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Goal-Directed Therapy and Hemodynamic Optimization in the Critical Care Setting: Practical Applications and Benefits

I. Introduction
In the operating room and in the intensive care units, the optimization of patient’s hemodynamics is key to improving morbidity and mortality. Evidence suggests that either too little or too much fluid administration during the perioperative period can worsen tissue perfusion and oxygenation leading to organ dysfunction. Further, this impairment may not be reliably revealed by alterations in conventional hemodynamic indices such as heart rate, urine output, central venous pressure or blood pressure. Numerous investigative studies in a spectrum of patient populations (sepsis, cardiovascular surgery, trauma, and other critical illnesses) have challenged the notion that these indicators accurately predict volume status.\(^1\)\(^2\) Goal directed therapy (GDT) is the concept of using indices of continuous blood flow and/or tissue oxygen saturation to optimize end organ function. By using the flow related parameters such as stroke volume (SV), cardiac output (CO), and markers of fluid responsiveness such as stroke volume variation (SVV), pleth variability index (PVI), and corrected aortic flow time (FTc), one is able to precisely infer where the patient is on their Frank Starling relationship, and thus, optimize oxygen delivery. Similarly, by using markers of tissue oxygenation/extraction, such as central venous saturation (ScVO\(_2\)) and somatic tissue oxygenation (StO\(_2\)), one is able to provide GDT therapy to improve end organ oxygenation. The body of evidence in favor of GDT continues to grow; therefore, GDT is rapidly becoming the standard of care in the ICU, emergency department, and in the operating rooms.

The body of evidence in favor of GDT continues to grow; therefore, GDT is rapidly becoming the standard of care in the ICU, emergency department, and in the operating rooms.

II. Goal-Directed Therapy in the Intensive Care Unit and in the Emergency Department
Shoemaker et al. were one of the first to show that in the critically ill patient, one should treat by physiologic criteria, and administration of therapy should be monitored to attain optimal physiologic goals.\(^3\) These concepts have been advanced by the landmark study by Rivers et al. that showed improved patient outcome using early goal directed therapy based on a protocol maintaining ScVO\(_2\) >70 % during treatment of severe sepsis and septic shock.\(^4\) Pearse et al. showed that it is possible to bridge intraoperative GDT to the ICU, and by maximizing patients oxygen delivery index, post-operative complications and duration of postoperative hospital stay can be decreased.\(^5\)

With regards to this, Emergency physicians (EPs) serve a key role in recognition of early disease presentation and the implementation of GDT therapy. During the past few years, several randomized, controlled trials in patients with severe sepsis and septic shock have demonstrated significant reductions in mortality rates with the institution of GDT therapies.\(^6\)\(^7\)

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While these have shown the importance of hemodynamic flow guided indices there are still many areas of clinical practice that need to be further developed. These include the more widespread use of SV optimization algorithms in the intensive care and emergency departments.

III. GDT in the Perioperative Period

The use of flow-related indices to guide intraoperative goal-directed fluid therapy has appeal since these parameters provide a numeric representation of the patient's volume status, which can frequently be difficult to ascertain using standard hemodynamic monitors, urine output or even CVP. Gan et al. in 2002 reported earlier return of bowel function, lower incidence of postoperative nausea and vomiting, and decrease in length of hospital stay in patients whose stroke volume was optimized using an esophageal Doppler. Intraoperative GDT has also reported to improve outcomes following surgery in high-risk patients, decreasing both morbidity and length of hospital stay. Previously published studies have shown decreased complications and hospital length of stay in high-risk patients undergoing major abdominal surgery with SVV guided GDT therapy. In addition, similar results have been shown in non-high risk surgical patients undergoing elective total hip arthroplasty and major abdominal surgery. These studies support that the use of flow guided parameters can aid in continuous maintenance of a euvoletic state by indicating the appropriate timing of fluid administration.

IV. Fluid Administration

Optimal fluid administration in the critically ill patient is important because prior reports indicate that both hypo- and hypervolemia may deleteriously affect perioperative organ function. High volume perioperative fluid therapy has shown to have deleterious effects on cardiac and pulmonary function, recovery of gastrointestinal motility (postoperative ileus), tissue oxygenation, wound healing and coagulation. On the other hand, one of the major concerns with intraoperative fluid restriction is unrecognized hypovolemia resulting in organ dysfunction, particularly postoperative acute renal failure. Given these considerations, the primary resuscitation goal in the critical patient is to restore tissue perfusion / cellular oxygenation, and maintain end-organ function through volume resuscitation. The optimal resuscitation fluid, however, remains a subject of debate.

The decision, whether to use crystalloid versus colloid as the primary resuscitation fluid in the critically ill remains contentious. Two previous meta-analyses of the numerous prospective, clinical trials in this area suggested that colloid resuscitation may be associated with increased patient mortality. A large multicenter, randomized, double-blind trial, however, documented the safety of colloid- based resuscitation using albumin, but failed to demonstrate either an economic or survival benefit to such therapy. The SAFE study authors subsequently performed a post hoc analysis of their data to confirm the suggestion that albumin is associated with a higher mortality rate in patients with traumatic brain injury (TBI). These studies do not refute the fact that: 1) colloids remain intravascular longer than crystalloids, 2) colloids expand plasma volume to a greater extent, and 3) crystalloids are more likely to cause edema formation.

V. Protocols for Goal-Directed Therapy

Many protocols have been proposed for Goal-Directed Therapy in the critical care setting. While they are relatively clear for the management of the septic patient in the emergency department and in the intensive care unit (i.e. the Rivers protocol is the most widely accepted), the range of protocols available for the perioperative setting is much wider and depends mainly on the patient’s vascular access and the availability of the monitors.
Goal-Directed Therapy Protocols in the Intensive Care Unit and the Emergency Department

In the intensive care unit and in the emergency department, the Rivers protocol for the management of the septic patient has been widely accepted. (Figure 1) This protocol is presented here as Figure 1. This protocol relies on the early optimization of mean arterial pressure, central venous pressure, and ScvO2. The interventions used in this protocol are volume expansion in order to keep central venous pressure between 8 and 12 mmHg, vasopressors to maintain mean arterial pressure between 65 and 90 mmHg, and transfusion and/or inotropes to keep ScvO2 more than 70%. The implementation of this protocol within 6 hours following the diagnosis of sepsis has been shown to decrease mortality in this setting.

Figure 1 - Rivers protocol for the management of the septic patient.

In the intensive care unit and in the emergency department, the Rivers protocol for the management of the septic patient has been widely accepted.
Goal-Directed Therapy Protocol in the Operating Room

The first step in the operating room is to identify the patient’s risk and then to define the vascular access. (Figure 2) Then, based on the vascular access, the monitoring approach is chosen and the hemodynamic optimization protocol is applied. Figure 2 is a suggestion for the choice of the hemodynamic monitoring system based on patient’s risk and vascular access.

![Proposed Algorithm for Hemodynamic Monitoring in the Perioperative Period.](image)

- **ΔPOP**: Respiratory variations in the SpO2 waveform
- **PVI**: Pleth Variability Index
- **A-line**: Arterial Line
- **SVV**: Stroke Volume Variation
- **PPV**: Pulse Pressure Variation
- **PAC**: Pulmonary Artery Catheter
- **TEE**: Transesophageal Echocardiography
**Protocol for Moderate Risk Surgery in a Patient Who is Not Equipped with an Arterial Line:**

Patients ASA 2 or 3, with expected blood loss less than 1,500 ml. Surgical procedures include: abdominal, peripheral angiography, head and neck, major orthopedic surgery, kidney transplantation, urology.

Vascular Access: one or two peripheral IV.

Monitoring: standard ASA monitors +/- respiratory variations in the plethysmographic waveform (Pleth Variability Index) if the conditions of applications are met (sinus rhythm, general anesthesia with mechanical ventilation, tidal volume > 7 ml/kg).

If a non-invasive cardiac output monitor is used, the NICE protocol can be applied (see Figure 4). The goal is to titrate fluid administration in order to maximize stroke volume.

**Figure 3 - Goal Directed Therapy protocol based on Pleth Variability index.**

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**Protocol for Low Risk Surgery**

Patients ASA 1 or 2, with expected blood loss less than 500 ml. Surgical procedures include: breast, stomatology, ophthalmology, gynecology, endocrinology (except pheochromocytoma and carcinoid tumor), plastic surgery, minor orthopedic surgery, minor urology surgery.

Vascular Access: one or two peripheral IV.

Monitoring: standard ASA monitors +/- respiratory variations in the plethysmographic waveform (Pleth Variability Index) if the conditions of applications are met (sinus rhythm, general anesthesia with mechanical ventilation, tidal volume > 7 ml/kg).

The protocol for fluid administration is shown in Figure 3. The goal is to use a baseline crystalloid administration of 3 to 5 ml/kg/h and to titrate volume expansion based on PVI.26
Protocol for Moderate Risk Surgery in a Patient Equipped with an Arterial Line

Monitoring: standard ASA monitors +/- stroke volume variation or pulse pressure variation (sinus rhythm, general anesthesia with mechanical ventilation, tidal volume > 7 ml/kg) and / or cardiac output monitoring based on arterial pressure waveform monitoring (pulse contour analysis or pulse power analysis) or non invasive cardiac output monitor (esophageal Doppler or bioreactance).

In this case, stroke volume can be optimized using the NICE protocol\textsuperscript{27} released in March 2011 by the National Health Service in the UK (see figure 4) or in conjunction with SVV or PPV monitoring (see figure 5). If only pulse pressure variation is monitored, a PPV minimization protocol aiming at keeping PPV below 13 % can be used (Figure 5).

In all cases, standard hemodynamic management for arterial pressure, urine output and heart rate must be respected.
Conclusion

We believe that GDT is a powerful clinical approach for managing critically ill patients. Evidence supporting the role of GDT in improving patient outcomes is becoming well-established. Further implementation of protocols of GDT will likely provide consolidation and streamlining of care for the patients by minimizing variability in clinical practice. This also has potential for improving resource utilization while implementing evidenced-based medicine.

References

27. NICE draft guidance on cardiac output monitoring device published for consultation [http://www.nice.org.uk/newsroom/pressreleases/DraftGuidanceOnCardiacOutputMonitoringDevice.jsp]
Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock

Goal-Directed Hemodynamic Management in the Emergency Department (ED)
Standardized algorithms are used in the ED and early ICU setting that to assist the clinician to apply timely evidence based therapy for acute myocardial infarction, stroke and trauma. A similar approach with sepsis originated when a randomized trial was conducted and published in 2001. This trial, which compared early goal-directed therapy (EGDT) versus standard care, was performed using specific criteria for the early risk stratification of septic patients (lactate), timely antibiotic administration and source control. This was followed by a consensus-derived protocol to reverse the hemodynamic perturbations of hypovolemia (CVP), vasoregulation (MAP), anemia (hemoglobin), myocardial suppression (ScvO2) and increased metabolic demands (ScvO2).

Key Benefits of Goal-Directed Therapy in the Emergency Department
EGDT is associated with a significant reduction in vasopressor use, sudden cardiopulmonary complications, mechanical ventilation and mortality (16%) over standard care. Over the last decade multiple investigations have validated the end-points used in EGDT. In addition, over 54 studies comprising over 18,000 patients and 3 meta-analyses have repeatedly shown the same or better outcome benefits than the original study (18%) in patients of similar illness severity. This robust mortality reduction has also been accompanied with a modulation of systemic inflammation, decreases in the progression of organ failure, decreased health care resource consumption (20% decrease in hospital costs). EGDT is a similar paradigm to the management of acute myocardial infarction, stroke, trauma and can save 1 out of every 6 patients presenting with severe sepsis and septic shock.
References


Key Benefits of Goal-Directed Therapy in the Operating Room

Introduction
The need to optimally manage the cardiovascular system in surgical patients and the critically ill is well recognised. This involves the administration of intravenous fluids, often in combination with inotropes and vasopressor therapies. It is accepted practice to adjust the dose of such treatments in response to some form of end-point. This approach is used to help strike a balance between the harmful effects of hypovolaemia, fluid overload and myocardial ischaemia. Simple end-points include urine output, core-peripheral temperature gradient and Glasgow coma score. However, in the more complex high-risk surgical patient or during critical illness, advanced haemodynamic invasive monitoring techniques are also used. The basis for the use of Goal-Directed Haemodynamic Therapy (GDHT) is that cardiac output related parameters provide a more reliable guide to the requirements for fluid and inotropes than basic invasive monitoring such as arterial pressure and central venous pressure. Although a number of studies suggest this approach is beneficial, there is still no clear consensus on which end-points should be used and how. The aim of this presentation will be to explore the physiological basis for the use of GDHT and clarify the current evidence base for its use.

Intra-operative Oesophageal Doppler Guided Fluid Therapy
The use of oesophageal Doppler cardiac output measurement to guide intravenous fluid therapy is perhaps the simplest form of GDHT. This intra-operative use of this monitor has proved popular, in part because of the simplicity of the technique but also because the anaesthetist will generally be able to gain access to the head during surgery. A number of studies suggest this approach will result in a reduction in post-operative complications and therefore a reduced duration of hospital stay. On average, the use of oesophageal Doppler derived cardiac output measurement does seem to be associated with a larger volume of fluid administration. However, it is important to note the wide variation in the volume of fluid required. This variability in estimated fluid requirements would suggest that the benefit of this approach does not relate to the administration of extra fluid but to the use of an accurate estimate of fluid volume requirements in each individual patient.

The basis for the use of Goal-Directed Haemodynamic Therapy (GDHT) is that cardiac output related parameters provide a more reliable guide to the requirements for fluid and inotropes than basic invasive monitoring such as arterial pressure and central venous pressure.
Peri-operative GDHT

Peri-operative GDHT involves the use of intra-venous fluids as well as inotropic agents to achieve a predefined ‘optimal’ goal for oxygen delivery to the tissues. Oxygen delivery is a parameter which is calculated from measurements of cardiac output, haemoglobin concentration, SaO$_2$ and PaO$_2$. This approach was developed following the observation that when routine parameters such as blood pressure and urine output, were stabilized in all surgical patients, survivors had consistently higher cardiac output, oxygen delivery and oxygen consumption than those who subsequently died. The median values attained by the surviving patients in these observational studies were subsequently incorporated into Goal-Directed Therapy protocols as haemodynamic goals. A number of studies have suggested that Goal-Directed Therapy may significantly reduce post-operative complication rates. Originally, Goal-Directed Therapy required the insertion of a pulmonary artery catheter and was continued throughout the peri-operative period. However, more recent evidence suggests this technique is most beneficial when applied for short periods during and after surgery. This can be performed using one of a number of less invasive monitoring techniques now available. Significant reductions in complication rates, and in some cases mortality, have been achieved with the use of GDHT commencing both before and after surgery.

Early GDHT in Septic Shock

Recent work has suggested that the use of central venous saturation may be an easily measured but effective tool in the delivery GDHT to patients presenting with septic shock in the Emergency Department. In one prominent single centre trial, use of a six hour early GDHT protocol resulted in a significant reduction in mortality, primarily because of a reduction in the incidence of ‘cardiovascular collapse’ in the subsequent hours. The findings of this study are in stark contrast to those of trials of the sustained use of GDHT in patients with established critical illnesses over periods of several days. In this scenario, GDHT is ineffective and possibly harmful. This observation has helped to shed light on the mechanism of action of GDHT which is now generally considered to be most effective during short periods of haemodynamic resuscitation.

References

Key Benefits of Goal-Directed Therapy and Personal Approach for Goal-Directed Hemodynamic Management in the Intensive Care Unit

The initial management of the hemodynamically unstable patient is often poorly reasoned. If there is clear evidence of tissue hypoperfusion, as manifested by oliguria, tachycardia and hypotension, most physicians give an initial bolus of fluids to see if their patient is volume responsive. However, after this initial “knee jerk” response, if blood pressure does not immediately rise, a more thoughtful approach follows. Most of our patients in extremis are also intubated and on mechanical ventilation, usually without spontaneous ventilatory efforts. Though we try to lessen sedation and promote spontaneous ventilation once hemodynamically stable, this is not the case during the initial resuscitation. We use invasive arterial pressure monitoring in most of these patients allowing immediate access to direct measures of arterial pulse pressure variation (PPV). If PPV is >10% by direct measure it is our practice to repeat the volume challenge with 250-500 ml crystalloid and if it remains >10% despite persistent hypotension (MAP < 60 mmHg) we start norepinephrine and titrate it to achieve a MAP > 60 mm Hg while continuing fluid resuscitation in rapid sequential bolus fashion. Once arterial hypotension is reversed our goal is to sustain adequate peripheral blood flow. To that regard we measure urine output, serum lactate and central venous O₂ saturation by blood gas analysis, usually as a paired analysis with an arterial blood gas sample. This allows us to estimate an arterial to venous PCO₂ gradient as well as central venous O₂ saturation. If either ScvO₂ < 70% or the V-a PCO₂ gradient > 10 mm Hg we continue to give fluids as long as PPV > 10% and if < 10% dobutamine. About this time in the bedside management we are approximately 15-20 minutes into the resuscitation. If the patient is still requiring pressors and/or inotropes we then transduce the arterial pressure into cardiac output using a minimally invasive cardiac output monitor with the goal of increasing cardiac output and thus calculated oxygen delivery (DO₂) to >450 ml/min/M². If we were treating a high risk patient prior to major surgery then our DO₂ goal would be >600 ml/min/M². From that point on, all resuscitation becomes highly individualized based on ventilatory status, renal response to increasing flow, changes in ScvO₂ or V-a PCO₂ gradient and dynamic changes in serum lactate. Our goal is a fully stabilized non-acidotic non-tachycardiac patient making urine by 120 to 180 minutes into the resuscitation. Since care at this point becomes individualized, the use of echocardiography or other imagining tools are used to define diagnosis and guide therapy relative the patient’s underlying condition, surgery, if relevant, and response to therapy. In practice, most patients rapidly stabilize if their condition is primarily due to hypovolemia (slow hemorrhage), loss of vasmotor tone (sepsis) or left sided pump failure. Clearly, acute coronary insufficiency, massive pulmonary embolism, fat embolism and surgical bleeding need to be treated independent of these resuscitation efforts. Resuscitation may stabilize the patient’s cardiovascular status but does not treat the underlying cause of the cardiovascular instability. Still, using a thoughtful physiologic approach to first maintain arterial pressure to sustain vital organ perfusion and then optimize flow to support metabolism, most patients can be rapidly returned to a stable plane allowing a more detailed diagnostic approach to identifying the exact cause for the instability and tailoring targeted treatment.
Conventional Hemodynamic Monitoring Parameters: Central Venous Pressure and Heart Rate. Should There Be a Target?

Central Venous Pressure (CVP)
There is very little evidence that supports the use of central venous pressure (CVP) to guide fluid therapy and hemodynamic management. The assessment of volume status is a major problem in the perioperative setting and in intensive care units. Due to the inability to accurately assess severity of hypovolemia and the patient’s response to treatment, hemodynamic status is often misdiagnosed. The results are delays in treatment or erroneous treatment, both of which lead to poor clinical outcomes. The dilemma in assessment of hypovolemia arises from the inability to directly measure blood flow, specifically stroke volume. Stroke volume is the perhaps the parameter of interest when a patient has volume loss. Most other compensatory sign occurs because of the reduction in stroke volume; such signs include increased heart rate, decreased cardiac output, decreased urine output, increased oxygen extraction, and reduced blood pressure. Even parameters such as CVP, which ostensibly measures cardiac volume is not helpful because it is not volume that is important, but blood flow. It is the loss of blood flow that threatens patients’ outcomes.

Further, CVP and pulmonary artery occlusion pressure (PAOP) or “wedge” pressure were designed to estimate volume status of the right and left ventricles. Unfortunately, no study of CVP and PAOP has shown that those pressures correlate well with volume or flow status. In addition, CVP and PAOP do not reveal any information about stroke volume. A sophisticated approach of measuring separately total blood volume and circulating blood volume, using a dye dilution technique, also did not demonstrate any correlation between values of CVP and blood volume, total or circulating (possibly total and stressed volumes). Dramatic changes in systemic hemodynamics may not be associated with any significant changes in CVP, e.g., significant decrease in mean arterial pressure and cardiac output during high thoracocervical epidural and general anesthesia, or drastic changes in arterial pressure, vascular resistance and venous capacity induced by changes in pressure within the carotid sinuses, or a significant decrease in arterial resistance and an increase in cardiac output induced by an infusion of prostaglandin E1 were not associated with any significant changes in CVP.

Values of intramural or even transmural central venous pressure (CVP) as well as values of pulmonary artery occluded pressure do not correlate with the values of measured circulating blood volume or with responsiveness to fluid challenge. The veins contain approximately 70% of the total blood volume and are 30 times more compliant than arteries, therefore, changes in blood volume within the veins are associated with relatively small changes in venous pressure. The main reason for a lack of correlation between CVP values and blood volume is that the body does everything possible to maintain homeostasis and

Marik et al in an excellent meta-analysis, recently recommended that CVP not even be used in intensive care units, emergency departments, and operating rooms because of its lack of accuracy.
adequate transmural CVP is a must for cardiovascular function. The most accurate measurement of volume status would be the mean circulatory filling pressure (MCFP), which cannot be measured in a clinical setting.

Marik et al in an excellent meta-analysis, recently recommended that CVP not even be used in intensive care units, emergency departments, and operating rooms because of its lack of accuracy. As demonstrated by this study, only about a half of patients administered a fluid bolus will demonstrate a positive hemodynamic response to the intervention. With an ROC of 0.56, the play of coin-toss will be as helpful as CVP in predicting which patients will respond to a fluid challenge. If fluid resuscitation is guided by CVP, it is likely that patients will have volume overload and pulmonary edema. Insufficient data exists demonstrating any benefit of using CVP as a target for achieving goal-directed hemodynamic management, or for improving patient outcomes.

Heart Rate

Elevated perioperative heart rate, an absolute increase in heart rate and heart rate lability have been suggested as independent predictors of both short- and long-term adverse outcomes in patients at cardiovascular risk undergoing major noncardiac surgery. Although prospective nonrandomized and retrospective data suggest heart rate control improves perioperative outcome, there is conflicting evidence from randomized trials that perioperative heart rate control improves outcome. This may be because drug-associated bradycardia influences mortality in the perioperative period. Therefore, any bradycardic manipulation of heart rate in the perioperative period must be accompanied by simultaneous attention to other physiological variables associated with increased morbidity and mortality. In a prospective randomized trial examining the efficacy of preoperative cardiac investigations in intermediate-risk vascular patients, all patients received beta-blockers as part of the protocol. A preoperative heart rate <65 beats.min-1 was associated with a decreased 30-day postoperative cardiac death or nonfatal myocardial infarction (OR 0.24, 95% CI 0.09 to 0.66, P=0.003) following vascular surgery. The incidence of the primary outcome was 5.2% in the group where the preoperative heart rate exceeded 65 beats.min-1.

Intraoperative studies suggest that a sustained elevated heart rate is associated with adverse short-term outcomes, while an elevated heart rate is associated with increased long-term mortality. In prolonged major vascular, major orthopedic, major urological, major gynecological and major general surgical procedure lasting more than 220 minutes, with median age 60 (interquartile range of 43 to 73 years) a median heart rate of >110 beats.min-1 for a five minute epoch resulted in a prolonged hospital stay associated with a morbid condition or in-hospital death (OR 2.7, P=0.01).

However, in patients undergoing surgery with an expected hospital stay of at least two days, intraoperative heart rate >120 beats.min-1 at any point intra-operatively was not predictive of postoperative myocardial ischemia. A fundamental difference with this studies definition of tachycardia and the previous studies discussed is that the previous studies suggest the importance of a time epoch of 5 or 10 minutes. This observation suggests that a sustained elevated heart rate is probably more important than merely an observed tachycardia, which may have been of short duration. Conversely, as opposed to the associated adverse in-hospital outcomes reported with a sustained intra-operative tachycardia, there appears to be an improved outcome associated with a lower intra-operative heart rate. Indeed, an increase in the lowest recorded intra-operative heart rate of surgical colectomy patients was shown to be an independent predictor of major surgical complications and death when adjusted for both pre- and intra-operative variables (OR 1.06, 95% CI 1.03 to 1.08, P <0.0001). An important study by Raby and colleagues showed that the use of esmolol to maintain a postoperative heart rate 20% below a Holter determined ischemic threshold decreased postoperative myocardial ischemia (RR 0.08, 95% CI 0.01 to 0.55, P <0.0001). Despite the obvious efficacy of beta-adrenergic blockade in decreasing myocardial ischemia, there is conflicting evidence from randomized prospective studies about whether heart rate control with beta-blockers is associated with an improved cardiac outcome.
References


What Do You Consider the Key Benefits of Goal-Directed Therapy in the Intensive Care Unit?

Goal-Directed Therapy (GDT) in the intensive care unit (ICU) is absolutely necessary and should not be limited to the use of “Early-Goal Directed Therapy for the Treatment of Sepsis and Septic Shock.” Patients arrive in the ICU in varying states of critical illness and medical complexity. Without clearly defined goals, whatever they may be, the patient, their family, and clinical providers will not have a clear objective upon which to apply their energy. For example, a patient arrives in the ICU with a presumed pneumonia in respiratory distress. The patient needs to be assessed, examined, admitted and stabilized. The family needs to be notified and have their needs addressed. In all of this activity, the patient’s presumed infection needs to be treated with the appropriate antibiotic coverage within 1 hour. This can have a significant impact upon patient mortality. Without goals upon which to focus our attention can be scattered. We need to cool patients to our ‘goal’ temperature quickly after cardiac arrest or stroke or brain injury. Seizing upon the “golden hour after heart attack” is certainly an example of ‘goal directed therapy’ in the ICU or ED. The benefits of goal directed are unified approach to a problem, facilitated communication, rapid reversal of pathophysiology (while still reversible) and improved morbidity and mortality for out patients.

What is Your Personal Approach for Goal-Directed Hemodynamic Management in the Intensive Care Unit?

My approach to Goal-Directed Hemodynamic management is one of using all the data that is available to me in a dynamic way at all times. I try to avoid the use of static hemodynamic parameters in isolation. For example, when using an arterial line for the assessment of adequacy of resuscitation or fluid responsiveness, I like to couple it with the respiro-phasic interactions (with the ventilator) or a straight leg lift. When using IVC diameter to assess volume status, I like to couple it with the same respiro-phasic interactions, either with the ventilator or a “sniff” test. These evocative maneuvers allow the clinician to assess their patients in a dynamic and non-static fashion. The system’s response to perturbation can be very telling. When using some of our more “traditional” hemodynamic parameters, I like to assess the “numbers” and then perturb the hemodynamics with volume, pressor, inotrope or vasodilator and see the response. The human cardiovascular system is not simple so should not be treated as such.
Key Benefits of Goal-Directed Therapy in the Operating Room

Goal-directed fluid and hemodynamic management (GDT) has been shown to benefit patients undergoing major surgery.\textsuperscript{1,2} It is particularly valuable when provided early: in the operating room during surgery, or even before, if possible. Based on the work of Shoemaker, who proposed benefits of maximizing tissue oxygen delivery,\textsuperscript{3} and Rivers, who demonstrated benefits of early GDT in sepsis,\textsuperscript{4} the anesthesiology and surgical communities are progressively accepting and applying GDT concepts to intraoperative care. It is generally accepted that either too little or too much fluid perioperatively is potentially harmful. Too little fluid results in poor tissue perfusion, with potential ischemic injury to vital organs such as the kidneys, liver, and bowel. Too much fluid results in airway edema, bowel edema, increased lung water, and increased risk for heart failure. Tailoring the fluid and hemodynamic management to individual patients and circumstances not only makes good medical sense, but also consistently results in fewer complications, shorter ICU length of stay, and shorter hospital length of stay.\textsuperscript{1,2} Tissue ischemia and injury result in local inflammation and edema, themselves impairing tissue perfusion and oxygenation. Providing GDT early, in the operating room, has the benefit of assuring good tissue perfusion and oxygenation at the outset, before tissue ischemia and injury may occur. Playing “catch-up” after damage has been done results in suboptimal outcome. Early, proactive perioperative GDT results in benefits lasting into the postoperative period, perhaps for years.\textsuperscript{5}

Goal-directed fluid and hemodynamic management involves the use of parameters in addition to basic vital signs such as heart rate and blood pressure to guide therapy. These may include central venous oxygenation, dynamic indices such as stroke volume variation (SVV) and pulse pressure variation (PPV), and cardiac stroke volume (SV) or output (CO). Therapy consists of a combination of adjustments in fluid administration, fluid boluses, and inotropic support. This author prefers to use dynamic parameters when available and appropriate, as they are the most reliable indicators of fluid responsiveness.\textsuperscript{6} When SVV or PPV are not appropriate (e.g. TV<8ml/kg, open chest, atrial fibrillation) SV is used. Optimizing fluid status prior to using inotropes and vasopressors is preferred by this author, administering 250-500ml colloid boluses until either SVV<13%, or SV does not increase. If SV index is low (e.g. <35ml/m2) despite adequate volume administration, an inotrope such as dobutamine or dopamine is considered along with investigation into the cause and extent of cardiac dysfunction (e.g. TEE/TTE). Importantly, the goals and fluid administration are adjusted according to the clinical situation. There may be a price to be paid for excessive fluid administration,\textsuperscript{7} as in lung surgery, so patient and surgical factors are carefully considered when fluid boluses and inotropes are used. This author strongly prefers starting GDT very early (at or before anesthetic induction). In off-pump coronary surgery, colloid fluid boluses are given early, both to assess response, and to prepare the patient for heart manipulations and their associated detrimental hemodynamic effects.
2\textsuperscript{nd} Goal-Directed Therapy Symposium

References


Key Components of Patient Blood Management

Given a growing body of evidence, allogeneic blood transfusion is faced with increasing scrutiny. It is becoming apparent that the risks associated with blood transfusion are not outweighed by the potential benefits in many patients who are routinely transfused. Studies have shown that clinical outcomes in patients who are treated without (or with less) allogeneic blood transfusion are often comparable or better than the outcomes of similar patients who are transfused or receive more blood. As such, “restrictive” transfusion strategies are being increasingly recommended by practice guidelines.1-3 Nonetheless, there has been a need for a more systematic approach with emphasis on improving patient outcomes (as opposed to mere focusing on usage of blood components). Patient Blood Management (PBM) is poised to meet this need.

Patient blood management has recently been recognized by the World Health Organization (WHO) as a means to “promote the availability of transfusion alternatives.” However, the scope of PBM goes beyond transfusions as reflected by its definition: the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome. This definition is derived from the observation that the vast majority of transfusions in perioperative period can be attributed to low preoperative hemoglobin levels, excessive surgical blood loss, and inappropriate transfusion practices. Accordingly, perioperative blood management (PBM) relies on three key strategies, which are commonly referred to as the “pillars” of PBM:

- Optimizing hematopoiesis
- Minimizing bleeding and blood loss, and
- Harnessing and optimizing physiological “tolerance” of anemia through application of all available modalities, leaving transfusion as the last resort.4

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The strategies utilized in PBM are broad and can span every stage of care of a patient; therefore, successful implementation of PBM often requires multidisciplinary teamwork using a combination of interventions (e.g. pharmacologic therapy and point of care testing). The treating clinician should assume a proactive role in applying PBM strategies to individual patient’s care, exercise clinical judgment, be prepared to modify routine practices (e.g. transfusion triggers) when appropriate, and anticipate and be prepared to address complications. A plan of proactive management for avoiding and controlling blood loss tailored to the clinical management of individual patients, including expected procedures should be formulated.5
Preventive measures play a key role in PBM. Whenever possible, planning and preparation in advance is needed to optimize the patient’s condition (e.g., treatment of anemia, adjustment of the dose of anticoagulant and anti-platelet agents). Similarly, detailed planning of procedures can result in more efficient management of the patient’s condition and less blood loss. For emergent and urgent cases, it is recommended that a general management plan for rapid control of bleeding and possibly transferring to an appropriate center is established in advance. Finally, integration of the PBM strategies as part of a hospital-wide program and establishment of effective data collection and monitoring systems for continuous evaluation and improvement of practices should be considered and implemented.

Throughout the care, judicious use of allogeneic blood components, in accordance with current guidelines will improve patient outcome. The guidelines all emphasize that blood products should be transfused when “clear” physiologic need exists, rather than blindly based on arbitrary hemoglobin or hematocrit “triggers.” The goal should be improving the patient’s health, rather than attaining a certain hemoglobin level.

In the preoperative period, detailed history taking, physical examination and current medications with special emphasis on risk factors for anemia and bleeding is very important. Anemia is not only a major risk factor for transfusion, but it is also an independent predictor of morbidity and mortality, and patients should be monitored for anemia throughout their course of care, particularly before surgery. Management of anemia consists of treating the underlying cause and use of appropriate hematinic agents to rapidly restore hemoglobin levels to normal by the time of surgery. Untreated anemia should be regarded as a contraindication of elective surgery.

PBM strategies during surgery generally focus on minimizing blood loss (e.g., using various systemic and topical hemostatic agents), autotransfusion techniques (e.g., acute normovolemic hemodilution and cell salvage), and optimizing physiologic “tolerance” of anemia, i.e., treating postoperative anemia with the appropriate medications. Vital signs should be closely monitored and unnecessary hypovolemia and tachycardia should be avoided.

PBM strategies continue after the surgery into the postoperative care unit and beyond. Blood salvage can be performed postoperatively. During the first few hours following the surgery, close attention must be given to continued blood loss, and the patient should be returned to the operating room for re-exploration promptly if bleeding persists. Again, vital signs must be thoughtfully monitored and cardiac output and ventilation/oxygenation should be optimized.

The clinical outcome of patients is the ultimate endpoint of interest and all treatments should be evaluated for their effect on improving patients’ outcomes. Lastly, emphasis on the appropriate use of blood components with the ultimate goal of improving patient outcomes using multimodality approaches remains a challenge. PBM modalities span every step in the care of patients and they include various pharmacologic, anesthetic, and surgical interventions. As mentioned above, when considering the use of any blood products, the physiologic need and expected benefit as well as the potential adverse effect on the outcome of the patients should be considered, rather than arbitrary threshold values of hemoglobin or hematocrit. Although the safety and efficacy of various modalities used in patient blood management should be evaluated individually, emerging data support PBM as a safe and effective concept in providing better care and improving patients’ outcomes while reducing transfusion of allogeneic blood components.

References
Perioperative Hemodynamic Optimization and Enhanced Surgical Recovery Program: A Quality Improvement Perspective

A well tailored anesthetic is key to optimal recovery from surgery. Fluid management, an inherent function of providing anesthesia care, has been a subject of great controversy in the past. With the availability of less invasive hemodynamic monitoring techniques (esophageal doppler, arterial waveform analysis), reliance on physiologic variables to guide perioperative fluid management has become more common. The results of systematic reviews show an impressive 37% decrease in mortality and 2-3 day reduction in hospital stay with this approach in high risk patients. Based on staggering evidence in favor of using physiologic variables to guide fluid therapy, we are implementing a quality initiative at UC Irvine using this approach as a part of our enhanced surgical recovery program. The program includes a pre implementation survey (pretest) to indentify gaps in knowledge. This will be followed by a multi-module training program with geared to enhance provider knowledge and experience in evaluating hemodynamic, macro and micro circulation, monitoring techniques, fluid management and goal directed fluid therapy (GDT). Use of simulation, coaching by experts, and availability of point of care decision support are essential parts of the program. The goal of the program is to provide a standardized approach to fluid management aimed at optimizing outcomes. A post implementation validation study and an evaluation of impact and sustainability will also be performed. The main challenge for a program like this is buy in from the surgeon and nurses and continuing GDT post operatively. However, we view this intervention very timely in the face of favorable medical evidence, changes in health care payment putting pressure on hospitals to decrease the length of stay, post op complications and readmission rates, and the expansion of the perioperative role of anesthesiologists (surgical home concept as promoted by the ASA).