018; 15(3):383–9.
10. Magder S. Heart-Lung interaction in spontaneous breathing subjects: the basics. Ann Transl Med 2018;6(18):348.
11. Condos WR, Latham RD, Hoadley SD, et al. Hemodynamics of the Mueller maneuver in man: right and left heart micromanometry and Doppler echocardiography. Circulation 1987;76(5):1020–8.
12. Keller M, Applefeld W, Acho M, et al. How I Teach auto-PEEP Applying the physiology of expiration. ATS Sch 2021;2(4):610–24.
13. Downs JB, Klein EF, Desautels D, et al. Intermittent mandatory ventilation: a new approach to weaning patients from mechanical ventilators. Chest 1973; 64(3):331–5.
14. Marini JJ, Smith TC, Lamb VJ. External work output and force generation during synchronized intermittent mechanical ventilation. Effect of machine assistance on breathing effort. Am Rev Respir Dis 1988;138(5):1169–79.
15. Alviar CL, Miller PE, McAreavey D, et al. Positive pressure ventilation in the cardiac intensive care Unit. J Am Coll Cardiol 2018;72(13):1532–53.
16. Cheifetz IM. Cardiorespiratory interactions: the relationship between mechanical ventilation and hemodynamics. Respir Care 2014;59(12):1937–45.
17. Pang D, Keenan SP, Cook DJ, et al. The effect of positive pressure airway support on mortality and the need for intubation in cardiogenic pulmonary edema: a systematic review. Chest 1998;114(4): 1185–92.
18. Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part II: practical implications in critical care. Intensive Care Med 2009;35(2):198–205.
19. Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part I: basic concepts. Intensive Care Med 2009; 35(1):45–54.
20. Mahmood SS, Pinsky MR. Heart-lung interactions during mechanical ventilation: the basics. Ann Transl Med 2018;6(18):349.
21. Slobod D, Assanangkornchai N, Alhazza M, et al. Right ventricular loading by lung inflation during controlled mechanical ventilation. Am J Respir Crit Care Med 2022;205(11):1311–9.
22. Haddad F, Doyle R, Murphy DJ, et al. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. Circulation 2008; 117(13):1717–31.
23. Scharf SM, Bianco JA, Tow DE, et al. The effects of large negative intrathoracic pressure on left ventricular function in patients with coronary artery disease. Circulation 1981;63(4):871–5.
24. Rasanen J, Nikki P, Heikkila J. Acute myocardial infarction complicated by respiratory failure. The effects of mechanical ventilation. Chest 1984;85(1):21–8.
25. Lemaire F, Teboul JL, Cinotti L, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. Anesthesiology 1988; 69(2):171–9.
26. Ouellette DR, Patel S, Girard TD, et al. Liberation from mechanical ventilation in critically ill Adults: an Official American College of chest Physicians/ American thoracic Society clinical Practice guideline: inspiratory pressure augmentation during spontaneous breathing trials, Protocols minimizing sedation, and noninvasive ventilation immediately after extubation. Chest 2017;151(1):166–80.
27. Andi Shahu MM, Soumya Banna M, Willard Applefeld M, et al. Liberation from mechanical

ventilation in the cardiac intensive care Unit. JACC (J Am Coll Cardiol): Advances 2023;2(1):100173.
28. Cabello B, Thille AW, Roche-Campo F, et al. Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. Intensive Care Med 2010;36(7):1171–9.
29. Ruiz-Bailén M, Cobo-Molinos J, Castillo-Rivera A, et al. Stress echocardiography in patients who experienced mechanical ventilation weaning failure. J Crit Care 2017;39:66–71.
30. Tehrani BN, Truesdell AG, Psotka MA, et al. A Standardized and comprehensive approach to the management of cardiogenic shock. JACC Heart Fail 2020;8(11):879–91.
31. Hrymak C, Strumpher J, Jacobsohn E. Acute right ventricle failure in the intensive care Unit: assessment and management. Can J Cardiol 2017;33(1):61–71.
32. Bootsma IT, Boerma EC, Scheeren TWL, et al. The contemporary pulmonary artery catheter. Part 2: measurements, limitations, and clinical applications. J Clin Monit Comput 2022;36(1):17–31.
33. Naeije R, Badagliacca R. The overloaded right heart and ventricular interdependence. Cardiovasc Res 2017;113(12):1474–85.
34. Lim HS, Gustafsson F. Pulmonary artery pulsatility index: physiological basis and clinical application. Eur J Heart Fail 2020;22(1):32–8.
35. Eskesen TG, Wetterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Med 2016;42(3):324–32.
36. Pinsky M, Kellum J, Bellomo R. Central venous pressure is a stopping rule, not a target of fluid resuscitation. Available at: Critical Care and Resuscitation 2014;16(4):245–6 www.jficm.anzca.edu.au/aaccm/journal/publi-.
37. Price LC, McAuley DF, Marino PS, et al. Pathophysiology of pulmonary hypertension in acute lung injury. Am J Physiol Lung Cell Mol Physiol 2012;302(9):L803.
38. Repessé X, Charron C, Vieillard-Baron A. Acute cor pulmonale in ARDS: rationale for protecting the right ventricle. Chest 2015;147(1):259–65.
39. Schmeisser A, Rauwolf T, Groscheck T, et al. Pressure-volume loop validation of TAPSE/PASP for right ventricular arterial coupling in heart failure with pulmonary hypertension. Eur Heart J Cardiovasc Imaging 2021;22(2):168–76.
40. Tavazzi G, Bergsland N, Alcada J, et al. Early signs of right ventricular systolic and diastolic dysfunction in acute severe respiratory failure: the importance of diastolic restrictive pattern. Eur Heart J Acute Cardiovasc Care 2020;9(6):649–56.
41. Imanishi J, Maeda T, Ujiro S, et al. Association between B-lines on lung ultrasound, invasive haemodynamics, and prognosis in acute heart failure patients. Eur Heart J Acute Cardiovasc Care 2023;12(2):115–23.
42. Picano E, Scali MC, Ciampi Q, et al. Lung ultrasound for the Cardiologist. JACC Cardiovasc Imaging 2018;11(11):1692–705.
43. Araujo GN, Silveira AD, Scolari FL, et al. Admission bedside lung ultrasound reclassifies mortality prediction in patients with ST-Segment-elevation myocardial infarction. Circ Cardiovasc Imaging 2020;13(6):E010269.
44. Bouhemad B, Brisson H, Le-Guen M, et al. Bedside ultrasound assessment of positive end-expiratory pressure-induced lung recruitment. Am J Respir Crit Care Med 2011;183(3):341–7.
45. Constantin JM, Grasso S, Chanques G, et al. Lung morphology predicts response to recruitment maneuver in patients with acute respiratory distress syndrome. Crit Care Med 2010;38(4):1108–17.
46. Kim WY, Suh HJ, Hong SB, et al. Diaphragm dysfunction assessed by ultrasonography: influence on weaning from mechanical ventilation. Crit Care Med 2011;39(12):2627–30.
47. Corradi F, Brusasco C, Vezzani A, et al. Computer-aided Quantitative ultrasonography for detection of pulmonary edema in mechanically ventilated cardiac surgery patients. Chest 2016;150(3):640–51.
48. Compton FD, Zukunft B, Hoffmann C, et al. Performance of a minimally invasive uncalibrated cardiac output monitoring system (Flotrac/Vigileo) in haemodynamically unstable patients. Br J Anaesth 2008;100(4):451–6.
49. Li-ping Q, Hong-wei L, Chang-ming H, et al. Safety and efficacy of pulse-induced contour cardiac output monitoring in elderly patients with coronary artery disease and severe heart failure at coronary care units. Front Cardiovasc Med 2022;9. https://doi.org/10.3389/FCVM.2022.910898.
50. Peyton PJ, Chong SW. Minimally invasive measurement of cardiac output during surgery and critical care: a meta-analysis of accuracy and precision. Anesthesiology 2010;113(5):1220–35.
51. Saraceni E, Rossi S, Persona P, et al. Comparison of two methods for cardiac output measurement in critically ill patients. Br J Anaesth 2011;106(5):690–4.
52. Grensemann J, Defosse JM, Willms M, et al. Validation of radial artery-based uncalibrated pulse contour method (PulsioFlex) in critically ill patients: a observational study. Eur J Anaesthesiol 2017;34(11):723–31.
53. Hadian M, Kim HK, Severyn DA, et al. Cross-comparison of cardiac output trending accuracy of LiDCO, PiCCO, FloTrac and pulmonary artery catheters. Crit Care 2010;14(6).
54. Saugel B, Hoppe P, Nicklas JY, et al. Continuous noninvasive pulse wave analysis using finger cuff technologies for arterial blood pressure and cardiac output monitoring in perioperative and intensive

care medicine: a systematic review and meta-analysis. Br J Anaesth 2020;125(1):25–37.
55. Segal E, Katzenelson R, Berkenstadt H, et al. Transpulmonary thermodilution cardiac output measurement using the axillary artery in critically ill patients. J Clin Anesth 2002;14(3):210–3.
56. Galarza L, Mercado P, Teboul JL, et al. Estimating the rapid haemodynamic effects of passive leg raising in critically ill patients using bioreactance. Br J Anaesth 2018;121(3):567–73.
57. Chopra S, Thompson J, Shahangian S, et al. Precision and consistency of the passive leg raising maneuver for determining fluid responsiveness with bioreactance non-invasive cardiac output monitoring in critically ill patients and healthy volunteers. PLoS One 2019;14(9).
58. Fathy S, Hasanin AM, Raafat M, et al. Thoracic fluid content: a novel parameter for predicting failed weaning from mechanical ventilation. J Intensive Care 2020;8(1).
59. Friesecke S, Heinrich A, Abel P, et al. Comparison of pulmonary artery and aortic transpulmonary thermodilution for monitoring of cardiac output in patients with severe heart failure: validation of a novel method. Crit Care Med 2009;37(1):119–23.
60. Volpicelli G, Skurzak S, Boero E, et al. Lung ultrasound predicts well extravascular lung water but is of limited usefulness in the prediction of wedge pressure. Anesthesiology 2014;121(2):320–7.
61. Vallabhajosyula S, Kashani K, Dunlay SM, et al. Acute respiratory failure and mechanical ventilation in cardiogenic shock complicating acute myocardial infarction in the USA, 2000-2014. Ann Intensive Care 2019;9(1).
62. Alviar CL, Rico-Mesa JS, Morrow DA, et al. Positive pressure ventilation in cardiogenic shock: review of the evidence and practical Advice for patients with mechanical circulatory support. Can J Cardiol 2020;36(2):300–12.
63. Van Diepen S, Hochman JS, Stebbins A, et al. Association between delays in mechanical ventilation initiation and mortality in patients with refractory cardiogenic shock. JAMA Cardiol 2020;5(8):965–7.
64. Rubini Giménez M, Elliott Miller P, Alviar CL, et al. Outcomes associated with respiratory failure for patients with cardiogenic shock and acute myocardial infarction: a Substudy of the CULPRIT-SHOCK trial. J Clin Med 2020;9(3).
65. Suter PM, Fairley HB, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. N Engl J Med 1975;292(6):284–9.
66. Grace MP, Greenbaum DM. Cardiac performance in response to PEEP in patients with cardiac dysfunction. Crit Care Med 1982;10(6):358–60.
67. Kontoyannis DA, Nanas JN, Kontoyannis SA, et al. Mechanical ventilation in conjunction with the intra-aortic balloon pump improves the outcome of patients in profound cardiogenic shock. Intensive Care Med 1999;25(8):835–8.
68. Mathru M, Rao TL, El-Etr AA, et al. Hemodynamic response to changes in ventilatory patterns in patients with normal and poor left ventricular reserve. Crit Care Med 1982;10(7):423–6.
69. Patzelt J, Zhang Y, Seizer P, et al. Effects of mechanical ventilation on heart geometry and mitral valve leaflet coaptation during percutaneous edge-to-edge mitral valve repair. JACC Cardiovasc Interv 2016;9(2):151–9.
70. Bellone A, Barbieri A, Ricci C, et al. Acute effects of non-invasive ventilatory support on functional mitral regurgitation in patients with exacerbation of congestive heart failure. Intensive Care Med 2002;28(9):1348–50.
71. Wiesen J, Ornstein M, Tonelli AR, et al. State of the evidence: mechanical ventilation with PEEP in patients with cardiogenic shock. Heart 2013;99(24):1812–7.
72. Shorofsky M, Jayaraman D, Lellouche F, et al. Mechanical ventilation with high tidal volume and associated mortality in the cardiac intensive care unit. Acute Card Care 2014;16(1):9–14.
73. Andrei S, Nguyen M, Berthoud V, et al. Determinants of arterial pressure of oxygen and carbon dioxide in patients supported by Veno-arterial ECMO. J Clin Med 2022;11(17).
74. Lorusso R, Shekar K, MacLaren G, et al. ELSO Interim guidelines for venoarterial extracorporeal membrane oxygenation in adult cardiac patients. ASAIO J 2021;67(8):827–44.
75. Schmidt M, Pellegrino V, Combes A, et al. Mechanical ventilation during extracorporeal membrane oxygenation. Crit Care 2014;18(1).
76. Guglin M, Zucker MJ, Bazan VM, et al. Venoarterial ECMO for adults: JACC scientific Expert Panel. J Am Coll Cardiol 2019;73(6):698–716.
77. Rali AS, Tran LE, Auvil B, et al. Modifiable mechanical ventilation targets are associated with improved survival in ventilated VA-ECLS patients. JACC Heart Fail 2023. https://doi.org/10.1016/J.JCHF.2023.03.023.
78. Tonna JE, Selzman CH, Bartos JA, et al. The association of modifiable mechanical ventilation settings, blood gas changes and survival on extracorporeal membrane oxygenation for cardiac arrest. Resuscitation 2022;174:53–61.
79. Thomas A, van Diepen S, Beekman R, et al. Oxygen Supplementation and hyperoxia in critically ill cardiac patients: from pathophysiology to clinical Practice. JACC Advances 2022;1(3):100065.
80. Jentzer JC, Miller PE, Alviar C, et al. Exposure to arterial hyperoxia during extracorporeal membrane oxygenator support and mortality in patients with cardiogenic shock. Circ Heart Fail 2023;16(4):E010328.

81. Montero S, Huang F, Rivas-Lasarte M, et al. Awake venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock. Eur Heart J Acute Cardiovasc Care 2021;10(6):585–94.
82. Jentzer JC, Wiley BM, Reddy YNV, et al. Epidemiology and outcomes of pulmonary hypertension in the cardiac intensive care unit. Eur Heart J Acute Cardiovasc Care 2022;11(3):230–41.
83. Barnett CF, O'Brien C, De Marco T. Critical care management of the patient with pulmonary hypertension. Eur Heart J Acute Cardiovasc Care 2022; 11(1):77–83.
84. Johannes J, Berlin DA, Patel P, et al. A technique of awake bronchoscopic endotracheal intubation for respiratory failure in patients with right heart failure and pulmonary hypertension. Crit Care Med 2017; 45(9):e980–4.
85. Kitamura T, Iwami T, Kawamura T, et al. Bystander-initiated rescue breathing for out-of-hospital cardiac arrests of noncardiac origin. Circulation 2010; 122(3):293–9.
86. Ogawa T, Akahane M, Koike S, et al. Outcomes of chest compression only CPR versus conventional CPR conducted by lay people in patients with out of hospital cardiopulmonary arrest witnessed by bystanders: nationwide population based observational study. BMJ 2011;342(7792):321.
87. Svensson L, Bohm K, Castrèn M, et al. Compression-only CPR or standard CPR in out-of-hospital cardiac arrest. N Engl J Med 2010;363(5):434–42.
88. Rea TD, Fahrenbruch C, Culley L, et al. CPR with chest compression alone or with rescue breathing. N Engl J Med 2010;363(5):423–33.
89. SOS-KANTO Study Group. Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): an observational study. Lancet 2007;369(9565):920–6.
90. Bobrow BJ, Spaite DW, Berg RA, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. JAMA 2010;304(13):1447–54.
91. Panchal AR, Bobrow BJ, Spaite DW, et al. Chest compression-only cardiopulmonary resuscitation performed by lay rescuers for adult out-of-hospital cardiac arrest due to non-cardiac aetiologies. Resuscitation 2013;84(4):435–9.
92. Lubrano R, Cecchetti C, Bellelli E, et al. Comparison of times of intervention during pediatric CPR maneuvers using ABC and CAB sequences: a randomized trial. Resuscitation 2012;83(12): 1473–7.
93. Sekiguchi H, Kondo Y, Kukita I. Verification of changes in the time taken to initiate chest compressions according to modified basic life support guidelines. Am J Emerg Med 2013;31(8):1248–50.
94. Marsch S, Tschan F, Semmer NK, et al. ABC versus CAB for cardiopulmonary resuscitation: a prospective, randomized simulator-based trial. Swiss Med Wkly 2013;143.
95. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American heart association guidelines for cardiopulmonary resuscitation and Emergency cardiovascular care. Circulation 2020;142:S366–468.
96. Berg RA, Hilwig RW, Kern KB, et al. "Bystander" chest compressions and assisted ventilation independently improve outcome from piglet asphyxial pulseless "cardiac arrest." Circulation 2000; 101(14):1743–8.
97. Nichol G, Leroux B, Wang H, et al. Trial of continuous or Interrupted chest compressions during CPR. N Engl J Med 2015;373(23):2203–14.
98. Aufderheide TP, Lurie KG. Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation. Crit Care Med 2004;32(9 Suppl).
99. Aufderheide TP, Sigurdsson G, Pirrallo RG, et al. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. Circulation 2004; 109(16):1960–5.
100. O'Neill JF, Deakin CD. Do we hyperventilate cardiac arrest patients? Resuscitation 2007;73(1):82–5.
101. Buunk G, Van Der Hoeven JG, Meinders AE. Cerebrovascular reactivity in comatose patients resuscitated from a cardiac arrest. Stroke 1997;28(8): 1569–73.
102. Cold GE. Cerebral blood flow in acute head injury. The regulation of cerebral blood flow and metabolism during the acute phase of head injury, and its significance for therapy. Acta Neurochir Suppl 1990;49:1–64. https://pubmed.ncbi.nlm.nih.gov/2275429/. [Accessed 25 June 2023].
103. Kågström E, Smith MLL, Siesgö BK. Cerebral circulatory responses to hypercapnia and hypoxia in the recovery period following complete and incomplete cerebral ischemia in the rat. Acta Physiol Scand 1983;118(3):281–91.
104. Safar P, Xiao F, Radovsky A, et al. Improved cerebral resuscitation from cardiac arrest in dogs with mild hypothermia plus blood flow promotion. Stroke 1996;27(1):105–13.
105. Eastwood G, Nichol AD, Hodgson C, et al. Mild hypercapnia or normocapnia after out-of-hospital cardiac arrest. N Engl J Med 2023. https://doi.org/10.1056/NEJMOA2214552.
106. Callaway CW, Donnino MW, Fink EL, et al. Part 8: post-cardiac arrest care: 2015 American heart association guidelines Update for cardiopulmonary resuscitation and Emergency cardiovascular care. Circulation 2015;132(18 Suppl 2):S465–82.
107. Roberts BW, Kilgannon JH, Chansky ME, et al. Association between postresuscitation partial pressure of arterial carbon dioxide and neurological

outcome in patients with post-cardiac arrest syndrome. Circulation 2013;127(21):2107–13.
108. Lee BK, Jeung KW, Lee HY, et al. Association between mean arterial blood gas tension and outcome in cardiac arrest patients treated with therapeutic hypothermia. Am J Emerg Med 2014; 32(1):55–60.
109. Ihle JF, Bernard S, Bailey MJ, et al. Hyperoxia in the intensive care unit and outcome after out-of-hospital ventricular fibrillation cardiac arrest. Crit Care Resusc 2013;15(3):186–90.
110. Kilgannon JH, Jones AE, Shapiro NI, et al. Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality. JAMA 2010;303(21):2165–71.
111. Vaahersalo J, Bendel S, Reinikainen M, et al. Arterial blood gas tensions after resuscitation from out-of-hospital cardiac arrest: associations with long-term neurologic outcome. Crit Care Med 2014;42(6): 1463–70.
112. Bellomo R, Bailey M, Eastwood GM, et al. Arterial hyperoxia and in-hospital mortality after resuscitation from cardiac arrest. Crit Care 2011;15(2).
113. Janz DR, Hollenbeck RD, Pollock JS, et al. Hyperoxia is associated with increased mortality in patients treated with mild therapeutic hypothermia after sudden cardiac arrest. Crit Care Med 2012; 40(12):3135–9.
114. Elmer J, Scutella M, Pullalarevu R, et al. The association between hyperoxia and patient outcomes after cardiac arrest: analysis of a high-resolution database. Intensive Care Med 2015;41(1):49–57.
115. Schmidt H, Kjaergaard J, Hassager C, et al. Oxygen targets in comatose Survivors of cardiac arrest. N Engl J Med 2022;387(16):1467–76.
116. Prekker ME, Driver BE, Trent SA, et al. Video versus direct laryngoscopy for Tracheal intubation of critically ill Adults. N Engl J Med 2023. https://doi.org/10.1056/NEJMOA2301601/SUPPL_FILE/NEJMOA2301601_DATA-SHARING.
117. Luecke T, Pelosi P. Clinical review: positive end-expiratory pressure and cardiac output. Crit Care 2005;9(6):607–21.
118. Pinsky MR. Cardiopulmonary interactions: physiologic basis and clinical applications. In: Annals of the American Thoracic Society. American Thoracic Society 2018;15:S45–8.
119. Laghi F, Goyal A. Auto-PEEP in respiratory failure. Minerva Anestesiol 2012;78(2):201–21.
120. Ranieri VM, Giuliani R, Cinnella G, et al. Physiologic effects of positive end-expiratory pressure in patients with chronic obstructive pulmonary disease during acute ventilatory failure and controlled mechanical ventilation. Am Rev Respir Dis 1993; 147(1):5–13.
121. Sullivan MJ, Higginbotham MB, Cobb FR. Increased exercise ventilation in patients with chronic heart failure: Intact ventilatory control despite hemodynamic and pulmonary abnormalities. Circulation 1988; 77(3):552–9.
122. Obokata M, Olson TP, Reddy YNV, et al. Haemodynamics, dyspnoea, and pulmonary reserve in heart failure with preserved ejection fraction. Eur Heart J 2018;39(30):2810–21.
123. Andrea R, López-Giraldo A, Falces C, et al. Lung function abnormalities are highly frequent in patients with heart failure and preserved ejection fraction. Heart Lung Circ 2014;23(3):273–9.
124. Woods PR, Olson TP, Frantz RP, et al. Causes of breathing inefficiency during exercise in heart failure. J Card Fail 2010;16(10):835–42.
125. Perlman CE, Lederer DJ, Bhattacharya J. Micromechanics of alveolar edema. Am J Respir Cell Mol Biol 2010;44(1):34–9.
126. Mauri T, Yoshida T, Bellani G, et al. Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. Intensive Care Med 2016;42(9):1360–73.
127. Talmor D, Sarge T, Malhotra A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359(20):2095–104.
128. Beitler JR, Sarge T, Banner-Goodspeed VM, et al. Effect of titrating positive end-expiratory pressure (PEEP) with an esophageal pressure-guided strategy vs an empirical high PEEP-Fio2 strategy on death and Days free from mechanical ventilation among patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA 2019; 321(9):846–57.
129. Repessé X, Vieillard-Baron A, Geri G. Value of measuring esophageal pressure to evaluate heart-lung interactions-applications for invasive hemodynamic monitoring. Ann Transl Med 2018; 6(18):351.