Exploration of Cardiology

Open Exploration

Open Access Review

Cardiopulmonary interaction during spontaneous breathing and mechanical ventilation

Angel Benjamin Rojas[1,2]*, Susana Vanoni[1,3], Carla Gobbi[1,4], Juan Carlos Vergottini[1,2]

[1]Faculty of Medical Sciences, National University of Córdoba, Córdoba X5000, Argentina
[2]Critical Care Unit, National Hospital of Clinics, Córdoba X5000, Argentina
[3]Department of Semiology, San Roque Hospital, Córdoba X5000, Argentina
[4]Department of Internal Medicine, Córdoba Hospital, Córdoba X5000, Argentina

***Correspondence:** Angel Benjamin Rojas, Faculty of Medical Sciences, National University of Córdoba, Córdoba X5000, Argentina. arojas@fcm.unc.edu.ar
Academic Editor: Dmitry Duplyakov, Samara State Medical University, Russian Federation
Received: February 4, 2026 **Accepted:** April 23, 2026 **Published:** May 12, 2026

Cite this article: Rojas AB, Vanoni S, Gobbi C, Vergottini JC. Cardiopulmonary interaction during spontaneous breathing and mechanical ventilation. Explor Cardiol. 2026;4:1012109. https://doi.org/10.37349/ec.2026.1012109

Abstract

Cardiopulmonary interaction is a fundamental physiological process during spontaneous breathing, but it is profoundly altered in critically ill patients receiving mechanical ventilation (MV). Positive-pressure ventilation modifies intrathoracic, pleural, and transpulmonary pressures, with major effects on pulmonary vascular hemodynamics and right ventricular performance. Among these consequences, acute pulmonary hypertension (aPH) has emerged as a clinically relevant yet frequently underrecognized complication. This review summarizes the current evidence on cardiopulmonary interaction during spontaneous breathing and MV, with particular emphasis on the mechanisms driving aPH and right ventricular dysfunction in critically ill patients. A narrative review was performed using PubMed, Embase, Scopus, Web of Science, and the Cochrane Library. Free-text terms and controlled vocabulary related to positive-pressure ventilation, right ventricular dysfunction, pulmonary hypertension (PH), pulmonary vascular resistance (PVR), right heart catheterization, intensive care, and respiratory compliance were combined using Boolean operators. Priority was given to studies involving adult patients, including systematic reviews, observational studies, clinical trials, and relevant reference lists. During spontaneous breathing, cardiopulmonary interaction is governed by negative intrathoracic pressure, venous return (VR), transpulmonary pressure, and physiological ventilation-perfusion relationships. In contrast, MV reverses this physiological pressure profile and may reduce VR, increase right ventricular afterload, impair ventricular interdependence, and increase PVR. High tidal volumes, excessive positive end-expiratory pressure, increased plateau pressure, hypercapnia, hypoxemia, alveolar overdistension, and diffuse lung injury all contribute to aPH, potentially disrupting right ventricle-pulmonary artery coupling and promoting right ventricular dysfunction. MV profoundly reshapes cardiopulmonary physiology and may precipitate aPH and right ventricular dysfunction. Early recognition of these mechanisms and the application of protective ventilatory strategies are essential to reduce pulmonary and hemodynamic complications.

Keywords

pulmonary hypertension, positive-pressure respiration, intensive care units, right ventricular dysfunction, lung compliance

Introduction

Physiological interactions occur among the different systems and organs of the human body. The heart and lungs are no exception, as they function in a closely integrated manner. This relationship involves a series of mechanisms that, under normal conditions, operate in a coordinated and orderly fashion. From an anatomical standpoint, the heart and lungs also lie in close proximity within the same thoracic cavity [1–3]. However, heart-lung interaction extends far beyond simple anatomical contiguity. A mechanical, functional, and even neuroendocrine interrelationship exists between these two systems [3, 4]. This interaction is so extensive that approximately 280 billion pulmonary capillaries perfuse between 300 million and 480 million alveoli [5].

The respiratory system generates negative pressure through contraction of the respiratory muscles, a process that depends on the integrity of neural pathways originating in the bulbar respiratory centers [5]. This negative pressure allows the lungs to expand in a bellows-like manner. During this process, the alveoli distend, and gas exchange occurs between inspired oxygen and exhaled carbon dioxide [2, 5].

By contrast, the cardiovascular system, composed of the heart as a propulsive pump and an extensive vascular network, operates through two major circuits: a) the systemic circulation, whose main vessel is the aorta and its branches, and whose function is to deliver oxygenated blood to peripheral tissues; and b) the pulmonary circulation, which carries venous blood through the right atrium, right ventricle (RV), and pulmonary artery to the alveolar-capillary membrane, where carbon dioxide and oxygen exchange takes place [5, 6].

In critically ill patients receiving mechanical ventilation (MV), these mechanisms are profoundly altered. This is particularly evident in those who require MV as a life-support intervention during critical illness. MV reverses the physiological pressure profile normally required to expand the lungs and maintain gas exchange, thereby inducing major changes in cardiopulmonary physiology [2, 7–10]. As a result, acute pulmonary hypertension (aPH) and right ventricular dysfunction may develop [1]. The occurrence of aPH represents a major hemodynamic event because it may increase right ventricular systolic pressure and reduce venous return (VR), potentially leading to acute cor pulmonale and right ventricular failure [11]. These effects are closely related to the tidal volume (VT) and positive end-expiratory pressure (PEEP) applied during ventilation [1].

MV is often indispensable in critically ill patients because of disease severity. However, it is not physiologically neutral, particularly when associated with aPH and right ventricular failure, conditions that may substantially increase mortality.

Objective and methods

The aim of this narrative review is to describe, on the basis of current evidence, the cardiopulmonary interaction that occurs during spontaneous breathing and MV, with particular emphasis on the development of aPH. This remains an underrecognized complication that should not be overlooked, as it may induce right ventricular dysfunction and directly affect morbidity and mortality in critically ill patients. The relevance of this review lies in its integrated analysis of cardiopulmonary interaction from spontaneous breathing to MV, while also providing practical tools to minimize or prevent the adverse effects of ventilatory support.

The literature search included PubMed, Embase, Scopus, Web of Science, and the Cochrane Library. Free-text terms and controlled vocabulary (MeSH and Emtree) related to positive-pressure MV, right ventricular dysfunction, pulmonary hypertension (PH), pulmonary vascular resistance (PVR), right heart catheterization, intensive care, and respiratory compliance were used. Terms were combined using the Boolean operators AND and OR. Studies involving adult patients, systematic reviews, observational research, and clinical trials were prioritized. Relevant reference lists were also manually reviewed. Articles were searched first in English and subsequently in Spanish, especially landmark literature on MV from earlier years, in order to include the fundamental concepts on which current knowledge is based.

Cardiorespiratory physiology

Ventilation

For ventilation to occur, a pressure gradient must exist between the atmosphere and the alveolus. Thus, inspiration occurs when alveolar pressure (PAlv) falls below atmospheric pressure. This indicates that physiological ventilation occurs under negative-pressure conditions. Alveoli cannot expand autonomously [5]. Rather, they expand according to the pressure difference between pleural pressure (Ppl) and PAlv. This difference is known as transpulmonary pressure (TP), according to the following formula [2, 5]:

$$TP = Alveolar\ pressure - Pleural\ pressure$$

Ppl changes from approximately −5 cmH_2O during expiration to −8 cmH_2O during inspiration, causing PAlv to reach subatmospheric values of approximately −1 cmH_2O during inspiration, thereby allowing air to enter the alveoli [5]. Thus, TP is approximately +5 cmH_2O during expiration and rises to +7 cmH_2O during inspiration [2, 5, 6]. Understanding the changes that occur in both Ppl and TP is crucial, as these pressures influence cardiovascular hemodynamics. Cardiac chambers and great vessels are primarily affected by Ppl, whereas pulmonary capillaries are mainly affected by TP [1].

Inspiration is an active process involving the diaphragm primarily and secondarily the intercostal muscles, whereas expiration is passive and results from the elastic recoil of the lungs and chest wall in opposite directions [2, 5]. The inspired VT is directly related to TP. However, there is a limit, known as the critical closing point, at which inspiration ceases because the inspiratory muscles have reached their maximum effort, thereby giving way to expiration [5].

Both inspiration and expiration occur because of a property of the respiratory system known as compliance, or distensibility, which is defined as the relationship between the volume of gas entering the lungs and the pressure required to distend them [2, 5, 7, 8].

During expiration, alveoli tend to collapse. From a physical standpoint, the elastic properties of alveoli favor their obliteration, since they are governed by Laplace's law [5].

According to this law, the smaller the radius, the greater the pressure, and vice versa. Therefore, at constant surface tension, alveoli with a smaller radius have higher pressure and tend to empty into alveoli with lower pressure or larger radius, thereby promoting collapse [2, 5].

Physiologically, two mechanisms promote alveolar stability and prevent collapse (Figure 1).

a) Alveolar interdependence: Because adjacent alveoli share walls or septa, retraction or stretching of one immediately distends its neighbor, thereby preventing collapse. During inspiration, the outermost lung regions are directly exposed to negative Ppls. These pressures tend to distend the more peripheral alveoli, leaving the more central alveoli less ventilated and more prone to collapse. Through alveolar interdependence, both central and peripheral alveoli are distended almost uniformly. Distension of one alveolus leads to distension of adjacent alveoli [5].

b) Surfactant: This is the other major mechanism that reduces the tendency toward alveolar collapse. Surfactant is a lipoprotein whose main function is to reduce surface tension at the alveolar air-liquid interface [5–7]. It is synthesized and secreted by type II pneumocytes and forms a lining layer within the alveolus. This substance is fundamental to respiratory physiology, since its absence leads to alveolar collapse [5–7]. This phenomenon is one of the mechanisms contributing to acute respiratory distress syndrome, whose pathophysiological core includes impaired surfactant production and function, ultimately leading to alveolar collapse and severe respiratory failure [8, 9].

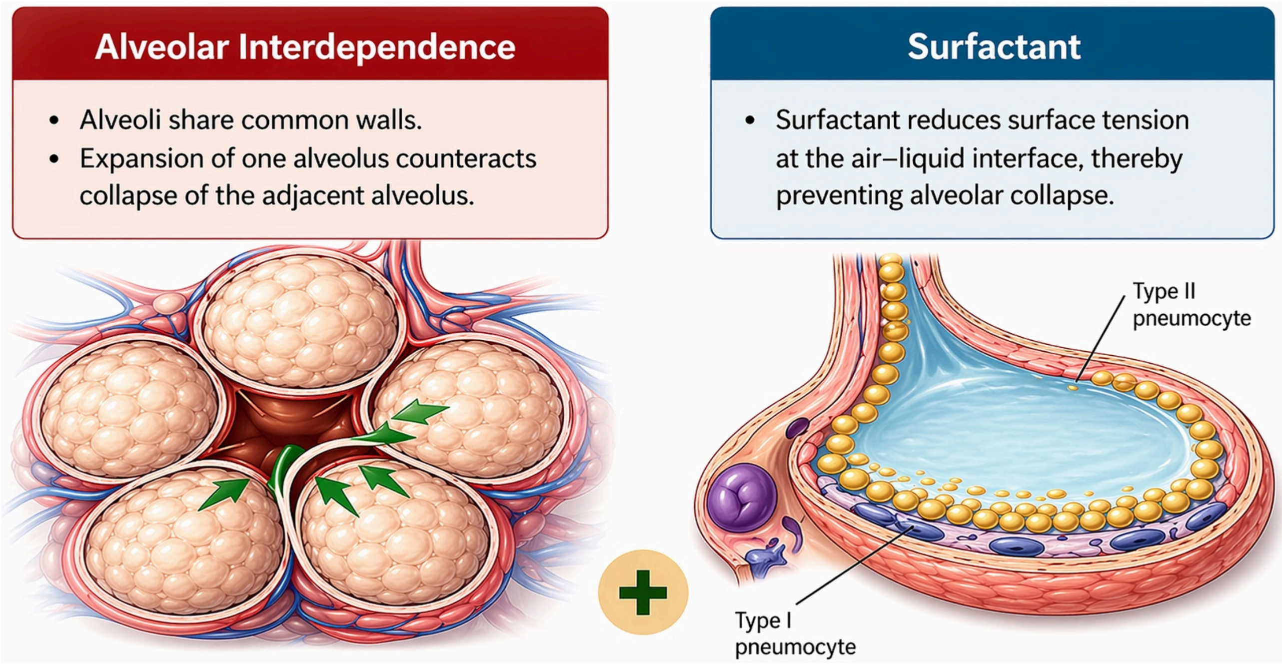

Figure 1. Mechanisms of alveolar stability. Alveolar stability is maintained mainly by alveolar interdependence and surfactant, which prevent collapse.

Right-sided hemodynamics and pulmonary circulation

Two circulatory systems supply blood to the lungs: a) the bronchial circulation, supplied by the bronchial artery, which receives only 2% of total cardiac output (CO); and b) the pulmonary circulation, which receives 100% of right ventricular output. Another important difference between these systems is that the bronchial arteries do not participate directly in gas exchange. However, they contribute to the physiological shunt, that is, the portion of deoxygenated blood that bypasses alveolar gas exchange. In addition, they are not part of the alveolar-capillary network [5].

The walls of the pulmonary artery are thinner than those of systemic arteries because they are capacitance vessels operating under low-pressure conditions. This makes them more compressible and distensible [5]. Because of their intrathoracic and juxta-alveolar location, they are exposed to changes in intrapleural, alveolar, and TPs [5, 12]. This underscores the importance of understanding the physical changes that occur within the respiratory system.

Pressures in the pulmonary circulation differ substantially from those in the systemic circulation. For example, left ventricular pressures are approximately 120 mmHg, whereas right ventricular pressures are around 25 mmHg. Physiologically, systemic arterial pressures are approximately 120/80 mmHg, whereas pulmonary artery pressures are approximately 25/8 mmHg [5, 6, 12]. These values clearly illustrate the marked differences between the two circulatory systems.

To understand right heart hemodynamics, it is important to recall that VR represents the amount of blood flow per minute returning from the venous circulation to the right atrium [3, 5–8, 12, 13]. VR is therefore determined by: a) right atrial pressure (RAP), which acts as the opposing back pressure; b) mean systemic filling pressure (MSFP), which drives blood toward the right heart; and c) resistance to venous return (RVR), two-thirds of which is venous, with the remaining third contributed by small pulmonary arteries and arterioles. MSFP represents the equilibrium pressure generated by the interaction between total blood volume and venous capacitance. Each of these variables directly affects VR, which behaves as a dependent variable within this system [5, 7].

For example, when RAP increases from 0 to +8 mmHg, VR progressively falls until it reaches zero, inevitably resulting in retrograde venous stasis. Conversely, when RAP falls below −2 mmHg, VR reaches a plateau because the right atrium becomes suction-like, causing collapse of the veins entering the thorax [7]. RAP is therefore a key determinant of the pressure gradient driving VR, whereas MSFP varies proportionally with circulating volume and changes in venous tone. For example, sympathetic stimulation, by inducing systemic vasoconstriction, can increase MSFP from 7 to 17 mmHg, thereby promoting sustained blood flow toward the right atrium. Conversely, sympathetic inhibition decreases MSFP. Thus, VR depends on the interaction among RAP, MSFP, and RVR [6].

In healthy adults, normal values are approximately as follows: VR 5 L/min, MSFP 7 mmHg, RAP 0 mmHg, and RVR 1.4 mmHg·min/L. These values favor blood return to the right atrium [6].

Once blood flow reaches the right atrium, constituting right-sided preload, and then the RV, it travels through the pulmonary artery and its branches toward the pulmonary capillaries, where gas exchange occurs. Oxygenated blood then returns through the pulmonary veins to the left atrium and left ventricle, from which it is ejected into the aorta during ventricular systole against its impedance, a physical phenomenon known as left ventricular afterload. From this arises the physiological concept of CO, whose normal value is approximately 5 L/min [5, 6, 8, 12]. Both the right and left ventricles generate their respective outputs. In the right-sided chambers, maintaining adequate CO is essential to eject sufficient blood volume and pressure into the pulmonary artery, since this same blood flow subsequently reaches the left atrium and left ventricle. This demonstrates the functional interdependence of the cardiac chambers [5, 6].

There is also a direct relationship between VR and CO. Whereas VR reflects the volume of blood returning from the peripheral circulation, CO is the volume of blood pumped by the heart into the great vessels each minute. Under normal conditions, VR equals CO. This becomes evident in clinical practice in conditions that reduce VR, such as moderate-to-severe hemorrhage, acute venous dilation, or obstruction of the great veins, all of which eventually lead to a decrease in CO [6].

However, because of the central role of CO in cardiac physiology, it depends not only on VR but also on other regulatory mechanisms. One of these is the Frank-Starling law, which states that when blood flow to the heart increases, myocardial fibers are stretched and contractile force rises accordingly [5, 6, 8, 12, 13]. Another is the Bainbridge reflex, which consists of an increase in heart rate in response to stimulation of stretch receptors located in the atrial walls [6]. This increase in heart rate may improve cardiac performance. It has also been described that sympathetic stimulation and parasympathetic withdrawal act as positive inotropic and chronotropic influences, respectively [6, 13].

PVR

PVR represents the force opposing normal blood flow within the pulmonary circulation [5, 6, 14, 15]. It is defined by the following formula:

$$PVR = \frac{mPAP - W}{\mathrm{CO}} \times 80$$

PVR is directly proportional to the difference between mean pulmonary arterial pressure (mPAP) and wedge pressure (W) and inversely proportional to CO, multiplied by a conversion factor of 80. Normal PVR values range from 20 to 120 dyn·s·cm^{-5}.

Physiologically, approximately one-third of PVR arises from the pulmonary arteries, one-third from the pulmonary capillaries, and one-third from the pulmonary veins [5].

PVR depends on the vascular transmural pressure gradient and on whether pulmonary vessels are alveolar or extra-alveolar in location [5]. In alveolar vessels, during normal expiration, the transmural gradient increases, the vessel diameter increases, and PVR decreases. During inspiration, the gradient and vessel diameter decrease, thereby increasing PVR. In extra-alveolar vessels, when Ppl becomes more negative during inspiration, the vessels distend and PVR decreases. During expiration, however, these vessels are compressed and PVR increases. Thus, during spontaneous breathing, PVR exhibits two peaks: the first at the onset of expiration because of extra-alveolar vessel constriction, and the second at the end of inspiration because of narrowing of alveolar vessels. Therefore, PVR reaches its lowest value at functional residual capacity [5, 6, 12]. These physiological observations show that any increase in extravascular pressure reduces pulmonary arterial diameter and thereby increases PVR [1].

Distribution of pulmonary blood flow and the ventilation/perfusion relationship

In the upright or seated patient, pulmonary blood flow is not distributed uniformly. Greater blood flow is observed in dependent lung regions, even though intravascular pressures are higher in these areas. This distribution is made possible by the phenomena of pulmonary vascular recruitment and distension [5, 6, 8, 9, 12].

As early as 1964, West et al. studied the relationship between ventilation and perfusion, leading to the description of the so-called West zones, which remain in use today [12, 16]. These zones are determined by the relationship among three variables at the pulmonary level: PAlv, pulmonary arterial pressure (PAP), and pulmonary venous pressure (PVP) [2, 3, 5, 6, 8, 9, 12, 16]. Zone 1 is characterized by PAlv being greater than PAP, which in turn is greater than PVP. This leads to compression of pulmonary vessels because of elevated PAlv and results in increased shunting. Intrapulmonary zone 1 corresponds to the uppermost lung regions and is characterized by being better ventilated than perfused. Zone 2 is characterized by PAP greater than PAlv, which in turn is greater than venous pressure, and corresponds to the middle lung regions. Zone 3 is characterized by PAP greater than PVP, which is greater than PAlv [5, 6, 8, 9, 12]. These are the best-perfused but less well-ventilated regions and correspond to the most dependent lung areas [12].

Taken together, these phenomena mean that the lung apices tend to have a ventilation/perfusion (V/Q) ratio > 1 and are therefore better ventilated than perfused, whereas the lower lung regions tend to have a V/Q ratio < 1 because they are more perfused [5, 6, 8, 9, 12].

This raises an important question: what happens when the V/Q relationship is altered? Two major effects may occur, both under physiological and pathological conditions. The first is the shunt effect, which occurs when V/Q is < 1. This happens when alveoli are hypoventilated or collapsed while remaining excessively perfused. Under these circumstances, the affected alveolus is inadequately ventilated despite being perfused. Pulmonary blood flow is therefore redirected toward alveoli that are better ventilated, producing a diversion from poorly ventilated areas toward adequately ventilated ones. This is known as the shunt effect. Examples include pneumonia, acute pulmonary edema, atelectasis, and states of pulmonary hyperperfusion [2, 5, 6, 8, 9, 12].

The second alteration occurs when the alveolus is well ventilated but poorly perfused or not perfused at all, giving rise to the alveolar dead-space effect, in which V/Q is > 1 [2, 5, 6, 8, 9, 12]. The classic example is pulmonary embolism, in which a branch of the pulmonary artery is occluded by a thrombus, impairing perfusion and gas exchange and causing refractory hypoxemia despite preserved alveolar structure. Another example occurs during positive-pressure MV, in which PAlv may become sufficiently high to compress pulmonary capillaries, resulting in V/Q > 1 [6–9, 12, 17].

Under normal conditions, these effects remain in dynamic balance, thereby preserving V/Q stability.

What happens during MV?

Mechanical ventilation

MV is a temporary and often unavoidable form of ventilatory and oxygenation support in the intensive care unit. It does not directly cure pulmonary or cardiovascular disease; rather, it provides the support needed to totally or partially replace respiratory muscle function through the generation of positive airway pressure and the application of PEEP. In addition, it delivers oxygen-enriched gas through the inspired oxygen fraction (FiO_2) and helps optimize the V/Q relationship [2, 7–9]. Based on these goals, the indications for MV include hypoxemic respiratory failure, hypercapnic respiratory failure, airway protection in patients with depressed consciousness, ventilatory failure with impending respiratory arrest, severe hemodynamic instability, and general anesthesia [2, 7].

To achieve these objectives, MV uses volume-controlled or assisted modes and pressure-controlled or assisted modes.

In volume-controlled ventilation, the ventilator delivers a preset VT selected by the operator. In this setting, VT is the independent variable. However, to deliver this VT, the respiratory system inevitably generates a certain pressure, both in the airway and globally. This pressure is the dependent variable. It varies according to the programmed VT, respiratory system compliance, airway resistance, and patient effort. In pressure-controlled ventilation, the operator sets the inspiratory pressure, which becomes the independent variable. In this mode, VT is the dependent variable and depends on the set pressure, lung compliance, airway resistance, inspiratory time, and, when present, patient effort [2, 7].

Mechanical ventilation is not physiologically neutral

During critical illness, cardiovascular physiology changes dramatically and may itself prompt the initiation of MV [18]. Although the need for MV in such patients is undeniable, it is also well established that MV is not physiologically neutral. Gattinoni et al. [10] referred to the nonphysiological increases in TP generated by increases in airway and Ppls during positive-pressure ventilation. The application of positive-pressure MV produces profound changes in both respiratory and cardiovascular physiology [2, 7–10].

In patients receiving positive-pressure ventilation, airway pressure rises, leading to an increase in intrathoracic pressure and greater external constraint on the heart [2]. Regardless of the ventilatory mode used, pulmonary physiology is inevitably altered. MV shifts the system from physiological negative-pressure breathing to nonphysiological positive-pressure ventilation in order to permit inspiration [10]. TP becomes more positive because alveolar and Ppls increase. This may, in turn, promote pulmonary edema and inflammation [10].

Cardiopulmonary interaction during MV

MV also induces substantial cardiovascular changes. In mechanically ventilated patients, ventricular systolic and diastolic volumes decrease, and these changes become more pronounced as PEEP levels rise [2, 7–10, 19]. In addition, the increase in TP raises RAP, which becomes more dependent on intrathoracic conditions and volemia. This increase in RAP inevitably reduces VR [2, 19, 20]. These phenomena are even more pronounced in states of hypovolemia, such as sepsis, hemorrhage, or major burns, in which collapse of the inferior vena cava is frequently observed, an unfavorable event for both right- and left-sided hemodynamics [12].

At the same time, the increase in intrathoracic pressure causes a rise in pericardial pressure [2]. Consequently, filling of the cardiac chambers depends not only on intracavitary pressure but also on pericardial pressure. PEEP increases pericardial pressure, thereby reducing left ventricular end-diastolic volume and impairing ventricular filling [2].

Within the right-sided chambers, elevation of intrathoracic pressure increases RAP and reduces the gradient between systemic venous pressure and right ventricular diastolic pressure. As a result, VR, right ventricular filling, and right ventricular stroke volume all decrease [2, 20, 21].

Both Ppl and TP affect right-sided hemodynamics [20, 21]. Changes in Ppl influence VR and right ventricular volume, that is, right ventricular preload, and therefore left ventricular end-systolic volume. By contrast, variations in TP primarily affect right ventricular end-systolic volume and left ventricular preload [1, 20–23].

Pressure changes also occur within the cardiac chambers. Any pressure change arising in one ventricle may affect the other. This mutual influence and dependence between the ventricles is known as ventricular interdependence. It is possible because both ventricles share myocardial fibers, the interventricular septum is a mobile structure capable of adapting to pressure changes, and the pericardium is a relatively nondistensible membrane surrounding both ventricles [13]. During MV, the reduction in VR leads to a decrease in right ventricular end-diastolic volume. However, when pulmonary resistance increases because of lung or chest wall factors, hemodynamic changes become predominantly pressure-driven rather than volume-driven.

Higher PEEP levels may increase PVR through compression of alveolar pulmonary capillaries, thereby increasing right ventricular afterload, right ventricular systolic pressure, and wall stress [1, 20]. This rise in right-sided pressures may favor leftward shift of the interventricular septum and further impair biventricular hemodynamics [2, 23, 24]. These observations reinforce the concept that pressure-related phenomena, rather than volume changes alone, are major determinants of hemodynamic impairment during MV.

Does aPH develop during MV?

Concept of PH

Based on the work of Kovacs et al. [25], it is now accepted that normal resting mPAP is 14 ± 3.3 mmHg. However, this pressure may increase pathologically, leading to the syndrome known as PH. According to the 2022 European Society of Cardiology/European Respiratory Society guidelines, PH is a pathophysiological disorder that may encompass multiple clinical conditions and may be associated with a wide variety of respiratory and cardiac diseases, resulting in substantial morbidity and mortality [26, 27].

PH is a progressive pathophysiological disorder currently defined by a mPAP > 20 mmHg at rest, with PVR used to further characterize the hemodynamic phenotype, particularly in precapillary disease [26, 28]. Sustained increases in pulmonary pressure and afterload may ultimately lead to right ventricular dysfunction and failure.

The 2022 ESC/ERS guidelines define PH as a mPAP > 20 mmHg measured by right heart catheterization [26]. Precapillary PH is defined as mPAP > 20 mmHg, pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg, and PVR > 2 Wood units. Isolated postcapillary PH is defined as mPAP > 20 mmHg, wedge pressure > 15 mmHg, and PVR ≤ 2 Wood units. Combined post- and precapillary PH is defined as mPAP > 20 mmHg, wedge pressure > 15 mmHg, and PVR > 2 Wood units. Exercise PH is considered when the relationship between mPAP and CO is > 3 mmHg/L/min. Finally, a more recently recognized category, unclassified PH, refers to elevated mPAP (> 20 mmHg) with low PVR (≤ 2 Wood units) and low wedge pressure (≤ 15 mmHg). These patients do not fulfill criteria for either precapillary or postcapillary PH and may present with congenital heart disease, liver disease, airway disease, lung disease, or hyperthyroidism. Clinical follow-up is recommended in such cases [26, 27, 29, 30]. These definitions are summarized in Table 1.

Table 1. Hemodynamic definitions of PH.

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg
	PAWP ≤15 mmHg
	PVR >2 WU
IpcPH	mPAP >20 mmHg
	PAWP >15 mmHg
	PVR ≤2 WU
CpcPH	mPAP >20 mmHg
	PAWP >15 mmHg
	PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min

CO: cardiac output; CpcPH: combined post- and precapillary pulmonary hypertension; IpcPH: isolated postcapillary pulmonary hypertension; mPAP: mean pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; PH: pulmonary hypertension; PVR: pulmonary vascular resistance; WU: Wood units. Some patients present with elevated mPAP (> 20 mmHg) but low PVR (≤ 2 WU) and low PAWP (≤ 15 mmHg); this haemodynamic condition may be described by the term 'unclassified PH'. Reprint with permission form [26]. © European Respiratory Society.

From a clinical standpoint, PH is also classified into five groups: Group 1, pulmonary arterial hypertension (PAH); Group 2, PH associated with left heart disease; Group 3, PH associated with lung disease and/or hypoxemia; Group 4, PH associated with pulmonary artery obstruction; and Group 5, PH associated with multifactorial and/or unclear mechanisms [26, 27, 29, 30] (Figure 2).

aPH and MV

The development of aPH in patients receiving positive-pressure ventilation is one of its major deleterious consequences [11].

During positive-pressure MV, each insufflation delivered by the ventilator provides the programmed VT. VT promotes the formation of new West zones I and II by generating PAlv greater than pulmonary arterial and venous pressures [5, 9, 21]. This, in turn, increases dead space and creates regions with a high V/Q ratio, that is, regions that are well ventilated but poorly perfused. The addition of PEEP further accentuates this phenomenon [31]. According to West and Luks [12], both mechanisms promote capillary collapse, leading to increased pulmonary pressure due to alveolar compression. As higher VT and PEEP levels are programmed, PAP increases further, thereby increasing the likelihood of aPH [1].

These concepts are especially applicable to noninjured lungs. However, in most cases, mechanically ventilated lungs are affected by conditions such as pneumonia, pulmonary edema, acute respiratory distress syndrome, or atelectasis. From a ventilatory standpoint, these conditions are characterized by reduced PaO_2/FiO_2, low static compliance reflecting stiff lungs, elevated driving pressure, higher PEEP requirements, increased shunt, hypoxemia, and a tendency toward hypercapnia. These phenomena promote the coexistence of alveolar units that are well perfused but poorly ventilated, units that are well ventilated but poorly perfused, and units with relatively preserved V/Q relationships, all heterogeneously distributed throughout both lungs. This heterogeneity contributes to the development of aPH through multiple mechanisms related both to the injured lungs themselves and to MV per se [32].

Patient position should also be considered. During MV, patients are generally supine, a position that favors the development of atelectasis in dependent lung regions because fluid and thoracic contents settle gravitationally over the lower lung zones, thereby worsening V/Q mismatch.

Therefore, the model proposed by West and Luks [12] does not fully explain the multifactorial pulmonary mechanisms involved, especially in patients with injured lungs, diffuse alveolar damage, and the supine position. Rather, it explains only part of the pathogenesis of aPH. In this setting, aPH is also driven by hypoxic vasoconstriction, hypercapnia, pulmonary microemboli, alveolar edema with reduced lung compliance, and, fundamentally, by the use of high PEEP and VT [33]. Taken together, these mechanisms increase total PVR and ultimately lead to aPH.

This increase in right ventricular afterload caused by elevated PVR results in increased ventricular wall tension, greater wall stress, reduced coronary perfusion, and ischemia of the right ventricular free wall [2–4]. Under these conditions, the RV must generate higher pressure to open the pulmonary valve. Vonk Noordegraaf et al. [4] proposed that these mechanisms lead to hypoxic vasoconstriction and subsequent precapillary aPH [3, 34]. In our study entitled Hemodynamic Behavior and Mortality During Mechanical Ventilation, an observational prospective analytical study of 18 patients, we found that the development of aPH was associated with higher mortality, metabolic acidosis, hypoxemia, hypercapnia, greater shunt, elevated wedge pressure, and stiff lungs, and that higher PEEP was associated with a greater increase in PVR [35]. These findings are consistent with the current literature.

Moreover, this acute increase in right ventricular afterload has a marked adverse effect on right ventricular physiology, since the RV belongs to a high-flow, high-compliance, low-resistance system with limited contractile reserve and poor adaptation to acute increases in PAP [34]. The rise in PVR leads to progressive disruption of RV-pulmonary artery coupling and may ultimately result in right ventricular dysfunction and failure [14, 15].

GROUP 1 Pulmonary arterial hypertension (PAH)
1.1 Idiopathic
1.1.1 Non-responders at vasoreactivity testing
1.1.2 Acute responders at vasoreactivity testing
1.2 Heritablea
1.3 Associated with drugs and toxins[a]
1.4 Associated with:
1.4.1 Connective tissue disease
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart disease
1.4.5 Schistosomiasis
1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
1.6 Persistent PH of the newborn
GROUP 2 PH associated with left heart disease
2.1 Heart failure:
2.1.1 with preserved ejection fraction
2.1.2 with reduced or mildly reduced ejection fraction[b]
2.2 Valvular heart disease
2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
GROUP 3 PH associated with lung diseases and/or hypoxia
3.1 Obstructive lung disease or emphysema
3.2 Restrictive lung disease
3.3 Lung disease with mixed restrictive/obstructive pattern
3.4 Hypoventilation syndromes
3.5 Hypoxia without lung disease (e.g. high altitude)
3.6 Developmental lung disorders
GROUP 4 PH associated with pulmonary artery obstructions
4.1 Chronic thrombo-embolic PH
4.2 Other pulmonary artery obstructions[c]
GROUP 5 PH with unclear and/or multifactorial mechanisms
5.1 Haematological disorders[d]
5.2 Systemic disorders[e]
5.3 Metabolic disorders[f]
5.4 Chronic renal failure with or without haemodialysis
5.5 Pulmonary tumour thrombotic microangiopathy
5.6 Fibrosing mediastinitis

Figure 2. Clinical classification of PH. [a] Patients with heritable PAH or PAH associated with drugs and toxins might be acute responders. [b] Left ventricular ejection fraction for HF with reduced ejection fraction: ≤ 40%; for HF with mildly reduced ejection fraction: 41–49%. [c] Other causes of pulmonary artery obstructions include: sarcomas (high or intermediate grade or

angiosarcoma), other malignant tumours (e.g., renal carcinoma, uterine carcinoma, germ-cell tumours of the testis), non-malignant tumours (e.g., uterine leiomyoma), arteritis without connective tissue disease, congenital pulmonary arterial stenoses, and hydatidosis. [d] Including inherited and acquired chronic haemolytic anaemia and chronic myeloproliferative disorders. [e] Including sarcoidosis, pulmonary Langerhans's cell histiocytosis, and neurofibromatosis type 1. [f] Including glycogen storage diseases and Gaucher disease. HF: heart failure; HIV: human immunodeficiency virus; PAH: pulmonary arterial hypertension; PCH: pulmonary capillary haemangiomatosis; PH: pulmonary hypertension; PVOD: pulmonary veno-occlusive disease. Reprint with permission form [26]. © European Respiratory Society.

In critically ill patients, right-sided hemodynamics are continuously exposed to powerful pulmonary vasoconstrictive stimuli. Consistent with our findings, Garnica Escamilla et al. [36] proposed that the vascular endothelium may trigger vasoconstriction and PH in the presence of tissue hypoxia, lactic acidosis, hypercapnia, sepsis, and pulmonary embolism in genetically susceptible individuals, ultimately leading to pulmonary artery remodeling with smooth muscle proliferation [3, 4, 33–35]. Hypoxic vasoconstriction is particularly common in lung regions where alveoli are hypoventilated or nonventilated because they are occupied or collapsed. Blood that does not undergo gas exchange is redirected toward unaffected alveoli capable of alveolar-capillary exchange, thereby generating intrapulmonary shunt [2, 15]. During our investigation, we found that increased intrapulmonary shunt and reduced static compliance correlated with higher mPAPs [35]. This suggests that the greater the degree of alveolar collapse and hypoventilation, the greater the intrapulmonary shunt toward better ventilated alveoli in the setting of low-compliance lungs and diffuse alveolar damage.

PEEP is essential in ventilated patients because it helps prevent atelectasis, reverse hypoxemia, and homogenize pulmonary ventilation [2, 7–9, 37]. Despite its clear utility, PEEP also carries risks and may amplify the hemodynamic disturbances inherent to positive-pressure ventilation [37]. At lower levels, PEEP may reduce right ventricular preload by decreasing VR; when excessive or poorly tolerated, it may increase PVR, reduce right ventricular stroke volume, raise right ventricular end-diastolic pressure, and impair CO through pulmonary capillary compression and overdistension [2, 7–9, 11, 37]. The acute rise in right-sided pressures may cause leftward shift of the interventricular septum, with secondary impairment of left ventricular filling [2, 7–9, 11, 23]. This phenomenon further illustrates how ventricular interdependence may be adversely affected by MV [38]. ARDS is a classic example and may lead to acute cor pulmonale as a consequence of right ventricular failure [2].

Abrupt and sustained increases in RAP may also favor reopening of the foramen ovale or aggravate a pre-existing right-to-left shunt. This occurs when RAP transiently exceeds left atrial pressure, allowing deoxygenated venous blood to pass into the left atrium through the foramen ovale. In this context, PEEP may increase right-to-left shunting in patients with a patent foramen ovale, especially when right-sided pressures rise; however, no absolute PEEP threshold can be considered universally predictive [39–41]. Reopening of the foramen ovale should be suspected in cases of hypoxemia refractory to increases in FiO_2 [39–43].

In addition to elevated PEEP and VT, other ventilatory mechanics parameters may contribute to aPH. One of these is plateau pressure (Pplat), which reflects PAlv [2, 9, 37]. High Pplat values imply alveolar overdistension and an increased risk of barotrauma [2, 9, 11, 37]. Excessive Pplat may increase RV afterload and favor the development of aPH. Accordingly, RV-protective approaches generally aim to keep Pplat below 27 cmH_2O whenever feasible. These variables should be continuously monitored in all mechanically ventilated patients.

A clinical approach derived from studies in ARDS has identified four variables associated with acute cor pulmonale and right ventricular failure in mechanically ventilated patients: pneumonia as the cause of ARDS, $PaO_2/FiO_2 < 150$ mmHg, driving pressure ≥ 18 cmH_2O, and $PaCO_2 \geq 48$ mmHg [44]. When several of these factors are present simultaneously, the risk of right ventricular dysfunction increases substantially.

Taken together, these observations indicate that critically ill patients receiving positive-pressure MV may develop aPH through multiple pathophysiological mechanisms arising from cardiopulmonary interaction [17, 19, 21, 31, 34, 38] (Figure 3).

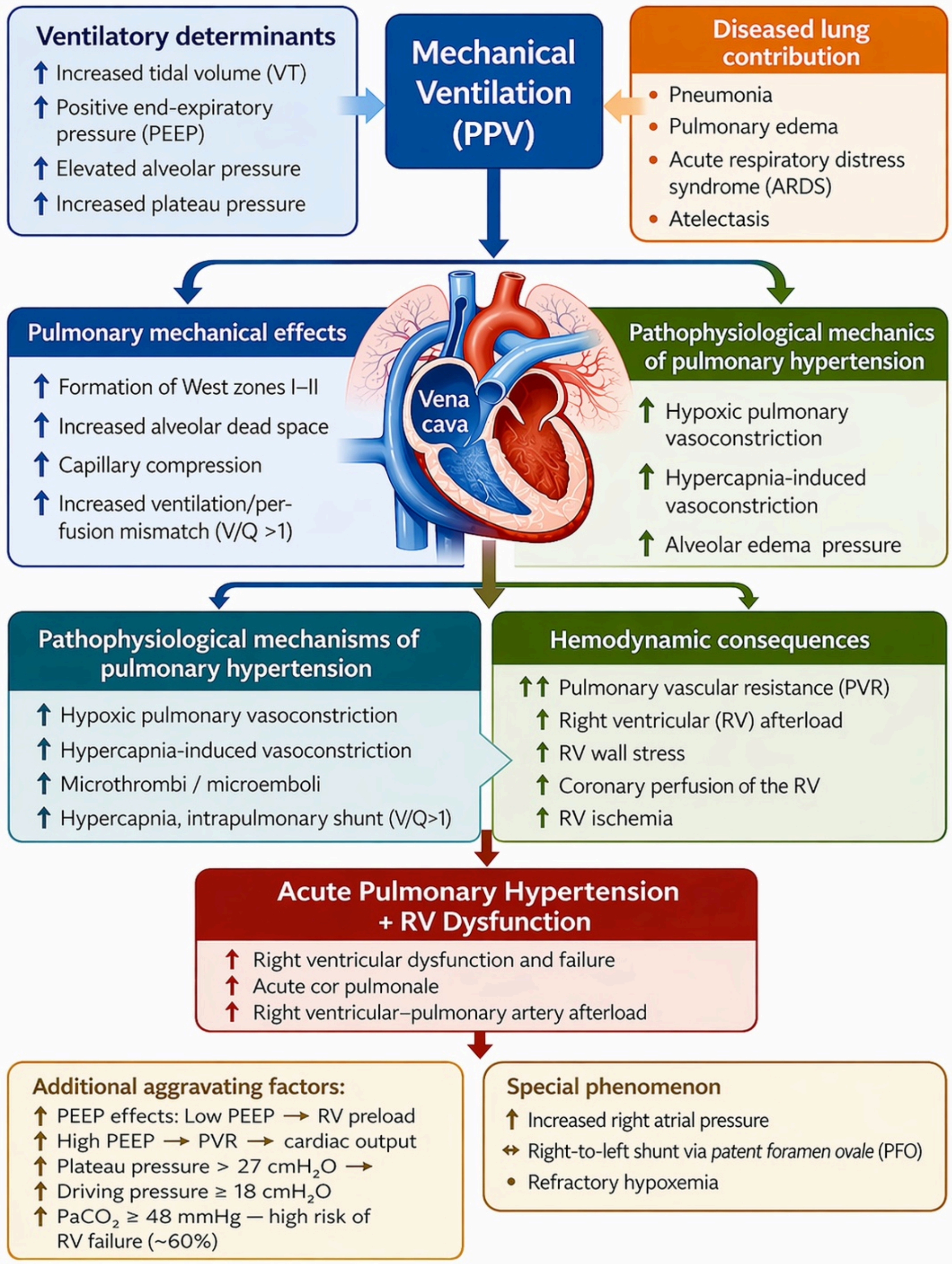

Figure 3. Acute pulmonary hypertension during mechanical ventilation.

Prevention of pulmonary and right-sided hemodynamic complications

To prevent, or at least minimize, the effects of MV on right-sided hemodynamics, the concept of lung- and RV-protective ventilation has been proposed. The goals of this strategy are as follows:

1. Use a low VT of 4–6 mL/kg predicted body weight; the more severely injured the lungs, the lower the VT should be whenever feasible [43].
2. Avoid high Pplat and keep it < 27 cmH_2O [44].
3. Avoid high driving pressure, ideally < 17 cmH_2O [44].
4. Maintain individualized PEEP, avoiding both alveolar collapse and overdistension [43, 44].
5. Correct hypoxemia, hypercapnia, and acidosis early [44].

6. Promote early prone positioning when PaO_2/FiO_2 is < 150 mmHg [43, 44].
7. Avoid aggressive recruitment maneuvers [43].
8. Avoid fluid overload [45, 46].
9. Consider invasive hemodynamic monitoring to distinguish hypovolemia from right ventricular failure when clinically indicated [44].

In summary, preventing respiratory and hemodynamic complications in critically ill patients admitted to the intensive care unit and receiving MV requires a lung- and RV-protective strategy. The RV is often overlooked when MV is instituted. To address this, alveolar overdistension, hypoxemia, hypercapnia, acidosis, and fluid overload should be avoided, and invasive hemodynamic monitoring may be considered to enable early recognition of right ventricular dysfunction whenever clinically appropriate (Figure 4).

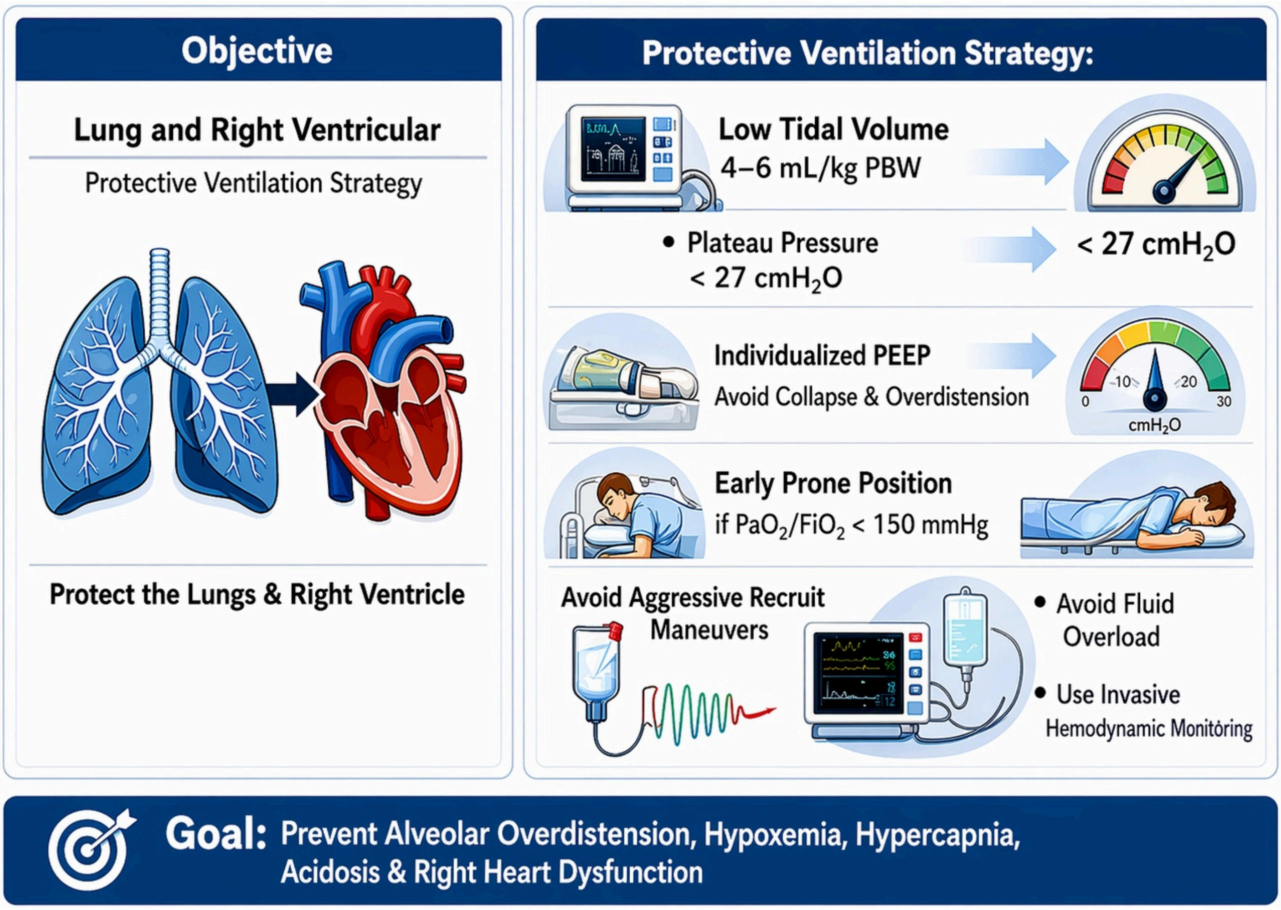

Figure 4. Prevention of pulmonary and right heart complications during mechanical ventilation. PBW: predicted body weight; PEEP: positive end-expiratory pressure.

These complications may also occur during anesthesia with positive-pressure ventilation. However, because ventilation in this setting is generally transient and applied to less severely injured lungs, typically with substantially lower pressure settings than those used in critically ill patients, their incidence is lower. Nevertheless, both settings share the same underlying pathophysiological mechanisms, including reduced VR, changes in ventricular preload and afterload, and a potential increase in right ventricular load. Under general anesthesia, the clinical relevance of these mechanisms becomes especially important in patients with COPD, PH, right ventricular dysfunction, hypovolemia, one-lung ventilation, cardiothoracic surgery, obesity, laparoscopic surgery with pneumoperitoneum, and related scenarios [47, 48].

Conclusions

The balance of normal cardiopulmonary interaction may be disrupted during critical illness.

Under such circumstances, MV is essential and often unavoidable. Ventilatory support must be provided whenever clinically indicated. Despite its clear benefits in critically ill patients, positive-pressure MV simultaneously induces a series of nonphysiological changes. The shift from the physiology of negative-pressure breathing to the pathophysiology of positive-pressure ventilation results in hemodynamic alterations even at relatively low levels of VT and PEEP. However, when VT, PEEP, Pplat, and driving pressure are elevated, the likelihood of aPH and right ventricular dysfunction increases substantially.

The development of aPH (mPAP > 20 mmHg) is profoundly deleterious to right ventricular function because it abruptly increases right ventricular afterload, thereby favoring right ventricular dysfunction, reopening of the foramen ovale, reduced left ventricular preload, and leftward displacement of the interventricular septum. In severe cases, these changes may impair left ventricular filling and contribute to obstructive hemodynamic compromise.

Preventing right ventricular dysfunction should therefore be considered a major clinical goal. Every appropriate measure should be taken to minimize its occurrence, including early implementation of protective ventilation strategies.

Abbreviations

aPH: acute pulmonary hypertension

CO: cardiac output

FiO_2: inspired oxygen fraction

mPAP: mean pulmonary arterial pressure

MSFP: mean systemic filling pressure

MV: mechanical ventilation

PAH: pulmonary arterial hypertension

PAlv: alveolar pressure

PAP: pulmonary arterial pressure

PEEP: positive end-expiratory pressure

PH: pulmonary hypertension

Ppl: pleural pressure

Pplat: plateau pressure

PVP: pulmonary venous pressure

PVR: pulmonary vascular resistance

RAP: right atrial pressure

RV: right ventricle

RVR: resistance to venous return

TP: transpulmonary pressure

V/Q: ventilation/perfusion

VR: venous return

VT: tidal volume

Declarations

Acknowledgments

During the preparation of the figures, the authors used ChatGPT (OpenAI, San Francisco, CA, USA) to create the three figures (Figures 1, 3, and 4) and visually optimize the table used in the review. After using the tool, authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Author contributions

ABR: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. SV: Validation, Writing—review & editing, Supervision. CG: Validation, Writing—review & editing, Supervision. JCV: Validation, Writing—review & editing, Supervision. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Copyright

Publisher's note

References

1. Zakynthinos GE, Tsolaki V, Mantzarlis K, Xanthopoulos A, Oikonomou E, Kalogeras K, et al. Navigating Heart-Lung Interactions in Mechanical Ventilation: Pathophysiology, Diagnosis, and Advanced Management Strategies in Acute Respiratory Distress Syndrome and Beyond. J Clin Med. 2024;13: 7788. [DOI] [PubMed] [PMC]
2. Chiapero GR, Ríos F, Setten M. Mechanical ventilation: book of the Critical Pneumology Committee of SATI. 3rd ed. Buenos Aires: Editorial Médica Panamericana; 2018.
3. Ortíz G, Dueñas C, Garay M, Díaz G. Fisiología respiratoria: aplicación en la práctica clínica. 1st ed. Bogotá: Editorial Distribuna; 2015.

4. Vonk Noordegraaf A, Chin KM, Haddad F, Hassoun PM, Hemnes AR, Hopkins SR, et al. Pathophysiology of the right ventricle and of the pulmonary circulation in pulmonary hypertension: an update. Eur Respir J. 2019;53:1801900. [DOI] [PubMed] [PMC]
5. Raff H, Levitzky M. Fisiología médica: un enfoque por aparatos y sistemas. 1st ed. México DF: McGraw-Hill Interamericana; 2013.
6. Barrett KE, Barman SM, Yuan JXJ, Brooks HL. Ganong's review of medical physiology. 26th ed. New York: McGraw-Hill; 2019.
7. Vega V. Diccionario ilustrado de rarezas, inverosimilitudes y curiosidades. 3rd ed. Barcelona: Gustavo Gili; 1965.
8. Lovesio C. Intensive Care Medicine. 6th ed. Rosario: Editorial Corpus; 2008.
9. Arata AL, Franceschini CM. Mechanical ventilation. 1st ed. Buenos Aires: Ediciones Journal; 2010.
10. Gattinoni L, Marini JJ, Collino F, Maiolo G, Rapetti F, Tonetti T, et al. The future of mechanical ventilation: lessons from the present and the past. Crit Care. 2017;21:183. [DOI] [PubMed] [PMC]
11. Vidal-Gordo F, Enciso-Calderón V. Acute respiratory distress syndrome, mechanical ventilation and right ventricular function. Med Intensiva. 2012;36:138–42. Spanish.
12. West J, Luks A. Fisiopatología pulmonar: fundamentos. 9th ed. Philadelphia: Wolters Kluwer; 2017.
13. Nava-López JA, Córdova-Rayas JC, de la Torre-de León T, Carrillo-Esper R, Silva-Blas L. Manejo anestésico del ventrículo derecho. Rev Mex Anestesiol. 2017;40:S191–8.
14. Pagnamenta A, Lador F, Azzola A, Beghetti M. Modern invasive hemodynamic assessment of pulmonary hypertension. Respiration. 2018;95:201–11. [DOI]
15. Ghio S, Schitinzi S, Pica S. Pulmonary arterial compliance: how and why should we measure it? Glob Cardiol Sci Pract. 2015;2015:58. [DOI]
16. Jozwiak M, Teboul JL. Heart-Lungs interactions: the basics and clinical implications. Ann Intensive Care. 2024;14:122. [DOI] [PubMed] [PMC]
17. Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. Anesthesiology. 2015;122:932–46. [DOI]
18. Barrett R, Biagioni BJ, Berger L, McDermid R. Mechanical ventilation outcomes in patients with pulmonary hypertension in the United States: a national retrospective cohort analysis. J Crit Care. 2016;32:588–92. [DOI]
19. Grübler MR, Wigger O, Berger D, Bloechlinger S. Basic concepts of heart-lung interactions during mechanical ventilation. Swiss Med Wkly. 2017;147:w14491. [DOI]
20. Silva PL, Ball L, Rocco PRM, Pelosi P. Physiological and Pathophysiological Consequences of Mechanical Ventilation. Semin Respir Crit Care Med. 2022;43:321–34. [DOI] [PubMed]
21. Vieillard-Baron A, Matthay M, Teboul JL, Bein T, Schultz M, Magder S, et al. Experts' opinion on management of hemodynamics in ARDS patients: focus on the effects of mechanical ventilation. Intensive Care Med. 2016;42:739–49. [DOI] [PubMed]
22. Price LC, Wort SJ, Finney SJ, Marino PS, Brett SJ. Pulmonary vascular and right ventricular dysfunction in adult critical care: current and emerging options for management: a systematic literature review. Crit Care. 2010;14:R169. [DOI] [PubMed] [PMC]
23. Das A, Haque M, Chikhani M, Cole O, Wang W, Hardman JG, et al. Hemodynamic effects of lung recruitment maneuvers in acute respiratory distress syndrome. BMC Pulm Med. 2017;17:34. [DOI] [PubMed] [PMC]
24. Santos Martínez LE. Fisiopatología de la falla ventricular derecha en la hipertensión arterial pulmonar. Arch Cardiol Mex. 2004;74:353–7.
25. Kovacs G, Berghold A, Scheidl S, Olschewski H. Pulmonary arterial pressure during rest and exercise in healthy subjects: a systematic review. Eur Respir J. 2009;34:888–94. [DOI] [PubMed]

26. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2023;61: 2200879. [DOI]
27. Moris MC, Soracio G, Echazarreta DF, Vulcano NO, Fernández Murga A, Caruso NA, et al. Recomendaciones para la realización de cateterismo cardíaco derecho en hipertensión pulmonar. Rev Fed Arg Cardiol. 2022;51:4–22.
28. Kovacs G, Bartolome S, Denton CP, Gatzoulis MA, Gu S, Khanna D, et al. Definition, classification and diagnosis of pulmonary hypertension. Eur Respir J. 2024;64:2401324. [DOI]
29. Galiè N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J. 2019;53:1802148. [DOI] [PubMed] [PMC]
30. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53: 1801913. [DOI] [PubMed] [PMC]
31. Pérez Nieto O, Zamarrón López E, Guerrero Gutiérrez MA, Tomas ED, Orozco RS, Sánchez Díaz JS, et al. PEEP: dos lados de la misma moneda. Med Crit. 2021;35:34–46. [DOI]
32. Estenssoro E, Dubin A. Síndrome de distrés respiratorio agudo. Medicina (B Aires). 2016;76:235–41.
33. Dunham-Snary KJ, Wu D, Sykes EA, Thakrar A, Parlow LRG, Mewburn JD, et al. Hypoxic pulmonary vasoconstriction: from molecular mechanisms to medicine. Chest. 2017;151:181–92. [DOI]
34. Hoeper MM, Granton J. Intensive care unit management of patients with severe pulmonary hypertension and right heart failure. Am J Respir Crit Care Med. 2011;184:1114–24. [DOI]
35. Rojas A, Vanoni S, Gobbi C, Vergottini J. Comportamiento hemodinámico y mortalidad durante la asistencia ventilatoria mecánica. Rev Fac Cien Med Univ Nac Cordoba. 2025;82.
36. Garnica Escamilla M, Carrillo Esper R. Hipertensión pulmonar y ventrículo derecho en anestesia. Rev Mex Anestesiol. 2017;40:S179–81.
37. Pérez-Nieto OR, Deloya-Tomás E, Lomelí-Terán JM, Pozos-Cortés KP, Monares-Zepeda E, Poblano-Morales M. Presión de distensión (driving pressure): principal objetivo para la protección alveolar. Neumol Cir Torax. 2018;77:222–7.
38. Ochoa Salmorán H, Martínez Martínez I, Cabrera Palos D, Lugo Bautista KS, Díaz Greene EJ. De la fisiología al ventilador: interacción corazón-pulmón durante la ventilación mecánica. Med Crit. 2020; 34:283–92. [DOI]
39. Mekontso Dessap A, Boissier F, Leon R, Carreira S, Campo FR, Lemaire F, et al. Prevalence and prognosis of shunting across patent foramen ovale during acute respiratory distress syndrome. Crit Care Med. 2010;38:1786–92. [DOI] [PubMed]
40. Lhéritier G, Legras A, Caille A, Lherm T, Mathonnet A, Frat JP, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: a multicenter study. Intensive Care Med. 2013;39:1734–42. [DOI]
41. Honda A, Yoshinaga K, Hirasaki Y, Iizuka Y, Otsuka Y. Dynamic shunt flow alterations through patent foramen ovale during off-pump coronary artery bypass grafting induced by airway pressure changes: a case report. JA Clin Rep. 2024;10:65. [DOI] [PubMed] [PMC]
42. Tsapenko MV, Tsapenko AV, Comfere TB, Mour GK, Mankad SV, Gajic O. Arterial pulmonary hypertension in noncardiac intensive care unit. Vasc Health Risk Manag. 2008;4:1043–60. [DOI] [PubMed] [PMC]
43. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, et al.; European Society of Intensive Care Medicine Taskforce on ARDS. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med. 2023;49: 727–59. [DOI] [PubMed] [PMC]

44. Arrigo M, Price S, Harjola VP, Huber LC, Schaubroeck HAI, Vieillard-Baron A, et al. Diagnosis and treatment of right ventricular failure secondary to acute cor pulmonale. Eur Heart J Acute Cardiovasc Care. 2024;13:304–12. [DOI]
45. Ziaka M, Exadaktylos A. Fluid management strategies in critically ill patients with ARDS: a narrative review. Eur J Med Res. 2025;30:401. [DOI] [PubMed] [PMC]
46. Sbaraini Zernini I, Nocera D, D'Albo R, Tonetti T. Acute Respiratory Distress Syndrome and Fluid Management: Finding the Perfect Balance. J Clin Med. 2025;14:2067. [DOI] [PubMed] [PMC]
47. Shelley B, McAreavey R, McCall P. Epidemiology of perioperative RV dysfunction: risk factors, incidence, and clinical implications. Perioper Med (Lond). 2024;13:31. [DOI] [PubMed] [PMC]
48. Di Cristo A, Segreti A, Tetaj N, Crispino SP, Guerra E, Stirpe E, et al. Hemodynamic Effects of Positive Airway Pressure: A Cardiologist's Overview. J Cardiovasc Dev Dis. 2025;12:97. [DOI] [PubMed] [PMC]