Goal-directed therapy in intraoperative fluid and hemodynamic management

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Abstract

Intraoperative fluid management is pivotal to the outcome and success of surgery, especially in high-risk procedures. Empirical formula and invasive static monitoring have been traditionally used to guide intraoperative fluid management and assess volume status. With the awareness of the potential complications of invasive procedures and the poor reliability of these methods as indicators of volume status, we present a case scenario of a patient who underwent major abdominal surgery as an example to discuss how the use of minimally invasive dynamic monitoring may guide intraoperative fluid therapy.

Keywords: high-risk surgery, hemodynamic, fluid, monitoring, goal-directed therapy

INTRODUCTION

One of the primary goals of hemodynamic monitoring is to alert the health care team to an impending cardiovascular crisis before organ injury ensues; it is routinely used in this manner in the operating room during high-risk surgery. Adequate volume replacement to achieve optimal cardiac performance is critical in hemodynamic management in order to prevent any deleterious consequence of under-resuscitation or fluid overload.

THE CONTROVERSY OVER "STANDARD" VS. "RESTRICTED" FLUID REGIMENS

The physiological response to injury involves, among other processes, a complex neuroendocrine response aimed at maintaining intravascular volume by conserving salt and water. Intravenous fluid management has evolved from the early attempts to "run patients wet" by giving them large volumes of fluid in the hope of preventing renal failure, to more restricted regiments and goal-directed fluid therapy aiming to minimize perioperative complications. It has been difficult to find the right balance; some fluid restricted regimens may not be able to meet the fluid requirements in as many as 25-28% of patients[1]. Recent studies have found that restricted postoperative IV fluid management in patients undergoing major abdominal surgery appears harmful because it is accompanied by an increased risk of major postoperative complications and a prolonged postoperative hospital stay.

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stay\textsuperscript{[2]}. On the other hand, several randomized controlled trials in recent years have shown that "restricting" fluid administration in patients undergoing elective abdominal surgery may result in better outcomes when compared with those receiving "standard or liberal" fluid therapy. Patients who received an excessive amount of fluid experienced a more prolonged gastric emptying time and more complications than those who received a restricted or goal-directed therapy, possibly because of marked intestinal wall edema\textsuperscript{[3-6]}. However, there is no consistency to the definitions of each therapy or to the endpoints. A recent meta-analysis found that perioperative outcomes favored goal-directed therapy rather than liberal fluid therapy. However, there was no certainty regarding whether goal-directed therapies are superior to restrictive fluid strategies\textsuperscript{[7]}. In summary, given the heterogeneity of the different studies regarding the amount of fluids given on each regime and the study endpoints, we can only infer that maintenance of intravascular fluid balance, rather than fluid restriction, seems to be the key to a better postoperative outcome.

**EMPIRICAL FORMULA TO CALCULATE THE FLUID NEEDS INTRAOPERATIVELY**

The widely used formula to calculate the maintenance fluid requirements during the intraoperative period evolved from pediatric studies extrapolated to adult population and is based on caloric expenditure rather than being based on the type of patient or the procedure\textsuperscript{[8]}. The traditional idea of restoring fasting deficit has been questioned after studies found that intravascular volume remains stable in healthy patients, even after 10 hours of fasting, unless additional losses are added\textsuperscript{[9]}. In addition, the existence of a third space has been disputed by some on the ground that different studies have been unable to localize or quantify it\textsuperscript{[10]}. For these reasons, it becomes necessary to find a more reliable way to guide perioperative fluid administration in a way that individualizes it according to type of patient and procedure. Here we use a case as an example to illustrate the quandary. The patient was a 63-year-old woman scheduled for choledochojejunostomy for cholelithiasis and a possible ampullary mass. Her BMI was 24. Past medical history was remarkable for multi-nodular goiter, essential tremor, developmental disorder, osteoporosis and phenylketonuria. The anesthetic plan included general endotracheal anesthesia, two big bore intravenous accesses, and an arterial line with FloTrac/Vigileo (Edwards Lifesciences, LLC, CA) monitoring to keep stroke volume variation (SVV) between 10% to 13% for fluid administration guidance. The procedure lasted 4 hours, and the surgical findings included cholelithiasis, choledocholithiasis and a cholecysto-choledoch fistula. She received a total of 2100 mL of intravenous fluid. Her urine output was 725 mL for the entire procedure (181 mL/h). Her vital signs remained stable intraoperatively with blood pressure ranging between 101/54 and 123/69 mmHg, and heart rate ranging between 82 and 92 per minute. The patient was extubated in the OR. The postoperative course was unremarkable and she was discharged home on post-operative day five. If we had used the standard fluid calculation for this patient for her weight (64.5 kg) following the 4-2-1 rule, calculating a deficit per 8 hours of fasting and insensitive losses including compensatory intravascular volume expansion plus evaporation losses of 10 mL/(kg.h)\textsuperscript{[11]}, plus the total blood loss of 500 mL, the total estimated amount of crystalloids needed was 6,366 mL (Table 1). The actual amount of crystalloids given was directed by SVV values with a goal to keep it between the ranges of 10% to 13%. The patient received a total of 2,100 mL. The urine output for the entire procedure was 725 mL (2.8 mL/(kg.h)).

**Table 1 Comparison of the empirical formula to the goal-directed method in calculating the fluid (mL) needs**

<table>
<thead>
<tr>
<th></th>
<th>1st hour</th>
<th>2nd hour</th>
<th>3rd hour</th>
<th>4th hour</th>
<th>Total</th>
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<td>209</td>
<td>418</td>
<td>836</td>
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<td>104.5</td>
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<td>418</td>
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<td>516</td>
<td>516</td>
<td>2,064</td>
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<tr>
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<td>387</td>
<td>387</td>
<td>1,548</td>
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<tr>
<td>Bleeding\textsuperscript{4}</td>
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<td></td>
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<td>1,500</td>
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<tr>
<td>Grand total calculated</td>
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<td></td>
<td></td>
<td></td>
<td>6,366</td>
</tr>
<tr>
<td>Total volume given\textsuperscript{5}</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2,100</td>
</tr>
</tbody>
</table>

1. Deficit and maintenance calculated following the 4-2-1 rule, with a fasting time of eight hours
2. Insensitive losses including compensatory intravascular volume expansion plus evaporation losses, calculated eight mL per kg
3. Third space losses calculated as six mL per kg
4. Total bleeding was 500 mL, calculating replacing with crystalloids at a 3:1 ratio
5. Volume administrated guided by SVV values with a goal of 10% to 15%
THE "GOLD STANDARD" FOR HEMODYNAMIC MONITORING

The pulmonary arterial catheter (PAC) has been considered to be the "gold standard" for monitoring preload, afterload, contractility, and tissue oxygenation. The invasiveness and high rate of complications associated with this device renders it as unsuitable for routine use in most cases. Besides, PAC uses right-sided pressures and flows to estimate the performance of systemic, or left-sided function, and its efficacy and performance remain to be justified. Since its introduction, more than 1,500 articles and abstracts have been published that examine the role of the PAC as a hemodynamic monitoring device in the management of the critically ill patient. Despite the extensive body of literature relating to the effects of PAC monitoring on outcomes, there have been only a few large prospective randomized clinical trials (RCT) that have studied the clinical outcomes with the use of PAC. The results showed that PAC utilization improves, worsens, or has no impact on morbidity or mortality, and its routine use in the majority of clinical circumstances, even in high-risk surgical and non-surgical patients, is not warranted.

Pulmonary arterial wedge pressure (PAWP) is a poor measure of left ventricular (LV) preload, but is a good measure of the back-pressure to pulmonary blood flow and the hydrostatic forces producing pulmonary edema.

Central venous pressure (CVP) is another widely used parameter to estimate blood volume and preload. It has been established, since as early as 1975, that there is no correlation between blood volume and CVP. It is suggested that inaccurate physiologic evaluation of critically ill patients is likely to jeopardize survival by inviting inappropriate and ineffective therapy. It has also been demonstrated that the standard preload indices, such as CVP or the changes in response to fluid challenges, reflect LV end-diastolic volumes (LVEDV) in patients receiving a fluid challenge for hemodynamic instability and they are not capable of predicting cardiac response to fluid therapy. CVP, on the other hand, is the back-pressure to systemic venous return and the clinical utility of CVP as a guide to diagnosis or therapy has not been demonstrated. Marik et al. measured 1,500 blood volume simultaneously with CVP in a heterogeneous cohort of 188 ICU patients and demonstrated no association between these two variables (r = 0.27). The receiver operator characteristic (ROC) in Marik’s study was 0.56 (0.8 to 0.9 indicates adequate accuracy with 0.7 to 0.8 being fair, 0.6 to 0.7 being poor, and 0.5 to 0.6 indicating failure). Bouchard et al. compared right and left ventricular stroke work index with echocardiography-derived indices of LV performance in cardiac surgery patients. Correlations between right and left ventricular stroke work index changes were poor. Thus, there is a significant discrepancy and limited relation between the right heart derived preload from the LV performance. Another study compared pulmonary artery pressure and CVP to LV end-diastolic area (LVEDA), an indicator for LV preload measured by transesophageal echocardiography (TEE), and found poor correlations among them. It was concluded that CVP is a measure of right atrial pressure alone; it is not a measure of blood volume or ventricular preload and, therefore, should no longer be routinely measured in the ICU, operating room, or emergency department.

TEE has been commonly utilized to examine cardiac function and hemodynamic parameters during the last decade. It can provide real-time information about both intra-cardiac volumes and cardiac function. The TEE measurement of LVEDA in the trans-gastric mid-papillary short axes view has been widely used intra-operatively to monitor the volume status. With this tool, direct observation of the left-side of the heart via ultrasound permits evaluation of information such as LV end systolic and end diastolic volumes, which are indicators of the LV preload and can be used to guide management and intervention to optimize a patient’s volume and cardiovascular status. When compared to PAWP, TEE measurement of the LVEDA has been shown to more accurately reflect the LV preload and improve the ability to detect changes in LV function and volume caused by acute blood loss. The value of LVEDA was lower in patients who subsequently responded to a fluid challenge and a significant relationship between the baseline LVEDA index and the changes in stroke volume induced by

Fig 1. Transesophageal echocardiography image of a left ventricular (LV) transgastric short axis view. The diastolic area is corresponding to the LV preload. AL: ante lateral papillary muscle; PM: postal medial papillary muscle.
volume expansion has been reported\textsuperscript{[25-27]}. With all the advantages of TEE, its measurements of the LV area or volume are considered by some to be the clinical "gold standard" of cardiac preload estimates\textsuperscript{[22,27]}. However, to utilize this technology, extensive training and expensive equipment are necessary, and is impractical for post-operative monitoring.

**ARTERIAL PRESSURE BASED CARDIAC OUTPUT**

The arterial pressure based cardiac output (APCO) is a CO monitoring system based on the analysis of the systemic arterial pressure wave form and back calculate the stroke volume (SV). The direct proportionality between arterial pulsatility and the stroke volume in conjunction with heart rate is used to calculate CO. Age, sex and the body surface area are used to correct for inter-individual differences in arterial compliance based on the model described by Langewouters and colleagues\textsuperscript{[27]}. Several algorithms for waveform analysis have been developed. The algorithms may include the area of the systolic pressure curve analysis, pulse-power analysis, standard deviation of the pressure trace, or pulse-contour methods to determine flow. Patient data characteristics, waveform morphology, and/or calibration with independent CO measurements are used to account for patient-specific aortic impedance, arterial compliance, and peripheral vascular resistance\textsuperscript{[29]}. Most importantly, it is minimally invasive and provides a measurement of the left heart function.

**STROKE VOLUME VARIATION/PULSE PRESSURE VARIATION**

SVV/Pulse pressure variation (PPV) is a naturally occurring phenomenon in which the arterial pulse pressure falls during inspiration and rises during expiration due to changes in intra-thoracic pressure secondary to negative pressure ventilation (spontaneously breathing). While on controlled mechanical ventilation, arterial pressure rises during inspiration and falls during expiration due to changes in intra-thoracic pressure secondary to positive pressure ventilation. PPV is the difference between the maximum and minimum values of the arterial pulse pressure (PP) during one mechanical breath divided by the mean of the two values (PP\textsubscript{max}-PP\textsubscript{min} / PP\textsubscript{mean}) with a normal value of less than 13%\textsuperscript{[30,31]}. SVV is calculated by taking the SV\textsubscript{max}-SV\textsubscript{min} / SV\textsubscript{mean} over a respiratory cycle or a period of time. Its normal value is less than 13%\textsuperscript{[32]}

The principles underlying the PPV and SVV are based on simple physiology that the inferior vena cava (IVC) is a compliant blood vessel subject to abdominal pressure and acts as a reservoir\textsuperscript{[33]}. Its caliber is altered by respiration, blood volume and right heart function\textsuperscript{[33-35]}. Demonstrated by using echocardiography, Morgan et al. first reported that mechanical ventilation induces cyclic changes in vena cava blood flow, pulmonary blood flow and aortic blood flow. During the inspiratory period of mechanical ventilation, the vena cava blood flow decreases first, followed by a decrease in pulmonary artery flow and then in aortic blood flow. The decrease in vena cava blood flow has been related both to an increase in right atrial pressure and to the compression of the vena cava due to the inspiratory increase in pleural pressure during mechanical ventilation\textsuperscript{[36]}. According to the Frank-Starling mechanism, the inspiratory decrease in right ventricular preload results in a decrease in right ventricular output and pulmonary artery blood flow that finally leads to a decrease in left ventricular filling and output\textsuperscript{[37]}.

Dynamic changes of arterial waveform-derived variables, such as SVV and PPV, during mechanical ventilation are highly accurate in predicting volume responsiveness in critically ill patients with an accuracy greater than that of traditional static indices of volume responsiveness. This technique, however, is limited to patients who receive controlled ventilation and who are not breathing spontaneously\textsuperscript{[39]}.

**PRE-LOAD AND CARDIAC OUTPUT RELATIONSHIP**

SV is determined by three factors: preload, afterload, and contractility. The preload gives the blood volume for the ventricle to pump, as well as the end diastolic length of the muscle. The contractility is the force that the muscle can create at the given length, and the afterload is the arterial pressure against which the muscle will contract. These factors establish the volume of blood pumped with each heartbeat. The direct relationship between end-diastolic fiber length and contractile force was first demonstrated experimentally by Frank and Starling\textsuperscript{[38,39]}. This Frank-Starling principle illustrates the relationship between CO and LVEDV. It is based on the length-tension relationship within the ventricle. If ventricular end diastolic volume (preload) is increased it follows that the ventricular fiber length is also increased, resulting in an increased 'tension' of the muscle. In this way, cardiac output is directly related to venous return, the most important determining factor of preload. When heart rate is constant, CO is directly related to preload (up to a certain point.). An increase in preload will increase the CO until very high end-diastolic volumes are reached. At this point CO will not increase with any further increase in preload, and may even decrease after a certain preload is reached (\textbf{Fig 2}). Also, any
increase or decrease in the contractility of the cardiac muscle for a given end diastolic volume will act to shift the curve up or down, respectively.

**CLINICAL APPLICATIONS**

In clinical practice, adequate volume replacement to achieve optimal cardiac performance is a primary goal of hemodynamic management in patients undergoing major surgeries. However, in only half of these patients, the CO increases after a fluid administration and thus only these can be considered as responders to fluid therapy. Therefore, physicians need reliable criteria to distinguish between responders and non-responders to avoid any deleterious consequences of fluid overload. The use of arterial pulse wave to determine the CO and volume status has intrigued both scientists and clinicians for decades, but only 1% of physicians consider the "swings" in blood pressure during respiration in their decision-making process regarding volume expansion. Only recently, this ability is its prediction of arterial compliance and beat-to-beat variability in cardiac function. Cardiac output is calculated with the Steward-Hamilton equation and applied with the pulse contour method to monitor beat-to-beat variability in cardiac function. PiCCO has been shown to more accurately reflect LV filling and volumes than the PAC in a number of studies. One unique aspect of the PiCCO system is that through a transpulmonary double indicator dilution technique, the extravascular lung water can be estimated. This information may be used as an indicator of pulmonary edema which can reflect excessive volume loading.

Both PiCCO and LiDCO make measurements applying pulse contour analysis using external calibration, which usually occurs at intervals of several hours. One device has the ability for self-calibration based on patient specific data and is known as FloTrac/Vigileo (Edwards Lifesciences, LLC, CA). The distinction of this ability is its prediction of arterial compliance and resistance based on age, sex, height, weight, and body surface area. There are some instances, such as non-traumatic intracranial hemorrhage, children with pulmonary hypertension or cardiomyopathy, or after cardiac transplantation, where the data has shown poor correlation with traditional thermodilution technique. In general, data have deemed the estimation of cardiac output by each of above systems to be interchangeable with that from a PAC.

**MINIMAL INVASIVE HEMODYNAMIC MONITORING DEVICES**

Several novel methods have been used to measure other hemodynamics of cardiac output. These include the FloTrac/Vigileo system, LiDCO (LiDCO, London, UK) and PiCCO (Pulsion Medical Systems, Munich, Germany) systems. The latter two used dilution analysis. The difference between them and PACs is that both LiDCO and PiCCO allow for dilution through the systemic or left-sided circulation versus just the right heart.

Initially described by Linton et al., lithium dilution was reported to have high correlation with PAC thermodilution CO. This technique involves the administration of a bolus of isotonic lithium chloride (0.002-0.004 mmol/kg) into a central or peripheral vein. Detection of lithium is later measured with a lithium ion specific electrode that is attached to an arterial line. The plasma concentration of lithium, as it varies over time, is then incorporated into the derivation of CO. Advantages of lithium are that it is neither protein bound nor normally present in blood, allowing for more accurate measurements at levels that are within the nontoxic range. In practice, LiDCO is commonly applied with a pulse contour analysis that allows continuous monitoring of cardiac output. This system has been shown to be clinically effective at predicting volume responsiveness even when compared to TEE.

The PiCCO system uses transpulmonary thermodilution to calibrate continuous cardiac output monitoring. Initial measurements are attained when cold saline injected into a central vein causes temperature fluctuations detected by a thermistor tipped arterial catheter placed in an axillary or femoral artery, although some studies suggest that the usage of a radial artery catheter provides similar accuracy. Cardiac output is calculated with the Steward-Hamilton equation and applied with the pulse contour method to monitor beat-to-beat variability in cardiac function. PiCCO has been shown to more accurately reflect LV filling and volumes than the PAC in a number of studies. One unique aspect of the PiCCO system is that through a transpulmonary double indicator dilution technique, the extravascular lung water can be estimated. This information may be used as an indicator of pulmonary edema which can reflect excessive volume loading.

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The use of minimally invasive hemodynamic moni-
Monitoring has gained popularity in the past few years. The devices have been validated, both intra-operatively and post-operatively, in various patients including on-pump and off-pump cardiac surgeries\[^{21,32-34}\]\(^{[21,32-34]}\), neurosurgery\[^{55}\]\(^{[55]}\), thoracic surgery\[^{56}\]\(^{[56]}\), open and laparoscopic abdominal surgeries\[^{57}\]\(^{[57]}\), urological surgery\[^{24}\]\(^{[24]}\), liver transplantation\[^{58}\]\(^{[58]}\), vascular surgery\[^{99}\]\(^{[99]}\) and post-operative ICU\[^{60-62}\]\(^{[60-62]}\). Its use has also been shown to improve the surgical outcomes by decreasing post-operative complications, days on mechanical ventilation, length of ICU stay and length of hospital stay in some small studies\[^{63,64}\]\(^{[63,64]}\). In our institution, more than 1,400 high-risk surgical cases were monitored using minimally invasive hemodynamic monitoring devices in 2009. The preload (SVV), contractility (CO) and afterload (systolic blood pressure) are the main parameters used to guide fluid administration and hemodynamic management (Fig 3).

**Fig 3. A sample algorithm to guide intraoperative hemodynamic management using blood pressure (BP), cardiac output (CO) and stoke volume variation (SVV) as the parameters.**

Loading should be more beneficial in a hypotensive patient with low CO and volume responsiveness than in a hypotensive patient with a high CO and lesser degree of volume responsiveness, for whom administration of vasopressors should be more logical. This emphasizes the great interest in new commercially available devices that monitor and display both CO and SVV/PVV together from beat-to-beat analysis of arterial pressure waveform.

Despite these encouraging findings, the above devices and technology are often compared and validated against what is now, or has been, common practices that include PAC and TEE\[^{21,24}\]\(^{[21,24]}\). Although there is strong agreement regarding patient volume status and cardiac function between those tested with minimally invasive hemodynamic monitoring devices and the results measured by the "gold standard" methods and devices, others have found discrepancies. The behavior of SVV, as it is influenced by known changes in volume loading through altering physical positioning (between Trendelenberg and reverse Trendelenberg) and normovolemic hemodilution, has also been documented\[^{24,65}\]\(^{[24,65]}\). Further studies are necessary for additional investigation of outcome measurements and goal-directed therapy using these new tools.

In conclusion, minimally invasive hemodynamic monitoring has a rising promise in the effort to improve continuous hemodynamic monitoring during cardiac and non-cardiac surgeries. More recently, it has been used to replace PAC in certain cardiac surgical patient populations. There may not be one ideal method that always preserves accuracy, as each method has its own set of limitations, but corroboration of new technology and innovation should justify the movement towards less invasive means of patient monitoring. This would reduce morbidity, cost less, yield similar if not higher quality physiologic data, and improve patient outcomes.

**TECHNOLOGY LIMITATIONS**

While the usefulness of using SVV/PPV and APCO to detect preload sensitivity is indisputable, a number of limitations must be remembered. The dynamic indices cannot be used in a patient who is spontaneously breathing and/or has arrhythmias. Even if the detection of fluid responsiveness is found to be of use in the decision-making process regarding volume expansion, two important points must be kept in mind. First, since both ventricles of a healthy subject operate on the steep portion of the preload/SV relationship, volume responsiveness is a physiological phenomenon related to a normal preload reserve. Therefore, detecting volume responsiveness must not automatically lead to a decision of infusing fluid. Second, it is reasonable to postulate that volume
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