

PRO: Perioperative Goal-Directed Fluid Therapy Is an Essential Element of an Enhanced Recovery Protocol

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Perioperative fluid management influences patients' outcomes. The type of fluid, the volume of fluid, and how we administer fluid all affect outcome. However, there is considerable variability in fluid administration among specialists (anesthesiologists, surgeons, nurses, perioperative physicians, and intensivists) and even within individual specialties. The volume of fluid administered to a surgical or critical care patient depends to a large extent on the individual practitioner,¹ with large interprovider and intraprovider variability.¹ Most practitioners use clinical end points such as urine output, mean arterial blood pressure, or central venous pressure that have little to do with the hemodynamic goals of fluid administration.² The end result is closer to random chaos than either art or science.³

The basic problem is that we do not know the ideal fluid volume a patient should receive during surgery. Contrary to physics, physiology is an imperfect science. Anesthesia, intensive care, and perioperative medicine are medical disciplines where level 1A evidence is rare. But it seems likely that huge interprovider variability cannot be good for our patients or for population health. Variability is the enemy of quality. Perioperative fluid administration should be standardized based on the best evidence available and on the most rational physiologic end points. We believe that perioperative goal-directed therapy is the rational approach for moderate- to high-risk patients. Put another way, if you were to undergo high-risk surgery tomorrow, would you rather be in the control (wild) group or in the goal-directed therapy group? We (MC and TJG) would want to be in the goal-directed therapy group as long as the physiologic endpoint of the goal-directed therapy group was rational and the crystalloid administration limited. We have overwhelming data to support the benefits of goal-directed therapy in high-risk patients or patients undergoing major procedures.

Over the past 10 years, several meta-analyses studying the impact of goal-directed therapy versus standard of care in patients undergoing moderate and major surgeries have been conducted and published in major journals.⁴⁻⁸ These meta-analyses have consistently shown that goal-directed therapy improves outcome compared with standard of care. However, some may argue that studies included in these meta-analyses are highly heterogeneous. These studies use different protocols, different physiologic end points, and different technologies to measure stroke volume and cardiac output, and these studies show that even patients in the goal-directed therapy groups received highly variable volumes of fluids. This is all true. However, we believe that this emphasizes the strength of the intervention. First, it is clear from these studies that a protocol of care is better than no protocol of care when it comes to fluid management and hemodynamic optimization. We do not know what the best end point is, but a rational physiologic goal seems better than no goal at all. Second, goal-directed therapy is not supposed to eliminate variability. No clinical pathway, protocol, or standard of care is meant to eliminate all forms of variability. Clinical care is fundamentally variable. It is expected that clinical care is variable because each patient is different. What is not desirable is variability of care related to the practitioners or the system. The whole philosophy of goal-directed therapy is that if one wants to improve hemodynamics, then give fluid whenever the patient is a responder to fluid. When the patient is not a responder to fluid and if the arterial blood pressure is still low, consider vasopressors instead. It is simple, straightforward, and rational. To apply this approach, we need to assess fluid responsiveness and/or monitor stroke volume or cardiac output. Negative studies are underpowered and conducted in relatively healthy patients with minimal blood loss.

Admittedly, there are some negative studies for goal-directed therapy, including a 2014 publication in *Anesthesia & Analgesia*.⁹ This was a well-conducted multicenter study that showed no difference in outcome. In addition, Pearse et al.⁵ reported the results of a multicentered randomized study showing "no improvement" in outcome in patients undergoing major surgery. However, the study by Pearse et al. is interesting in the sense that the sample size was calculated based on an expected 30-day complication incidence of 50% (yes, 50%) in the control group and a 37.5% incidence in the goal-directed group. When the study was conducted (in the United Kingdom, where enhanced recovery after surgery [ERAS] is widely popular and consistently applied nationwide for abdominal surgery), the incidence

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of complications was only 43.4% in the control group and 36.6% in the goal-directed therapy group ($P = 0.07$). Thus, the initial sample size calculation was based on a much higher incidence of postoperative complications than expected, and hence, the study was underpowered to show a difference. Instead of continuing the study (which would have required more funding), the authors chose to include their results in an updated meta-analysis. In this manner, the authors demonstrated that the treatment effect was still positive. In addition, according to the authors of this study, "In the prespecified adherence-adjusted analysis conducted using established methods, the observed treatment effect was strengthened when the 65 patients whose care was non adherent were assumed to experience the same outcome as if they had been allocated to the alternative group (RR, 0.80; 95% CI, 0.61–0.99; $P = 0.04$)." In other words, when the goal-directed therapy protocol was consistently applied, the treatment effect was strengthened. Finally, there was no risk associated with the goal-directed therapy protocol (specifically, no increased cardiac morbidity). Several countries including the United Kingdom and France have chosen to apply this approach consistently to patients undergoing major surgery and have made it part of their national expert recommendations.^{10–12}

We agree that some questions related to goal-directed fluid therapy remain incompletely answered. What is the ideal end point? What is the best technology? What should be the baseline crystalloid administration rate? What is the ideal patient population? Should goal-directed therapy protocols include inotropic support? Even though the answers to these questions are not clear, having a hemodynamic goal is better than having no goals at all. Should we wait for these questions to be answered before we adopt goal-directed therapy? Institutions and departments have protocols and standardized pathways for pain management, despite the absence of level 1A evidence. This is done to reduce variability of care and improve quality. In our view, we should do the same for hemodynamic and fluid management. We should encourage institutions that do not have an ERAS program in place to apply goal-directed therapeutic strategies, because the current evidence supports patient benefit.

We believe that goal-directed therapy has the potential to reduce length of stay in the hospital and decrease postoperative complications in patients undergoing major and high-risk surgery. In fact, recent studies using goal-directed therapy in an ERAS setting have demonstrated a reduction in length of stay and complications.^{13,14}

Goal-directed therapy can rely on pulse pressure variation minimization alone, which permits use in the absence of a cardiac output monitor and in clinical settings where more advanced monitoring is not available. As a result, there is almost no incremental cost with implementing goal-directed therapy. Goal-directed therapy can improve outcome in settings where ERAS protocols are not implemented. Thus, neither the presence nor the absence of ERAS protocols should limit the application of goal-directed therapy.

One of the cornerstones of modern medicine is to increase quality of care. Variability is the enemy of quality. Standardization of fluid administration could be achieved using basic crystalloid restriction strategies in low- to moderate-risk surgery. However, for moderate- to high-risk

surgeries, it is foolish to believe that crystalloid restriction alone can achieve this goal. For complex surgeries, clinicians need to follow basic physiologic end points to make fluid administration rational, consistent, and standardized. That is the main goal of perioperative goal-directed therapy. ■■

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