

Fluid Resuscitation and Volume Assessment

Volume replacement remains the cornerstone of resuscitation in the critically ill and injured patient. The initial therapeutic intervention in hypotensive patients, oliguric patients, and patients with evidence of poor organ/tissue perfusion is volume resuscitation. However, both under-resuscitation and volume overload increase morbidity and mortality in critically ill patients. Uncorrected hypovolemia, leading to inappropriate infusions of vasopressor agents, may increase organ hypoperfusion and ischemia.¹ However, overzealous fluid resuscitation has been associated with increased complications, increased length of ICU and hospital stay, and increased mortality.^{2,3} The resuscitation of all critically ill patients therefore requires an accurate assessment of the adequacy of organ/tissue perfusion (and oxygenation), the patients' intravascular volume status, and fluid responsiveness (the hemodynamic response following a fluid challenge). Fluid management is one of the most important (and difficult) issues in the critically ill patient. However, the volume status of each and every ICU patient needs to be assessed on an ongoing basis. The intensivist needs to ask the following questions:

- Does this patient have adequate organ perfusion?
 - Mean arterial pressure (cerebral and abdominal perfusion pressures)
 - Urine output
 - Mentation
 - Capillary refill
 - Skin perfusion/mottling
 - Cold extremities
 - Cold knee's (Marik's sign; temperature gradient between thigh and knee)

- Blood lactate
- Arterial pH, BE, and HCO_3
- Mixed venous oxygen saturation (SmvO_2) or central venous oxygen saturation (ScvO_2)
- Mixed venous pCO_2
- Tissue pCO_2 (sublingual capnometry or equivalent)
- Gastric impedance spectroscopy
- Skeletal muscle tissue oxygenation StO_2
- What is this patient's intravascular volume?
 - See below
- Does this patient have tissue edema?
 - Generalized edema
 - Pulmonary edema on chest radiograph
 - Increased extravascular lung water (PiCCO technology)
 - Increased intra-abdominal pressure
- Is this patient volume responsive?
 - Pulse pressure variation (PPV) and/or stroke volume variation (SVV)
- Does this patient have preserved LV function?
 - ECHO
- If the patient has inadequate organ perfusion and is volume responsive, what volume expander do I use?
 - Lactated Ringer's solution (Hartmann's solution)
 - 5% albumin
 - Normal saline
 - 1/2 normal saline
 - Blood

■ VOLUME DEPLETION

The intravascular volume of an average 70 kg man is approximately 5 L of which 2 L is red cell volume and 3 L plasma volume. The intravascular, extracellular fluid compartment equilibrates with the extracellular, extravascular fluid compartment ($\text{ECF} \sim 11 \text{ L}$), with a reduction in one compartment leading to a reduction of the other. However, critically ill patients may have an expanded extracellular, extravascular compartment (tissue edema) with a contracted intravascular compartment. It is important to distinguish between these forms of volume depletion as the management may differ:

Volume Depletion with Depleted Extravascular Compartment

- Acute blood loss
 - Trauma
 - GI bleed

- Gastrointestinal tract losses (diarrhea, vomiting, fistula)
- Decreased fluid intake due to acute medical conditions
- Diabetic ketoacidosis
- Heat exhaustion
- “Dehydration”

Volume Depletion with Expanded Extravascular Compartment

- Sepsis
- Pancreatitis
- Trauma
- Surgery
- Burns
- Liver failure
- Cardiac failure

A reduction in intravascular volume results in a fall in stroke volume, which is initially compensated for by an increase in heart rate thereby maintaining cardiac output. However, with further volume depletion cardiac output and then blood pressure falls. This is associated with a reduction in organ perfusion. At the organ level, local autoregulatory mechanism comes into play in an attempt to maintain tissue perfusion. A reduction in renal perfusion normally results in dilatation of the glomerular afferent arteriole and constriction of the glomerular efferent arteriole so that glomerular capillary hydrostatic pressure and glomerular filtration rate (GFR) remain constant. However, a decrease in *renal perfusion pressure* below the autoregulatory range (mean arterial pressure < 70 mmHg) leads to an abrupt fall in GFR and urine output (oliguria). In the elderly and in patients with diseases affecting the integrity of the afferent arterioles, lesser degrees of hypotension may cause a decline in renal function and oliguria. While primary renal disease and urinary tract obstruction may lead to oliguria, intravascular volume depletion with renal hypoperfusion is the commonest cause of oliguria in clinical practice. Other features of intravascular volume depletion include the following:

- Concentrated urine
- Postural hypotension
- Tachycardia (and postural tachycardia)
- Pulse pressure variation (PPV) and stroke volume variation (SVV)

■ IS MY PATIENT FLUID RESPONSIVE?

Fundamentally the only reason to give a patient a fluid challenge is to increase stroke volume and cardiac output. This assumes that the

patient is on the ascending portion of the Frank–Starling curve and has “recrutable” cardiac output. Once the left ventricle is functioning near the “flat” part of the Frank–Starling curve, fluid loading has little effect on cardiac output and only serves to increase tissue edema and to promote tissue dysoxia. In normal physiologic conditions, both ventricles operate on the ascending portion of the Frank–Starling curve.⁴ This mechanism provides a functional reserve to the heart in situations of acute stress.⁴ In normal individuals, an increase in preload (with volume challenge) results in a significant increase in stroke volume. In contrast, only about 50% of patients with circulatory failure will respond to a fluid challenge.⁵ It is therefore crucial during the resuscitation phase of all critically ill patients to determine whether the patient is fluid responsive or not; this determines the optimal strategy of increasing cardiac output and oxygen delivery.

ALERT

The only reason to give a patient a fluid challenge is to increase stroke volume. The concept of “filling up the tank” is meaningless and reflects a poor understanding of human physiology.

■ “STATIC” MEASURES OF INTRAVASCULAR VOLUME

The Central Venous Pressure (CVP) and Pulmonary Capillary Wedge Pressure (PCWP)

The central venous pressure (CVP) is frequently used to guide fluid management. The basis for using the CVP comes from the dogma that the CVP reflects intravascular volume; specifically it is widely believed that patients’ with a low CVP are volume depleted while patients with a high CVP are volume overloaded. Furthermore, the “5-2” rule which was popularized in the 1970s is still widely used today for guiding fluid therapy.⁶ According to this rule, the change in CVP following a fluid challenge is used to guide subsequent fluid management decisions.

While the CVP describes the pressure of blood in the thoracic vena cava it is a very poor indicator of both intravascular volume and fluid responsiveness. In a recent report the pooled correlation coefficient between the CVP and the measured blood volume was 0.16 (95% CI 0.03–0.28).⁷ The pooled correlation coefficient between the baseline CVP and change in stroke index/cardiac index was 0.18 (95% CI 0.08–0.28). The pooled area under the ROC curve was 0.56 (95% CI 0.51–0.61). The pooled correlation between the delta-CVP and the

change in stroke index/cardiac index was 0.11 (95% CI 0.015–0.21). The results of this systematic review clearly demonstrate that there is no association between the CVP and circulating blood volume and that the CVP does not predict fluid responsiveness. It is very important to note that a patient with a CVP of 2 mmHg is as likely to be fluid responsive as a patient with a CVP of 20 mmHg.⁸ Based on this data the CVP should no longer (NEVER) be measured in the ICU, operating room, or emergency room.

Since the introduction of the pulmonary artery catheter (PAC) almost 30 years ago, the pulmonary artery wedge pressure (PCWP) was assumed to be a reliable and valid indicator of left ventricular preload. However, it was not long after the introduction of the PAC that studies began to appear demonstrating that the PCWP was a poor reflection of preload. Recent studies have clearly demonstrated that the PCWP is a poor predictor of preload and volume responsiveness.^{5,8,9} Indeed, the PCWP suffers many of the limitations of the CVP. The PCWP is an indirect reflection of left ventricular end-diastolic pressure (LVEDP) and not left ventricular end-diastolic volume or LV preload.

ALERT

The CVP is a relic from the past and should never be measured in modern critical care medicine (except in acute cor pulmonale). The CVP and PCWP are no more useful than the “phases of the moon” in evaluating a patient’s volume status.

Other Static Indices of Intravascular Volume

The right ventricular end-diastolic volume (RVEDV), left ventricular end-diastolic area (LVEDA), inferior vena-caval diameter, intrathoracic blood volume index (ITBVI), and global end-diastolic volume index (GEDVI) have all been shown to be poor predictors of volume responsiveness and should not be used to guide volume replacement.¹⁰

■ “DYNAMIC” MEASURES OF INTRAVASCULAR VOLUME

As discussed above, multiple studies have demonstrated that the CVP, PCWP, RVEDVI, and LVEDA do not predict volume responsiveness.^{7,11,12} It has therefore become generally accepted that “estimates of

intravascular volume based on any given level of filling pressure (or volume) do not reliably predict a patient's response to fluid administration."¹² Over the last decade a number of studies have been reported which have used heart–lung interactions during mechanical ventilation to assess fluid responsiveness. Specifically, the pulse pressure variation (PPV) derived from analysis of the arterial waveform and the stroke volume variation (SVV) derived from pulse contour analysis have been shown to be highly predictive of fluid responsiveness.

Stroke Volume Variation (SVV) and Pulse Pressure Variation (PPV)

The principles underlying the PPV (and SVV) are based on simple physiology (see Figure 8-1). Intermittent positive pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles. Mechanical insufflation decreases preload and increases afterload of the right ventricle (RV). The RV preload reduction is due to the decrease in the venous return pressure gradient that is related to the inspiratory increase in pleural pressure.¹¹ The increase in RV afterload is related to the inspiratory increase in transpulmonary pressure. The reduction in RV preload and increase in RV afterload both lead to a decrease in RV stroke volume, which is at a minimum at the end of the inspiratory period. The inspiratory reduction in RV ejection leads to a decrease in LV filling after a phase lag of two or three heart beats because of the long blood pulmonary transit time. Thus the LV preload reduction may induce a decrease in LV stroke volume, which is at its minimum during the expiratory period. The cyclic changes in RV and LV stroke volume are greater when the ventricles operate on the steep rather than the flat portion of the Frank–Starling curve (see Figure 8-2). Therefore, the magnitude of the respiratory changes in LV stroke volume is an indicator of biventricular preload dependence.¹¹

A recent meta-analysis demonstrated that the PPV and SVV measured during volume controlled mechanical ventilation predicted with a high degree of accuracy (ROC of 0.94 and 0.84, respectively) those patients likely to respond to a fluid challenge as well as the degree to which the stroke volume is likely to increase.¹³ The predictive value was maintained in patients with poor LV function. Furthermore, with remarkable consistency these studies reported a threshold PPV/SVV of 12–13%. In this study the area under the ROC curves was 0.55 for the CVP, 0.56 for the GEDVI, and 0.64 for the LVEDAI. The enormous appeal of using the PPV/SVV as a marker of volume responsiveness is that it dynamically predicts an individual patient's position on his or her Starling curve and this is independent of ventricular function and compliance as well as pulmonary pressures and mechanics (see Figure 8-3).

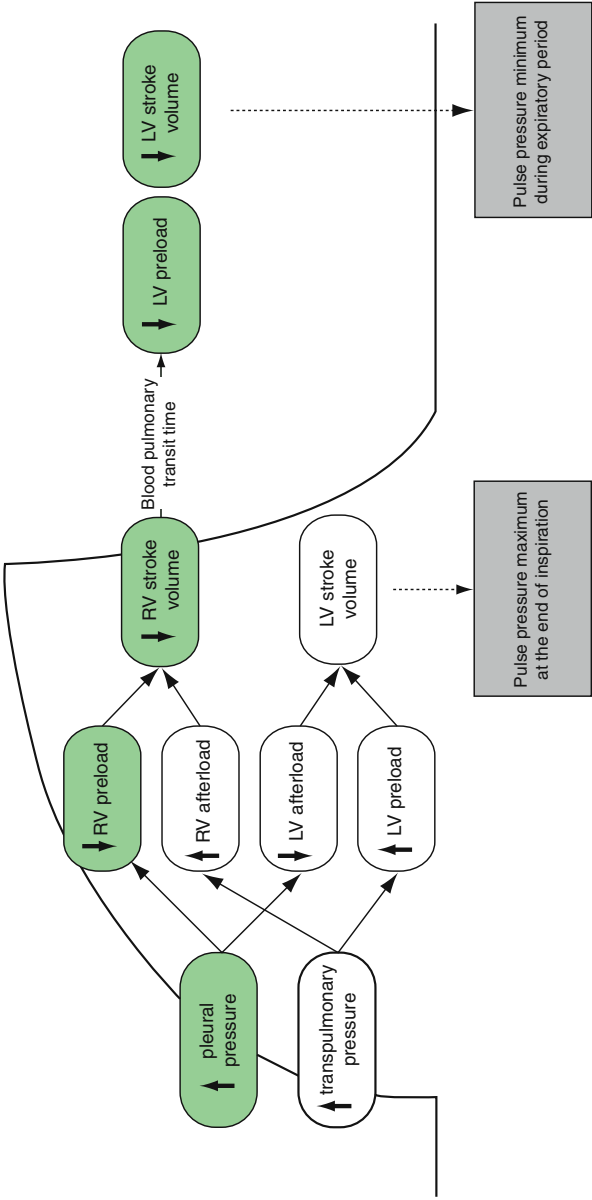


Figure 8-1. Hemodynamic effects of mechanical ventilation. The cyclic changes in LV stroke volume are mainly related to the expiratory decrease in LV preload due to the inspiratory decrease in RV filling. reproduced with permission from Crit Care/Current Science Ltd.

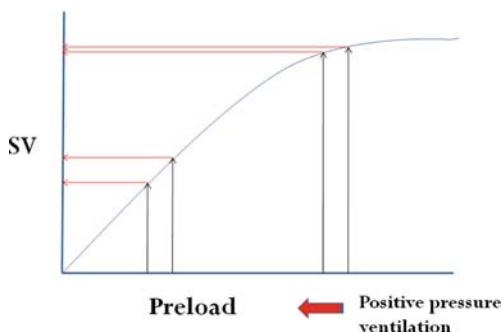


Figure 8-2. The cyclic changes in RV and LV stroke volume are greater when the ventricles operate on the steep rather than the flat portion of the Frank-Starling curve.

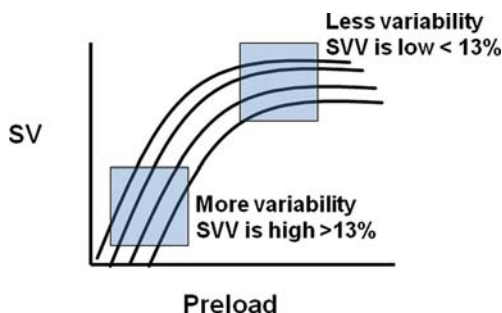


Figure 8-3. Arterial waveform analysis during positive pressure ventilation predicts an individual patients' position on his/her Starling curve and allows optimization of cardiac performance.

While the respiratory variation in vena-caval diameter and stroke volume as measured by echocardiography (see below) has been demonstrated to predict fluid responsiveness, they do not perform as well as the PPV/SVV, require intensivists with a high degree of expertise in echocardiography, and are not conducive to minute-to-minute monitoring. This suggests that currently the PPV/SVV is the most accurate predictor of volume responsiveness in critically ill patients. It should be noted that the PPV was a more accurate predictor of volume responsiveness than the SVV. This may be related to the fact that the PPV is a direct measurement, while the SVV is derived from pulse contour analysis which makes

a number of assumptions. Changes in vascular tone alter the contour of the pulse wave which may result in erroneous calculations of stroke volume.^{14,15}

It should be appreciated that both arrhythmias and spontaneous breathing activity will lead to misinterpretations of the respiratory variations in pulse pressure/stroke volume. Furthermore, for any specific preload condition the PPV/SVV will vary according to the tidal volume. Reuter and colleagues demonstrated a linear relationship between tidal volume and SVV.¹⁶ De Backer and colleagues evaluated the influence of tidal volume on the ability of the PPV to predict fluid responsiveness.¹⁷ These authors reported that the PPV was a reliable predictor of fluid responsiveness only when the tidal volume was at least 8 mL/kg. For accuracy, reproducibility and consistency we suggest that the tidal volume be increased to 8–10 mL/kg ideal body weight prior to and after a fluid challenge.

Dynamic Changes in Aortic Flow Velocity/Stroke Volume Assessed by Esophageal Doppler

The esophageal Doppler technique measures blood flow velocity in the descending aorta by means of a Doppler transducer. The probe is introduced into the esophagus of sedated, mechanically ventilated patients and then rotated so that the transducer faces the aorta and a characteristic aortic velocity signal is obtained. The cardiac output is calculated based on the diameter of the aorta (measured or estimated), the distribution of the cardiac output to the descending aorta, and the measured flow velocity of blood in the aorta. As esophageal Doppler probes are inserted blindly, the resulting waveform is highly dependent on correct positioning. The clinician must adjust the depth, rotate the probe, and adjust the gain to obtain an optimal signal.¹⁸ Poor positioning of the esophageal probe tends to underestimate the true cardiac output. There is a significant learning curve in obtaining adequate Doppler signals and the correlations are better in studies where the investigator was not blinded to the results of the cardiac output obtained with a PAC.¹⁹

A meta-analysis by Dark and Singer demonstrated a 86% correlation between cardiac output as determined by esophageal Doppler and PAC.²⁰ Although the correlation between the two methods was only modest, there was an excellent correlation between the change in cardiac output with therapeutic interventions. Furthermore, the respiratory variation in aortic blood flow velocity with positive pressure ventilation has been demonstrated to be a reliable predictor of fluid responsiveness.²¹ While esophageal Doppler has utility in aiding in the assessment of the hemodynamic status of critically ill patients, this technology has been slow to be

adopted. This is likely the consequence of a number of factors including the less than ideal accuracy of the cardiac output measurements, the long learning curve, the inability to obtain continuous reliable measurements, and the practical problems related to presence of the probe in the patients' esophagus.

Positive Pressure Ventilation Induced Changes in Vena-Caval Diameter

Cyclic changes in superior and inferior vena-caval diameter as measured by echocardiography have been used to predict fluid responsiveness.^{22,23} This technique has a number of limitations, including the fact that sub-costal echocardiography may be difficult in obese patients and those that have undergone laparotomy. Furthermore, changes in IVC diameter are affected by intra-abdominal pressure making this technique unreliable in patients with high intra-abdominal pressure.

Dynamic Changes in Aortic Flow Velocity/Stroke Volume Assessed by Echocardiography

The respiratory changes in aortic flow velocity and stroke volume can be assessed by Doppler echocardiography. Feissel and colleagues demonstrated that the respiratory changes in aortic blood velocity predicted fluid responsiveness in mechanically ventilated patients.²⁴ In this study the LVEDAI was unable to predict fluid responsiveness.

The dynamic indices of volume responsiveness reviewed above are dependent on the cyclic changes in intrathoracic pressure induced by positive pressure ventilation and are not applicable to spontaneously breathing patients. However, changes in aortic flow velocity and stroke volume induced by passive leg raising in non-ventilated patients have been demonstrated to be predictive of volume responsiveness.^{25,26}

Echocardiographic methods of assessing volume status (aortic flow velocity, stroke volume, LVEDAI, IVC/SVC diameter) require intensivists with specialized expertise and skill who have undergone rigorous training in these techniques. There is a long learning curve with a lack of reproducibility. Furthermore, the requirement for 24 h availability and the non-continuous nature of the data limit the applicability of these techniques in the ICU environment. However, as more intensivists embrace this technology, in the hands of experienced operators it can be a useful adjunctive tool to determine fluid responsiveness as well as to assess ventricular function.

■ END-POINTS OF VOLUME RESUSCITATION

Not all patients who are volume responsive require additional fluid challenges. The ideal end-point(s) of fluid resuscitation remains the “holy grail” of critical care medicine. This is complicated by the fact that both under- and over-resuscitation are associated with increased morbidity and mortality. Therefore the patient should receive sufficient fluid to restore “adequate organ perfusion and not a drop more.” An integration of the following parameters will allow the intensivist to determine the adequacy of volume resuscitation and if/when a vasopressor agent should be initiated:

- Urine output
- Urine sodium and osmolarity
- Mean arterial pressure (cerebral and abdominal perfusion pressure)
- BUN
- PPV (or SVV)
- Heart rate
- Lactate
- Arterial pH, BE, and HCO_3
- Mixed venous oxygen saturation SmvO_2 or ScvO_2
- Mixed venous pCO_2
- Tissue pCO_2 (sublingual capnometry or equivalent)
- Gastric impedance spectroscopy
- Skeletal muscle tissue oxygenation StO_2 as measured by NIRS
- Extravascular lung water (see below)
- Intra-abdominal pressure (see below)
- Technology yet to be developed

Once resuscitated, it is preferable to keep patients with ARDS and sepsis (and SIRS) on the “dry side of the road”; allow the BUN to creep up to 30–40 mg/dL; however, do not allow acute renal failure to develop.³ Monitoring of extravascular lung water and intra-abdominal pressure is very useful in this setting (see below).

It is important to note that while “lactic acidosis,” $\text{SmvO}_2/\text{ScvO}_2$, and StO_2 may reflect the adequacy of tissue perfusion and oxygenation in patients with hypovolemic, hemorrhagic, and cardiogenic shock this does NOT apply to patients with severe sepsis/septic shock/SIRS. In patients with sepsis, tissue CO_2 tension (microvascular flow) and gastric impedance spectroscopy (cellular well being) may be better end-points of resuscitation (see Chapter 10).

■ MEASURES OF VOLUME OVERLOAD

While the dynamic changes in pulse pressure and stroke volume together with clinical indices of organ perfusion are useful for detecting intravascular volume depletion we have few reliable measures of volume overload. An elevated CVP and PCWP are measures of RV and LV dysfunction (failure) and not volume status. Some have suggested that patients receive volume resuscitation until they develop pulmonary edema (indicating that the “tank is full”); this is clearly an absurd approach.²⁷ Radiographic and clinical signs of pulmonary edema and clinical evidence of anasarca are late signs of volume overload and poor end-points for fluid resuscitation. Extravascular lung water as determined by transpulmonary thermodilution and intra-abdominal pressure monitoring are two techniques that “measure” tissue edema and may aid in the assessment of volume overload.

Extravascular Lung Water

Extravascular lung water (EVLW) may be calculated from the descending limb (indicator dissipation) of the transpulmonary thermodilution curve and is a method of quantifying the degree of pulmonary edema (hydrostatic and permeability).²⁸ This technique has been shown to compare favorably with the double indicator dilution technique and the ex vivo gravimetric method.^{29–31} Furthermore, this technique can detect small (10–20%) increases in lung water.³² The “normal” value for EVLW is reported to be 5–7 mL/kg with values as high as 30 mL/kg during severe pulmonary edema. In an intriguing study, Sakka et al. found that the mortality was about 65% in ICU patients with an EVLW > 15 mL/kg whereas the mortality was 33% in patients with an EVLW < 10 mL/kg.³³ EVLW has been demonstrated to be an accurate indicator of the severity of lung injury and a reliable prognostic indicator in patients with sepsis-induced acute lung injury.^{34,35} EVLW should be indexed to IBW rather than actual body weight.³⁶ It is likely that using EVLW to guide fluid therapy *may* reduce positive fluid balance, duration of mechanical ventilation, and ultimately patient outcome.

Intra-Abdominal Pressure Monitoring

Intra-abdominal pressure (IAP) is the pressure concealed within the abdominal cavity.³⁷ The World Society of the Abdominal Compartment Syndrome (WSACS, www.wsacs.org) has recently developed consensus definitions outlining standards for IAP measurement as well as diagnostic

criteria for intra-abdominal hypertension (IAH). According to the consensus guidelines IAH is defined as an intra-abdominal pressure ≥ 12 mmHg and abdominal compartment syndrome (ACS) is defined as an IAP above 20 mmHg with evidence of organ dysfunction/failure.³⁸ The abdominal perfusion pressure (APP) is a more accurate predictor of visceral perfusion (MAP-IAP) with a target above 60 mmHg correlating with improved survival.³⁷ Major risk factors for intra-abdominal hypertension (IAH) include the following:

- Abdominal surgery/trauma
- High volume fluid resuscitation ($> 3,500$ mL/24 h)
- Massive blood transfusion (> 10 units/24 h)
- Large burns
- Ileus
- Damage control laparotomy
- Liver failure with ascites
- Severe pancreatitis
- Liver transplantation

Physical examination is inaccurate in detecting IAH. Currently IAP is best measured using the intravesicular method. Continuous methods for monitoring IAP have been reported.³⁹ The following key principles must be followed in the measurement of IAP:

- IAP should be expressed in mmHg
- IAP should be measured at end-expiration and in Complete supine position (note: elevated HOB increases IAP)
- Transducer zeroed in midaxillary line at level of iliac crest
- Maximal instillation of 25 mL sterile saline
- IAP should be measured 30–60 s after instillation of fluid

The IAP should be measured in all “at-risk patients” with repeated measures in those with IAH and following clinical deterioration.

Management of IAH

The 24 h fluid balance has been shown to be an independent predictor of IAH.⁴⁰ Therefore a restrictive fluid strategy is recommended in patients at risk of IAH and those with IAH (however MAP must be maintained with cautious volume loading and vasopressors if required). Resuscitation with 5% albumin should be considered in these patients (see below); maintain APP > 60 mmHg:

- Improve abdominal wall compliance
 - Sedation and analgesia
 - Avoid HOB $> 30^\circ$

- Evacuate intra-abdominal contents
 - Orogastric tube decompression
 - Rectal decompression
 - Prokinetic agents
- Evacuate abdominal fluid collections
 - Paracentesis
 - Percutaneous drainage
- Correct positive fluid balance
 - “cautious diuresis”
 - Ultrafiltration
- Optimize ventilation
 - Keep mean airway pressures as low as possible
 - Prevent ventilator dyssynchrony
- Surgical decompression

■ WHAT TYPE OF FLUID?

This age-old debate has become somewhat of a non-issue in recent years and may be best summarized as follows:

- Hydroxyethyl starch (HES) solutions are associated with an increased risk of renal failure (and death) and have a “limited” role in critical care medicine⁴¹
- Albumin (5% in NaCl) is SAFE⁴² and may have a role (together with lactated Ringer’s solution) in the resuscitation of patients with
 - Sepsis
 - Cirrhosis
 - Pancreatitis
 - Burns
- Packed –red blood cells AND lactated Ringer’s (LR) are the volume expanders of choice in hemorrhagic shock
 - In traumatic blood loss, RBC should be given with FFP and platelets in a ratio of 1:1:1 (see Chapter 51, blood transfusion)
- 0.9% NaCl is better known as “AbNormal Saline,” is associated with the following complications, and is best avoided
 - Decreased glomerular filtration rate (GFR)
 - Metabolic acidosis; both hyperchloremic non-AG as well as AG acidosis
 - Coagulopathy with increased bleeding
- Patients with traumatic head injury should be resuscitated with crystalloids (LR); albumin should be avoided⁴²
- A glucose (5 or 10%) containing solution should be used in patients with cirrhosis (high risk of hypoglycemia)

ALERT

0.9% NaCl (AbNormal Saline) is a non-physiologic solution (sodium 154 mEq/L, Cl 154 mEq/L, and pH < 6) with limited indications.

5% Albumin

While the type of fluid used in the resuscitation of patients with sepsis has not been definitively shown to affect outcome, subgroup analysis of the SAFE study suggested a trend toward a favorable outcome in patients who received albumin.⁴² This is supported by experimental studies⁴³ and patients with malaria (similar pathophysiology to gram-negative sepsis).⁴⁴ Albumin has a number of features that may be theoretically advantageous in patients with sepsis (and SIRS) including the following:

- Maintains endothelial glycocalyx and “endothelial function”
- Anti-oxidant properties
- Anti-inflammatory properties
- May limit “third” space loss

Our preference is to give a mixture of both albumin and LR ($\pm$ 50–50) in patients with sepsis (and SIRS) in an attempt to maintain intravascular volume and yet limit the total amount of fluid given.

Albumin should be considered the volume expander of choice in patients with underlying liver disease (cirrhosis).^{45,46} Albumin is particularly useful in patients with spontaneous bacterial peritonitis, hepatorenal syndrome, and following a paracentesis (see Chapter 33).

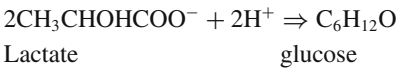
Lactated Ringer’s (Hartmann’s Solution) vs. 0.9% NaCl (AbNormal Saline)

Despite differences in composition, normal saline and lactated Ringer’s solution are frequently considered equivalent and lumped under the term “balanced salt solution.” For reasons that are unclear, normal saline appears to be the preferred replacement fluid of medical physicians while lactated Ringer’s solution is the choice of surgeons. Furthermore, while no body fluid has an electrolyte composition similar to that of normal saline, this fluid is frequently referred to as “physiologic salt solution” (PSS). However, both experimental and clinical data have demonstrated that these fluids are NOT equivalent (see below) and that in most clinical situations LR is the fluid of choice.

Metabolic Acidosis

Numerous studies have demonstrated the development of a hyperchloremic metabolic acidosis in human volunteers and patients resuscitated with normal saline.⁴⁷⁻⁵⁰ While the clinical implications of these findings are unclear, the additional loss (renal) of HCO_3^- in the setting of reduced buffering capacity only adds to the acid-base burden characteristic of hypoperfused states.⁴⁸ Furthermore, resuscitation with normal saline may produce a “dilutional acidosis.”

In addition it should be noted that the lactate (in LR) is converted to glucose (mainly in the liver); this reaction consumes hydrogen ions, thereby generating HCO_3^- .⁵¹:



Many erroneously believe that LR may worsen or cause a “lactic acidosis”; this is impossible as lactate (the base) has already donated H^+ ions; LR generates HCO_3^- in the liver and kidney. Although the lactate concentration (base) may increase with LR this increase is associated with an increase in HCO_3^- and an increase in pH (even with liver disease). This observation was elegantly demonstrated by Phillips et al., who in a swine hemorrhagic shock model compared the acid-base status of animals resuscitated with LR and NS (see Table 8-1 below).⁵²

Table 8-1. Laboratory data at end of study (Phillips et al.).

	<i>Normal Saline</i>	<i>Ringer's Lactate</i>
Lactate	1.3	6.0
HCO_3^-	16.7	27.8
pH	7.17	7.41

These results are strikingly similar to the work of Healey et al. who compared resuscitation with blood + normal saline vs. blood + lactated Ringer's solution in a murine massive hemorrhage model (see Table 8-2 below).⁵³ Note the significantly improved survival in the LR group.

Table 8-2. Laboratory data at end of study (Healey et al.).

	<i>NS + Blood</i>	<i>LR + Blood</i>
pH	7.14	7.39
Na	147	135
Cl	130	109
HCO_3^-	9.4	19.7
Survival	50%	100%

Coagulopathy

Studies in surgical patients have demonstrated that as compared to LR volume replacement with NS results in greater blood loss with a greater need for blood transfusion.⁴⁹ The cause of the coagulopathy is unclear and is only partly explained by the difference in Ca^{2+} between the two solutions.

Renal Function

Solutions high in chloride have been shown experimentally to reduce GRF (due to tubulo-glomerulo feedback).⁵⁴ Clinical studies have found indices of renal function to be worse in surgical patients randomized to NS as opposed to RL.

D-Lactate

It should be noted that LR solution is a racemic mixture containing both the L- and D-isomers of lactate. Small animal hemorrhagic shock models have suggested that the D-isomer is pro-inflammatory and increases apoptotic cell death.^{55–57} The clinical implication of these findings is unclear.

ALERT

As LR has added potassium (K^+ 4–5 mEq/L) this solution should be used with caution in patients with acute renal failure and hyperkalemia.

■ RESUSCITATION IN SPECIFIC DISEASE STATES

Hemorrhage

In patients who have lost blood, fluid moves from the interstitial to the intravascular compartment in an attempt to restore blood volume; the hemoglobin concentration falls by hemodilution (in the absence of volume resuscitation it takes about 72 h for Hct to stabilize). Therefore, both the intravascular and extravascular, extracellular compartments are decreased following blood loss. Experimental hemorrhage models have demonstrated a higher mortality when animals are resuscitated with blood alone, as compared to blood and crystalloids. Patients who have lost blood should therefore be resuscitated with crystalloid (LR), followed by

blood. Due to both a consumptive and a dilutional coagulopathy, patients with traumatic hemorrhage should proactively receive platelets and FFP together with packed red blood cells (in a ratio of 1:1:1). In all other patients, platelets and FFP should only be transfused based on coagulation parameters and ongoing bleeding. In both “medical” and surgical bleeding, the goal should be to restore tissue perfusion and oxygenation and not to achieve a “normal” hemoglobin (a hemoglobin above 7–8 g/dL is usually just fine) (see Chapter 51).

Dehydration

Patients who are dehydrated (from diarrhea, vomiting, diabetic osmotic diuresis, etc.) have lost both intravascular and extravascular, extracellular fluid. Volume replacement with crystalloids (LR) will resuscitate both compartments.

Sepsis (and SIRS)

As a consequence of “leaky capillaries” and “third space loss” these patients have a decreased effective intravascular compartment and tissue edema (enlarged interstitial compartment). As less than 20% of infused crystalloid remains intravascular in these patients, the volume of crystalloids should be limited. The combination of albumin and LR is recommended.

Burns

Due to the thermal injury these patients have a massive loss of interstitial fluid as well as a generalized capillary leak. Patients should be resuscitated with crystalloid (LR) during the first 24 h.

■ MANAGEMENT OF OLIGURIA

While primary renal diseases and urinary tract obstruction may lead to oliguria, intravascular volume depletion with renal hypoperfusion is the commonest cause of oliguria in clinical practice (see Chapter 42). The management of oliguria due to intravascular volume depletion is *aggressive fluid resuscitation*. “Lasix is not a volume expander!”

Diuresis with loop diuretics in patients with normal or reduced effective intravascular volume is invariably associated with a fall in intravascular volume, a fall in plasma volume, a fall in GFR, and a rise in blood urea nitrogen (BUN). The fall in GFR has been correlated with the fall

in intravascular volume. Contraction of the intravascular volume and fall in GFR may occur in the absence of a fall in cardiac output. Volume depletion is associated with a greater rise in the BUN than in the plasma creatinine due to increased passive reabsorption of urea which follows the hypovolemia-induced increase in sodium and water resorption in the kidney. An increasing BUN/creatinine ratio in a patient receiving a diuretic is a reliable sign of intravascular volume depletion and should prompt the immediate discontinuation of these agents.

ALERT

Lasix® is the “Devil’s medicine” and has no role in acute oliguria/acute renal failure.

Contrary to popular belief the GFR falls (rather than rises) with loop diuretics. In the mammalian kidney there is close coordination between the processes of glomerular filtration and tubular reabsorption. Coordination between the glomerulus and tubule is mediated by a system of tubulo-glomerular feedback which operates within the juxtaglomerular apparatus of each nephron. Microperfusion experiments have demonstrated that an increase in flow rate of tubule fluid through the loop of Henle following the use of a loop diuretic is followed by a reduction in single nephron GFR. This has been shown to be mediated via feedback control by the macula densa which is the flow-dependent distal sensing site. When the tubular glomerular feedback pathway is interrupted with a loop diuretic, there is an attenuation of the pressure-induced afferent arteriolar dilatation with impairment in blood flow autoregulation. In patients with extracellular volume depletion this effect is exaggerated with a dramatic fall in GFR.

■ CLINICAL PEARLS

- The initial treatment of hypotension is a fluid challenge (lactated Ringer’s solution)
- The initial treatment of oliguria is a fluid challenge (lactated Ringer’s solution)
- Lactated Ringer’s is the replacement fluid of choice in most clinical scenarios
- Pulse pressure variation (on mechanical ventilation) should be used to determine “fluid responsiveness”
- The measurement of extravascular lung water and intra-abdominal pressure should be used to prevent volume overload during “large volume” resuscitation

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