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Review

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Perioperative fluid management-Goal Directed Therapy (GDT)

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Abstract

Perioperative goal-directed hemodynamic therapy is a protocolized treatment strategy aimed at optimization of global cardiovascular dynamics, including oxygen delivery to tissues and organ perfusion pressure. This is achieved by titrating fluids, vasopressors, and inotropes to predefined physiological target values of hemodynamic variables. Its scope is to reduce complications (acute kidney disease, pulmonary oedema, respiratory distress syndrome, wound infections), decrease major abdominal and systemic postoperative complications, length of stay and postoperative morbidity and mortality mainly in high-risk patients undergoing major surgery. Identifying patients in whom perioperative goal-directed hemodynamic therapy can actually improve postoperative outcomes is crucial. This is a review focusing on all the aspects of GDFT compared to standard fluid therapy during surgery.

Key words: fluid management, goal directed therapy

Introduction

Perioperative goal-directed hemodynamic therapy is a protocolized treatment strategy aimed at optimization of global cardiovascular dynamics, including oxygen delivery to tissues and organ perfusion pressure. This is achieved by titrating fluids, vasopressors, and inotropes to predefined physiological target values of hemodynamic variables. In an editorial, Saugel et al. suggested the "5 Ts" to specifically describe the concept and framework of perioperative goal-directed hemodynamic therapy: target population, timing of the intervention, type of intervention, target variable, and target value1. Hence, not all surgical patient populations benefit from perioperative goal-directed hemodynamic therapy. For perioperative goal-directed hemodynamic therapy to be effective, the target population needs to be at substantial risk for postoperative complications. Perioperative goal-directed hemodynamic therapy reduces postoperative morbidity and mortality compared with standard care mainly in high-risk patients undergoing major surgery. Identifying patients in whom perioperative goal-directed hemodynamic therapy can actually improve postoperative outcomes is the first step in applying perioperative goal-directed hemodynamic therapy wisely. Perioperative goal-directed hemodynamic therapy should thus start early in the intraoperative period rather than only in the postoperative phase. To optimize organ perfusion pressure and tissue oxygen delivery, different therapeutic interventions are used including fluids, vasopressors and inotropes. Perioperative goal-directed hemodynamic therapy can exhibit a sustained improvement in postoperative outcomes only if both fluids and vasoactive agents are part of the treatment protocol.

To improve patient-centered outcomes, perioperative goal-directed hemodynamic therapy should primarily include variables reflecting blood flow as targets and not solely dynamic cardiac preload variables or even static cardiac preload variables that have been shown to be unsuitable to guide fluid therapy. To tailor target values of hemodynamic variables to the individual patient's cardiovascular physiology, functional hemodynamic monitoring, adaptive targets, personalized targets, and multiparametric approaches including physiological targets should be used[1]. In FEDORA trial they evaluated postoperative complications in patients having major elective surgery using esophageal Doppler monitor-guided goal-directed hemodynamic therapy, in which administration of fluids, inotropes, and vasopressors was guided by stroke volume, mean arterial pressure, and cardiac index[2]. This resulted in fewer complications (acute kidney disease, pulmonary oedema, respiratory distress syndrome, wound infections, etc.), and a shorter hospital stay in the goal directed therapy group, with no difference in mortality at 180 days. In a pilot matched-controlled study aiming to determine the effects of continuous CO and SVV monitoring by pulse contour analysis providing goal-directed fluid management, as compared to standard care, they concluded that in high-tumor load gynecological patients without comorbidities who receive radical and prolonged surgery, intraoperative use of this novel goal directed protocol helped limit fluids administration with safety[3].

In patients undergoing peritonectomy with HIPEC, the use of a restrictive fluid therapy regimen combined with a GDT (FloTrac/Vigileo system) while maintaining the minimum threshold of CI greater than or equal to 2.5 l/min/m2 decreased the incidence of major abdominal and systemic postoperative complications and length of stay compared to standard fluid therapy protocol; the incidence of mortality although improved is not statistically significant[4]. The use of a monitoring and hemodynamic GDT anesthetic protocol (FloTrac-Vigileo® Edwards Lifesciences S.L. 4.0) in CRS and HIPEC makes it possible to individually adjust the fluid therapy and vasoactive drugs (VD) use, avoiding over-hydration and ensuring hemodynamic stability in all surgery phases[5].

Jan Benes et al, used for the management of intraoperative fluid and hemodynamic stability Vigileo/FloTrac and stroke volume variation in 120 high risk surgical patients. The goal of this trial was stroke volume variation (SVV) lower than 10% and cardiac index (CI) higher than 2.5 $l/min/m^2$. Colloids infusion and dobutamine were used in order to reach these goals. Intraoperative fluid optimization with the use of stroke volume variation and Vigileo/FloTrac system showed further from a significant improvement in morbidity an economic benefit. The mean savings observed in the overall costs of postoperative care (namely clinical care, costs of antimicrobial treatments and ward stay costs) trend to offset the investment needed to perform the GDT strategy and intraoperative monitoring. In addition, important differences in complication associated costs between East and West Euro- pean countries were observed. The median hospital length of stay was reduced to 9 days (8 to 12) in the GDT group compared to 10 days (8 to 19) in controls ($p = 0.042$)[6].

According to John Diaper et al, the GDFT group received much more intravenous fluid (mean 10,8 mL/kg/h) during major open abdominal surgery than normovolemic therapy group (RNT), meaning fixed rate infusion of crystalloids with the concomitant administration of vasopressors (mean of 7.2 mL/kg/h).In this study for the evaluation of stroke volume index and cardiac index all patients were connected to LiDCO monitor. Both groups have shown positive effects on postoperative morbidity and hospital duration of stay. Postoperative mortality was almost similar, in the 30-day and 1-year mortality rates were 1.0% and 11.7% in the GDHT group and 0.5% and 10.6% in the RNT group[7].

Meticulous perioperative care is critical to optimize outcomes for women undergoing radical CRS for advanced ovarian cancer. A key aspect of perioperative care is fluid management.110 patients undergoing CRS for stage III or IV EOC were studied to investigate the impact of fluid status on perioperative outcomes. They concluded that perioperative fluid excess is common in patients undergoing CRS for epithelial ovarian cancer (EOC) and was associated with unscheduled reoperation, anastomotic leak, surgical site infections (SSI), and length of stay >5 days[8].

In a double-blind pilot study including 50 patients with primary ovarian cancer undergoing cytoreductive surgery, the use of balanced crystalloid or balanced starch solutions administered to optimize stroke volume by esophageal Doppler using a goal-directed hemodynamic algorithm was compared[9]. Results revealed that the balanced hydroxyethyl starch group required less study fluid and less transfusion of fresh-frozen plasma as it had a longer intravascular effect. Furthermore it was associated with better hemodynamic stability, higher stroke volume, cardiac index, corrected flow time and lower systemic vascular resistance. This demonstrates that within a goal-directed hemodynamic algorithm, a colloid solution reduces intraoperative fluid demand and provides improved circulatory flow measured by stroke volume and cardiac output.

Crystalloids and colloids are the primary options for intravenous fluid resuscitation. Crystalloid solutions are isotonic plasma volume expanders that contain electrolytes and are used for expanding and maintaining plasma volume, while colloids are gelatinous solutions that maintain a high osmotic pressure in the blood and thus expand volume. In a double-blinded multicenter randomized trial they tested the effect of intraoperative goal-directed administration of balanced crystalloids versus colloids on major postoperative morbidity, having moderate- to high-risk open and laparoscopically assisted abdominal surgery. The authors concluded that Doppler-guided intraoperative hydroxyethyl starch administration did not reduce composites of minor or serious complications and the duration of hospitalization[10]. There was no indication of renal or other toxicity. As starch colloids are more expensive than crystalloids and apparently do not reduce perioperative complications, they should sparingly be used in surgical patients.

A meta-analysis concerning perioperative coagulation competence, hemorrhage and outcome was conducted studying the efficacy and safety of the use of hydroxyethyl starches, dextran, or albumin versus crystalloids during major elective surgery[11]. Patients admitted to hydroxyethyl starches administration were exposed to decreased coagulation competence evaluated by TEG-MA while perioperative hemorrhage tended to increase compared to crystalloids and albumin. The stratified meta-analysis disclosed that increased blood loss was found during non-cardiovascular surgery among patients receiving hydroxyethyl starch compared with crystalloids, followed by a marked reduction in TEG-MA, while infusion of 3rd generation hydroxyethyl starch products (HES 130/0.4) did not influence the results significantly.

Postoperative wound infection may be prevented by achieving sufficient tissue oxygen tension. A single centre randomized controlled study investigated whether increased tissue oxygen tension would benefit from perioperative goal directed colloid infusion when compared with crystalloid infusion[12]. Tissue oxygen tension was measured subcutaneously in the upper arm and surgical wound in patients undergoing open abdominal surgery. There was no difference in perioperative tissue oxygenation between goal-directed colloid and crystalloid fluid therapy. In a goal-directed fluid management strategy, the type of fluid was not important for tissue oxygen tension levels. In another systematic review and meta-analysis, the authors determined the effects of perioperative hemodynamic goal-directed therapy on postoperative infection rates[13]. They concluded that flow-directed hemodynamic therapy designed to optimize oxygen delivery protects surgical patients against postoperative hospital-acquired infections and must be strongly encouraged, particularly in the high-risk surgical population[13].

A systematic review and meta-analysis including 45 eligible randomized controlled trials of available evidence suggests that the use of perioperative goal-directed hemodynamic therapy could improve postoperative recovery following major abdominal surgery, as demonstrated by a reduction of postoperative morbidity, improvement of survival, and earlier return of gastrointestinal function[14].

Goal-directed fluid management improves major outcomes, such as cardiopulmonary function, gastric motility, wound healing and reduces hospital length of stay. A meta-analysis of 32 trials by Cecconi and colleagues reported that patients with the highest risk of surgical mortality benefited the most from goal-directed therapy[15]. In a cohort study of colorectal cancer patients treated within an ERAS protocol concluded that a restrictive (total iv administered volume of<3000 ml) compared with a non-restrictive perioperative fluid therapy on the day of surgery may be associated with lower short-term complication rates, faster recovery, shorter length of stay and improved 5-year survival[16].

In new era goal-directed fluid therapy can be automatically administrated using the closed-loop system with invasive CO and SVV monitoring. Joosten et al performed a prospective randomized trial in 38 patient undergoing intermediate- or high-risk abdominal or orthopedic surgery. Computer assisted GDFT group was based on mean arterial pressure (MAP) and stroke volume, as many studies have been shown that intraoperatively MAP less than 55 to 65 mmHg is associated with a higher risk of morbidity. To minimize intraoperative hypotension norepinephrine was used. Co-administration of mini-fluid challenge and vasopressor was achieved for the normal stroke volume index. Patients in computer-assisted group had lower intraoperative hypotension case time, higher cardiac index and SV competed to manually adjusted GDFT (1.2% [0.4 to 2.0] vs 21.5% [14.5 to 31.8] $P < 0.001$). This study also demonstrated lower lactate concentrations on arrival in the PACU using automatically adjusted GDFT. Computer- assisted GDFT systems provides hemodynamic stability by targeting MAP and SV. The incidence of postoperative complications was not significantly different in the two groups[17].

Major surgeries have been linked to higher incidence of post-operative pulmonary complications. The commonest reported postoperative pulmonary complications are acute respiratory distress syndrome (ARDS), acute lung injury (ALI), pulmonary embolism (PE) and pulmonary oedema (PO)[18]. A large systematic review and meta-analysis (66 studies) based on moderate quality evidence, was performed by Dushianthan et al. to determine the reduction of post-operative pulmonary complications through augmenting blood flow by GDHT with specified measured goals[19]. Intraoperatively hemodynamic monitoring was implemented by pulmonary artery catheterization, esophageal Doppler, minimally invasive and non-invasive. The devices observed specific hemodynamic parameters: cardiac output(CO), stroke volume(SV), systolic pressure variation (SPV), pulse pressure variation(PPV), oxygen delivery (DO2), oxygen consumption (VO2), mixed venous oxygen saturation and oxygen extraction ration (O2ER). This systematic review has shown that the use of GDHT using fluids in combination with inotropes and/or vasopressors significantly reduces the rates of post-operative respiratory tract infections, acute respiratory failure and pulmonary oedema. Overall, in the intervention group pulmonary complications were 11,5 % (549/4772) in contrast to 14% (676/4774) in the control group. There was no difference in ARDS or pulmonary embolism. Moreover, the GDHT group received more colloid (+280 ml) and less crystalloid (−375 ml) solutions than the control group. (P = 0.0003)[18].

Anesthesia can cause vasodilation and reduce cardiac function. In addition, surgery may disturb microcirculation and induce systematic inflammation. This can provoke an imbalance between oxygen delivery and consumption in vital organs, increasing the risk of perioperative acute organ injury and long-term mortality. As we already noticed, GDFT plays a significant role to maintain patient's normal physiology in the perioperative period, thus optimizing patient outcomes without complications. One of the first systematic reviews and meta-analysis including 31 studies (3176 patients) evaluated all available evidence regarding the effect of GDFT with the application of alpha-1 adrenergic agonists compared with the conventional fluid therapy on postoperative outcomes following noncardiac surgery. Infusion or injection of alpha-1 adrenergic agonists (Phenylephrine, Norepinephrine) with GDFT maintains appropriate vascular tension, blood pressure and organ perfusion and can be used to treat anesthesia-induced vasodilatation by increasing systemic vascular resistance. The primary outcomes which included the postoperative mortality rate and length of hospital stay (LOS) were significant reduced. Facilitated GI functional recovery, as demonstrated by shortening the time to first flatus pass and time to toleration of oral solid food was studied as secondary outcome. Shuai Feng et al. confirmed that the treatment with norepinephrine during the perioperative period had no adverse effects on microcirculatory blood flow or tissue oxygen tension in the regarding intestinal tract. This finding was consistent with the result of the present study indicating a significant improved postoperative recovery, reducing LOS and postoperative complications[20].

Obesity is associated with a higher risk of developing tissue perfusion and oxygen delivery problems under anesthesia. Therefore, perioperative subcutaneous tissue oxygen tension (PsqO2) is significantly reduced. J. Mühlbacher et al. randomly assigned 60 obese patients (BMI ≥ 30 kg/m^2) undergoing laparoscopic bariatric surgery to have esophageal Doppler-guided goal directed fluid management or conventional fluid treatment. The goal of this study was to measure intra and postoperative subcutaneous tissue oxygen tension (Psq02) and intra- postoperative PsqO2 measured with a polarographic electrode in the subcutaneous tissue of the upper arm. In this study, no effect was seen intraoperatively but overall subcutaneous tissue oxygen tension increased significantly in the early post- operative period in obese patients receiving Doppler-guided fluid administration. Maintaining adequate tissue oxygenation remains one of the most significant tasks for anesthetists, however, newer minimally invasive devices are promising, but still require initial validation before assessing their impact upon clinical outcomes[21,22].

GDFT can be guided by using pulse-pressure variation (PPV) or pleth variability index (PVI). Coeckelenbergh et al performed a randomized controlled trial in 76 patients undergoing low-to-moderate risk surgery. These dynamic indicators are based on cardiopulmonary interaction and can predict fluid responsiveness. PVI, is noninvasive and requires only a pulse oximeter, while PPV requires the insertion of an arterial catheter and its inherent risks. PVI and PPV guided GDFT are considered similar the primary outcomes of hospital LOS, amount of fluid, and postoperative complications. However this study showed that low-risk patients undergoing surgical procedures while optimizing stroke volume may have limited impact on outcome[23].

Attenuating postspinal hypotension during cesarean delivery remains less explored. Postspinal hypotension is a reduction in baseline systolic blood pressure (SBP) by >20% and it is a challenge for the anesthesiologist. Continuous noninvasive finger cuff devices such as the ClearSight System, can provide noninvasive monitoring stroke volume value, to perform GDFT before spinal anesthesia. The ClearSight System provides hemodynamic parameters including stroke volume, cardiac output, and stroke volume variation. 71 consecutive full-term pregnant women were randomly divided into a control group (n=34) and a GDFT group (n=37). Before spinal anesthesia, the control group received a fixed dose (1000mL) of crystalloid fluid, and the GDFT group received repeated 3mL/kg body weight of crystalloid fluid challenges within 3 minutes with a 1-minute interval based on stroke volume incremental changes obtained by ClearSight System (targeting a stroke volume increase of ≥5% after a fluid challenge). One limitation of the study was that stroke volume variation is unreliable in patients breathing spontaneously. The major findings of this study was that GDFT preload was not effective in ameliorating post spinal hypotension but only reduced post spinal nausea[24].

Most GDT studies analysis were done with pulmonary artery catheters, esophageal Doppler and calibrated pulse contour methods. Uncalibrated pulse contour (uPC) techniques are an appealing alternative, but their accuracy has been questioned. In a meta-analysis of 19 randomized controlled trials GDT with uPC methods is associated with a significant decrease in postoperative morbidity. It also shows that it does not increase the volume of fluid administered and decrease the variability of fluid volumes. Therefore, their findings support the notion that uPC methods are useful to guide hemodynamic therapy solely during the perioperative period[25]. In the perioperative setting, not only the type of fluid but also the volume administered can impact a patient's outcome following major surgery. Fluid volume should be guided by predefined physiologic targets, using an individualized hemodynamic algorithm. It is of prime importance that intravenous fluids be administered with the same care as any other drug, with strict indications and contraindications and precautions regarding potential adverse effects[26]. GDT evidence has been considered strong enough as to allow the creation of national recommendations in the UK, in France, and by the European Society of Anesthesiology. GDT has been recognized as the standard of care in the anesthesia setting as it demonstrates strong clinical evidence and benefit in reducing rates of postoperative complications Despite all the evidence demonstrating the benefit of GDT, there is still no clear consensus about the most effective goals and the most appropriate monitoring device for guiding therapy[27].

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