REVIEWS

What every ICU clinician needs to know about the cardiovascular effects caused by abdominal hypertension

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Abstract

The effects of increased intra-abdominal pressure (IAP) on cardiovascular function are well recognized and include a combined negative effect on preload, afterload and contractility. The aim of this review is to summarize the current knowledge on this topic. The presence of intra-abdominal hypertension (IAH) erroneously increases barometric filling pressures like central venous (CVP) and pulmonary artery occlusion pressure (PAOP) (since these are zeroed against atmospheric pressure). Transmural filling pressures (calculated by subtracting the pleural pressure from the end-expiratory CVP value) may better reflect the true preload status but are difficult to obtain at the bedside. Alternatively, since pleural pressures are seldom measured, transmural CVP can also be estimated by subtracting half of the IAP from the end-expiratory CVP value, since abdominothoracic transmission is on average 50%. Volumetric preload indicators, such as global and right ventricular end-diastolic volumes or the left ventricular end-diastolic area, also correlate better with true preload. When using functional hemodynamic monitoring parameters like stroke volume variation (SVV) or pulse pressure variation (PPV) one must bear in mind that increased IAP will increase these values (via a concomitant increase in intrathoracic pressure). The passive leg raising test may be a false negative in IAH. Calculation of the abdominal perfusion pressure (as mean arterial pressure minus IAP) has been shown to be a better resuscitation endpoint than IAP alone. Finally, it is re-assuring that transpulmonary thermodilution techniques have been validated in the setting of IAH and abdominal compartment syndrome. In conclusion, the clinician must be aware of the different effects of IAH on cardiovascular function in order to assess the volume status accurately and to optimize hemodynamic performance.

Key words: abdominal hypertension, abdominal pressure, abdominal compartment syndrome, cardiovascular, hemodynamic, barometric, volumetric, preload, afterload, contractility, cardiac output, functional hemodynamic, fluid responsiveness, passive leg raising

Obviously, any mechanically ventilated patient that is at risk of developing intra-abdominal hypertension (IAH) or abdominal compartment syndrome (ACS) with shock should be hemodynamically monitored [1]. Conversely, since IAH has an impact on every organ within and outside the abdomen any patient that develops one or more organ failure should be screened for increased intra-abdominal pressure (IAP) [2–4]. IAH affects multiple organ systems in a graded fashion and in order to better understand the clinical presentation and management of IAH, one must understand the physiologic derangements within each organ system separately [5]. It is beyond the scope of this review to give a complete overview of the pathophysiologic implications of raised IAP. We will only discuss some key messages related to cardiovascular function that will affect the daily clinical practice of the ICU physician and we will provide the reader with some practical hints and tips for patient management decisions. Cardiovascular dysfunction and failure and hemodynamic instability are commonly encountered in patients with IAH or ACS and the different effects are listed in Table 1 [6]. As such, accurate assessment and optimization of preload, contractility, and afterload, together with appropriate goal-directed resus-

Table 1. Cardiovascular effects related to increased IAP*

Diaphragm elevation and cardiac compression ↑
Pleural and intrathoracic pressure (ITP) ↑
Difficult preload assessment
Pulmonary artery occlusion pressure (PAOP) ↑
Central venous pressure (CVP) ↑
Mean systemic filling pressure ↑
Transmural filling pressure =↘
Intra thoracic blood volume (ITBV) =↘
Global end-diastolic volume (GEDV) =↘
Right ventricular end-diastolic volume (RVEDV) =↘
Right, global and left ventricular ejection fraction =↘
Extra vascular 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, edema, ulcers ↑
Venous thrombosis ↑
Pulmonary embolism# ↑
Mixed venous oxygen saturation ↓
Central venous oxygen saturation ↓
False negative passive leg raising test ↑
Functional hemodynamic thresholds for fluid responsiveness ↑

*cardiovascular effects are exacerbated in case of hypovolemia,
haemorrhage, ischemia, auto-PEEP or high PEEP ventilation
#risk of pulmonary embolism upon decompression
↑ — increase; ↑↑ — huge increase; ↗ — small increase; ↘ — small decrease;
↓ — decrease; ↓↓ — huge decrease

citation are essential in restoring end-organ perfusion [7]. A Medline and Pubmed literature search was performed in order to find an answer to the question "What is the impact of increased IAP on cardiovascular function?", using the search terms "abdominal compartment syndrome" or "abdominal hypertension" or "abdominal pressure" and "cardiac output" or "preload" or "afterload" or "contractility" or "cardiovascular" or "hemodynamic". This search yielded many references, most of which were not relevant to the subject of this paper. The

selected abstracts were screened and selected on the basis of relevance, methodology, and scientific merit. Full text articles of the selected abstracts were used to supplement the authors' expert opinion and experience. The references of the selected papers were also checked for other relevant material. The resulting references were included in the current review on the basis of relevance and scientific merit.

CARDIOVASCULAR EFFECTS ASSOCIATED WITH INTRA-ABDOMINAL HYPERTENSION

IAH is associated with a number of effects on the cardiovascular system that are caused by multiple factors [1, 8]. First of all, due to the upward movement of the diaphragm during IAH, the intrathoracic pressure (ITP) and hence also pleural pressure will rise. Animal and human experiments have shown that between 20% and 80% or thus on average 50% of the IAP is transmitted to the thorax [9, 10]. Cephalad movement of the diaphragm leads to direct compression on the heart with reduction of the right and left ventricle end-diastolic volumes. Secondly, the cardiac preload decreases due to decreased venous return from the abdomen and the systemic afterload is increased due to direct compression of vascular beds and activation of the renin-angiotensin-aldosteron pathway [11]. This leads to decreased cardiac output (CO). Although mean arterial blood pressure (MAP) may rise initially due to the shunting of blood away from the abdominal cavity (a sort of autotransfusion effect), it usually normalizes, or even decreases thereafter. The different effects on preload, afterload and contractility are summarized in Figure 1. The cardiovascular effects can be aggravated in hypovolemic patients and with the application of high levels of positive end-expiratory pressure (PEEP) [12, 13], whereas hypervolemia usually has a temporary protective effect [14]. Cardiac function may be distilled into three essential components: preload, contractility, and afterload. Moreover, elevated IAP has negative effects on all three of these interrelated components as will be explained below [15].

EFFECT OF INTRA-ABDOMINAL HYPERTENSION ON PRELOAD
PATHOPHYSIOLOGY

Increased IAP results in direct vascular compression and diaphragm elevation. Vascular compression on the inferior vena cava (IVC) reduces the flow, while diaphragm elevation increases ITP and causes cardiac compression (Fig. 1). Since barometric filling pressures are zeroed against atmospheric pressure, preload assessment becomes difficult in patients with IAH/ACS [1]. First, as originally described by Coombs, intrathoracic pressure (ITP) is increased as a result of a cephalad movement of the diaphragm due to increased IAP [16]. The elevated ITP is directly transmitted to the intravascular pressures, such as the central venous (CVP) and pulmonary
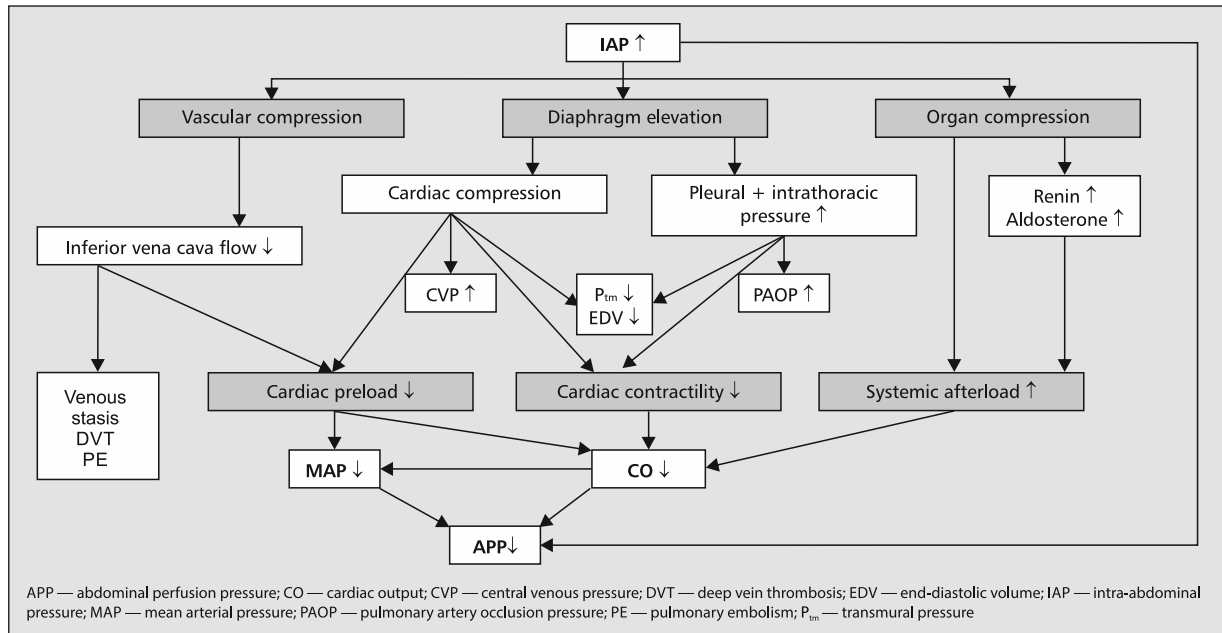
APP — abdominal perfusion pressure; CO — cardiac output; CVP — central venous pressure; DVT — deep vein thrombosis; EDV — end-diastolic volume; IAP — intra-abdominal pressure; MAP — mean arterial pressure; PAOP — pulmonary artery occlusion pressure; PE — pulmonary embolism; P_{tm} — transmural pressure

Figure 1. Cardiovascular effects (on preload, afterload and contractility) related to increased intra-abdominal pressure

artery occlusion pressure (PAOP). As suggested, the elevated ITP also decreases blood flow through the IVC and limits blood return from below the diaphragm in a pressure-dependent manner [9, 17]. Together with increased IVC and femoral vein pressures, parallel changes in IAP can be observed. Some have even suggested that IVC pressure could be used as a surrogate for IAP [18]. Secondly, when IAP rises, the cranial deviation of the diaphragm compresses and narrows the IVC as it passes through the diaphragm, further reducing venous return, and this may occur at an IAP as low as 10 mm Hg [19]. The resulting reduced venous return has an immediate effect on CO through decreased stroke volume (SV). As a result, mixed venous and central venous oxygen saturation may fall. Similar effects are encountered during laparoscopic surgery and these changes place the patient with IAH at risk of deep venous thrombosis and pulmonary embolism at the time of abdominal decompression [20, 21]. Lower extremity hydrostatic venous pressure increases and clinical examination may show venous stasis, edema and leg ulcers in cases of chronic IAH, as seen with obesity.

INTRACARDIAC FILLING PRESSURES ARE INACCURATE DURING IAH

According to the Frank-Starling principle, ventricular preload is defined as myocardial muscle fiber length at end-diastole (Fig. 2). Ideally, the appropriate clinical correlate would be left ventricular end-diastolic volume (LVEDV),

but this physiologic parameter is not easily measured on a serial basis [1, 8]. If we assume that a patient's ventricular compliance remains constant, changes in ventricular volume should be reflected by changes in ventricular pressure through the following relationships:

$$\text{Compliance} = \Delta \text{ Volume} / \Delta \text{ Pressure}$$
$$\text{and}$$
$$\Delta \text{ Volume} \cong \Delta \text{ Pressure}$$

Based upon the assumption of stable ventricular compliance, pressure-based parameters such as left ventricular end-diastolic pressure (LVEDP), left atrial pressure (LAP), and PAOP, have long been utilized clinically as surrogate estimates of intravascular volume. Although likely to be valid in normal healthy individuals, the multiple assumptions necessary to utilize PAOP and CVP as estimates of left and right ventricular preload status respectively, are not necessarily true in the critically ill patient with IAH or ACS (Fig. 2).

Hemodynamic monitoring can only improve patient care and outcomes when clinicians thoroughly understand both the appropriate utilization, as well as the potential measurement errors associated with the use of parameters such as PAOP and CVP. Due to the physiologic complexity of patients with IAH or ACS, resuscitation to arbitrary, absolute PAOP or CVP values should be avoided as such a practice can lead to inappropriate therapeutic decisions, under-resuscitation, and organ failure.
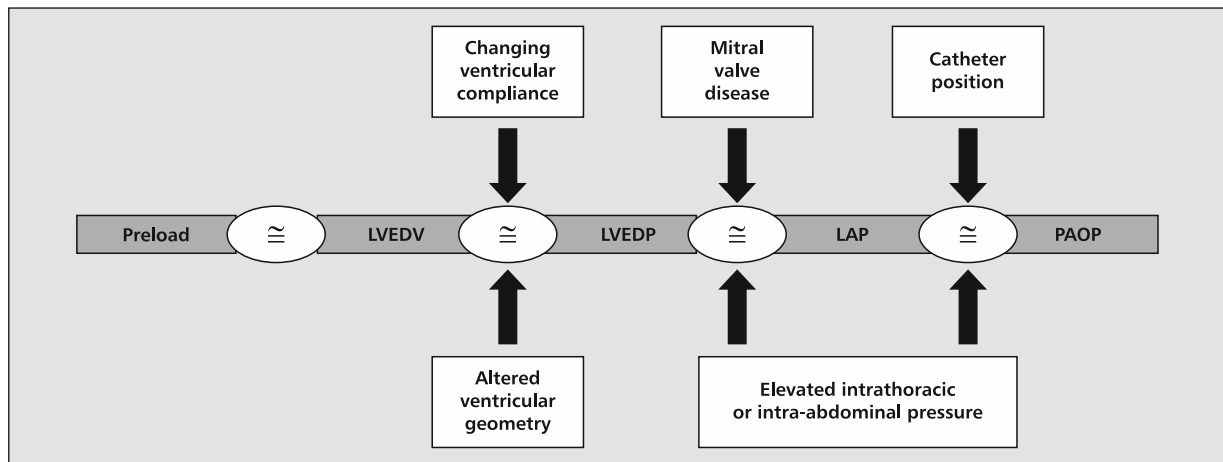
Figure 2. "The PAOP Assumption": why intracardiac filling pressures like pulmonary artery occlusion pressure do not accurately estimate preload status. First, ventricular compliance is constantly changing in the critically ill, resulting in a variable relationship between pressure and volume. As a result, changes in intracardiac pressure no longer directly reflect changes in intravascular volume. The presence of IAH will decrease LV compliance by rightward shift and flattening of the Frank-Starling curve. Second, the elevated ITP associated with IAH has been demonstrated to increase PAOP and CVP measurements by an amount that is difficult to predict, further confounding their validity. This apparent deviation from Starling's Law of the Heart is due to the fact that both PAOP and CVP are measured relative to atmospheric pressure but are actually the sum of both intravascular pressure and intrapleural pressure. Third, mitral valve disease can confound the use of PAOP as an estimate of intravascular volume status. Patients with IAH-induced pulmonary hypertension or acute lung injury demonstrate increased PVR and are at significant risk for mitral valve regurgitation. Fourth, accurate PAOP measurements are dependent upon proper placement of the PAC. Compression of the pulmonary parenchyma as a result of elevated IAP can markedly alter the normal progression of alveolar distention and pulmonary capillary pressures defined in West's lung zones 1, 2 and 3. IAH-induced cardiac and pulmonary dysfunction can further alter the normal pulmonary artery waveforms making proper placement of the PAC tip in West's lung zone 2 difficult. Inadvertent placement of the tip in apical zone 1 commonly results in PAOP measurements that more appropriately reflect alveolar pressure. Adapted from Cheatham et al [1] "The PAOP Assumption": why intracardiac filling pressures like pulmonary artery occlusion pressure do not accurately estimate preload status. Caption: LVEDV — left ventricular end-diastolic volume; LVEDP — left ventricular end-diastolic pressure; LAP — left atrial pressure; PAOP — pulmonary artery occlusion pressure.

IMPROVEMENT OF BAROMETRIC PRELOAD INDICES (TRANSMURAL CARDIAC FILLING PRESSURES)

Recognizing the impact of elevated IAP and ITP on the validity of intracardiac filling pressure measurements, some authors have suggested calculating the transmural PAOP ($PAOP_{tm}$) or CVP (CVP_{tm}) in an attempt to improve the accuracy of PAOP and CVP as resuscitation endpoints in animal studies with IAH [9, 10, 22]. Assuming the proper placement of a PAC and the absence of other confounding factors, $PAOP_{tm}$ may be calculated as end-expiratory PAOP ($PAOP_{ee}$) minus ITP with CVP_{tm} calculated as CVP_{ee}-ITP.

- Theoretical transmural (tm) filling pressures, calculated as the endexpiration value (ee) minus the ITP may better reflect true preload.
  - $CVP_{tm} = CVP_{ee} - ITP$
  - $PAOP_{tm} = PAOP_{ee} - ITP$

The ITP is usually estimated by pleural pressure (P_{pl}) which in turn is typically determined by measuring lower esophageal pressure using a balloon catheter. Studies showed that there is a good correlation between P_{pl} and IAP [9, 23, 24]. Different studies found that around 20–80% (or on average 50%) of IAP is transmitted to the thorax, a feature which is termed the abdomino-thoracic index of transmission [10]. 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 [25].

- A quick estimate of transmural filling pressures can also be obtained by subtracting half of the IAP from the end-expiratory filling pressure
  - $CVP_{tm} = CVP_{ee} - IAP/2$
  - $PAOP_{tm} = PAOP_{ee} - IAP/2$

Alternatively, one can calculate the index of transmission, which can easily be calculated at the bedside (Fig. 3). This can be done by looking at changes in IAP (ΔIAP, e.g. by means of a Velcro belt or abdominal compression) versus changes in CVP (ΔCVP). The abdomino-thoracic index of transmission (ATI) can thus be calculated as ΔCVP divided by ΔIAP.

- The real transmural filling pressures can be calculated as follows:
  - $CVP_{tm} = CVP_{ee} - (ATI \times IAP)$
  - With ATI = ΔCVP/ ΔIAP
  - $PAOP_{tm} = PAOP_{ee} - (ATI \times IAP)$

It has not been shown that real measurement of pleural pressure by an esophageal catheter improves the ability of PAOP alone to predict volume recruitable increases in CO [1, 25]. Although physiologically sound, the use of transmural filling pressures cannot be recommended in clinical practice as no studies have investigated this.
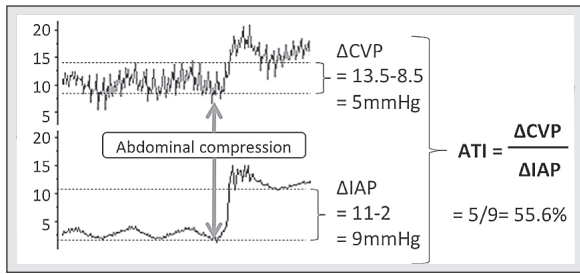
Figure 3. Calculation of the abdomino-thoracic index (ATI) of transmission at the bedside. Simultaneous central venous pressure (CVP) and intra-abdominal pressure (IAP) tracing before and during abdominal compression (e.g. by applying an abdominal velcro belt). The abdomino-thoracic index of transmission (ATI) can be calculated as follows: the change in end-expiratory CVP (ΔCVP_{ee} = 13.5 – 8.5 mm Hg = 5 mm Hg) divided by the change in end-expiratory IAP (ΔIAP_{ee} = 11 – 2 = 9 mm Hg) and expressed as a percentage. The abdomino-thoracic index (ATI) of transmission = $\Delta CVP/\Delta IAP$ = 5/9 = 55.6%

The calculation of transmural pressures may be better to estimate preload in patients with IAH or ACS for a number of reasons. This is because both PAOP and CVP are measured relative to atmospheric pressure and are actually the sum of intravascular pressure and ITP. Furthermore, ventricular compliance is dynamically changing from beat-to-beat in the critically ill, resulting in a variable relationship between pressure and volume [26]. As a result, changes in intravascular pressure no longer reflect changes in intravascular volume, further reducing the accuracy of intracardiac filling pressures such as PAOP and CVP as estimates of preload status.

THE ROLE OF VOLUMETRIC PRELOAD MONITORING IN IAH

Volumetric preload monitoring can be done with either the continuous right ventricular end-diastolic volume index (RVEDVI) obtained with the PAC (transcardiac thermodilution) or via the intermittent global end-diastolic volume index (GEDVI) obtained with either the PiCCO (Pulsion Medical Systems, Munich, Germany) or EV1000 (Edwards Lifesciences, Irvine, CA, USA) system (transpulmonary thermodilution, TPTD). To calculate the RVEDVI, the right ventricular ejection fraction (RVEF) reflecting the patient's right ventricular contractility and afterload, is utilized using the following equation (where SVI = stroke volume index):

$$RVEDVI = SVI / RVEF$$

Independent of the effects of changing ventricular compliance and increased ITP or IAP, RVEDVI has been shown in multiple studies to be an accurate indicator of preload

recruitable increases in CO in a variety of patient populations [27, 28]. With concerns over the safety and efficacy of the PAC in the management of the critically ill, several less invasive hemodynamic monitoring technologies have been proposed [29, 30]. The PiCCO system is less invasive and combines two techniques namely, intermittent TPTD (as calibration) and an estimation of SV based upon analysis of a patient's arterial pressure waveform or contour. This technique, known as arterial pulse contour analysis, has been proposed as a less invasive alternative [31]. Due to the unique mechanical characteristics of each patient's arterial tree, initial calibration of the monitoring system using the TPTD technique and the Stewart Hamilton equation is needed and this greatly improves accuracy compared to uncalibrated continuous pulse contour CO techniques like Lidco rapid or Vigileo, as has been recently shown [32].

Assessment of the mean transit time (MTT) and downslope time (DST) during the TPTD, allows the calculation of other derived parameters: global ejection fraction (GEF), an estimate of ventricular contractility, and several intravascular volume measurements including GEDV and extravascular lung water (EVLW), as surrogate predictors of cardiac preload and capillary leak.

$$GEF = (4 \times SVI)/GEDVI$$

VOLUMETRIC PRELOAD INDICES BETTER REFLECT THE TRUE PRELOAD STATUS IN IAH

The value of RVEDVI over traditional intracardiac filling pressures is especially notable in patients with elevated ITP or IAP where PAOP and CVP are at greatest risk for providing erroneous information regarding preload status. Elevated ITP and IAP result in significant decreases in GEDVI despite paradoxical increases in measured PAOP and CVP [13, 33]. Based upon these studies and others, although it is clear that IAH significantly depletes intravascular volume and that these changes in preload status are appropriately detected by volumetric measurements of intravascular volume such as RVEDVI or GEDVI, this does not apply to pressure-based measurements such as PAOP and CVP.

IMPROVEMENT OF VOLUMETRIC PRELOAD INDICES

IAH, as discussed above, commonly results in cardiac dysfunction and decreased EF, which are identified by decreases in RVEF and GEF. As a result of this constantly changing ventricular compliance, there cannot be a single value of RVEDVI or GEDVI that can be considered the goal of resuscitation for all patients with IAH or ACS [27, 28]. Each patient must therefore be resuscitated to the end-diastolic volume that optimizes cardiac preload and systemic perfusion in that particular situation and at that particular moment in time during his or her critical illness. By "correction" of the
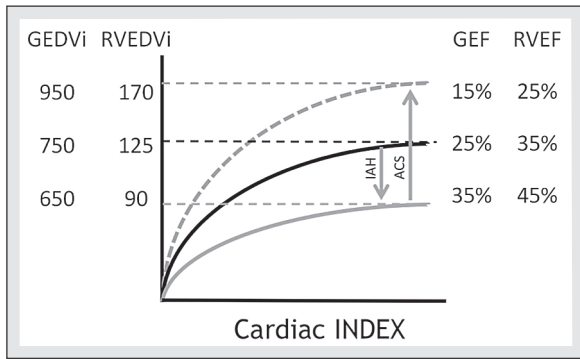
Figure 4. Ventricular Function Curves by by Global Ejection Fraction (GEF) and Right Ventricular Ejection Fraction (RVEF). Cardiac contractility in the critically ill can be described as a series of "ventricular function curves". Each curve has an associated ejection fraction, describing the ventricle's contractility, and an optimal end-diastolic volume, identifying the plateau of the ventricular function curve. Resuscitation to this plateau end-diastolic volume is widely believed to optimize a patient's intravascular volume, cardiac function, and end-organ perfusion. As ventricular function changes, the patient "shifts" from one Frank-Starling curve to another with the identification of both a new, optimal plateau end-diastolic volume as a resuscitation endpoint and a new ejection fraction. Therefore, the patient's global end-diastolic volume index (GEDVI) and right ventricular end-diastolic volume index (RVEDVI) must be interpreted in conjunction with the patient's GEF or RVEF. Adapted from Malbrain et al. [34].

GEDVI for the underlying GEF the predictive power for GEDVI as preload parameter or even fluid responsiveness indicator improves [34]. This is illustrated in Figure 4.

EFFECT OF INTRA-ABDOMINAL HYPERTENSION ON CONTRACTILITY
PATHOPHYSIOLOGY

Diaphragmatic elevation and increased ITP can also have marked effects on cardiac contractility via direct cardiac compression and increased ITP (Fig. 1). Compression of the pulmonary parenchyma increases pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR), while simultaneously reducing left ventricular preload. As right ventricular afterload increases, the right side of the heart must play a more active role in maintaining CO. In response, the thin-walled right ventricle dilates with a decrease in RVEF. The interventricular septum may bulge into the left ventricular chamber impeding left ventricular function with further decreases in CO. Cardiac ultrasound can provide useful information in patients with IAH [35, 36]. Animal studies have shown consistently a drop in CO with increases in IAP [9, 17, 22, 37]. This is illustrated in Figure 5. Right ventricular dysfunction can become severe in the presence of marked IAH leading to significant reductions in left ventricular contractility as a result of "interventricular interdependence" [38, 39]. In a dog model where IAP was increased up to 40 mm Hg with fluid infusion in the peritoneal cavity, a rightward and
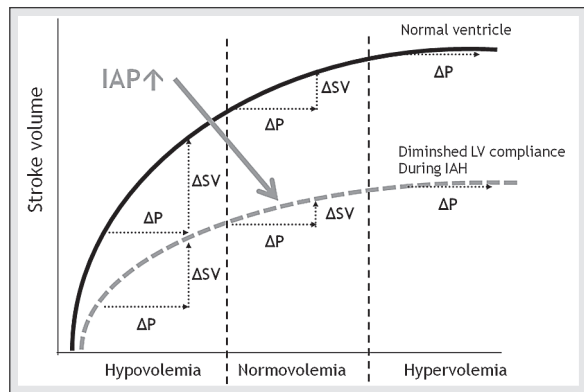

Figure 5. Frank Starling curves with suggested effects on left ventricular (LV) compliance related to increased intra-abdominal pressure. Especially in the "middle zone" of normovolemia (between dotted vertical lines), increased IAP (dotted Frank-Starling line) can have deleterious effects on LV compliance making a correct assessment of fluid responsiveness important. The ΔP indicates a change in preload versus ΔSV, the resulting change in stroke volume

downward shift of the Frank-Starling curve was observed [40]. Huetteman et al. showed that anteroseptal left ventricle wall motion assessed with transesophageal echocardiography was significantly decreased at IAP levels of only 12 mm Hg in 8 children during laparoscopic herniorrhaphy [41, 42]. In patients with congestive heart failure, increased CVP and increased IAP are independent predictors for the development of acute renal failure [43]. This association has recently been termed cardio-abdomino-renal syndrome or CARS [4]. While initially responsive to fluid loading and inotropic support at lower levels of IAH, the reduced biventricular contractility of advanced IAH/ACS can only be effectively treated by nonoperative measures to reduce IAP or abdominal decompression.

IMPORTANCE OF ABDOMINAL PERFUSION PRESSURE

During the early evolution of IAH and ACS, attempts were made to identify a single "critical" IAP that could be used to guide decision making concerning patients with IAH. This oversimplifies what is actually a highly complex and variable physiologic process. While IAP is a major determinant of patient outcomes during critical illness, the IAP that defines both IAH and ACS clearly varies from patient to patient, and even within the same patient, as their disease process evolves [2, 44, 45]. As a result, a single threshold value of IAP cannot be globally applied to decision making regarding all critically ill patients (Fig. 6) [46]. In order to improve the sensitivity of IAP for decision making, one can include it in an assessment of abdominal perfusion pressure (APP) as a resuscitation endpoint. Similar to the widely accepted and utilized concept of cerebral perfusion pressure (CPP), APP, calculated as MAP minus IAP, has been
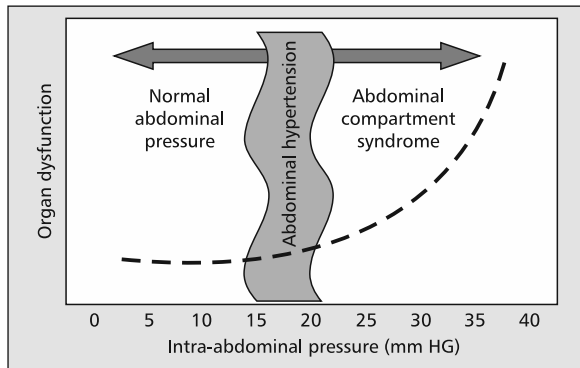
Figure 6. Distinctions between normal intra-abdominal pressure, intra-abdominal hypertension (IAH), and abdominal compartment syndrome (ACS). The shaded area illustrating IAH may undergo shifts to the right or left depending on the clinical scenario. Courtesy of David J.J. Muckart, MD, University of Natal Medical School, Republic of South Africa, and Rao Ivatury, MD, PhD, Virginia Commonwealth University, Virginia, USA, and adapted from Malbrain et al. [46]

proposed as a more accurate marker of critical illness and endpoint for resuscitation in patients with IAH, although a large prospective multicentric validation of this parameter is still pending.

$$APP = MAP - IAP$$

Target APP values can be achieved through a balance of judicious fluid resuscitation and the application of vasoactive medications. Maintaining an APP of 50 to 60 mm Hg may appear to be a better resuscitation endpoint compared to other macro and microcirculatory parameters. Multiple regression analysis has demonstrated that APP is superior as a resuscitation endpoint parameter compared to arterial pH, base deficit, arterial lactate, and hourly urinary output in surgical patients [47]. The authors concluded that using APP can allow one to predict survival from IAH or ACS that is not identified by IAP alone [47]. However, studies with regard to APP are scarce, often retrospective and include only small patient numbers. Therefore, APP as a resuscitation parameter cannot be recommended based on the current literature.

USE OF TRANSPULMONARY THERMODILUTION IN IAH

The continuous CO measured by TD or pulse contour with different devices (Pulsioflex, PiCCO, Swan Ganz) showed good agreement with TPTD in 10 pigs without IAH, and reflected an increase in CO following fluid loading [48]. Induction of IAH via the pneumoperitoneum did not significantly influence the CO measured by all devices. However, in IAH, an increase in CO following fluid loading was indicated by calibrated CO but not by uncalibrated CCO methods using arterial waveform analysis. In the critically ill patient, recalibration of continuous arterial waveform CO methods

should be performed after fluid loading or before a major change in treatment is initiated [49]. The relative position of the catheters used for TPTD measurements may also be relevant. Huber et al. found that performing TPTD via a femoral central venous line (CVL) had a significant impact on the calculated variables [50]. Thus, they found that CI measured with TPTD via a jugular CVL can be calculated with the following formula:

$$0.931 \times CI_{fem} + 1.45 - 0.00042 \times GEDVI_{fem} + 0.028 \times CVP_{fem} - 0.009 \times height$$

(with CI_{fem}, $GEDVI_{fem}$ and CVP_{fem} respectively the CI, GEDVI and CI when measured with TPTD via a femoral CVL).

Since IAP and CVP_{fem} are closely related especially from grade III to IV IAH, this formula suggests that IAP may have an impact on TPTD CI when bolus injection is performed via a femoral CVL [18, 51]. The GEDVI and EVLWI values were also affected when performing TPTD via a femoral CVL. This phenomenon can be explained by the fact that the calculation of these volumetric parameters is based upon the MTT and DST, and since venous return is diminished in IAH, transit times may be affected when the thermodilution bolus is injected via the femoral CVL.

EFFECT OF INTRA-ABDOMINAL HYPERTENSION ON AFTERLOAD

Elevated ITP and IAP can cause increased systemic vascular resistance (SVR) through direct compressive effects on the aorta and systemic vasculature and increased PVR through compression of the pulmonary parenchyma. Organ compression may also result in alterations in the renin-angiotensin-aldosterone mechanism [11, 52]. More commonly, however, increased SVR occurs as compensation for the reduced venous return and falling stroke volume outlined above. As a result of this physiologic compensation, MAP typically remains stable in the early stages of IAH/ACS despite reductions in venous return and cardiac output. These increases in afterload may be poorly tolerated by patients with impaired cardiac contractility or inadequate intravascular volume [27, 53–55].

The concept of abdominal vascular zones may be present in the patient with IAH, analogous to the pulmonary vascular zone conditions described by West. In this concept, an increased IAP increases venous return when the transmural IVC pressure (defined as IVC pressure minus IAP) at the thoracic inlet significantly exceeds the critical closing transmural pressure (=zone 3 abdomen) [15]. This is most often the case in hypervolemic patients with a high IVC pressure. In zone 3 conditions, the abdominal venous compartment functions as a capacitor. In contrast, when

the transmural IVC pressure at the thoracic inlet is below the critical closure transmural pressure (=zone 2 abdomen), venous return is significantly decreased. This is most often the case in hypovolemic patients and by extension in most non-cardiogenic shock patients. In zone 2 conditions, the abdominal venous compartment functions as a collapsible starling transistor [56]. This model clearly illustrates why hypovolemia (and especially in combination with positive pressure ventilation and high levels of PEEP) predisposes patients to lower CO in response to elevated IAP than does normovolemia [57].

For the same reasons mean systemic filling pressure may also increase during IAH as was found in pregnant woman with pre-eclampsia [58]. This may explain the marked susceptibility to pulmonary edema seen with even minimal volume administration.

USE OF FUNCTIONAL HEMODYNAMICS IN IAH
IMPACT OF IAP ON FLUID RESPONSIVENESS

An increase in IAP will result in a concomitant increase in ITP and, as such, also in an increase in stroke volume variation (SVV) and pulse pressure variation (PPV) [59, 60]. Other studies have also shown increases in systolic pressure variation (SPV) that were mainly related to the Δup component and not to a Δdown phenomenon. As different mechanisms have been suggested, the increases seen in functional hemodynamic parameters may not univocally correspond to fluid responsiveness [61]. These include the following firstly, a change in aortic compliance and an increase in aortic transmural pressure induced by increased IAP (either via direct compression or increased vasomotor tone); secondly, errors in the measurement of dynamic indices in conditions of increased IAP, or, if we assume that no measurement errors are induced by IAP, then this implies that these indices do not perform well during IAH (since SVV and SPV no longer predict fluid responsiveness); and thirdly, changes in extramural pressure, ITP or chest wall compliance. Although in several animal studies, PPV (but not SVV) maintained its ability to predict fluid responsiveness even at IAP levels of 25 mm Hg, a receiver operating characteristics (ROC) curve analysis identified 20.5% as the best threshold for fluid responsiveness (instead of the classical 12% and the 9.5% identified in this study at baseline) [62–64]. This means that we cannot use the same thresholds for different conditions. The threshold value will depend on the amount of tidal volume, PEEP application or increased ITP and consequent changes in pleural pressure and chest wall compliance, the presence of obesity, heart failure with changes in right and left ventricular preload and afterload, pulmonary hypertension, the use of a pneumoperitoneum or increased IAP and may also differ in children or neonates [65]. Moreover, PPV has been shown to be superior to SVV in order to predict fluid responsiveness in the patients. This is somewhat surprising since PPV is a surrogate of SVV (derived from a pulse contour analysis based on a complex algorithm) and the latter should be less influenced by changes in vasomotor tone. Changes in pulse contour due to increased ITP may be more complex than previously thought. A recent animal study on severe pancreatitis showed that goal-directed hemodynamic management guided by SVV led to improved survival, tissue oxygenation, and microcirculatory perfusion, as well as less histopathologic damage [66]. Although the authors did not measure actual IAP, the model was interesting and can provide useful information for patients with IAH [67].

VALIDITY OF THE PASSIVE LEG RAISING TEST IN IAH

Recent data have shown that about 25% of critically ill patients with a PPV above 12% are not fluid responsive, suggesting different thresholds for different conditions [68]. Similar false positive PPV values have been reported previously and were related to right ventricular dysfunction. This also shows that the PLR test can be a 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. Care should be taken when a PLR test is performed, and an IAP measurement is needed whilst interpreting the result of a PLR test. The PLR test is difficult to standardise since it does not provide information on the exact amount of endogenous transfusion and there is some debate whether the starting position should be supine or upright (HOB) or whether the Trendelenburg position should be used. In fact, depending on patient anthropomorphism, the amount of fluid loading with a PLR may vary. During IAH one can expect an increase in baseline PPV especially in the 45° HOB position (Fig. 7). Performing a PLR maneuver from HOB (with the least risk for ventilator associated pneumonia) will further increase IAP and will only result in a marginal venous return from the legs but not from the mesenteric veins. Performing a PLR maneuver from the supine position will have a neutral effect on IAP and result in a better venous return from the legs but not from the mesenteric veins. At the same time, the Trendelenburg position will have a beneficial effect on IAP and, depending on body anthropomorphism, will result in a more pronounced venous return from the legs, as well as from the mesenteric veins [69].

CARDIOVASCULAR OPTIMIZATION IN IAH
IMPROVEMENT OF PRELOAD

Although initial fluid loading may improve venous return and restore CO, fluid overload must be avoided, especially in the setting of a capillary leak [70, 71]. To solve this

Panel A. Schematic overview comparing the possible effects and (dis)advantages of different PLR tests during normal IAP

TYPE	STARTING POSITION	POSITION DURING PLR	ADVANTAGES	DISADVANTAGES
HOB-PLR	PPV↑	PPV↘	No risk for VAP	Laborious Only small endogenous transfusion from legs
SUP-PLR	PPV↑	PPV↓ (45°)	Not labour intensive Combination of endogenous transfusion from legs and mesenteric veins	Risk for VAP Risk for ICP increase
TRENDELENBURG	PPV↗	PPV↓↓ (45°)	Not labour intensive Biggest endogenous transfusion from legs and mesenteric veins	Biggest risk for VAP Biggest increase in ICP

Panel B. Schematic overview comparing the possible effects and (dis)advantages of different PLR tests during increased IAP

TYPE	STARTING POSITION	POSITION DURING PLR	ADVANTAGES	DISADVANTAGES
HOB-PLR	PPV↑↑ IAH	PPV↑↑ IAP↑	No risk for VAP	Labour intensive Increases IAP (lung compression) No endogenous transfusion
SUP-PLR	PPV↑↑ IAH	PPV↑ IAP= (45°)	No increase in IAP (no lung compression) Not labour intensive	Risk for VAP Risk for ICP increase Only small endogenous transfusion (from legs)
TRENDELENBURG	PPV↑ IAH	PPV↘ IAP↓ (45°)	Decrease in IAP (effects on lungs unclear) Not labour intensive Best endogenous transfusion in case of IAH	Biggest risk for VAP Biggest increase in ICP

Figure 7. Comparison of different types of passive leg raising tests. The PLR can be performed from HOB (first row) or supine (second row) position or putting the patient in the Trendelenburg position (third row). Panel A shows the effects of different PLR tests in patients with normal IAP while Panel B hypothesizes on the effects in patients with IAH. Endogenous fluid resuscitation comes from venous return from the legs (oblique arrow) and the mesenteric veins (horizontal arrow). The amount endogenous fluid resuscitation is indicated by the thickness of the arrow (dotted line is smallest while 3mm line is largest amount), a dotted line marked with a "X" indicates the absence of endogenous transfusion (adapted from Malbrain et al. [69]); HOB — head of bed; IAH — intra-abdominal hypertension; IAP — intra-abdominal pressure; ICP — intra cranial pressure; PLR — passive leg raising; PPV — pulse pressure variation; SUP — supine; VAP —ventilator associated pneumonia; ↑ — increase; ↑↑ — huge increase; ↗ — small increase; ↘ — small decrease; ↓ — decrease; ↓↓ — huge decrease

problem, the use of colloids or hyperoncotic solutions like hypertonic lactated saline or albumin 20% have been shown to reduce fluid intake whilst at the same time preserving urine output in severely burnt patients [72, 73]. The net result was a lower IAP and higher APP [72]. An important question in these patients is whether they are truly volume depleted,

and the use of parameters such as those mentioned above should always be correlated with clinical parameters of volume depletion. As fluids are the major contributor to secondary ACS, the judicious use of fluids is recommended [74]. As for all organ dysfunctions, decreasing IAP is another effective way of decreasing the negative cardiac effects described above.

IMPROVEMENT OF CONTRACTILITY

Non-operative measures to decrease IAP will result in a caudal movement of the diaphragm and decrease of cardiac compression, while the concomitant drop in ITP will improve cardiac contractility. After the initial resuscitation, a positive inotrope like dobutamine, levosimendan or milrinone can be considered if the patient has a low CO, increased lactate or low $S_{cv}O_2$. Although dobutamine infusion reverses the decrease in CO, it cannot restore superior mesenteric artery blood flow; however, intestinal mucosal blood flow returns to baseline levels [75]. Dopamine should not be used, since studies have shown no beneficial effect on splanchnic hemodynamic variables [75].

IMPROVEMENT OF AFTERLOAD

Preload augmentation through volume administration appears to ameliorate, at least partially, the injurious effects of IAH-induced increases in afterload. It has also been proposed, that the use of a moderate level of PEEP might efficiently reduce the increase in ventricular afterload [37, 40, 76, 77].

CONCLUSIONS AND KEY MESSAGES

— Cardiovascular dysfunction and failure (low CO, low contractility, high SVR) are common in IAH or ACS.
— Clinical evaluation of a patient is essential when interpreting the hemodynamic parameters obtained.
— Before administering fluids to patients with IAH or ACS, carefully check whether the patient is truly intravascular fluid depleted – do not act solely on preload parameters.
— Accurate assessment and optimization of preload, contractility, and afterload is essential to restore end-organ perfusion and function.
— Traditional hemodynamic monitoring techniques must be re-evaluated in IAH/ACS since pressure-based estimates of intravascular volume as PAOP and CVP can be erroneously increased.
  - The clinician must be aware of the interactions between ITP, IAP, PEEP, and intracardiac filling pressures.
  - Misinterpretation of the patient's minute-to-minute cardiac status may result in the administration of inappropriate and potentially detrimental treatment.
  - Transmural filling pressures may better reflect preload in the setting of increased IAP.

- The mean systemic filling pressure may increase in IAH.
- The Surviving Sepsis Campaign guidelines targeting initial and ongoing resuscitation towards a CVP of 8 to 12 mm Hg and other studies targeting a MAP of 65 mm Hg should be interpreted with caution in cases of IAH/ACS to avoid unnecessary over- and under resuscitation.
- There is insufficient data to recommend resuscitation towards an APP > 60 mm Hg.
— Volumetric estimates of preload status such as right ventricular end-diastolic volume index (RVEDVI), global end-diastolic volume index (GEDVI) or left ventricular end-diastolic area (LVEDA), can be useful because of the changing ventricular compliance with elevated ITP.
— Clinicians must be aware of abdominal West abdominal zones.
— Although functional hemodynamic parameters such as PPV (but not SVV nor SPV) should be used to assess volume responsiveness, the traditional thresholds need to revised.
  - About 25−35% of patients with IAH and a PPV > 12% are non-responders to fluids.
  - The best threshold to predict fluid responsiveness in grade II IAH (15 to 20 mm Hg) is a PPV > 20%.
— IAH can be a cause of a false negative passive leg raising test.
— IAH causes pulmonary hypertension via increased ITP with direct compression on lung parenchyma and vessels and via the diminished left and right ventricular compliance.
— Transpulmonary thermodilution CO measurements are validated in the setting of IAH.
— Cardiovascular effects are aggravated by hypovolemia and the application of PEEP, whereas hypervolemia has a temporary protective effect.

References

1. *Cheatham ML, Malbrain ML:* Cardiovascular implications of abdominal compartment syndrome. Acta Clin Belg Suppl 2007; 62: 98–112.

2. *Cheatham ML, Malbrain ML, Kirkpatrick A et al.:* Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. II. Recommendations. Intensive Care Med 2007; 33: 951–962.

3. *Malbrain ML, Cheatham ML:* Cardiovascular effects and optimal preload markers in intra-abdominal hypertension. In: Yearbook of intensive care and emergency medicine. Vincent J-L (ed.) Springer-Verlag, Berlin 2004: 519–543.

4. *Verbrugge FH, Mullens W, Malbrain MLNG:* Worsening Renal Function during Decompensated Heart Failure: The cardio-abdomino-renal syndrome (CARS). In: Yearbook of intensive care and emergency medicine. Vincent J-L (ed.) Springer-Verlag, Berlin 2012: 577–590.

5. *Malbrain ML, De laet IE:* Intra-abdominal hypertension: evolving concepts. Clin Chest Med 2009; 30: 45–70, viii. doi: 10.1016/j.ccm.2008.09.003.

6. *Malbrain MLNG, De Waele J:* Section 4. Consequences of intra-abdominal hypertension: why to worry? In: Core critical care series: intra-abdominal hypertension. Vuylsteke A (ed.). Cambridge University Press, Cambridge 2013.

7. *Sugerman HJ, Bloomfield GL, Saggi BW:* Multisystem organ failure secondary to increased intraabdominal pressure. Infection 1999; 27: 61–66.

8. *Malbrain ML, Ameloot K, Gillebert C, Cheatham ML:* Cardiopulmonary monitoring in intra-abdominal hypertension. Am Surg 2011; 77 Suppl 1: S23–30.

9. *Wauters J, Claus P, Brosens N et al.:* Relationship between abdominal pressure, pulmonary compliance, and cardiac preload in a porcine model. Crit Care Res Pract 2012; 2012: 763181. doi: 10.1155/2012/763181.

10. *Wauters J, Wilmer A, Valenza F:* Abdomino-thoracic transmission during ACS: facts and figures. Acta Clin Belg Suppl 2007; 62: 200–205.

11. *Gudmundsson FF, Gislason HG, Myking OL, Viste A, Grong K, Svanes K:* Hormonal changes related to reduced renal blood flow and low urine output under prolonged increased intra-abdominal pressure in pigs. Eur J Surg 2002; 168: 178–186.

12. *Simon RJ, Friedlander MH, Ivatury RR, DiRaimo R, Machiedo GW:* Hemorrhage lowers the threshold for intra-abdominal hypertension-induced pulmonary dysfunction. J Trauma 1997; 42: 398–403.

13. *Schachtrupp A, Graf J, Tons C, Hoer J, Fackeldey V, Schumpelick V:* Intravascular volume depletion in a 24-hour porcine model of intra-abdominal hypertension. J Trauma 2003; 55: 734–740.

14. *Schachtrupp A, Lawong G, Afify M, Graf J, Toens C, Schumpelick V:* Fluid resuscitation preserves cardiac output but cannot prevent organ damage in a porcine model during 24 h of intraabdominal hypertension. Shock 2005; 24: 153–158.

15. *Ameloot K, Gillebert C, Desie N, Malbrain ML:* Hypoperfusion, shock states, and abdominal compartment syndrome (ACS). Surg Clin North Am 2012; 92: 207–220, vii. doi: 10.1016/j.suc.2012.01.009.

16. *Coombs HC:* The mechanism of the regulation of intra-abdominal pressure. Am J Physiol 1922; 61: 159–170.

17. *Wauters J, Claus P, Brosens N, McLaughlin M, Malbrain M, Wilmer A:* Pathophysiology of renal hemodynamics and renal cortical microcirculation in a porcine model of elevated intra-abdominal pressure. J Trauma 2009; 66: 713–719. doi: 10.1097/TA.0b013e31817c5594.

18. *De Keulenaer BL, Regli A, Dabrowski W et al.:* Does femoral venous pressure measurement correlate well with intrabladder pressure measurement? A multicenter observational trial. Intensive Care Med 2011; 37: 1620–1627. doi: 10.1007/s00134-011-2298-x.

19. *Diamant M, Benumof JL, Saidman LJ:* Hemodynamics of increased intra-abdominal pressure: Interaction with hypovolemia and halothane anesthesia. Anesthesiology 1978; 48: 23–27.

20. *Korkmaz A, Alkis M, Hamamci O, Besim H, Erverdi N:* Hemodynamic changes during gaseous and gasless laparoscopic cholecystectomy. Surg Today 2002; 32: 685–689.

21. *Hazebroek EJ, Haitsma JJ, Lachmann B et al.:* Impact of carbon dioxide and helium insufflation on cardiorespiratory function during prolonged pneumoperitoneum in an experimental rat model. Surg Endosc 2002; 16: 1073–1078.

22. *Ridings PC, Bloomfield GL, Blocher CR, Sugerman HJ:* Cardiopulmonary effects of raised intra-abdominal pressure before and after intravascular volume expansion. J Trauma 1995; 39: 1071–1075.

23. *Talmor D, Sarge T, Malhotra A et al.:* Mechanical ventilation guided by esophageal pressure in acute lung injury. New Engl J Med 2008; 359: 2095–2104. doi: 10.1056/NEJMoa0708638.

24. *Talmor D, Sarge T, O'Donnell CR et al.:* Esophageal and transpulmonary pressures in acute respiratory failure. Crit Care Med 2006; 34: 1389–1394.

25. *De laet I, Malbrain ML:* ICU management of the patient with intra-abdominal hypertension: what to do, when and to whom? Acta Clin Belg Suppl 2007; 62: 190–199.

26. *Stocks J, Quanjer PH:* Reference values for residual volume, functional residual capacity and total lung capacity. ATS Workshop on Lung Volume Measurements. Official Statement of The European Respiratory Society. Eur Respir J 1995; 8: 492–506.

27. *Cheatham ML, Safcsak K, Block EF, Nelson LD:* Preload assessment in patients with an open abdomen. J Trauma 1999; 46: 16–22.

28. *Cheatham ML, Nelson LD, Chang MC, Safcsak K:* Right ventricular end-diastolic volume index as a predictor of preload status in patients on positive end-expiratory pressure. Crit Care Med 1998; 26: 1801–1806.

29. *Harvey S, Harrison DA, Singer M et al.:* Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. Lancet 2005; 366: 472–477.

30. *Connors AF, Jr., Speroff T, Dawson NV et al.:* The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA 1996; 276: 889–897.

31. *Malbrain ML, De Potter P, Deeren D:* Cost-effectiveness of minimally invasive hemodynamic monitoring. In: Yearbook of intensive care and emergency medicine. Vincent J-L (ed.) Springer-Verlag, Berlin 2005: 603–618.

32. *Palmers P, Vidts W, Ameloot K et al.:* Assessment of three minimally invasive continuous cardiac output measurement methods in critically ill patients and a review of the literature. Anaesthesiol Intensive Ther 2012; 44: 188–189.

33. *Sutcliffe R, Meares H, Auzinger G, Wendon J:* Preload assessment in severe liver disease associated with intra-abdominal hypertension. Intensive Care Med 2002, 28 (Suppl. 1): S177.

34. *Malbrain ML, De Potter TJ, Dits H, Reuter DA:* Global and right ventricular end-diastolic volumes correlate better with preload after correction for ejection fraction. Acta Anaesthesiol Scand 2010; 54: 622–631. doi: 10.1111/j.1399-6576.2009.02202.x.

35. *Mahjoub Y, Plantefeve G:* Cardiac ultrasound and abdominal compartment syndrome. Acta Clin Belg Suppl 2007; 62: 183–189.

36. *Yi M, Leng Y, Bai Y, Yao G, Zhu X:* The evaluation of the effect of body positioning on intra-abdominal pressure measurement and the effect of intra-abdominal pressure at different body positioning on organ function and prognosis in critically ill patients. J Crit Care 2011; 27: 222.e1–6. doi: 10.1016/j.jcrc.2011.08.010

37. *Richardson JD, Trinkle JK:* Hemodynamic and respiratory alterations with increased intra-abdominal pressure. J Surg Res 1976; 20: 401–404.

38. *Pinsky MR:* Heart-lung interactions. Curr Opin Criti Care 2007; 13: 528–531.

39. *Robotham JL, Wise RA, Bromberger-Barnea B:* Effects of changes in abdominal pressure on left ventricular performance and regional blood flow. Crit Care Med 1985; 13: 803–809.

40. *Kashtan J, Green JF, Parsons EQ, Holcroft JW:* Hemodynamic effect of increased abdominal pressure. J Surg Res 1981; 30: 249–255.

41. *Huettemann E, Sakka SG, Petrat G, Schier F, Reinhart K:* Left ventricular regional wall motion abnormalities during pneumoperitoneum in children. Br J Anaesth 2003; 90: 733–736.

42. *Sakka SG, Huettemann E, Petrat G, Meier-Hellmann A, Schier F, Reinhart K:* Transoesophageal echocardiographic assessment of haemodynamic changes during laparoscopic herniorrhaphy in small children. Br J Anaesth 2000; 84: 330–334.

43. *Mullens W, Abrahams Z, Skouri HN et al.:* Elevated intra-abdominal pressure in acute decompensated heart failure: a potential contributor to worsening renal function? J Am Coll Cardiol 2008; 51: 300–306. doi: 10.1016/j.jacc.2007.09.043.

44. *Malbrain ML, De laet I, Cheatham M:* Consensus conference definitions and recommendations on intra-abdominal hypertension (IAH) and the abdominal compartment syndrome (ACS) — the long road to the final publications, how did we get there? Acta Clin Belg Suppl 2007; 62: 44–59.

45. *Malbrain ML, Cheatham ML, Kirkpatrick A et al:* Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. Intensive Care Med 2006; 32: 1722–1732.

46. *Malbrain ML, Deeren D, De Potter TJ:* Intra-abdominal hypertension in the critically ill: it is time to pay attention. Curr Opinion Crit Care 2005; 11: 156–171.

47. *Cheatham ML, White MW, Sagraves SG, Johnson JL, Block EF:* Abdominal perfusion pressure: a superior parameter in the assessment of intra--abdominal hypertension. J Trauma 2000; 49: 621–626.

48. *Gruenewald M, Renner J, Meybohm P, Hocker J, Scholz J, Bein B:* Reliability of continuous cardiac output measurement during intra-abdominal hypertension relies on repeated calibrations: an experimental animal study. Crit Care 2008; 12: R132. doi: 10.1186/cc7102.

49. *Cecconi M, Malbrain ML:* Cardiac output obtained by pulse pressure analysis: to calibrate or not to calibrate may not be the only question when used properly. Intensive Care Med 2013; 39: 787–789. doi: 10.1007/s00134-012-2802-y.

50. *Saugel B, Umgelter A, Schuster T, Phillip V, Schmid RM, Huber W:* Transpulmonary thermodilution using femoral indicator injection: a prospective trial in patients with a femoral and a jugular central venous catheter. Crit Care 2010; 14: R95. doi: 10.1186/cc9030.

51. *Regli A, De Keulenaer BL, Hockings LE, Musk GC, Roberts B, van Heerden PV:* The role of femoral venous pressure and femoral venous oxygen saturation in the setting of intra-abdominal hypertension: a pig model. Shock 2011; 35: 422–427. doi: 10.1097/SHK.0b013e3181fddf45.

52. *Bloomfield GL, Blocher CR, Fakhry IF, Sica DA, Sugerman HJ:* Elevated intra--abdominal pressure increases plasma renin activity and aldosterone levels. J Trauma 1997; 42: 997–1004.

53. *Malbrain ML:* Intra-abdominal pressure in the intensive care unit: Clinical tool or toy? In: Yearbook of Intensive Care and Emergency Medicine. Vincent JL (ed.) Springer-Verlag, Berlin 2001: 547–585.

54. *Cheatham M:* Intra-abdominal hypertension and abdominal compartment syndrome. New Horizons 1999; 7: 96–115.

55. *Malbrain ML:* Abdominal pressure in the critically ill. Curr Opin Crit Care 2000; 6: 17–29.

56. *Bonadonna G, Valagussa P, Moliterni A, Zambetti M, Brambilla C:* Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: the results of 20 years of follow-up. New Engl J Med 1995; 332: 901–906.

57. *Takata M, Wise RA, Robotham JL:* Effects of abdominal pressure on venous return: abdominal vascular zone conditions. J Appl Physiol 1990; 69: 1961–1972.

58. *Crozier TM, Wallace EM, Parkin GW:* Guyton, the mean systemic filling pressure and pre-eclampsia: making sense of a restrictive fluid strategy in the "hypovolemic" woman. Pregnancy Hypertens 2015; 5: 40–41. doi: 10.1016/j.preghy.2014.10.079.

59. *Malbrain ML, de Laet I:* Functional hemodynamics and increased intra--abdominal pressure: same thresholds for different conditions...? Crit Care Med 2009; 37: 781–783. doi: 10.1097/CCM.0b013e318194c397.

60. *Malbrain ML, De Laet I:* Functional haemodynamics during intra-abdominal hypertension: what to use and what not. Acta Anaesthesiol Scand 2008; 52: 576–577. doi: 10.1111/j.1399-6576.2007.01567.x.

61. *Bliacheriene F, Machado SB, Fonseca EB, Otsuke D, Auler JO, Jr., Michard F:* Pulse pressure variation as a tool to detect hypovolaemia during pneumoperitoneum. Acta Anaesthesiol Scand 2007; 51: 1268–1272.

62. *Jacques D, Bendjelid K, Duperret S, Colling J, Piriou V, Viale JP:* Pulse pressure variation and stroke volume variation during increased intra--abdominal pressure: an experimental study. Crit Care 2011; 15: R33. doi: 10.1186/cc9980.

63. *Duperret S, Lhuillier F, Piriou V et al.:* Increased intra-abdominal pressure affects respiratory variations in arterial pressure in normovolaemic and hypovolaemic mechanically ventilated healthy pigs. Intensive Care Med 2007; 33: 163–171.

64. *Vivier E, Metton O, Piriou V et al.:* Effects of increased intra-abdominal pressure on central circulation. Br J Anaesth 2006; 96: 701–707.

65. *Mahjoub Y, Pila C, Friggeri A et al.:* Assessing fluid responsiveness in critically ill patients: False-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of right ventricle. Crit Care Med 2009; 39: 2570–2575. doi: 10.1097/CCM.0b013e3181a380a3.

66. *Trepte CJ, Bachmann KA, Stork JH et al.:* The impact of early goal-directed fluid management on survival in an experimental model of severe acute pancreatitis. Intensive Care Med 2013; 39: 717–726. doi: 10.1007/s00134-012-2775-x.

67. *Huber W, Malbrain ML:* Goal-directed fluid resuscitation in acute pancreatitis: shedding light on the penumbra by dynamic markers of preload? Intensive Care Medi 2013; 39: 784–786. doi: 10.1007/s00134-012-2783-x.

68. *Mahjoub Y, Touzeau J, Airapetian N et al.:* The passive leg-raising maneuver cannot accurately predict fluid responsiveness in patients with intra-abdominal hypertension. Crit Care Med 2010; 38: 1824–1829. doi: 10.1097/CCM.0b013e3181eb3c21.

69. *Malbrain ML, Reuter DA:* Assessing fluid responsiveness with the passive leg raising maneuver in patients with increased intra-abdominal pressure: Be aware that not all blood returns! Crit Care Med 2010; 38: 1912–1915. doi: 10.1097/CCM.0b013e3181f1b6a2.

70. *Malbrain MLNG, Van Regenmortel N:* Fluid overload is not only of cosmetic concern (Part I): Exploring a new hypothesis. ICU Management 2012; 12: 30–33.

71. *Malbrain MLNG, Cordemans C, Van Regenmortel N:* Fluid overload is not only of cosmetic concern (Part II): Results from a meta-analysis and practical approach. ICU Management 2012; 12: 34–37.

72. *Oda J, Ueyama M, Yamashita K et al.:* Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. J Trauma 2006; 60: 64–71.

73. *Cordemans C, De Laet I, Van Regenmortel N et al.:* Aiming for a negative fluid balance in patients with acute lung injury and increased intra-abdominal pressure: a pilot study looking at the effects of PAL-treatment. Ann Intensive Care 2012; 2 Suppl 1: S15. doi: 10.1186/2110-5820-2--S1-S15.

74. *Malbrain ML, Chiumello D, Cesana BM et al.:* A systematic review and individual patient data meta-analysis on intra-abdominal hypertension in critically ill patients: the wake-up project. World initiative on Abdominal Hypertension Epidemiology, a Unifying Project (WAKE-Up!). Minerva Anestesiol 2014; 80: 293–306.

75. *Agusti M, Elizalde JI, Adalia R, Cifuentes A, Fontanals J, Taura P:* Dobutamine restores intestinal mucosal blood flow in a porcine model of intra-abdominal hyperpressure. Crit Care Med 2000; 28: 467–472.

76. *Caldwell CB, Ricotta JJ:* Changes in visceral blood flow with elevated intraabdominal pressure. J Surg Res 1987; 43: 14–20.

77. *Bloomfield G, Dalton J, Sugerman H, Ridings P, DeMaria E, Bullock R:* Treatment of increasing intracranial pressure secondary to the acute abdominal compartment syndrome in a patient with combined abdominal and head trauma. J Trauma 1995; 39: 1168–1170.

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