Impact of Goal-Directed Perioperative Fluid Management in High-Risk Surgical Procedures: A Literature Review

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Guidelines for the perioperative administration of fluid are often based on static hemodynamic targets such as central venous pressure, and delayed volume status indexes such as blood pressure, heart rate, capillary refill, and urine output. Traditional fluid management protocols also rely heavily on algorithmic estimates of fluid deficit, intravascular fluid volume status, fluid loss, and basal fluid requirements to guide perioperative fluid administration. Such formulaic approaches lack definitive physiologic endpoints for determining fluid optimization and fail to address the roles of tissue oxygenation and end-organ perfusion in achieving positive long-term patient outcomes. Recent advances in hemodynamic monitoring have produced sophisticated dynamic measures of volume status, such as stroke volume variation and pulse pressure variation, which may serve as functional indexes for perioperative fluid administration.

This article reviews randomized controlled trials measuring the impact of perioperative goal-directed therapy on outcomes among patients undergoing high-risk surgical procedures. A broad literature search was conducted, and 12 studies met the inclusion criteria. Studies were evaluated for design, population, goal-directed therapy targets, monitoring devices used, clinical endpoints, methods, and results. Goal-directed therapy was associated with decreased hospital stay compared with the control group (in 7 studies) and reduced number of postoperative complications (7 studies).

Keywords: Fluid management, goal-directed therapy, hemodynamic monitoring, optimization, perioperative.

Meticulous perioperative administration of intravenous fluids and blood products is an integral part of anesthesia practice. Conventional fluid management approaches have used formulas and fixed-volume methods to maintain physiologic stability by calculating patients' basal fluid requirements, estimating their preoperative fluid deficits, assessing clinical and diagnostic indicators of volume status, managing effects of anesthetic agents on venous capacitance, and anticipating blood and fluid losses based on type and duration of surgery. Anesthesia providers integrate these inputs with static and dynamic intraoperative indicators such as mean arterial pressure, heart rate, central venous pressure, urine output, actual blood loss, and arterial blood gas analyses to guide their perioperative fluid therapy.[1,2] Despite the historical safety and efficacy of such approaches, recent improvements in minimally invasive hemodynamic monitoring modalities, along with an increased focus on outcome-driven anesthesia, have prompted a surge of renewed interest among anesthesia providers in identifying the safest and most effective approaches toward perioperative fluid management, particularly of high-risk or medically complex patients undergoing major surgical procedures.[3]

Primary research efforts over the past 2 decades have highlighted the emergence of goal-directed therapies (GDT), a spectrum of fluid management strategies that use patient-specific hemodynamic outcomes to optimize physiologic stability, cardiovascular volume, tissue oxygenation, nutrient delivery, microvascular flow, and end-organ perfusion while minimizing the long-term sequelae associated with perioperative fluid volume depletion or overload.[4-6] The aim of this article is to review recent, methodologically sound literature that compares conventional perioperative fluid management with GDT strategies to determine best outcomes in patients undergoing high-risk surgical procedures.

Methods

A broad literature review was conducted using 3 electronic databases: MEDLINE/PubMed, The Cochrane Library, and Cumulative Index to Nursing & Allied Health Literature. The authors used the following search terms: *perioperative, goal-directed, fluid management, hemodynamic monitoring, fluid optimization*, and *intraoperative*. Search results were filtered by date (January 1, 1990, to May 1, 2012) and study design (randomized controlled human trials). Results were further narrowed by excluding trials of critical care patients outside the perioperative arena, and trials comparing fixed-volume fluid management approaches with other fixed-volume

strategies. All remaining search results yielded studies of patients undergoing high-risk surgical procedures. Twelve studies were analyzed for study design, patient population, targets of control strategies and GDT, monitoring devices used, measured clinical endpoints, and results (Table 1). All studies had clearly stated research questions and objectives, well-defined inclusion and exclusion criteria, reproducible intervention strategies, and objective outcome measures. Studies also were evaluated for methodologic quality using these and other parameters derived from guidelines for rating of evidence, such as randomization techniques, presence of double blinding, sufficient study power, subject withdrawal or loss to follow-up, and intent-to-treat analysis.[7-11] A Jadad score was calculated for each study based on an instrument validated by Jadad et al[12] as a measure of evidence quality for each study (Table 1). The Jadad score provides a bias assessment by scoring 3 parameters: randomization, double blinding, and description of withdrawals and dropouts. Research studies were scored from 0 to 5, with 5 representing the least biased study. One point was given for each of the 3 parameters addressed; 1 point was added for adequate description of an appropriate method of randomization sequence generation and/or an appropriate blinding technique; and 1 point was deducted for description of inappropriate method of randomization and/or inappropriate blinding technique.[12] All studies represented level 2 evidence, and all are generalizable to patients undergoing high-risk surgical procedures.[13] Studies were also evaluated in terms of limitations (Table 2).[14] Additional studies are cited for historical context.

History and Review of the Literature

Early research efforts aimed at identifying meaningful goals for targeted fluid therapy were introduced during the latter half of the 1980s and into the mid-1990s in response to growing awareness of the limitations of conventional perioperative fluid therapy. Particularly in high-risk surgical and critical care patients, traditional perioperative fluid management strategies failed to address tissue oxygenation and metabolic demands without contributing to fluid volume impairment or metabolic derangements.[2,15,16] Despite scientific advances in cellular physiology contributing to increased knowledge of metabolic tissue stress during surgery and need for altered fluid and blood delivery targets, the primary hemodynamic monitoring modality clinically available during the early 1990s was the thermodilutional pulmonary artery catheter (PAC).[17,18] The highly invasive nature of the PAC necessarily limited its use to critically ill patients in whom the benefits of hemodynamic monitoring clearly outweighed the risks of placement.[19] Furthermore, lack of use in patients with normal cardiovascular physiology led to uncertainty regarding optimal hemodynamic endpoints.[16]

The introduction of the esophageal Doppler monitor (EDM) into mainstream clinical practice in the early portion of the 21st century provided a less invasive means for measuring central hemodynamic indexes. This technique also helped generate a wave of research efforts aimed at defining targets for GDT among a variety of patients undergoing high-risk surgical procedures who might not otherwise have met the risk-benefit qualifications for receiving a PAC.[20-22] The studies selected for review in this article reflect the increasing array of minimally invasive hemodynamic monitoring devices introduced in the past decade, such as the FloTrac sensor and Vigileo monitor hemodynamic monitoring system (Edwards Lifesciences), the LiDCO plus/PulseCO hemodynamic monitoring system (LiDCO Ltd), and the PiCCO plus hemodynamic monitor (Pulsion Medical Systems AG).[23,24] These studies emphasize the importance of using measurable "flow-related" indexes rather than standardized formulas to optimize individual patient volume status and end-organ perfusion and to mitigate the complications associated with poorly managed perioperative fluid therapy. Such complications include hypovolemia, metabolic derangements, fluid overload, cardiovascular compromise, decreased tissue oxygenation, pulmonary edema, prolonged mechanical ventilation, and organ dysfunction or failure.[25,26]

Discussion of State of the Art: Goal-Directed Therapy and Anesthesia Management

The emerging body of research on GDT indicates that targeted fluid management strategies improve perfusion, total volume status, and cellular oxygen delivery, thus reducing perioperative complications and improving patient outcomes among high-risk surgical patients.[27,28] The work of Cecconi et al[23] stresses that "high risk patients" include not only those at risk of mortality, but those whose baseline physiologic status or planned surgical procedures place them at risk of all perioperative complications. Evaluation of the study articles revealed several GDT strategies and real-time hemodynamic monitoring technologies that are clinically available and used extensively in many hospitals and practice settings. By employing these technologies and tailoring perioperative fluid therapy to achieve individualized hemodynamic endpoints, the anesthesia provider can optimize hemodynamic volume, intravascular flow, and tissue oxygen delivery (Figure).

- ***Pulse Contour and Arterial Waveform Analyses.*** Pulse contour and arterial waveform analysis technologies use software-based monitoring systems to integrate arterial waveform or pulse oximetry plethysmography inputs with end-tidal capnography data of mechanically ventilated patients. These systems provide a means for calculating measures of fluid-responsive hypovolemia, such as stroke volume variation (SVV), systolic pressure

variation (SPV), pulse pressure variation, and pleth variability index.[1] The concept of fluid-responsive hypovolemia relates to the Frank-Starling law of the heart, which states that up to a certain point along a defined volume/pressure curve, increased preload (left ventricular end diastolic volume) causes myocardial wall stretch, which contributes to increased cardiac contractility, increased stroke volume, and therefore increased cardiac output (CO). During hypovolemic states, the heart is at the "responsive" end of the Frank-Starling curve and (in the absence of wall motion abnormalities or ventricular dysfunction) should respond to fluid administration by increasing contractility and CO. In the presence of adequate ventricular volume, the heart is at the "unresponsive" end of the Frank-Starling curve and has maximized stretch-related contractility; further fluid administration will only overload the heart.[1] The measurement of hemodynamic waveforms over the respiratory cycle provides a surrogate indicator of CO variability related to positive pressure ventilation. The increased intrathoracic pressure associated with each positive pressure inhalation decreases left ventricular preload; the subsequent decrease in intrathoracic pressure upon mechanical exhalation provides a "test" of volume responsiveness by flooding the heart with a "bolus" of venous return. If stroke volume and, therefore, CO and systolic pressure increase, a respiratory cycle variation is noted in the hemodynamic waveform, and the degree of variability indicates the degree of fluid-responsive hypovolemia.[1,29]

By providing measures of fluid-responsive hypovolemia (Table 3), devices such as the FloTrac/Vigileo and the PiCCO plus allow the anesthesia provider prediction of fluid-responsive hypovolemic states. The higher the SVV, the more likely the patient is to respond to changes in preload.[1,30] These systems can also provide hemodynamic indexes such as stroke volume, oxygen delivery index (Do_2I), and CO when combined with appropriate bedside monitoring devices and given inputs, including patients' hemoglobin and arterial oxygen saturation (Sao_2) concentrations.[30]

Cecconi et al[23] demonstrated a decrease in major cardiac complications, an increase in total intraoperative fluid administration and intraoperative urine output, and no statistically significant change in time to hospital discharge among patients in the GDT group compared with the control group. Their target hemodynamic endpoints were to maximize stroke volume and to maintain Do_2I above 600 mL/min/m^2. They employed a GDT strategy involving the administration of colloid boluses to maximize stroke volume and the infusion of a positive inotropic agent to augment Do_2I if the target Do_2I was not obtained when maximal stroke volume was achieved.[23] Their GDT protocol included a transfusion threshold to maintain a hemoglobin concentration greater than 10 g/dL in the GDT group, thus mitigating the effects of anemia on Do_2I.[23] The FloTrac/Vigileo system that Cecconi et al used derives the Do_2I by combining patient hemoglobin and Sao_2 inputs with measured values by using the standard equation: $Do_2I = Cao_2 \times CI \times 10$, where Cao_2 indicates arterial oxygen content and CI indicates cardiac index.[23,31,32] Normal resting values for Do_2I range from 400 to 650 mL/min/m^2; many GDT protocols aim to achieve a target Do_2I of 600 mL/min/m^2 to optimize oxygen delivery in the context of increased oxygen consumption (eg, surgical stress, painful or noxious stimuli, critical illness).[23,31-34]

Lopes et al[35] used pulse contour analysis to integrate arterial waveform data with end-tidal capnography to calculate changes in pulse pressure. By administering colloid boluses to maintain the GDT group at a target of less than 10% of changes in pulse pressure, the researchers increased the total intraoperative fluid volume administered and decreased length of hospital stay in the GDT compared with the control group.[35] Mayer et al[36] set target hemodynamic goals of stroke volume index (SVI) greater than 35 mL/m^2 and cardiac index greater than 2.5 L/min/m^2 among patients at high cardiac risk who were undergoing major abdominal surgery. By optimizing these hemodynamic parameters in the GDT group, Mayer et al[36] demonstrated a statistically significant decrease in perioperative complications, a reduced duration of hospital stay, an increase in colloid administration, and a decrease in crystalloid administration with no significant difference in total fluid volume administration compared with the control group.

• ***Dilutional Analyses.*** The archetypical dilutional monitoring device is the thermodilutional PAC, which calculates hemodynamic parameters based on the thermodilution of a fixed volume of a chilled saline injectate. The LiDCO plus system uses the foundational hemodynamic monitoring principles of the thermodilutional PAC and applies them to the arterial catheter with a chemical dilution technique. Using lithium chloride as an indicator, the LiDCO plus derives real-time hemodynamic parameters such as CO from the area beneath the lithium concentration-time curve.[37] The accompanying PulseCO software system applies pulse contour analysis to the arterial waveform to calculate SVV, heart rate variation, SPV, and other hemodynamic measures of fluid-responsiveness.[37] With the input of venous oxygen saturation values from venous blood gas analyses, the PulseCO also provides Do_2I and measures of oxygen consumption. These indicators are particularly valuable in the perioperative period, where surgical stress can contribute to profound changes in perfusion and metabolic demand.[28]

The PiCCO plus hemodynamic monitor uses both thermodilution and pulse waveform analysis to provide measures such as CO, SVI, SVV, and SPV.[38] Buettner et al[24] used the PiCCO plus to evaluate SPV in patients un-

Source	Study design	Type of patients (n)	Goals of fluid strategy	Device used	Fluid strategy	Measured endpoints	Results	Jadad score[12]
Pulse contour and arterial waveform analysis								
Benes et al,[29] 2010	Prospective single-center RCT	High-risk patients undergoing major abdominal surgery with anticipated operation time > 120 min or anticipated blood loss > 1,000 mL (n = 120)	• SVV < 10% (GDT) • CI 2.5-4 L/min/m^2 (GDT) • CVP 8-15 mm Hg (all) • MAP > 65 mm Hg (control) • UO > 0.5 mL/kg/h (control) • HR < 100/min (control)	• Arterial catheter with FloTrac/Vigileo device (Edwards Lifesciences) • CVC	• *Control:* Basal fluid replacement at 8 mL/kg/h of crystalloid. Fluid management at anesthesiologist's discretion to maintain MAP, CVP, and UO within goals. Transfusion of PRBCs to maintain hemoglobin > 90 g/L and of fresh frozen plasma in response to acute blood loss > 20% of calculated circulating blood volume. • *GDT:* Basal fluid replacement at 8 mL/kg/h of crystalloid. Measurement of baseline SVV and CI. If SVV > 10% and CVP < 15 mm Hg, bolus of 3 mL/kg of colloid administered over 5 min. If SVV < 10% or CI increased > 10% and CVP ↑ by 3 mm Hg, additional 250-mL colloid bolus administered. If SVV < 10% and CI ↓ or did not change from < 2.5 L/min/m^2, dobutamine infusion initiated to maintain CI between 2.5 and 4 L/min/m^2. If SVV < 10% and CI > 2.5 L/min/m^2, no change from control. SVV and CI monitored during next 5 min. Transfusion of PRBCs to maintain hemoglobin > 90 g/L and of fresh frozen plasma in response to acute blood loss > 20% of calculated circulating blood volume.	• Primary: Postoperative morbidity based on number of infections and other organ complications until POD 30 • Secondary: Hospital LOS, ICU LOS, all-cause mortality	• 48.5% ↓ in 30-day incidence of postoperative morbidity based on infections and other organ complications (P = .0033) • 55.8% ↓ in overall 30-day incidence of postoperative complications (P = .0066) • 1-day ↓ in median hospital LOS per protocol analysis (P = .0421); no significant difference in median hospital LOS ITT analysis (P = .0937) • No significant difference in ICU LOS (P = .789) or all-cause mortality (P > .99) • 425-mL ↑ in median intraoperative colloid administration (P < .003) • 42.8% ↓ in median number of intraoperative hypotensive events (P = .0001)	2
Cecconi et al,[23] 2011	Prospective single-center RCT	Patients undergoing total hip arthroplasty under spinal anesthesia (n = 40)	• MAP > 65 mm Hg (all) • Maximized stroke volume (GDT) • DO_2I > 600 mL/min/m^2 (GDT)	• Arterial catheter with FloTrac/Vigileo device	• *Control:* Crystalloid at 10 mL/kg/h started 30 min before induction and continued until end of surgery when rate ↓ to 100 mL/h. Initial bolus of 250 mL of colloid given before induction. Boluses of 250 mL of colloid if MAP < 65 mm Hg. Boluses of 10 mg of ephedrine at anesthesiologist's discretion for MAP < 65 mm Hg not responding to fluid challenge. • *GDT:* Crystalloid at 10 mL/kg/h started 30 min before induction and continued until end of surgery when rate ↓ to 100 mL/h. Step 1: Boluses of 250 mL of colloid administered up to a maximum of 25 mL/kg until stroke volume failed to ↑ by a factor of 10%. If maximum colloid administered, boluses of 250 mL of crystalloid administered. Step 2: If DO_2I at this point was < 600 mL/m^2, dobutamine started at 3 µg/kg/min and increased by 3 µg/kg/min every 20 min until DO_2I goal achieved. Transfusion used to achieve hemoglobin > 10 g/dL.	• Total fluid administered intraoperatively and for 1 h postoperatively • Minor postoperative complications (uncomplicated abdominal or urinary infection, hypotension, anemia) • Major postoperative complications (pneumonia, pulmonary embolism, tachyarrhythmias, ACS, renal)	• 3,397-mL ↑ in mean total intraoperative fluid volume (crystalloids, colloids, blood) (P < .0001) • 925-mL ↑ in median intraoperative UO (P < .0001) • No significant change in time to hospital discharge (P = .618) • 25% ↓ in incidence of minor postoperative complications (uncomplicated infections, hypotension, anemia) (P < .05) • No overall significant change in major postoperative complications (P = .076) • 25% ↓ in incidence of major cardiac complications (tachyarrhythmias, ACS; P < .05) • No mortality of patients within 28 d of enrollment	3
Forget et al,[26] 2010	Prospective single-center RCT	Patients undergoing major abdominal surgeries (n = 88)	• PVI < 13% (GDT) • MAP > 65 mm Hg (all) • CVP > 6 mm Hg (all)	• CVC • Arterial catheter • Pulse oximeter	• *Control:* Crystalloids, 500 mL, administered during induction of anesthesia, followed by a continuous infusion of crystalloids at 4-8 mL/kg/h. Colloid bolus administered for acute blood loss > 50 mL, MAP < 65 mm Hg, or CVP < 6 mm Hg. If desired criteria not met within 5 min after bolus, an additional colloid bolus administered. If MAP < 65 mm Hg unresponsive to fluid, norepinephrine titrated to maintain MAP > 65 mm Hg. • *GDT:* Crystalloids, 500 mL, administered during induction of anesthesia, followed by a continuous infusion of crystalloids 2 mL/kg/h. If PVI > 13% for > 5 min, 250 mL colloid bolus administered. Dose repeated every 5 min until goal of PVI < 13% met. Norepinephrine titrated to maintain MAP > 65 mm Hg.	Lactate levels as a surrogate indicator of organ perfusion, as measured by arterial blood gas analysis at time of incision, hourly intraoperatively, and at 6, 12, 24, 36, and 48 h postoperatively	• 452-mL ↓ in mean intraoperative crystalloid administration (P = .004) • 524-mL ↓ in mean mL of total intraoperative fluid volume administration (P = .049) • 25% median ↓ in maximum intraoperative lactate levels (P = .04); 22.2% median ↓ in lactate levels at 24 h (P = .02); 14.3% median ↓ in lactate levels at 48 h (P = .03) • 92.8% ↓ in incidence of high lactate levels (> 1.7 mmoL/L) at 24 h (P < .0001) and 100% ↓ in incidence of high lactate levels at 48 h (P = .003) • No significant difference in incidence of postoperative complications (infection, cardiovascular complications, coagulopathy, PONV, hemorrhage, anastomotic leak), morbidity, mortality, duration of mechanical ventilation, or LOS (P = .08-1)	2

Source	Study design	Type of patients (n)	Goals of fluid strategy	Device used	Fluid strategy	Measured endpoints	Results	Jadad score[12]
Lopes et al,[35] 2007	Prospective single-center RCT	Patients in ASA classes 2, 3, and 4 undergoing high-risk surgery (n = 33)	• ΔPP < 10% (GDT)	Arterial catheter and capnogram to measure PPV with positive pressure mechanical ventilation, where ΔPP = 100 × (PPmax – PPmin)/[(PPmax – PPmin)/2]	• *Control:* Standard fluid management at anesthesiologist's discretion • *GDT:* Boluses of colloid to maintain ΔPP ≤ 10%	• Primary: Hospital LOS • Secondary: Number of postoperative complications per patient, duration of mechanical ventilation, duration of ICU stay.	• 10-day ↓ in median hospital LOS ($P < .01$) • 64.1% ↓ in number of postoperative complications (infection, respiratory, cardiovascular, abdominal, coagulopathy, renal) per patient ($P < .05$) • 4-day ↓ in median duration of mechanical ventilation ($P < .05$) • 6-day ↓ in median ICU LOS ($P < .01$) • 172.6% ↑ in mean milliliters of total intraoperative fluid administration ($P < .0001$)	2
Mayer et al,[36] 2010	Prospective single-center RCT	High-risk patients (ASA 3 with 2 or more Lee Cardiac Risk Index factors) undergoing major abdominal surgery (n = 60)	• MAP 65-90 mm Hg (all) • CVP 8-12 mm Hg (control) • UO > 0.5 mL/kg/h (control) • CI ≥ 2.5 L/min/m^2 (GDT) • SVI > 35 mL/m^2 (GDT) • SVV < 12% (GDT)	• Arterial catheter with Flotrac/Vigileo Device • CVC	• *Control:* Crystalloid, 500 mL, administered for MAP < 65 or CVP < 8 mm Hg. If MAP, CVP, and UO within goal after fluid bolus, status reevaluated after 5 min. If MAP still < 65 mm Hg or CVP < 8 mm Hg, 250-mL colloid bolus administered. If MAP < 65 mm Hg or CVP < 8 mm Hg after initial colloid therapy, additional 250-mL colloid bolus administered or vasopressor/inotrope therapy (norepinephrine/dobutamine) initiated. Blood transfused for hemoglobin < 8 mg/dL. • *GDT:* If CI ≥ 2.5 L/min/m^2, MAP > 65 mm Hg, and SVI > 35 mL/m^2, no change from control. If CI ≥ 2.5 L/min/m^2 and MAP < 65 mm Hg, norepinephrine administered at 100 μg/h. If CI < 2.5 L//min/m^2, SVI < 35 mL/m^2, and SVV > 12%, 500 mL of crystalloid administered. If SVI then > 35 mL/m^2, status reevaluated after 5 min. If SVI < 35 mL/m^2, 250-mL colloid bolus administered. If SVI still < 35 mL/m^2, additional 250-mL colloid bolus administered. If CI < 2.5 L/min/m^2 and SVI > 35 mL/m^2, dobutamine, 50 mg/50 mL, administered at 10 mL/h and increased by 5 mL/h every 5 min to maintain CI ≥ 2.5 L/min/m^2. Blood transfused for hemoglobin < 8 mg/dL.	• Primary: Hospital LOS • Secondary: Incidence of perioperative complications, ICU LOS, amount and type of intraoperative fluids, amount and type of intraoperative vasoactive and positive inotropic support	• 4-day ↓ in median LOS ($P = .006$) • 65.3% ↓ in total number of complications (infection, respiratory, cardiovascular, abdominal, renal, hemorrhage, death) until hospital discharge ($P = .001$) • No significant difference in ICU LOS ($P = .70$) • No significant difference in postoperative mechanical ventilation ($P = .14$) • 371 mL ↑ in mean intraoperative colloid administration ($P = .006$) • 664 mL ↓ in mean intraoperative crystalloid administration ($P = .02$) • No significant difference in total fluids ($P = .95$) • 26.3 μg/kg/h ↑ in mean positive inotropic support with dobutamine ($P = .01$) • No significant difference in vasoactive treatment with norepinephrine, epinephrine, or nitrates	2
Dilutional analyses								
Buettner et al,[24] 2008	Prospective single-center RCT	ASA class 1, 2, and 3 patients undergoing major elective abdominal or gynecologic surgery with bowel resection and anticipated blood loss > 500 mL (n = 80)	• SPV < 10% (GDT) • MAP > 70 mm Hg (all)	• CVC • Arterial catheter with PiCCO plus (Pulsion Medical Systems AG) • LiMon finger clip (Pulsion Medical Systems AG) for measurement of indocyanine green plasma disappearance rate, a surrogate indicator of hepatosplanchnic blood flow • Tonometric gastric catheter to measure gastric mucosal perfusion	• *Control:* Standard fluid management at discretion of anesthesiologist blinded to SPV, SVV, $ScvO_2$, indocyanine green plasma disappearance rate, and PCO_2 gap data. • *GDT:* Fluid administered to maintain SPV < 10%. Blood products administered if clinically indicated and for hematocrit < 23%, platelet count < 100,000/L, PT > 1.5× control, aPTT > 1.5× control. Anesthesiologists for GDT group also blinded to ScvO2, indocyanine green plasma disappearance rate, and PCO_2 gap data.	• Duration of mechanical ventilation, ICU LOS, total hospital LOS, in-hospital mortality • Indocyanine green plasma disappearance rate • Indicators of oxygen transport and organ function ($ScvO_2$, lactate, bilirubin, and creatinine)	• No significant difference in duration of mechanical ventilation, ICU LOS, total hospital LOS, or incidence of in-hospital mortality • 1 mm Hg ↑ in median SPV in control group at 3 h ($P = .04$) and 3 mm Hg ↑ in median SPV in control group at 6 h ($P = .01$) • No significant difference in oxygen transport as measured by indocyanine green plasma disappearance rate and $ScvO_2$ • No significant difference in organ function as measured by lactate, bilirubin, and creatinine	1

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Source	Study design	Type of patients (n)	Goals of fluid strategy	Device used	Fluid strategy	Measured endpoints	Results	Jadad score[12]
Esophageal Doppler monitoring								
Challand et al,[27] 2012	Prospective single-center stratified RCT	• *Fit strata:* Patients undergoing major colorectal surgery whose oxygen consumption at anaerobic threshold with cardiopulmonary exercise test was > 11 mL O_2/kg/min (n = 123) • *Unfit strata:* Patients undergoing major colorectal surgery whose O_2 consumption at anaerobic threshold with cardiopulmonary exercise test was 8.0-10.9 mL O_2/kg/min (n = 56)	• Maximized stroke volume	Esophageal Doppler	• *Control:* If bowel preparation given, 1-2 L of crystalloid administered in the 12 h before surgery. Standard fluid therapy at discretion of anesthesiologist aiming for a maintenance rate of 10 mL/kg/h of crystalloid. • *GDT:* If bowel preparation given, 1-2 L of crystalloid administered in the 12 h before surgery. Baseline stroke volume measured. A 200-mL colloid challenge given over 5 min. If stroke volume ↑ by > 10%, a further bolus administered. If stroke volume did not ↑ by > 10%, stroke volume monitored and additional fluid boluses administered only if stroke volume ↓ by > 10%.	• Primary: Time of readiness for discharge as measured by predefined criteria • Secondary: Actual LOS, critical care admission, 30- and 90-day mortality, 30-day readmission rate	• *Fit:* 2.3 day ↑ in median time until readiness for discharge (P = .01) • *Unfit:* No significant difference in time until readiness for discharge (P = .47) • *Fit:* 2.8-day ↑ median LOS (P = .01) • *Unfit:* No significant difference in median LOS (P = .54) • *Fit:* 63.7% ↑ in incidence of critical care admission (P = .03) • *Unfit:* No significant difference in critical care admission (P = .8) • *Fit:* No significant difference in 30- and 90-day mortality and 30-day readmission rate (P = .36-.46) • *Unfit:* No significant difference in 30- and 90-day mortality and 30-day readmission rate (P = .59-.72) • *Inclusive* (both fit and unfit strata): No significant difference in time to readiness for discharge, median LOS, incidence of critical care admission, 30- and 90-day mortality and 30-day readmission rate (P = .09->.99)	4

Source	Study design	Type of patients (n)	Goals of fluid strategy	Device used	Fluid strategy	Measured endpoints	Results	Jadad score[12]
Gan et al,[5] 2002	Prospective single-center RCT	ASA class 1, 2, and 3 patients undergoing major elective general, urologic, gynecologic surgery with anticipated blood loss > 500 mL (n = 100)	• UO > 0.5 mL/kg/h (control) • FTc > 0.35 s (GDT) • Maximized stroke volume (GDT)	Esophageal Doppler	• *Control:* Fluid bolus of 5 mL/kg crystalloid before induction of anesthesia followed by crystalloid infusion at 5 mL/kg/h until end of surgery. Fluid administration at discretion of anesthesiologist blinded to Doppler data. Crystalloid, 200 mL, administered for UO < 0.5 mL/kg/h, ↑ in HR > 20/min above baseline or > 110/min, ↓ in BP < 20% below baseline or < 90 mm Hg, or CVP < 20% baseline until target restored to goal. Fluid boluses also administered at anesthesiologist's discretion if clinically indicated. Blood loss replaced 3:1 with crystalloid. Blood products administered when "clinically indicated" and for hematocrit < 23%, PT > 1.5× control, aPTT > 1.5× control, or fibrinogen < 100 mg/dL. • *GDT:* Fluid bolus of 5 mL/kg crystalloid before induction of anesthesia followed by crystalloid infusion at 5 mL/kg/h until surgery end. If FTc < 0.35 s, 200 mL of colloid administered. If FTc still < 0.35 s, repeat colloid bolus. If FTc > 0.35 s but ≤ 0.4 s and stroke volume increased > 10%, repeat colloid bolus. Additional colloid boluses as warranted up to max of 20 mL/kg of colloid if FTc ↓ to < 0.35 s or stroke volume decreased > 10%. Blood loss replaced 3:1 with crystalloid. Blood products administered when "clinically indicated" and for hematocrit < 23%, PT > 1.5× control, aPTT > 1.5× control, or fibrinogen < 100 mg/dL.	• Primary: Hospital LOS • Secondary: Postoperative surgical morbidity	• 2-day ↓ in mean LOS (P = .03) • 61.1% ↓ in incidence of PONV requiring rescue antiemetic (P < .05) • 1.7-day ↓ in mean time to toleration of oral solid regimen (P = .01) • 565 mL ↑ in mean intraoperative colloid administration (P < .01)	3
Noblett et al,[22] 2006	Prospective single center RCT	Patients undergoing colorectal resection (n = 103)	• FTc > 350 ms (GDT) • Maximized stroke volume (GDT)	Esophageal Doppler	• *Control:* Standard fluid and hemodynamic management at discretion of anesthesia provider blinded to Doppler data • *GDT:* Baseline FTc and stroke volume measured. If FTc < 350 ms, 7 mL/kg colloid bolus administered. If FTc > 350 ms but < 400 ms following bolus and stroke volume ↑ by > 10%, additional 3 mL/kg colloid bolus administered. If FTc > 350 ms but < 400 ms following bolus and stroke volume did not ↑ 10% OR if FTc > 400 ms with or without Δ in stroke volume, FTc and stroke volume monitored to maintain FTc > 350 ms and to prevent stroke volume ↓ > 10%.	• Primary: Hospital LOS • Secondary: Return of GI function, morbidity, critical care unit LOS, cytokine indicators of inflammation	• 2-day ↓ in median hospital LOS (P = .005) • 3-day ↓ in median readiness for discharge (P = .003) • No significant difference in return of GI function as measured by return of bowel movement (P = .709) • 2-day ↓ in median time to toleration of oral diet (P = .029) • 86.6% ↓ in incidence of intermediate or major postoperative complications (P = .043) • 6 patients in control group and 0 patients in GDT group required unplanned critical care admission (P = .012) • ↓ rise in perioperative cytokine interleukin 6 markers (P = .039)	4
Wakeling et al,[21] 2005	Prospective single-center RCT	Patients undergoing colorectal resection (n = 128)	• CVP 12-15 mm Hg (control) • Maximized stroke volume (GDT)	• Esophageal Doppler • CVC	• *Control:* Bowel preparation given and crystalloid, 1-2 L, administered overnight before surgery. Standard fluid management at discretion of anesthesiologist blinded to Doppler measurements to maintain CVP at 12-15 mm Hg. • *GDT:* Bowel preparation given and crystalloid, 1-2 L, administered overnight before surgery. Baseline CVP and stroke volume measured. Colloid 250-mL fluid challenge administered over 2 min. If stroke volume ↑ by ≥ 10% and CVP did not ↑ by 3 mm Hg within 5 min after fluid challenge, fluid challenge repeated. If stroke volume did not ↑ by 10% or CVP ↑ by ≥ 3 mm Hg, CVP and stroke volume measured every 10 min. Colloid 250-mL fluid boluses administered for 10% ↓ in stroke volume.	• Primary: Postoperative hospital LOS • Secondary: Time taken until patient able to tolerate full diet	• 1.5-day ↓ in median postoperative hospital stay (P = .031) • 1.5-day ↓ in median readiness for discharge (P = .012) • 1-day ↓ in median time to resumption of full diet (P < .001) • 68.8% ↓ in incidence of GI morbidity (P < .001) • 36.7% ↓ in total number of patients with complications (P = .013)	4
Measures of tissue oxygenation								
Donati et al,[6] 2007	Prospective multicenter RCT	ASA class 2, 3, and 4 patients undergoing major abdominal procedures at 9 hospitals (n = 135)	• MAP > 80 mm Hg until POD 1 (all) • UO > 0.5 mL/kg/h until POD 1 (all) • CVP 8-12 cm H_2O until POD 1 (all) • O_2ERe < 27% (GDT)	• CVC • Arterial catheter	• *Control:* Standard fluid management at anesthesiologist discretion to maintain MAP, UO, and CVP as described • *GDT:* If O_2ERe ≤ 27%, no change from control. If O_2ERe > 27% and CVP < 10 mm Hg, fluid challenge of colloids 250-1,000 mL infused over 30 min. If O_2ERe > 27% and CVP > 10 mm Hg, dobutamine in incremental doses of 3-15 µg/kg/min. If O_2ERe > 27% and hemoglobin < 10 g/dL or intraoperative blood loss > 1,000 mL, PRBCs.	• Primary: New postoperative organ failure described using a standardized scoring system • Secondary: Organ failures during ICU stay, hospital LOS, in-hospital mortality	• 60.4% ↓ in incidence of new postoperative organ failure (P < .05) • 66.6% ↓ in total number of organ failures (P < .001) • 2.1-day ↓ in mean LOS (P < .05) • No significant difference in in-hospital mortality	3

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Source	Study design	Type of patients (n)	Goals of fluid strategy	Device used	Fluid strategy	Measured endpoints	Results	Jadad score[12]
Jammer et al;[25] 2010	Prospective multicenter RCT	ASA class 1, 2, and 3 patients undergoing colorectal surgery at 2 hospitals (n = 241)	• UO > 0.5 mL/kg/h (all) • $ScvO_2$ > 75% (GDT)	CVC	• *Control:* Crystalloid 1,000 mL during first hour intraoperatively followed by 10-12 mL/kg/h to maintain UO as described. First 500 mL blood loss replaced 1:4 with crystalloid; blood loss > 500 mL replaced 1:1 with colloid. Blood transfusion and use of vasopressors at anesthesiologist's discretion. Colloid also given perioperatively or postoperatively when "considered necessary" for ↓ BP. Glucose 5%, 1,000 mL, prescribed postoperatively and "extra fluid" given postoperatively for clinical indicators of hypovolemia. Fluid managed by research protocol until 8 AM on POD 1. • *GDT:* If bowel preparation: 500 mL crystalloid bolus preoperatively. Maintained on crystalloid, 100 mL/h. If $ScvO_2$ ≥ 75%, no change from control; $ScvO_2$ rechecked every 60 min or with change in BP. If $ScvO_2$ < 75%, 3 mL/kg colloid over 10-15 min followed by repeat $ScvO_2$ analysis after 5 min. Blood loss replaced 1:1 with colloid. Blood transfusion and use of vasopressors at anesthesiologist's discretion. Maximum total colloid at 50 mL/kg/24 h. Postoperative glucose 5% at 80 mL/h. Postoperative loss from stomas or drains replaced with crystalloid 1:1. Extra fluid given for clinical signs of hypovolemia or $ScvO_2$ < 75%. Fluid managed by research protocol until 8 AM on POD 1.	• Primary: Postoperative complications within 30 d • Secondary: Postoperative serum creatinine, SpO_2 (measured on POD 1 after 5 min without supplemental oxygen), weight	• No significant difference in postoperative complications (OR = 0.98; 95% confidence interval 0.6-1.6) • No significant difference in serum creatinine (OR = 1.6; 95% confidence interval 0.6-4.3) • No significant difference in SpO_2 (P = .07) • 68% ↓ in mean kilograms of weight gain (P < .001) • 2,094-mL ↓ in mean perioperative Ringer's acetate administration (P < .001) • 79-mL ↑ in mean perioperative "other crystalloid" administration (P = .008) • 153-mL ↑ in mean perioperative colloid administration (P = .004) • 2,622-mL ↓ in mean total fluid administration until 8 AM on POD 1 (P < .001)	3

Table 1. Analysis of Studies Reviewed

Abbreviations: ACS, acute coronary syndrome; aPTT, activated partial thromboplastin time; BP, blood pressure; CI, cardiac index; CO_2, carbon dioxide; CVC, central venous catheter; CVP, central venous pressure; ΔPP, change in pulse pressure; DO_2I, oxygen delivery index; FTc, corrected flow time; GDT, goal directed therapy; GI, gastrointestinal; HR, heart rate; ICU, intensive care unit; ITT, intention-to-treat; LOS, length of stay; MAP, mean arterial pressure; O_2ERe, oxygen extraction ratio estimate; OR, odds ratio; PAC, pulmonary artery catheter; O_2, oxygen; PACU, postanesthesia recovery unit; PE, pulmonary embolism; POD, postoperative day; PONV, postoperative nausea and vomiting; PPmax, maximum pulse pressure; PPmin, minimum pulse pressure; PPV, pulse pressure variation; PRBCs, packed red blood cells; PT, prothrombin time; PVI, pleth variability index; RCT, randomized controlled trial; SaO_2, arterial oxygen saturation; $ScvO_2$, central venous oxygen saturation; SpO_2, pulse oximetry measure of blood oxygen saturation; SPV, systolic pressure variation;; SVI, stroke volume index; SVV, stroke volume variation; UO, urine output; ↑, increase; ↓, decrease.

dergoing major abdominal surgery. Patients in the GDT group received intraoperative fluid therapy guided by a target SPV below 10%. Central venous oxygen saturation ($ScvO_2$) was also used from central venous blood sample analysis as a surrogate measure of mixed venous oxygen saturation, or $S\bar{v}O_2$, and as an index of the adequacy of tissue oxygenation.[39] Buettner et al[24] demonstrated that by guiding intraoperative fluid therapy according to a target SPV, they were able to significantly reduce the degree of fluid-responsive hypovolemia in the GDT group, as measured by SPV at 3 hours postoperatively. No significant differences in duration of mechanical ventilation, duration of critical care stay, duration of hospital stay, and incidence of in-hospital mortality were identified between the GDT and control groups.[24]

• ***Esophageal Doppler Ultrasonography.*** The dual-sensor EDM uses ultrasound technology to transduce changes in pressure in the aorta over time. The EDM then provides a real-time measure of aortic pulse wave velocity as well as calculated hemodynamic indicators, including aortic compliance, stroke volume, and corrected flow time, a derived parameter based on heart rate correction which provides a surrogate measure of systemic vascular resistance and a parameter for indicating fluid-responsive hypovolemia.[5,20] Both Gan et al[5] and Noblett et al[22] used corrected flow time greater than 350 ms as their primary GDT target; both demonstrated decreased length of hospital stay and reduced postoperative complications in their respective GDT groups.

• ***Measures of Tissue Oxygenation.*** By using laboratory data derived from mixed venous blood samples to determine $ScvO_2$ and data derived from arterial blood samples to determine SaO_2, Donati et al[6] were able to calculate an oxygen extraction ratio estimate (O_2ERe) as a surrogate target endpoint for their multicenter GDT group to ensure adequate tissue oxygenation and end-organ perfusion among ASA class 2, 3, and 4 patients undergoing major abdominal procedures. Central venous oxygen saturation and its counterpoint, O_2ERe, are valuable real-time measures of tissue perfusion and metabolic demand; they are also important indicators of physiologic decompensation.[6,39]

In healthy individuals under normal conditions, $ScvO_2$ ranges from 70% to 80%; this reflects that 20% to 30% of DO_2I is extracted by the tissues (O_2ERe) to meet the metabolic demand, the oxygen consumption index ($\dot{V}O_2I$).[39] The normal compensatory cardiovascular response to increased $\dot{V}O_2I$ (due to exercise, stress, and pain) is to increase CO and O_2ERe to maintain DO_2I.

- Partial blinding or lack of blinding[5,6,21,24,26,29,35,36]
- Length of stay as an outcome metric is dependent on individual institutional protocol regarding discharge[5,6,21-24,29,35]
- Single-site study (possible source of systematic bias associated with institutional protocols or standards of care for perioperative and postoperative care and discharge planning)[5,21-24,26,29,35,36]
- Lack of predefined discharge criteria[29]
- Small sample size[23,24,35,36]
- Lack of intent-to-treat analysis (possible source of measurement bias)[10,24]
- Inclusion of only very physiologically high-risk patients limits generalizability to healthy patients undergoing high-risk procedures[36]
- Difference in size of strata (fit strata significantly larger than unfit strata)[27]
- Patients in GDT group had 250 mL ↑ in median intraoperative blood loss ($P = .006$)[27]
- Instrument used for evaluation of postoperative complications did not differentiate well between minor and serious complications[27]
- Statistically significant difference in age of control and GDT groups[25]
- Loss of secondary postoperative outcomes data among patients in both groups. Spo_2 data: 11 patients (4 in control and 7 in GDT group); weight data: 15 patients (7 in control and 8 in GDT group); creatinine data: 14 patients (8 in control and 6 in GDT group)[25]
- Incidence of peripheral vascular disease 34.2% ↑ in GDT group ($P = .04$)[35]

Table 2. Limitations of Studies Reviewed

Abbreviations: GDT, goal-directed therapies; Spo_2, oxygen saturation as measured by pulse oximetry; ↑, increase.

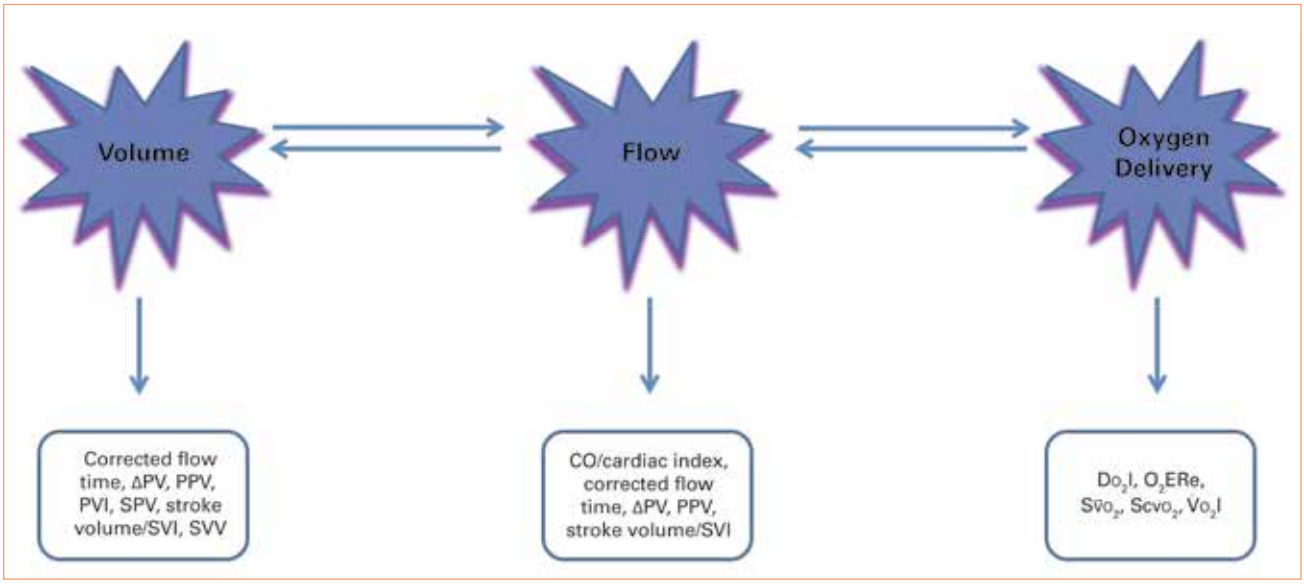

Figure. Targets of Goal-Directed Therapy and Individualized Hemodynamic Parameters Used to Assess Patient Outcomes

Abbreviations: CO, cardiac output; ΔPV, change in peak velocity; Do_2I, oxygen delivery index; O_2ERe, oxygen extraction ratio estimate; PPV, pulse pressure variation; PVI, pleth variability index; $ScvO_2$, central venous oxygen saturation; SPV, systolic pressure variation; SV, stroke volume; SVI, stroke volume index; $S\bar{v}o_2$, mixed venous oxygen saturation; SVV, stroke volume variation; $\dot{V}o_2I$, oxygen consumption index.

This increased O_2ERe may result in a mild decrease in $Scvo_2$ without a decrease in Do_2I or its associated cellular consequences. Under pathologic conditions or extreme states of stress (surgery, infection, trauma) and in the presence of organ dysfunction, $\dot{V}o_2I$ increases considerably, and compensatory mechanisms may be insufficient to maintain Do_2I. The resultant decrease in $Scvo_2$ and Do_2I reflects tissue hypoxia, anaerobic metabolism and metabolic derangements associated with lactic acid accumulation, cellular death, and organ dysfunction or failure.[39-41] By optimizing O_2ERe to below 27% in the GDT group, Donati et al[6] demonstrated a decrease in postoperative and total organ failure and a decrease in length of hospital stay compared with the control group.

Summary

Evaluation of the literature regarding GDT reveals many advantages of these strategies in terms of hemodynamic stability, oxygen transport balance, organ protection, and patient outcomes. By using multimodal hemodynamic monitoring technologies to derive specific target parameters, anesthesia providers can optimize perioperative fluid administration even in the presence of comorbidities, major surgical procedures, and large fluid shifts.

Abbreviation	Parameter	Measures	Clinical significance
CO/CI	Cardiac output/ cardiac index	CO measures volume of blood pumped by the left ventricle in 1 min; CI is an individual measure of CO normalized for body surface area (BSA)	Indicator of volume status and left ventricular function. Most often used for goal-directed therapy (GDT) in combination with measures of fluid-responsive hypovolemia such as stroke volume variation (SVV). If CI is decreased (↓) and SVV is ↑, fluid is administered to optimize CI. If CI is decreased (↓) and SVV is ↓, positive inotropes are given to optimize CI.[30,35]
Do_2I	Oxygen delivery index	Calculated value that combines inputs (hemoglobin concentration, hemoglobin carrying capacity, CI, and arterial oxygen saturation) to provide an individualized BSA-based indicator of tissue perfusion	Indicator of oxygen delivery; ↓ Do_2I indicates ↓ tissue perfusion; Most often used for GDT in combination with those inputs that comprise it (hemoglobin concentration, hemoglobin carrying capacity, CI, and arterial oxygen saturation), and with measures of fluid-responsive hypovolemia. If Do_2I is ↓, hemoglobin is evaluated and optimized first with transfusion if needed. If hemoglobin and arterial oxygen concentrations are otherwise within normal or expected limits, other measures are used to optimize Do_2I. If, for example, Do_2I is ↓ and SVV is ↑, fluid is given to optimize Do_2I. If Do_2I is ↓ and SVV is ↓, inotropes or vasopressors are administered to optimize Do_2I.[21,22]
FTc	Corrected flow time	Measures the forward flow of blood through the aorta during systole (flow time) and corrects it to a heart rate of 60/ min; FTc is a surrogate indicator of left ventricular ejection time	Indicator of left ventricular preload (larger end diastolic volume requires more time to eject); also sensitive to changes in left ventricular function and systemic vascular resistance. Often used for GDT in combination with measures of stroke volume (SV) or SVV. If FTc is ↓ (< 350 ms), SV is ↓, and SVV is ↑, fluid is administered and the SV/ SVV responses assessed. An ↑ in SV and/or ↓ in SVV following fluid indicates fluid-responsive hypovolemia. If FTc is ↓ and SV/SVV are normal, or if SV does not improve following fluid administration, further fluid administration is not indicated. The causes of ↓ FTc in the presence of normal SV/SVV could include poor left ventricular function or ↑ left ventricular afterload.[5,22]
O_2ER/O_2ERe	Oxygen extraction ratio/oxygen extraction ratio estimate	O_2ER is a direct measure of the difference between arterial and venous oxygen saturation at a given location (eg, heart, kidneys); O_2ERe is a calculated value based on the difference between arterial and mixed or central venous oxygen saturation	Indicator of tissue oxygenation; ↑ O_2ERe indicates ↑ oxygen extraction (↑ metabolism, stress, trauma) or ↓ oxygen delivery (anemia, hypovolemia). Used for GDT in conjunction with measures of volume such as SVV as well as hemoglobin concentration. If O_2ERe is ↑ and hemoglobin is ↓, hemoglobin is optimized with transfusion if needed. If hemoglobin concentration and arterial oxygen concentration are otherwise within normal or expected limits, other measures are used to optimize O_2ERe. Measures can be taken to ↓ oxygen extraction (↑ depth of anesthesia, ß-blockade, antipyretics as appropriate) and ↑ oxygen delivery. If, for example, O_2ERe is ↑ and SVV is ↑, fluid is administered to optimize O_2ERe. If O_2ERe is ↑ and SVV is ↓, inotropes or vasopressors may be given to optimize O_2ERe.[6]
ΔPV	Change in peak velocity	Changes in peak aortic pulse wave velocity over the positive pressure controlled ventilation (PPCV) respiratory cycle	Indicator of volume status; ↑ ΔPV indicates fluid-responsive hypovolemia.[26]
PPV/ΔPP	Pulse pressure variation/ change in pulse pressure	Variation in arterial pulse pressure over the PPCV respiratory cycle	Indicator of volume status; ↑ PPV/ΔPP indicates fluid-responsive hypovolemia[27]
PVI	Pleth variability index	Calculated variability in amplitude of pulse oximetry plethysmography over multiple PPCV respiratory cycles	Noninvasive indicator of volume status; ↑ PVI indicates fluid-responsive hypovolemia[26]
$Scvo_2$	Central venous oxygen saturation	Venous oxygen saturation of blood in the superior vena cava as measured by a central venous catheter	Indicator of oxygen consumption and of oxygen supply and demand ratio; ↓ $Scvo_2$ indicates ↑ oxygen consumption ($\dot{V}o_2$) or ↓ oxygen delivery (Do_2); $Scvo_2$ values are typically 2%-8% lower than $S\bar{v}o_2$ values because they reflect cerebral oxygen consumption alone without mixing of venous blood from the inferior vena cava[25,39,41]

SPV	Systolic pressure variation	Variation in systolic pressure over the PPCV respiratory cycle calculated based on pulse contour analysis of area beneath systolic arterial waveform curve	Indicator of volume status; ↑ SPV indicates fluid-responsive hypovolemia[24]
SV/SVI	Stroke volume/ stroke volume index	SV measures volume of blood pumped by the left ventricle in 1 heartbeat; SVI is an individual measure of SV normalized for BSA	Indicator of volume status and left ventricular function. Primary goal of many GDT strategies is to maximize SV/SVI by administering blood or fluid (depending on hematocrit concentration) until SV/SVI no longer ↑ by ≥ 10% in response to fluid therapy.[5,21,23,27]
$S\bar{v}O_2$	Mixed venous oxygen saturation	Venous oxygen saturation of blood in the pulmonary artery as measured by a pulmonary artery catheter	Indicator of oxygen consumption and of oxygen supply and demand ratio; ↓ $S\bar{v}O_2$ indicates ↑ oxygen consumption ($\dot{V}O_2$) or ↓ oxygen delivery ($\dot{D}O_2$); $S\bar{v}O_2$ values are typically 2%-8% higher than $ScvO_2$ values because they reflect mixed venous blood from the superior and inferior vena cavae, including blood from organs with low basal oxygen extraction such as the kidneys[25,39,41]
SVV	Stroke volume variation	Variation in stroke volume during PPCV respiratory cycle calculated by esophageal Doppler monitoring measurements or based on pulse contour analysis of area beneath arterial waveform curve	Indicator of volume status; ↑ SVV indicates fluid-responsive hypovolemia[29]

Table 3. Definition and Clinical Significance of Some Endpoint Measures Used in Goal-Directed Fluid Therapy Strategies

Many of the studies analyzed demonstrated common themes in results obtained; among the most notable are the decrease in hospital stay among the GDT group compared with the control group (n = 7 studies), and the decrease in postoperative complications (n = 7 studies).

However, despite evidence that traditional fluid management protocols rely on static and lagging hemodynamic measures, new knowledge about the effects of stress and surgical trauma on vascular integrity, and general acknowledgment that formulaic volume status estimates are insufficient to optimize perioperative fluid administration, traditional protocols persist as "routine care" in many institutions. Given the current advances in hemodynamic and monitoring technology, the increasing acuity of our surgical population, and the demonstrated need for improvement in our approach to perioperative fluid management, there is a need for ongoing research. Large multisite trials of perioperative GDT among patients in all risk strata for perioperative morbidity and mortality and comparison trials of various GDT protocols are needed to further evaluate the effects of GDT modalities. Based on the strength of current evidence supporting the use of perioperative GDT to guide fluid management, the National Institute for Health and Clinical Excellence in the United Kingdom released a medical technology guideline in 2011 recommending the use of EDM for perioperative GDT of high-risk surgical patients or those undergoing major surgery.[42] The application of continued research toward the development of practice guidelines for perioperative GDT will help ensure that all patients experience individualized fluid management, improved hemodynamic stability, optimized tissue perfusion, enhanced oxygen transport balance, and decreased perioperative complications.

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