
3.1 Definition

Pulmonary hypertension (PH) is defined as an elevated level of pulmonary pressure above the normal range, and several hemodynamic parameters are used in defining pulmonary hypertension [1]. A systolic pulmonary pressure (PP) >30 mmg Hg, a mean PP >25 mmHg, or a pulmonary vascular resistance >200–300 dyn.s.cm⁻⁵ are the most common used definition. Pulmonary arterial hypertension (PAH) is a disease of the small pulmonary arteries that is, in part, due to vasoconstriction and remodeling of the vascular wall. These processes contribute to a characteristic progressive increase in pulmonary vascular resistance (PVR) and subsequent effects on the right ventricle that will eventually lead to death. Several of these definitions have been used in cardiac surgery, but information are obtained before the procedure and usually from an awake patient. For these reasons, the severity could be underestimated. This preoperative information could be acquired through preoperative catheterization or, more frequently, estimated *via* transthoracic echocardiography by using the Bernoulli's equation. Right ventricular function is described by pressure-volume relationships and is a major parameter of risk during PH. Acute PH expose to right ventricular (RV) failure after a short period of inotropic adaptation by the Anrep's law [2]. The RV chronically exposed to pulmonary hypertension undergoes hypertrophic changes and an increase in contractility, allowing for preserved flow output until decompensation.

3.2 Etiology

PAH is typically classified as capillary, precapillary, or postcapillary, depending on the site where the cause of PAH is present. The 2003 World Symposium on PAH proposed a classification based on five groups, and this classification has been modified in Nice [3] in 2013 (Table 3.1).

Pulmonary hypertension related to left heart disease (LHD) by far represents the most common form of PAH, accounting for 65–80% of cases. The distinction between pulmonary arterial hypertension and PH-LHD may be challenging, and it has direct therapeutic consequences [4].

Regardless of the origin, PH is defined by a mean pulmonary artery pressure (PAP) ≥ 25 mmHg. Based on the left-sided filling pressure determined either as LV end-diastolic pressure (LVEDP), left atrial pressure (LAP), or pulmonary arterial wedge pressure (PAWP), the hemodynamic definition further distinguishes pre- (≤ 15 mmHg) and postcapillary PH (> 15 mmHg). In postcapillary PH, the elevation of PAWP leads to a proportionate increase of the mean PAP, maintaining a normal transpulmonary pressure gradient ($\text{TPG} = \text{mPAP} - \text{PAWP}$) < 12 mmHg and low pulmonary vascular resistance ($\text{PVR} < 3$ Wood units (WU) or < 240 dynes s cm^{-5}). However, chronic elevation of the left-sided filling pressure associated with neurohormonal and mediator activation may cause excess vasoconstriction with or without vascular remodeling leading to a “disproportionate” increase of the PAP and thus resulting in an elevated TPG and PVR, which has been described as “reactive,” “out-of-proportion,” or “combined” post- and precapillary PH (Cpc-PH) [5].

Heart failure (HF) is now separated between HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF), with similar clinical syndrome of “heart failure,” but distinct entities regarding pathophysiology, cardiopulmonary interaction, and response to therapy. In HFrEF, the prevalence of PH was reported to be between 40 and 75% [6]. In patients with HFpEF, recent studies indicated a PH prevalence in a range between 36 and 83%. The prevalence of Cpc-PH in patients with HF is 12–38%. All the data indicate that PH and RV dysfunction are frequent and associated with a poor outcome in patients with LV HF.

During many years, the heterogeneity of PH was not understood and the reasons why some patients develop severe PH and RV dysfunction, whereas others do not, unclear. Two factors are now well described: the susceptibility for pulmonary vascular disease (due to genetic factors and/or environmental stressors and/or comorbidities) and the factor “time.” Genetic factors as gene *BMPR2*, which was the first discovered, can be researched now by many laboratories (see Table 3.1). For the Eisenmenger syndrome, time factor is determinant. Prolonged overcirculation-induced pulmonary arterial hypertension is a cause of right ventricular failure.

Table 3.1 Updated clinical classification of PH (Nice 2013)

1. Pulmonary arterial hypertension (PAH)
1.1. Idiopathic
1.2. Heritable
1.2.1. BMPR2
1.2.2. ALK1, ENG, SMAD9, CAV1, KCNK3
1.2.3. Unknown
1.3. Drug and toxin induced
1.4. Associated with:
1.4.1. Connective tissue diseases
1.4.2. HIV infection
1.4.3. Portal hypertension
1.4.4. Congenital heart diseases
1.4.5. Schistosomiasis
1'. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1". Persistent pulmonary hypertension of the newborn (PPHN)
2. Pulmonary hypertension due to left heart disease
2.1. Left ventricular systolic dysfunction
2.2. Left ventricular diastolic dysfunction
2.3. Valvular disease
2.4. Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
3. Pulmonary hypertension due to lung disease and/or hypoxia
3.1. Chronic obstructive pulmonary disease
3.2. Interstitial lung disease
3.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4. Sleep-disordered breathing
3.5. Alveolar hypoventilation disorders
3.6. Chronic exposure to high altitude
3.7. Developmental abnormalities
4. Chronic thromboembolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear multifactorial mechanisms
5.1. Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2. Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

3.3 Treatment Available

Standard medical therapies include oxygen, anticoagulant, prevention of fluid overload, and cardiac support. Calcium channel blockers decrease blood pressure and are appropriate for a small minority of patients (<10%) demonstrating a favorable response to vasodilator testing at the time of heart catheterization. But specific treatments have been progressively discovered over the past two decades and have changed the prognosis of these severe patients. Three major pathways (the prostacyclin, endothelin, and nitric oxide (NO) pathways) have been established as being key to the development and progression of PAH [7]. These pathways have been targeted by PAH-specific therapies (Table 3.2) that fall into three main drug classes in practice: prostacyclin analogues, endothelin receptor antagonists (ERAs), and phosphodiesterase-5 inhibitors (PDE-5i). As for antibiotics, it is not recommended to associate two drugs of the same class, but can be switched.

Whereas targeted therapies are available for pulmonary arterial hypertension (PAH), these treatments have not been adequately evaluated or are not indicated and may even be harmful in patients with PH related to LHD [8]. All of these treatments

Table 3.2 Specific treatments of PAH

Endothelin receptor antagonists (ERAs)
• Ambrisentan (Letairis®)
• Bosentan (Tracleer®)
• Macitentan (Opsumit®)
NO pathway
• Nitric oxide (NO)
Phosphodiesterase inhibitors (PDE-5 inhibitors)
• Sildenafil (Revatio™)
• Sildenafil (Revatio™) for pediatric use
• Tadalafil (Adcirca®)
Soluble guanylate cyclase stimulators
• Riociguat (Adempas®)
Prostacyclin pathway
Oral
• Oral Treprostinil (Orenitram®)
• Oral IP prostacyclin receptor agonists selexipag (Upravi®)
Inhaled treatment options
• Iloprost (Ventavis®)
• Inhaled Treprostinil (Tyvaso™)
Intravenous treatment options
• Intravenous Treprostinil (Remodulin®)
• Epoprostenol (Flolan®)
• Room Temperature Stable Epoprostenol (Veletri®)
Subcutaneous treatment options
• Subcutaneous Treprostinil (Remodulin®)

Table 3.3 Drugs trial and results

Drugs	Study	Hemodynamics	Combined test	Survival
<i>Endothelin pathway</i>				
Bosentan	BREATHE-1	++	+	
Ambrisentan	ARIES-1 and 2	+	+	
<i>NO pathway</i>				
Sildenafil	SUPER-1	+	+	
Tadalafil	PHIRST	+	—	
<i>Prostacyclin pathway</i>				
Intravenous epoprostenol		+		+
Inhaled iloprost	AIR	+	+	
Subcutaneous treprostinil		+	+	
Inhaled treprostinil	TRIUMPH		—	
Oral beraprost	ALPHABET	—	+	

Analyse inspired by Galiè [9]

NO nitric oxide, *Hemodynamics* PH or vascular resistance, *Combined* combination of 10% improvement in 6 min walking distance combined with an absence of clinical deterioration, +/— parameter improved or not

are not available in all countries, depending of national health authority. Some of them are prescribed only by reference centers, and differences are observed between clinical effects during trial [9] (Table 3.3). All these treatments should be known preoperatively by the anesthetist in order to continue them during perioperative period without any rupture or additive to intravenous or inhaled treatment. Nitric oxide [10, 11], prostacyclin [12], and PDE-5i [13, 14] like sildenafil or similar are the most common drugs used in ICU after cardiac surgery or during cardiac transplantation. Side effects are frequent and specific of each product (flush, hypotension, biological effects like transaminase increase or platelets effects) and should be monitored. The endothelin receptor antagonist bosentan has been reported to improve overcirculation-induced pulmonary hypertension [15].

During acute PH, norepinephrine restored arterial pressure, increased RV contractility, and increased but did not normalize RV-PA coupling and cardiac output. Dobutamine restored arterial pressure, markedly increased RV contractility, and normalized RV-PA coupling and cardiac output. Compared with norepinephrine, dobutamine decreased PA resistance and elastance and increased RV contractility and RV-PA coupling. In case of right ventricular failure due to PH, norepinephrine added to a pulmonary vasodilator is the most common choice, but levosimendan restores right ventricular-pulmonary arterial coupling, because of combined pulmonary vasodilation and increased right ventricular contractility, and has been tested [16].

Early appropriate treatment is necessary to reverse acute PH and RV failure. If not appropriate, a persistent right ventricular failure appears, and it is now demonstrated that this organ damage is related to an early activation of apoptotic pathways and to a local overexpression of tumor necrosis factor-alpha, a proinflammatory cytokine [17]. New drugs like riociguat are under evaluation or appropriate in some countries. Riociguat is a stimulator of soluble guanylate cyclase (sGC) that targets the NO pathway. Riociguat also sensitizes sGC to NO and promote vasorelaxation [18].

3.4 Risk Factors and Hemodynamic Parameters

For research trial or cath lab, the gold standard of RV systolic function is maximum elastance (E_{\max}), which is the maximal value of the pressure/volume ratio. This value is few sensitive to changes in loading conditions. The gold standard of after-load is arterial elastance (E_a), defined by the ratio of pressure at E_{\max} to stroke volume. The optimal coupling of ventricular function to the arterial circulation occurs at an E_{\max}/E_a ratio between 1.5 and 2 [2]. Patients with severe pulmonary hypertension often present an increased E_{\max} , a decreased E_{\max}/E_a , and increased RV dimensions. The normal subject had an E_{\max}/E_a ratio of 2. The E_{\max}/E_a ratio was decreased to 1 in the PAH patient.

In clinical practice, pulmonary artery systolic pressure (PASP) estimated by echocardiography strongly predicted all-cause and cardiovascular mortality independently of known predictors of outcome. While the TPG is influenced by volume load and cardiac function and does not prognosticate outcome in PH-LHD, the diastolic pressure gradient (DPG), defined by the difference between diastolic PAP and PAWP, is assumed to be less dependent of stroke volume and loading conditions and was shown to correlate with pulmonary vascular remodeling in PH-LHD [19]. These findings led to the current terminology and classification of postcapillary PH [5] as either isolated postcapillary PH (Ipc-PH), if the DPG is <7 mmHg and/or $PVR \leq 3$ WU, or combined post- and precapillary PH (Cpc-PH), if the DPG is ≥ 7 mmHg and/ or $PVR > 3$ WU. A combination of elevated PAP and reduced RV systolic function was particularly associated with an unfavorable outcome in HFrEF. Furthermore, HFpEF patients commonly display RV dysfunction, but elevated PAP occurs at more advanced stages and represents a strong predictor of death. The prognostic value of the DPG in PH-LHD is not yet conclusive.

A TAPSE of less than 1.8 cm is associated with greater RV systolic dysfunction, right heart remodeling (right atrial area index, 17.0 vs. 12.1 cm²), and RV-left ventricular (LV) disproportion (RV/LV diastolic area, 1.7 vs. 1.2), versus a TAPSE of 1.8 cm or greater. In patients with pulmonary arterial hypertension, the one-year survival rate was 94% vs. 60%, in groups with TAPSE $>$ or < 1.8 cm. Reduced RV free wall peak longitudinal strain was associated with an increased risk for RV failure among patients undergoing LVAD implantation [20].

During surgery for mechanical assistance, emergency situation, creatinine clearance, and bilirubin levels were more important risk factors of right ventricular failure than pulmonary pressure [21]. Many scoring systems have been proposed.

3.5 PAH in Practice: Anesthesia

During general anesthesia, risk factors for major complications in a PAH population of 114 patients [22] are reported as an elevated right atrial pressure (OR 1.1), a 6-min walking distance < 399 m at the last preoperative assessment (OR 2.2), the perioperative use of vasopressors (OR 1.5) and the need for emergency surgery (OR 2.4). Although there is consensus among anesthesiologists that regional anesthesia

is preferred over general anesthesia in patients with PAH, this is not possible in cardiac surgery. Hemodynamic monitoring is essential to detect the onset of an acute PAH crisis [23] but also to give direct information on the efficacy of treatment. The care of PAH patients for cardiac catheterization performed at a pulmonary hypertension center with expertise [24] is associated with low complication rates (1.2%) and mortality (0.2%). During valvular surgery, PH may be challenging, and the incidence of postcardiotomy acute refractory right ventricular failure ranges from 0.04 to 0.1%. But PAP returns to near-normal values in patients with severe preoperative PH and to normal values in patients with mild preoperative PH immediately after mitral valve replacement [25]. The outcome after surgery in patients with severe PH is comparable to those with mild PH and depends mainly on the right ventricular function.

Acute pulmonary hypertension may induce a series of mechanically triggered biologic events, which include an activation of proapoptotic pathways and local TNF overexpression that could contribute to persistently depressed RV function and ventriculo-arterial decoupling. So a particularly strict adaptation of pulmonary circulation and ventilation is needed to prevent a prolonged complication and death.

Inhalation but not IV anesthetics are reported to decrease pulmonary vascular resistance. Different animal models (hypoxic, overflow, or pulmonary banding) could have conflicting results. Isoflurane and desflurane markedly impair RV-PA coupling efficiency in dogs, during hyperoxia and hypoxia, both by increasing RV afterload and by decreasing RV contractility [26]. But isoflurane compared to propofol impaired RV vascular coupling caused by the decrease of RV contractility, while afterload may be unchanged [27]. Sevoflurane causes significant depression of global RV function associated with a qualitatively different effect on inflow and outflow tracts, without any modification of PVR [28].

PH is frequent in pediatric cardiac surgery [29]. Incidence of cardiac arrest was 0.78% for cardiac catheterization procedures, 10% for major surgical procedures, and 1.6% for all procedures. Ketamine administration was not associated with increased complications [30]. No differences were found between dexmedetomidine/fentanyl and midazolam/fentanyl in terms of the duration of sedation, mechanical ventilator use, and CICU stay in children with PAH [31], but a lower incidence of delirium than patients in the midazolam group.

3.6 PAH in Practice: Intensive Care

3.6.1 PH and Transplantation or LVAD

Acute refractory right ventricular failure has also been reported in 2–3% patients after a heart transplant and in almost 20–30% patients who receive a left ventricular assist device (LVAD) support. PH is not considered now as a contraindication for heart transplantation, but a risk factor [32]. Nevertheless adaptation of the right ventricle after the end of CPB should be considered as a difficult period for the anesthetist. Pulmonary vascular resistance over 450 dynes s cm^{-5} is the cutoff

for risk factor. Reversibility during pharmacological test could be tested before transplantation. All cofactors increasing pulmonary pressure like hypoxia, bleeding, and pain should be avoided. Monitoring pulmonary pressure is recommended.

During LVAD procedure, right ventricular failure increases the risk of death. Due to low cardiac output evaluation of pulmonary pressure and resistance could be difficult, so the level of pulmonary pressure is not directly the main risk factor. The need for right ventricular assistance is so far difficult. Nevertheless clinical experience during prolonged LVAD has proved the reversibility of disproportioned vascular resistance during the first 6 months [33]. But if measurement of right ventricular load (effective arterial elastance, pulmonary vascular compliance, and pulmonary vascular resistance) improves between the pre- and early post-LVAD time periods, the early phase could be different. Despite decreasing load and pulmonary artery wedge pressure (PAWP), RAP could be unchanged and the RAP/PAWP ratio worsened early post-LVAD (0.44 vs. 0.77 $p < 0.001$), suggesting a worsening of RV adaptation to load [34]. For that reason most patients are treated by NO or sildenafil in the early postoperative period. One of the most challenging period is the beginning of the left assistance, when PH acts as a barrier from right to left filling of the LVAD.

3.6.2 Mechanical Ventilation

The normal RV wall is thin and is able to accommodate to large changes in venous return, but unable to maintain flow output during sudden increase in pulmonary artery pressure or intrathoracic pressure. Patients with PAH who undergo invasive mechanical ventilation have an in-hospital mortality of 39% [35]. The types of patients who benefit most from advanced respiratory support in a critical care setting is not clearly defined. Peak pressure and plateau pressure should be monitored and right ventricular effect assessed by echocardiography after intubation.

Conclusion

Pulmonary hypertension is a high-risk situation for anesthesia, specifically during cardiac surgery. Significant progresses in specific medical treatments have changed the prognosis, but PH associated with left heart failure need more evaluation.

What Every Anaesthetist Needs to Know About Respiratory and Cardiovascular Dynamics in Patients with Obesity or Intra-abdominal Hypertension

7

7.1 Introduction

Worldwide, the incidence of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) is still underestimated by clinicians working in the emergency department (ED), operating room (OR) or intensive care unit (ICU). Increased intra-abdominal pressure (IAP) can have an immense impact on organ function, not only within but also outside the abdominal cavity including the brain, the cardiovascular system, and the lungs as summarised in Fig. 7.1. We will focus on cardiovascular and respiratory function as these are the closest monitored functions during surgery and anaesthesia. Respiratory failure can be defined as an imbalance between ventilatory capacity and ventilatory load. Whilst ventilatory capacity is mainly determined by respiratory drive, neuromuscular transmission and muscle strength, ventilatory load depends on minute volume, airway resistance and lung and chest wall compliance. Table 7.1 summarises the factors that affect chest wall compliance, IAP being one of the most important ones. In particular, because increased IAP affects the mechanical properties of the chest wall, it will

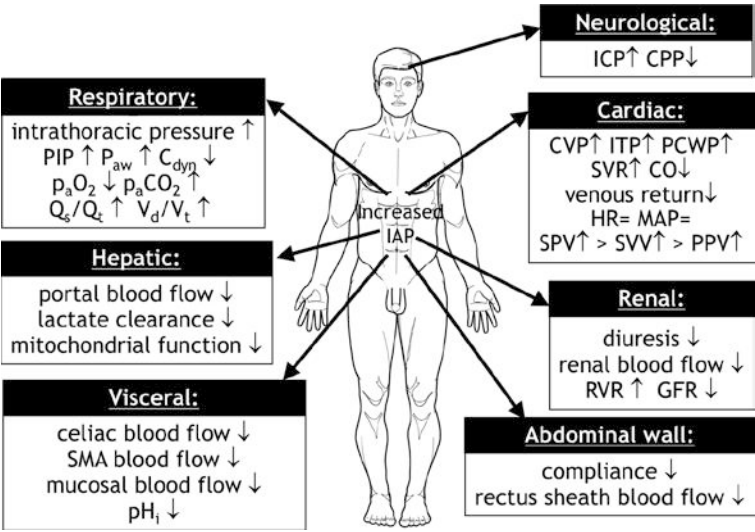


Fig. 7.1 Summary of the most important pathophysiologic effects of increased intra-abdominal pressure on end-organ function within and outside the abdominal cavity. Figure legend: *Cdyn* Dynamic respiratory compliance, *CO* Cardiac output, *CPP* Cerebral perfusion pressure, *CVP* Central venous pressure, *GFR* Glomerular filtration rate, *HR* Heart rate, *ICP* Intracranial pressure, *ITP* Intrathoracic pressure, *MAP* Mean arterial pressure, *PIP* Peak inspiratory pressure, *Paw* Airway pressures, *PCWP* Pulmonary capillary wedge pressure, *pHi* Intramucosal gastric pH, *Qs/Qt* Shunt fraction, *RVR* Renal vascular resistance, *SMA* Superior mesenteric artery, *SVR* Systemic vascular resistance, *Vd/Vt* Dead space ventilation

Table 7.1 Factors that affect chest wall compliance

• Pleural effusion
• Lung transplant
• Sternotomy (post-CABG)
• Obesity
• Ascites
• Fluid overload
• Rib fractures
• Abdominal distension
• Intra-abdominal hypertension (IAH)
• Abdominal compartment syndrome (ACS)

consequently also affect the respiratory function in different conditions [1]. In this chapter, we will start by listing the consensus definitions on IAH and ACS, followed by the different effects of IAH and ACS on ventilator-induced lung injury (VILI), respiratory mechanics, lung recruitment manoeuvre, lung oedema and lymphatic function. Table 7.2 summarises the respiratory effects induced by IAH and ACS. Afterwards, we will discuss what every anaesthetist needs to know about the cardiovascular effects of IAH and ACS (Table 7.3). Finally, we will translate these findings into clinical management suggestions. After reading this chapter, the way you will look at and treat your patients in the ED, OR and ICU especially those with obesity and IAH will never be the same, but it will save lives.

Table 7.2 Pulmonary effects of intra-abdominal hypertension and abdominal compartment syndrome. Adapted from Pelosi et al. [1]

Pulmonary effects related to increased IAP
Diaphragm elevation ↑
Intrathoracic pressure ↑
Pleural pressure ↑
Peak airway pressure ↑ (volume-controlled MV)
Mean airway pressure ↑
Plateau airway pressure ↑
Functional residual capacity (FRC) ↓
All lung volumes (TLC, TV, etc.) ↓ (~restrictive disease)
Extrinsic compression lung parenchyma ↑
Auto-PEEP ↑
Compression atelectasis ↑
Pulmonary vascular resistance ↑
Alveolar baro-/volutrauma = ↑
Compliance ↓
Respiratory system compliance ↓
Chest wall compliance ↓↓
Lung compliance =
Upper inflection point on PV curve ↓
Lower inflection point on PV curve ↑
Hypercarbia—pCO ₂ retention ↑
PaO ₂ ↓ and PaO ₂ /FiO ₂ ↓
Alveolar oxygen tension ↓
Oxygen transport ↓
Dead space ventilation ↑
Intrapulmonary shunt ↑
Ventilation perfusion mismatch ↑
Ventilation diffusion mismatch ↑↑
Oxygen consumption ↑
Metabolic cost and work of breathing ↑
Alveolar oedema ↑
Extravascular lung water (EVLW) = ↗
Pulmonary vascular permeability index (PVPI) = ↗
Prolonged ventilation
Difficult weaning
Activated lung neutrophils (experimental) ↑
Pulmonary inflammatory infiltration (experimental) ↑
Pulmonary infection rate (experimental) ↑

Table 7.3 Cardiovascular effects of intra-abdominal hypertension and abdominal compartment syndrome. Adapted from Malbrain et al. [2]

Cardiovascular effects related to increased IAP ^a
Diaphragm elevation and cardiac compression ↑
Pleural and intrathoracic pressure (ITP) ↑
Difficult preload assessment
Pulmonary capillary wedge pressure (PCWP) ↑
Central venous pressure (CVP) ↑
Mean systemic filling pressure ↑
Transmural filling pressure = ↓
Intrathoracic blood volume (ITBV) = ↓
Global end-diastolic volume (GEDV) = ↓
Right ventricular end-diastolic volume (RVEDV) = ↓
Right, global and left ventricular ejection fraction = ↓
Extravascular lung water (EVLW) = ↗
Stroke volume variation (SVV) ↗
Pulse pressure variation (PPV) ↗
Systolic pressure variation (SPV) ↗ (Δdown =, Δup ↑)
Inferior vena caval flow ↓
Venous return ↓
Left ventricular compliance and contractility ↓
Downward and rightward shift of Frank-Starling curve
Cardiac output ↓
Systemic vascular resistance (SVR) ↑
Mean arterial pressure (MAP) ↗ = ↓
Pulmonary artery pressure (PAP) ↑
Pulmonary vascular resistance (PVR) ↑
Heart rate ↗ =
Lower extremity hydrostatic venous pressure ↑
Venous stasis, oedema, ulcers ↑
Venous thrombosis ↑
Pulmonary embolism ^b ↑
Mixed venous oxygen saturation ↓
Central venous oxygen saturation ↓
False negative passive leg raising test ↑
Functional haemodynamic thresholds for fluid responsiveness ↑

^aCardiovascular effects are exacerbated in case of hypovolaemia, haemorrhage, ischaemia, auto-PEEP or high PEEP ventilation

^bUpon decompression

7.2 Epidemiology

Around one in four patients will have signs and symptoms of IAH on ICU admission, whilst around one out of two will develop IAH within the first week of ICU stay [3]. Moreover, 1 in 20 patients will develop overt ACS, a lethal syndrome with a mortality rate above 75% when left untreated [4]. To this day, patients may have unrecognised IAH. The major risk factors of IAH include abdominal surgery, surgery performed in the emergency setting, severe poly-trauma, abdominal trauma, severe haemorrhagic shock, severe burns, severe acute pancreatitis, large volume fluid resuscitation (especially crystalloid) resulting in fluid overload, ileus and liver dysfunction [5].

7.3 Consensus Definitions

Recently the World Society of the Abdominal Compartment Syndrome (WSACS) changed its name into the Abdominal Compartment Society (www.wsacs.org) [6]. As the focus concerning ACS becomes less paramount as it becomes less frequent, it became even more apparent that the actual name of the Society was limiting in terms of reflecting the true breadth and depth of the Society's mission. The ACS emphasises the most dramatic condition to be addressed, but it does not reflect upon the full scope of the Society's interests and activities [6]. In order to reflect the evolving science and to embrace important concepts related to abdominal wall anatomy and function, the focus was broadened from ACS to formally appreciating the abdominal compartment as a whole within all the body's interrelated compartments [6]. Hereby follows a short list of the latest consensus definitions as formulated by the WSACS, the Abdominal Compartment Society [7].

Definition 1: Intra-abdominal pressure IAP is the steady-state pressure concealed within the abdominal cavity.

Definition 2: Abdominal perfusion pressure In analogy to cerebral perfusion pressure, abdominal perfusion pressure (APP) is defined as mean arterial pressure (MAP) minus IAP.

Definition 3: IAP measurement IAP should be expressed in mmHg and measured at end expiration in the complete supine position after ensuring that abdominal muscle contractions are absent and with the transducer zeroed at the level where the mid-axillary line crosses the iliac crest.

Definition 4: Gold standard IAP measurement method The reference standard for intermittent IAP measurements is via the bladder with a maximal instillation volume of 25 mL of sterile saline.

- Paediatric-specific definition: The reference standard for intermittent IAP measurement in children is via the bladder using 1 mL/kg as an instillation volume, with a minimal instillation volume of 3 mL and a maximum installation volume of 25 mL of sterile saline.

Definition 5: Normal IAP Normal IAP is approximately 5–7 mmHg and around 10 mmHg in critically ill adults.

- Paediatric-specific definition: IAP in critically ill children is approximately 4–10 mmHg.

Definition 6: Intra-abdominal hypertension IAH is defined by a sustained or repeated pathologic elevation of IAP ≥ 12 mmHg.

- Paediatric-specific definition: IAH in children is defined by a sustained or repeated pathological elevation in IAP >10 mmHg.

Definition 7: IAH grading IAH is graded as follows:

- Grade I: IAP 12–15 mmHg
- Grade II: IAP 16–20 mmHg
- Grade III: IAP 21–25 mmHg
- Grade IV: IAP >25 mmHg

Definition 8: Abdominal compartment syndrome ACS is defined as a sustained increased IAP ≥ 20 mmHg (with or without an APP <60 mmHg) that is associated with new organ dysfunction or failure.

- Paediatric-specific definition: ACS in children is defined as a sustained elevation in IAP of greater than 10 mmHg associated with new or worsening organ dysfunction that can be attributed to elevated IAP.

Definition 9: Primary IAH/ACS Primary IAH/ACS (formerly also known as surgical or abdominal) is a condition associated with injury or disease in the abdomino-pelvic region that frequently requires early surgical or interventional radiological intervention.

Definition 10: Secondary IAH/ACS Secondary IAH/ACS (formerly also known as medical or extra-abdominal) refers to conditions that do not originate from the abdomino-pelvic region.

Definition 11: Recurrent IAH/ACS Recurrent IAH/ACS (formerly also known as tertiary) refers to the condition in which IAH/ACS redevelops following previous surgical or medical treatment of primary or secondary IAH/ACS.

Definition 12: Polycompartment syndrome A polycompartment syndrome is a condition where two or more anatomical compartments have elevated compartmental pressures. This will be discussed further.

Definition 13: Abdominal compliance Abdominal compliance (C_{ab}) quantifies the ease of abdominal expansion and is determined by the elasticity of the abdominal wall and diaphragm. C_{ab} is expressed as the change in intra-abdominal volume per change in intra-abdominal pressure in L/mmHg.

Definition 14: Open abdomen An open abdomen (OA) is any abdomen requiring a temporary abdominal closure (TAC) due to the skin and fascia not being closed after laparotomy. The technique of temporary abdominal closure should be explicitly described.

Definition 15: Open abdomen classification The open abdomen is classified with the following grading system:

- 1—No fixation.
 - 1A: Clean, no fixation.
 - 1B: Contaminated, no fixation.
 - 1C: Enteric leak, no fixation.
- 2—Developing fixation.
 - 2A: Clean, developing fixation.
 - 2B: Contaminated, developing fixation.
 - 2C: Entero-atmospheric/cutaneous fistula, developing fixation.
- 3 and 4—Frozen abdomen.
 - 3: Frozen abdomen, no fistula.
 - 4: Frozen abdomen with entero-atmospheric/cutaneous fistula.

Definition 16: Lateralization Lateralization of the abdominal wall refers to the phenomenon whereby the musculature and fascia of the abdominal wall, most well seen by the rectus abdominis muscles and their enveloping fascia, move laterally away from the midline with time.

7.4 Effects of Intra-abdominal Hypertension on Respiratory Mechanics

7.4.1 Intra-abdominal Hypertension and Ventilator-Induced Lung Injury (VILI)

Animal studies have shown that increasing IAP during mechanical ventilation may result in cytokine release and subsequent lung injury. Rezende-Neto et al. showed in a study of 50 rats that 60–90 min of IAH (IAP of 20 mmHg via insufflated

intraperitoneal air) resulted in increased plasma levels of IL-6, increased polymorphonuclear leucocyte activity in the lungs as evaluated by myeloperoxidase (MPO) assay [8], and intense pulmonary inflammatory infiltration including atelectasis and alveolar oedema on lung histology. Schachtrupp et al. showed in a study of 12 pigs that 24 hours of IAH (IAP of 30 mmHg) also resulted in histological findings similar to those found in VILI (interstitial and alveolar leucocytes and fibrin) but also proximal tubular necrosis in the kidneys and paracentral necrosis in the liver [9]. Since the strain on lung structures leading to VILI depends on transpulmonary pressure, it is not unreasonable to imagine that the frequently used relative too low transpulmonary pressures in the context of IAH will cause shear stress with increased repetitive opening and closing of alveoli units.

7.4.2 Effect of Intra-abdominal Hypertension on Respiratory Mechanics

As stated above lung distension is in part regulated by chest wall mechanics. The stiffer the chest wall, the less lung distension will occur during mechanical ventilation for a given airway pressure. In a Chinese study of 16 patients undergoing decompressive laparotomy (DL), different lung volumes were calculated with computed tomography (CT) at baseline, before and after DL. Compared to controls ($n = 6$), patients ($n = 16$) had lower total lung and higher non-aerated lung volumes [10]. This is illustrated in Fig. 7.2. Whereas chest wall elastance accounts in normal conditions for only 15% of the total respiratory system elastance, this number may increase up to 50% during IAH with IAP above 20 mmHg (due to the stiffening of the chest

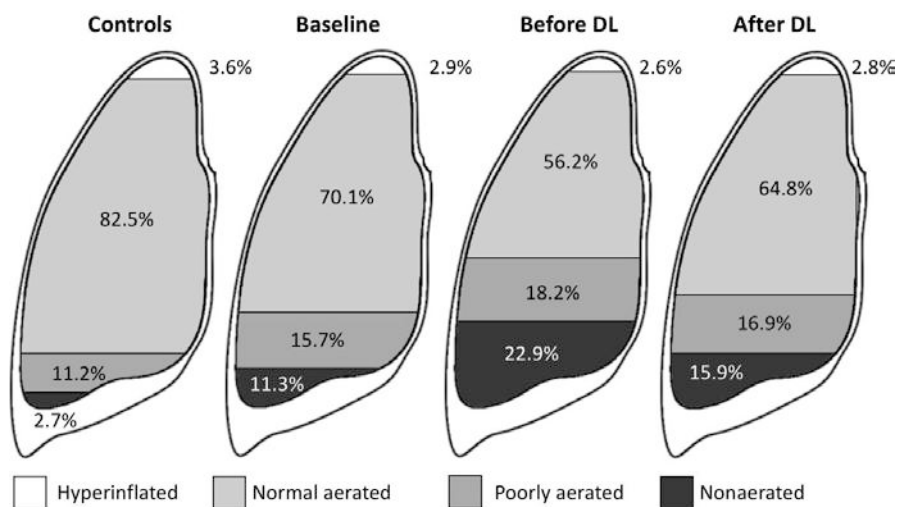


Fig. 7.2 Effect of abdominal hypertension and decompressive laparotomy on total lung volumes expressed percentages of different aerated lung volumes. Adapted from Zhou et al. [10]

wall). According to the polycompartment model (as will be discussed further down), IAH can increase intrathoracic pressure (ITP) and subsequently increase alveolar pressures [11]. We previously showed in a pig study ($n = 11$) that IAH up to 30 mmHg (with abdominal saline infusion intraperitoneally) resulted in an abdomino-thoracic transmission index (ATI) between 17% and 62% when looking at end-expiratory vs end-inspiratory oesophageal pressures, respectively [12]. With increasing IAP, both total respiratory system (C_{RS}) and chest wall (C_{CW}) compliance decreased significantly. The decrease was more pronounced for the chest wall and showed a strong inverse correlation with IAP ($r = -0.84$, $p < 0.0001$). A pilot study in 14 mechanically ventilated patients with acute lung injury (ALI) showed that the application of an abdominal Velcro belt increased IAP from 8.6 to 15.4 mmHg with a concomitant increase in alveolar plateau pressures (Pplat) from 18 to 23.3 cmH₂O (data on file). These changes were paralleled by a decrease in dynamic respiratory compliance from 37 to 28 mL/cmH₂O. This probably explains why the suggested lung-protective ventilation strategies are difficult to apply in patients with IAH or those with diminished chest wall compliance like in morbid obesity. Previous animal and human 'PV curve' studies focusing on the importance of IAH showed that abdominal and subsequently chest wall compliance improves after abdominal decompression [13, 14].

Acute respiratory distress syndrome (ARDS) is a syndrome and not a disease, and as a consequence, not all ARDS patients are the same which may be a possible explanation why there are conflicting results in previous ARDS studies. Ranieri et al. found that patients with ARDS had different respiratory mechanics depending upon the underlying aetiology and the presence of IAH. He found that surgical patients had stiffer chest walls compared to medical patients, probably due to the increased presence of abdominal distension [13]. Respiratory system and chest wall compliance improved after DL in these patients. Unfortunately, the effect of positive end-expiratory pressure (PEEP), forced residual capacity (FRC) and IAP was not measured. Mergoni and colleagues studied respiratory system mechanics partitioned between the lung and chest wall and showed that in a subgroup of ARDS patients in which the lower inflection point (LIP) was mainly determined by chest wall (C_{CW}) PEEP was not as effective in improving pO₂ [15]. In contrast, in ARDS patients in which LIP was determined by the lung compliance (C_L), PEEP was effective.

These findings are somewhat in contradiction with those found by Gattinoni and co-workers, and this can in part be explained by the difference in measurement manoeuvres and techniques as well as the assumptions used [16]. Gattinoni showed that the localised character of parenchymal involvement in primary ARDS (with primary lung involvement, e.g. pneumonia) resulted in decreased lung but normal chest wall compliance, whilst secondary ARDS (mainly as a result of abdominal sepsis) presented with preserved lung but decreased chest wall compliance, and PEEP allows to recruit lung units markedly only in secondary but not in primary ARDS [16]. The results imply that the application of PEEP in pulmonary ARDS may cause over-distension of already open lung units, making these patients more prone to ventilator-induced lung injury (VILI) than patients with extrapulmonary ARDS and IAH. The same phenomenon may be responsible for the change in respiratory mechanics seen in morbidly obese patients [17]. Measuring IAP may therefore provide an easy bedside method to

estimate altered chest wall mechanics and avert the need to measure oesophageal pressure (as surrogate for ITP). Measuring oesophageal pressure is not easy due to some practical problems at the bedside [1]. IAP also influences the shape of the PV curve (with downward flattening and rightward shifting) of the total respiratory system and the chest wall, whilst the lung mechanics basically remain unaffected [18].

7.4.3 Effect of Intra-abdominal Hypertension on Lung Recruitment

The most frequent performed recruitment manoeuvre is a 40-by-40 manoeuvre (40 s holding 40 cmH₂O inspiratory pressure). It is estimated that transpulmonary opening pressure equal to 30 cmH₂O is required to open atelectasis. In the setting of IAH with altered C_L/C_{RS} ratio from 0.85 to 0.5, the resulting transpulmonary pressure during a 40-by-40 recruitment manoeuvre may only be 20 cmH₂O; hence, the alveolar units with long-time constants would remain collapsed [19]. Therefore in the setting of IAH, higher opening pressures closer to 40 cmH₂O + IAP/2 may be required [20]. Lung-protective ventilation implies opening the lungs (with a recruitment manoeuvre or thus peak alveolar pressures) and keeping the lungs open (with appropriate PEEP setting) [21]. The altered lung mechanics and the different recruitment manoeuvres needed in IAH have also an impact on lung-protective ventilation (limiting Pplat below 30 cmH₂O) as this will result in very low tidal volumes (TV) in the setting of IAH or ACS. Therefore, Pplat should be limited towards a maximal peak alveolar pressure of '30 cmH₂O + IAP/2', or stated otherwise, transpulmonary Pplat calculated as $P_{plat} - IAP/2$ should be kept below 30 (to 35) cmH₂O. This statement is supported by the fact that Talmor and co-workers found that IAP (e.g. measured via the stomach) and oesophageal pressure (e.g. measured via an oesophageal balloon) are closely correlated [22]. Therefore, not only opening pressures but also closing pressures are increased during IAH and ACS and as such higher PEEP levels are required to prevent end-expiratory lung collapse. Keeping the lungs open is equally important after a recruitment manoeuvre to avoid shear stress of opening and closing lung units that may induce VILI. As a rule of thumb, PEEP (in cmH₂O) can be set equal to IAP (in mmHg). This assumption takes into account the fact that the ATI is not 100% as the conversion factor from mmHg to cmH₂O is 1.36. Some experimental data suggested the use of higher TVs around 10 mL/kg (as compared to 6 mL/kg) in IAH/ACS, but this strategy cannot be recommended yet in patients [23].

7.4.4 Effect of Intra-abdominal Hypertension on Lung Oedema and Lymphatic Drainage

A landmark paper by Quintel and co-workers showed that IAH causes an increase in lung oedema in a pig model of acute lung injury (induced by oleic acid) [18]. When IAP was increased from 0 to 20 cmH₂O, lung oedema distribution changed from the dorsobasal regions to the complete lung. In keeping with this, Schachtrupp showed an increase in extravascular lung water (EVLW) in and histological lung alterations

at IAP levels of 30 cmH₂O [24, 25]. An epidemiologic study in humans also found a correlation between IAP, fluid balance and EVLW in patients with acute lung injury, suggesting a link between sepsis, capillary leak, fluid overload, abdominal hypertension and lung oedema [26]. This may explain why active fluid removal or so-called de-resuscitation with PAL treatment (PEEP in cmH₂O set at the level of IAP in mmHg, followed by hyperoncotic albumin 20% and Lasix®) was able to reduce IAP and EVLWI in a pilot study of 57 patients matched with historical controls [27, 28].

Fluid drainage from the lungs can take place via three mechanisms: transpleural, via the lung hilum or transabdominal [29]. The effects of different ventilatory settings and increasing IAP on thoracic and abdominal lymph flow were studied in a porcine endotoxin sepsis model [30]. The study was performed in three parts and data were collected from a total of 32 pigs. In summary the authors found that lipopolysaccharide infusion increased IAP and lymphatic flow, that PEEP increased IAP and lymph production but impeded lymphatic drainage across the diaphragm, that spontaneous breathing improved transdiaphragmatic lymph drainage and finally that increased IAP diminished lymphatic flow. Although often overlooked, the role of lymphatic flow is complex but very important to determine not only the fluid balance in the lung but also in the peripheral organs [31]. Different pathologies and treatments can markedly influence the pathophysiology of the lymphatics with dramatic effects on end-organ function.

7.5 Effects of Intra-abdominal Hypertension on Cardiovascular Dynamics

7.5.1 Effect of Intra-abdominal Hypertension on Cardiac Contractility

Diaphragmatic elevation and increased ITP exert direct mechanic effects on cardiac contractility. This will be accompanied by an increase in pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) with a simultaneous decrease in left ventricular preload, finally leading to a decrease in cardiac output (CO). Animal studies have demonstrated a rightward and downward shift of the Frank-Starling curve in a dog model of IAH up to 40 mmHg created with fluid infusion in the peritoneal cavity [32]. Left ventricle wall motion assessment with trans-oesophageal echocardiography showed a significant decrease at the level of the anteroseptal wall in eight children during laparoscopic herniorraphy (with IAP levels of only 12 mmHg) [33]. Increases in central venous pressure (CVP) and IAP have also been observed in patients with congestive heart failure developing acute renal failure [34]. Whilst initially responsive to fluid loading and inotropic (dobutamine but not dopamine) support at lower levels of IAH, the deleterious cardiovascular effects in patients with ACS can only be effectively treated by nonoperative measures to reduce IAP or abdominal decompression. The APP seems a promising target to guide resuscitation in combination with less invasive haemodynamic monitoring like the transpulmonary thermodilution technique. After induction of IAH via pneumoperitoneum in ten pigs, an increase in CO following fluid loading was only indicated by calibrated CO but not by uncalibrated continuous CO methods using arterial waveform analysis [35].

7.5.2 Effect of Intra-abdominal Hypertension on Cardiac Preload

As described above, increased IAP causes a concomitant increase in ITP (via the ATI) and diaphragm elevation. This will result in direct compression of the heart and the vascular structures within the thorax. Vascular compression reduces the flow in the inferior vena cava (IVC) limiting blood return from below the diaphragm in a pressure-dependent manner (Fig. 7.3). When IAP increases, the cranial deviation of the diaphragm compresses and narrows the IVC where it enters the diaphragm, further reducing venous return (already at IAP levels of 10 mmHg) [2]. The resulting reduced venous return has an immediate effect on CO through decreased stroke volume. Since barometric filling pressures are zeroed against atmospheric pressure, they will be erroneously increased in patients with IAH and ACS because the elevated ITP is directly transmitted to the intravascular pressures like the central venous (CVP) and pulmonary capillary wedge pressure (PCWP), making (barometric) preload assessment difficult [36]. Mean systemic filling pressure may also increase during IAH explaining the marked susceptibility to pulmonary oedema, even minimal volume administration [37]. Finally, mixed venous and central venous oxygen saturation may fall.

7.5.3 Effect of Intra-abdominal Hypertension on Cardiac Afterload

As explained above (and as illustrated in Fig. 7.3), IAP can increase systemic and pulmonary vascular resistance via compression of the aorta, systemic and pulmonary vasculature, mesenteric splanchnic pool and pulmonary parenchyma. Accompanying

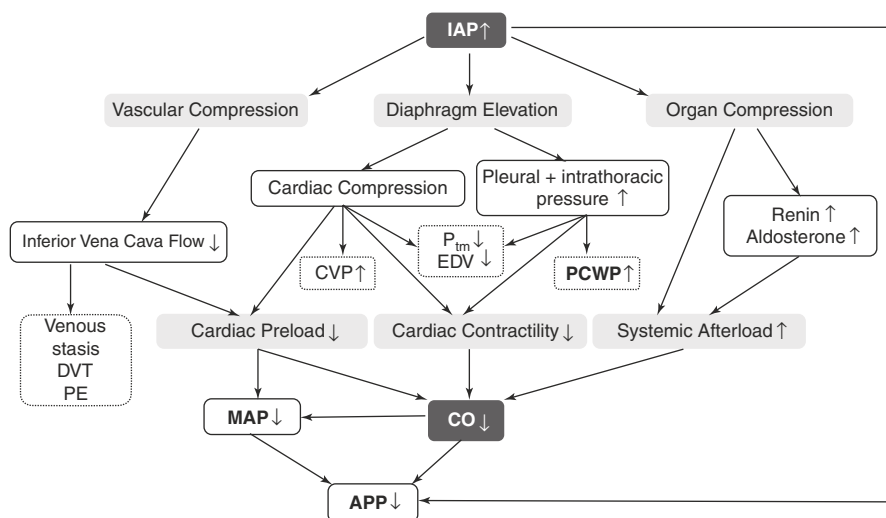


Fig. 7.3 Cardiovascular effects on preload, afterload and contractility related to increased intra-abdominal pressure. Adapted from Malbrain et al. [2]. Figure legend: APP Abdominal perfusion pressure, CO Cardiac output, CVP Central venous pressure, DVT Deep vein thrombosis, EDV End-diastolic volume, IAP Intra-abdominal pressure, MAP Mean arterial pressure, PCWP Pulmonary capillary wedge pressure, PE Pulmonary embolism, P_{tm} Transmural pressure

alterations in the renin-angiotensin-aldosterone mechanism have also been described [38]. The increased afterload also compensates for the reduced venous return. As a result of this physiologic compensation, MAP typically remains stable in the early stages of IAH and ACS. The cardiovascular effects are poorly tolerated in patients with impaired contractility, systemic underfilling or mechanical ventilation with high PEEP levels.

7.5.4 Effect of Intra-abdominal Hypertension on Functional Haemodynamics

Experimental data has shown that increased IAP resulting in increased ITP (ATI around 50%) will also increase functional haemodynamic parameters like stroke volume variation (SVV), pulse pressure variation (PPV) or systolic pressure variation (SPV) by exerting pressure on the thoracic vessels. This means that our usual thresholds (of 12–15%) defining fluid responsiveness may need to be changed in the setting of IAH or ACS. In fact, a summary of previous animal reports concludes that an increase in IAP up to 20 mmHg almost doubles the values of SVV and PPV suggesting thresholds around 24–30% to identify a fluid responder [39]. The increase in SPV seen during IAH is most likely a Δ_{up} phenomenon rather than a Δ_{down} phenomenon (Fig. 7.4), only the latter being correlated with fluid responsiveness [40].

7.6 Practical Implications at the Bedside

7.6.1 ARDS Definitions

In view of the above-cited clear differences between pulmonary and extrapulmonary ARDS, the current Berlin definition is inappropriate at the bedside for several reasons [41]. First, chest radiography has several limitations in mechanically ventilated patients in supine position as it lacks sensitivity and specificity to detect

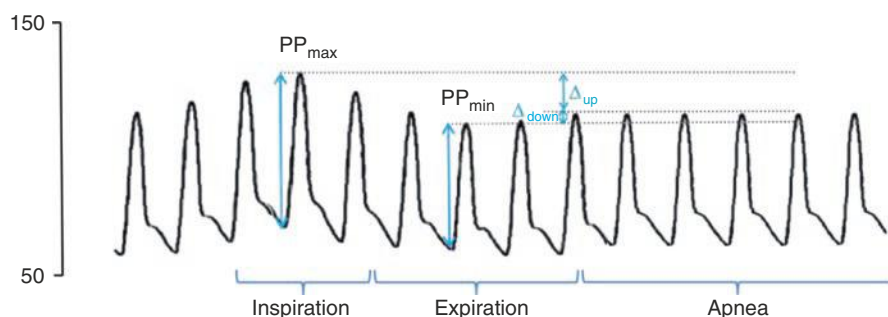


Fig. 7.4 Effects of abdominal hypertension on pulse and systolic pressure variations. Increased pulse (PPV) and systolic pressure variations (SPV) in a patient with IAP of 18 mmHg. The PPV can be calculated as $[(PP_{max} - PP_{min})/PP_{mean}] \times 100 (\%)$. After an apnoea test, it becomes clear that the increased SPV and PPV seen on the monitor are mainly related to a Δ_{up} phenomenon as only a smaller portion is caused by Δ_{down} . This means that the increased PPV and SPV are not necessarily correlated to fluid responsiveness and higher thresholds are probably needed

Table 7.4 A new definition for acute lung injury and ARDS, adapted from Michard et al. [45]

1. A pulmonary disease process known to increase pulmonary vascular permeability (normal IAP)
(a) Viral or bacterial pneumonia
(b) Gastric or smoke inhalation
(c) Etc.
Or
2. An extrapulmonary disease process known to increase pulmonary vascular permeability (increased IAP >12 mmHg)
(a) Chest trauma and/or poly-trauma and/or polytransfusion
(b) Pancreatitis or severe burns or severe sepsis or septic shock
(c) Etc.
With
3. Evidence for lung oedema
(a) Bilateral pulmonary infiltrates on chest radiography (with exclusion of pleural effusion or atelectasis)
(b) EVLWI >10 ml/kg PBW
(c) PVPI >2.5
(d) Bilateral consolidations on chest CT scan
And
4. The need for:
(a) FiO_2 between 0.4 and 0.6 to maintain $\text{S}_a\text{O}_2 > 95\%$ (ALI)
(b) $\text{FiO}_2 > 0.6$ to maintain $\text{S}_a\text{O}_2 > 95\%$ (ARDS)
(c) Regardless of PEEP level

pulmonary oedema [42] and may be mistaken with pleural effusions that are not necessarily related to increased EVLW [43]. Second, it is well established that the $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio depends on F_iO_2 , the relationship between the numerator and the denominator being non-linear. Moreover, this ratio also depends on the level of PEEP used. Third, as mentioned above, the definition also does not take into account the differences that may exist between primary and secondary ALI/ARDS and the role of IAP [26]. Finally, the evidence for cardiac dysfunction does not imply causality as patients with chronic cardiac diseases have an abnormal cardiac function on echocardiography also when they develop lung injury [44]. Therefore, the existence of a disease known to increase pulmonary vascular permeability seems more important than the lack of left ventricular dysfunction in order to accurately diagnose ALI/ARDS. Table 7.4 suggests a possible new ARDS definition [45].

7.6.2 Polycompartment Syndrome (PCS)

The abdominal compartment has unique effects because it is geographically situated ‘upstream’ from the extremities and ‘downstream’ from the thorax and the cranium [11]. Therefore, IAH and ACS may influence the physiology and pathophysiology of each of these other compartments. The presence of a compartment syndrome often plays a role when we are dealing with a therapeutic conflict, which is a dilemma

where each of the possible therapeutic decisions carries potential harm, e.g. the decision about fluid administration in particular should be done within this context in patients with ACS and haemodynamic instability accompanied with increased EVLW. Because the abdomen plays a major role in the interactions between different compartments, IAP affects portal and hepatic vein pressure hence facilitating blood shunting away from the lungs. This can be referred to as hepato-abdominal-pulmonary syndrome (HAPS) [11]. Similarly, IAP has also recently been identified as the missing link triggering renal failure (via increased renal vein pressures) in patients with chronic congestive heart disease, referred to as CARS or cardio-abdominal-renal syndrome [46]. Likewise deteriorating kidney function in patients with liver cirrhosis may be referred to as HARS or hepato-abdominal-renal syndrome.

7.6.3 Obese Patients

Studies have shown that obese patients with a body mass index higher than 35–40 kg/m² have higher IAP values compared to nonobese patients [47, 48]. Similarly to patients with IAH and ACS, the increased IAP values seen in obese patients will equally result in impairment in respiratory mechanics and gas exchange and decreased lung volumes particularly during sedation, paralysis and mechanical ventilation. As a consequence, the mechanical load exerted on the diaphragm is increased, especially in the supine position both during spontaneous breathing and general anaesthesia [1].

7.7 Respiratory Management in Intra-abdominal Hypertension: Hints and Tips

7.7.1 Recruitment

As stated above, in order to recruit the lung in IAH/ACS, higher than usual opening pressures are needed. As a rule of thumb, a 40 plus IAP/2-by-40 manoeuvre may be required. In fact, the transpulmonary peak pressure will open the lungs, and the higher the IAP, the lower the chest wall compliance and thus the higher the opening pressure (whilst transpulmonary opening pressure will remain unaffected).

7.7.2 Ventilator Settings During Lung-Protective Ventilation

Lung-protective ventilation is ideally set below P_{plat} 30 cmH₂O. In the context of IAH, higher P_{plat} may be required. When using an oesophageal balloon, lung-protective ventilation can be set targeting transpulmonary P_{plat} below <30 (to 35) cmH₂O. The application of PEEP by itself may increase IAP at the level of the diaphragm but only if PEEP is significantly higher than IAP. In a study of 30 patients with ALI/ARDS, the application of moderate PEEP of 12 cmH₂O resulted in a 3 mmHg increase in IAP [49], the effects being more pronounced in patients with underlying IAH. A recent review summarising different studies looking at the effects of PEEP on IAP found an average increase in IAP with 1.5 mmHg for a PEEP setting of 15 cmH₂O [47]. As

discussed previously, recent experimental data suggests the possibility for using a higher TV in IAH/ACS; however, to date, there is no hard human data to support this statement, and moreover this may be potentially dangerous [23].

7.7.3 Best PEEP

To date, the best PEEP in the setting of patients with IAH is largely unknown. As stated above, in IAH/ACS, the lung will collapse at higher closing pressures during expiration. As a rule of thumb, PEEP (cmH₂O) can be set at the level of IAP (mmHg) to prevent end-expiratory lung collapse. Different animal and scarce human data have looked into this hypothesis. A first study was conducted in 13 pigs with healthy lungs, and IAH was created with an inflatable balloon; the PEEP levels (5, 8, 12 and 15 cmH₂O) were unmatched to the level of IAP [50]. The conclusions were that commonly applied PEEP levels, set below the IAP level, cannot prevent FRC decline. Noteworthy was that IAP reached 18 mmHg or thus 25 cmH₂O, whilst PEEP was only set up to a maximum of 15 cmH₂O. In a second study, conducted in nine pigs with healthy lungs, IAH was again created with an inflatable balloon, and the PEEP levels were now matched for IAP [51]. The authors found a preservation of end-expiratory lung volume (EELV) without improvement in arterial oxygen tension but with a reduction in CO. In a third study, conducted in eight pigs with ALI induced by saline lavage and IAH created with CO₂ insufflation up to 20 mmHg, the PEEP levels (27 cmH₂O) were matched for IAP [52]. The major findings during PEEP application were lower LIP (reversal of shifting of PV curve to right with flattening), improved compliance and decreased D(A-a)O₂ (less shunt). In a fourth animal study in nine pigs, IAH induced by an inflatable balloon was combined with oleic acid-induced lung injury, and PEEP levels were matched to IAP [53]. The authors found better EELV, lower shunt fraction, lower dead space and a better P/F ratio. So far only one human study looked at 20 patients with ALI/ARDS with normal IAP or grade II IAH treated in the surgical ICU. There was no difference in oxygenation; however, EVLW was decreased in ALI/ARDS patients with IAH and high PEEP. The authors observed a decreased elastance of the respiratory system and the lung at PEEP of 15 cmH₂O. There were however many limitations: the numbers were small as only two times ten patients were included (underpowered), the values of IAP were relatively low (16 vs 8 mmHg) and there was no real matching between PEEP and IAP.

7.7.4 Prone and Other Positioning

Placing ARDS patients in the prone or upright position does not result in univocal beneficial effects on respiratory mechanics and oxygenation parameters [54]. Mure and co-workers demonstrated in an interesting animal model that the prone position improves pulmonary gas exchange to a greater degree in the presence of IAH as shown by increases in PaO₂ and decreases in D(A-a)O₂ and V/Q heterogeneity [55]. The observed decrease in IAP (estimated via gastric pressure), resulting in a concomitant decrease in pleural pressure (ITP) in the prone position, may be a possible

explanation for these observations, hence facilitating regional ventilation in the dependent lung zones near the diaphragm. The 45° head-of-bed or upright position can also affect respiratory mechanics. We previously published a case of ACS in an obese patient on non-invasive ventilation via face mask (with aerophagia) resulting in cardiovascular collapse after being put in the upright position [56]. Return of spontaneous circulation was only achieved after abdominal decompression via placement of a nasogastric tube and evacuation of the stomach contents. There seems to be a merit for unloading the abdomen (with suspensions) during prone ventilation. The pressure exerted by the chest suspension will result in a decreased C_{CW} , whilst the suspension at the level of the symphysis pubis will make sure that the abdomen can hang freely, hence exerting a ‘gravity’ effect limiting transmission of IAP towards the dorsobasal lung regions and diaphragm. This decreases IAP and improves C_{ab} avoiding atelectasis via dorsobasal recruitment. The theoretical benefits of proning a patient with IAH/ACS need to be outweighed against the practical risks (e.g. especially in case of an open abdomen). Further studies are required in patients with IAH although weightlessness appears to be beneficial for patients with ARDS [57]. Instead of proning, the combination of a weight placed on the chest with a vacuum shell placed on the abdomen may have similar effects to that of weightlessness with reducing C_{CW} and improving C_{ab} (Fig. 7.5) [58].

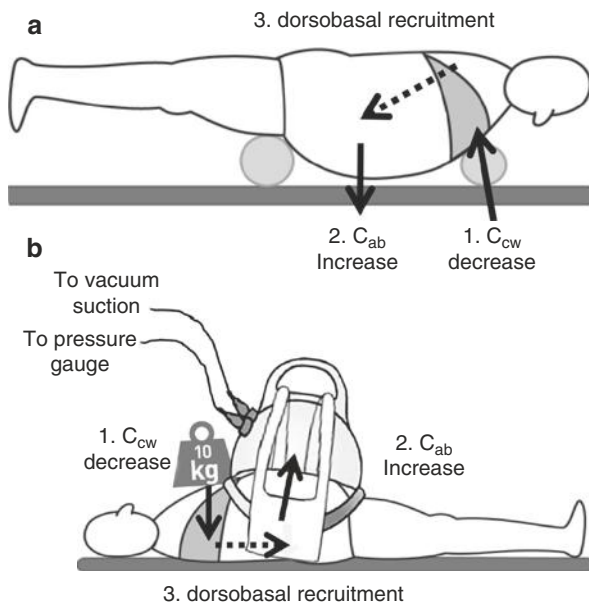


Fig. 7.5 Effects of positioning on chest and abdominal wall compliance. *Panel A:* Effects of prone positioning with abdominal suspension on chest and abdominal wall compliance. The suspension placed under the chest will reduce chest wall compliance, whilst the abdominal suspension placed at the level of the symphysis will exert a gravitational effect that will increase abdominal wall compliance. This will result in recruitment of dorsobasal lung regions. *Panel B:* Effects of supine positioning in combination with weight placed on the chest and vacuum bell on the abdomen. The weight placed on the chest will reduce chest wall compliance, whilst the abdominal vacuum bell will increase abdominal wall compliance. This will result in recruitment of dorsobasal lung regions

7.8 Cardiovascular Management in Intra-abdominal Hypertension: Hints and Tips

7.8.1 Improvement of Barometric Preload Indices (Calculation Transmural Cardiac Filling Pressures)

Because of the impact of IAP and ITP on the validity of intracardiac filling pressures like CVP and PCWP, a quick estimation of the transmural PCWP ($PCWP_{tm}$) or CVP (CVP_{tm}) at the bedside may improve the accuracy of barometric preload indicators as resuscitation endpoints [2, 12]. Theoretically, transmural ($_{tm}$) filling pressures are calculated as the end-expiratory value ($_{ee}$) minus the ITP or thus CVP_{tm} calculated as $CVP_{ee} - ITP$ and $PCWP_{tm}$ calculated as $PCWP_{ee} - ITP$.

The ITP is usually estimated from the pleural pressure which in turn is typically determined by measuring lower oesophageal pressure using a balloon-tipped catheter and is closely correlated to IAP [22]. As discussed previously, the ATI is around 20–80%, so that on average 50% of IAP is transmitted to the thorax [59]. As a rule of thumb, a quick estimate of transmural filling pressures can be obtained by subtracting half of the IAP from the measured filling pressure at end expiration or thus CVP_{tm} calculated as $CVP_{ee} - IAP/2$ and $PCWP_{tm}$ calculated as $PCWP_{ee} - IAP/2$. The calculation of transmural pressures is a better way to estimate true preload in patients with IAH or ACS for a number of reasons. First, since both PCWP and CVP are measured relatively to atmospheric pressure and are in fact actually the sum of intravascular pressure and ITP, the transmural pressures will more closely reflect true intracardiac pressures. Second, ventricular compliance is dynamic and changes from beat to beat in the critically ill, resulting in a variable relationship between pressure and volume, and as a result, changes in intravascular pressure will no longer reflect changes in intravascular volume, further reducing the accuracy of absolute intracardiac filling pressures.

7.8.2 Volumetric Preload Indices Better Reflect the True Preload Status in Intra-abdominal Hypertension

The value of volumetric preload indices like right ventricular end-diastolic volume (RVEDV) or global end-diastolic volume (GEDV) over traditional intracardiac filling pressures is especially notable in patients with elevated ITP or IAP where, as stated above, PCWP and CVP are at greatest risk for providing erroneous information regarding preload status [60]. Elevated ITP and IAP result in marked decrease in GEDV despite paradoxical increases in PCWP and CVP [61]. As IAH significantly depletes intravascular volume, it becomes clear that these changes are most appropriately detected by volumetric and not by pressure-based measurements of intravascular volume. Volumetric preload indicators can be further ‘improved’, as IAH also commonly results in cardiac dysfunction and decreased ejection fraction (EF). As a result of this constantly changing ventricular compliance, there cannot be a single value of GEDV that can be considered the goal of resuscitation for all patients with IAH [2]. Therefore, each patient must be resuscitated to the GEDV that optimises cardiac preload and systemic perfusion at any given moment. By ‘correction’ of the GEDV for the underlying EF, the predictive power improves [62].

7.8.3 Importance of Abdominal Perfusion Pressure

To improve the sensitivity of a single threshold value of IAP (that cannot be globally applied to the decision-making in all critically ill patients), one could include it in an assessment of APP. Similar to the widely accepted concept of cerebral perfusion pressure (CPP), APP, calculated as MAP minus IAP, has been proposed as a more accurate endpoint for resuscitation in patients with IAH or ACS. Reaching an APP of 50–60 mmHg appears to be superior over other macro- and microcirculatory parameters [63]. However, in order to achieve the target APP, the ICU physician needs to find a judicious balance between fluid resuscitation and the use of vasoactive medication. So far, studies with regard to APP are scarce, often retrospective and including only small numbers of patients [2].

7.8.4 Validity of the Passive Leg Raising Test in Intra-abdominal Hypertension

Since about 25% of critically ill patients with a PPV above 12% are not fluid responsive, this suggests different thresholds for different conditions [64]. Within this respect, it is important for the ED, OR and ICU physician to realise that the PLR test can be false negative in responders to fluid administration, and this can be related to increased IAP and diminished venous return from the legs and mesenteric veins. Therefore, care should be taken and IAP should be measured whilst interpreting the result of a PLR test.

7.9 Medical Management

Medical management strategies for raised IAP may be divided into five categories according to their proposed mechanism of action:

- First, improvement of abdominal wall compliance (sedation and analgesia, neuromuscular blockade, epidural anaesthesia and body positioning changes)
- Second, evacuation of intra-luminal contents (nasogastric or rectal decompression and use of prokinetic agents)
- Third, drainage of intra-abdominal fluid collections (paracentesis or percutaneous catheter drainage)
- Fourth, avoidance of excessive fluid resuscitation and correction of a positive patient fluid balance (with judicious use of fluids, e.g. rather hypertonic solutions instead of crystalloids)
- Fifth, organ support (respiratory and cardiovascular monitoring as outlined above)

It would be beyond the scope of this chapter to discuss the different medical management strategies into detail. An overview of the WSACS IAH/ACS medical management algorithm (and the associated grades of recommendations) is shown in Fig. 7.6.

IAH / ACS MEDICAL MANAGEMENT ALGORITHM

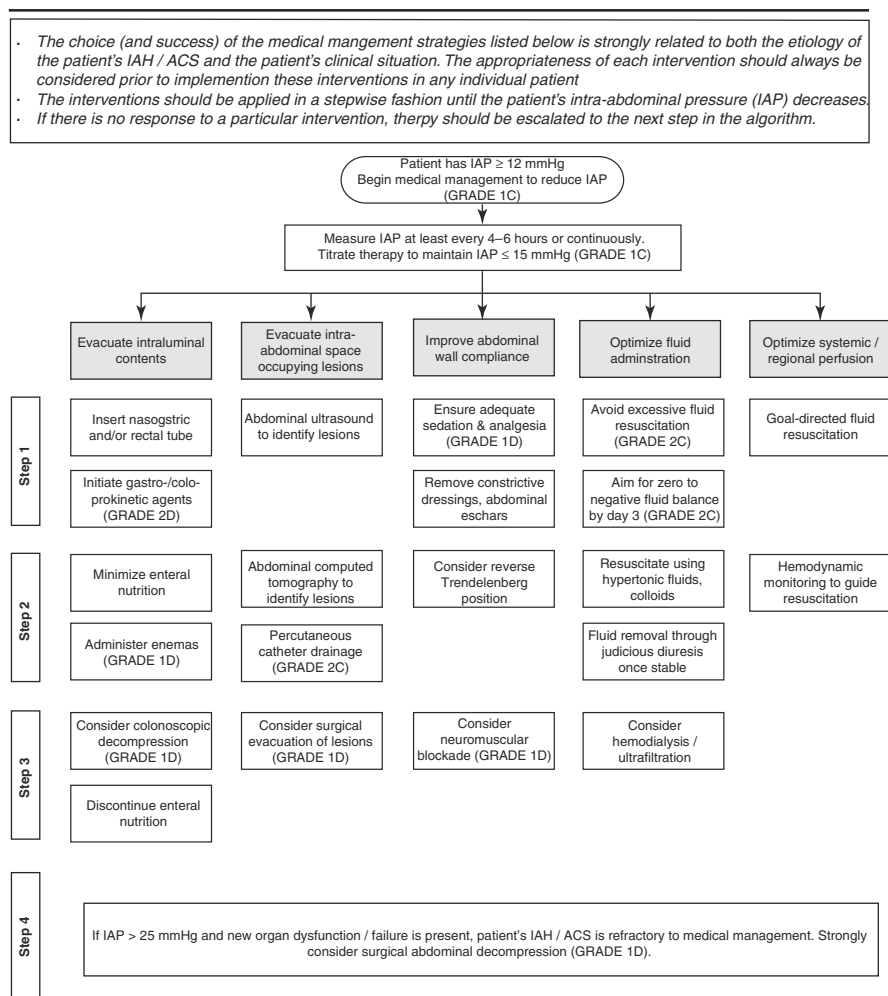


Fig. 7.6 WSACS 2013 intra-abdominal hypertension/abdominal compartment syndrome medical management algorithm. IAP intra-abdominal pressure. Figure reproduced with permission from Kirkpatrick et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated guidelines and consensus definitions from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med* 2013;39 [8]:1190–1206 [7]

7.10 Take-Home Messages

With regard to ventilator setting in patients with ALI/ARDS and abdominal hypertension, it is important to measure IAP and if possible also oesophageal pressure as surrogate for ITP [65]. Of note IAH can lead to the polycompartment syndrome with the associated interactions between different compartmental pressures [11].

Within this respect, one should avoid HOB above 45° in patients with high BMI. The ICU physician should get an idea of the ATI and TAI by looking at changes in IAP vs changes in airway (P_{aw}), intrathoracic (ITP) and filling pressures (CVP). During lung recruitment, higher opening pressures need to be used in patients with IAH or ACS. This cannot be done with a standard 40-by-40 manoeuvre, but rather a $(40 + IAP/2)$ -by-40 manoeuvre should be used instead. In addition, higher PEEP settings are required in order to prevent end-expiratory lung collapse. The best PEEP (in cmH_2O) can be calculated by performing a low-flow PV loop (with best PEEP equal to $LIP + 2 \text{ cmH}_2\text{O}$), but as a rule of thumb, best PEEP (cmH_2O) can be set equal to IAP (mmHg). During recruitment manoeuvres, haemodynamic status (CO) needs to be monitored. And in view of the exponential deleterious effects, it is worthwhile monitoring EVLW and pulmonary vascular permeability (calculated with transpulmonary thermodilution and defined as EVLW divided by pulmonary blood volume). Deep sedation with a short course of neuromuscular blocking agents may be used in selected patients or as a bridge towards decompressive laparotomy. Body positioning is important, and the anti-Trendelenburg position or proning with abdominal suspension may have beneficial effects on respiratory mechanics. During lung-protective ventilation, transmural or transpulmonary airway pressures are preferred, and as a rule of thumb, transpulmonary pressures, calculated as P_{plat} minus $IAP/2$, should be kept below 30–35 cmH_2O .

With regard to cardiovascular optimisation, the ED, OR and ICU physician must realise that cardiovascular dysfunction and failure (low CO, low contractility, high SVR) are common in IAH and ACS. Clinical evaluation of the patient is important when interpreting the haemodynamic parameters. Before administering fluids to patients with IAH or ACS, one should carefully check whether the patient is truly intravascular fluid depleted and fluid responsive. Accurate assessment and optimization of preload, contractility and afterload are essential to restore end-organ perfusion and function. Traditional haemodynamic monitoring techniques must be re-evaluated in IAH/ACS since pressure-based estimates of intravascular volume as PCWP and CVP can be erroneously increased. Mean systemic filling pressure may also be increased in IAH. The clinician must be aware of the interactions between ITP, IAP, PEEP and intracardiac filling pressures as misinterpretation of the patient's minute-to-minute cardiac status may result in the institution of inappropriate and potentially dangerous treatment. Transmural filling pressures may better reflect the true preload status in the setting of increased IAP, and resuscitation towards an APP $>60 \text{ mmHg}$ may be a good alternative resuscitation endpoint. Volumetric estimates of preload status such as global end-diastolic volume (GEDV) can be very useful because of the changing ventricular compliance with elevated ITP. Functional haemodynamic parameters such as PPV (rather than SVV or SPV) should be used to assess volume responsiveness, but the traditional thresholds need to be revised as around 25–35% of patients with IAH and a $PPV >12\%$ are nonresponders. The best threshold to predict fluid responsiveness in grade II IAH (15–20 mmHg) is a $PPV >20\text{--}25\%$. One also needs to bear in mind that IAH can be a cause for a false negative passive leg raising test. Finally, the cardiovascular effects are aggravated by hypovolaemia and the application of PEEP, whereas hypervolaemia may have a temporary protective effect.

Conclusions

Although considerable progress has been made over the past decades with regard to the identification and understanding of IAH and ACS, a number of important questions remain relating to the consequences and the optimal management of these conditions. Still, every day, patients may be exposed to the risks of unrecognised pathological increases in IAP. Every ED, OR and ICU physician should therefore learn to understand these pathophysiological mechanisms in order to positively impact organ function during IAH and ACS. IAP measurement is a first step, followed by prevention and medical management to lower the IAP. Monitoring of the respiratory and cardiovascular function during anaesthesia and surgery is of great importance. With our improved understanding of the pathophysiology and epidemiology, future randomised studies should be focused on defining whether targeted or multifaceted medical (and minimally invasive surgical) interventions aimed at reducing IAP and improving C_{ab} will ultimately improve outcomes in patients with IAH and ACS.