Goal-directed therapy: what we know and what we need to know

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Goal-directed therapy: what we know and what we need to know

Jason B O’Neal1* and Andrew D Shaw2

Abstract
Goal-directed therapy (GDT) utilizes monitoring techniques to help guide clinicians with administering fluids, vasopressors, inotropes, or other treatments to patients in various clinical settings. Multiple studies have investigated the potential benefits of GDT, but no consensus on the use of GDT exists. Future trials which address fluid and inotrope choice as well as expanding the results to evaluate patient-centered outcomes in addition to survival are warranted.

Background
Achieving hemodynamic stability during and after surgery to ensure adequate perfusion and oxygenation is a goal of every perioperative physician. We have several types of invasive and non-invasive monitoring techniques that influence our decisions to give intravenous fluids, start vasopressors, or initiate inotropes on a patient. Goal-directed therapy (GDT) utilizes these monitors to assess cardiovascular performance and thus guides the clinician to intervene as necessary based on a predetermined algorithm. Many investigators have conducted studies to examine the potential benefits of GDT in surgical patients and also in the intensive care unit (ICU) [1,2]. Two recent large multi-center, randomized controlled trials, the Australasian Resuscitation In Sepsis Evaluation (ARISE) and Protocolized Care for Early Septic Shock (ProCESS) studies, examined GDT in early septic shock [3,4]. The ARISE study found no reduction in all-cause mortality at 90 days, and the ProCESS study showed no improvement in outcomes including 60-day in-hospital mortality, 90-day mortality, 1-year mortality, or the need for organ support. A paper in Critical Care Medicine, using a simulation model of a tertiary care hospital in the United Kingdom, found a cost benefit of goal-directed therapy. The short-term model suggested that GDT reduced the hospital length of stay and was also associated with fewer complications [5]. Although there is a vast number of publications on GDT, and a possible cost benefit, no general consensus on the use of GDT exists. A study published in JAMA, the Optimisation of Cardiovascular Management to Improve Surgical Outcome (OPTIMISE) trial, examined the effect of GDT in high-risk gastrointestinal (GI) surgical patients on outcomes following surgery [6].

The OPTIMISE trial was a multi-center, randomized, observer blinded trial of 734 high risk patients undergoing major GI surgery in 17 hospitals in the United Kingdom. The aim of the study was to evaluate a GDT algorithm using intravenous fluid boluses and an inotrope (dopexamine). Cardiac output was measured with the LiDCO (hemodynamic monitor), and the intervention group received non-standardized 250 cc colloid fluid boluses and were started on a dopexamine infusion at a set rate to attain an adequate stroke volume. The management between the intervention and usual care groups was similar except more colloid was administered in the intervention group, and also the intervention group received more blood products both during and after surgery.

The primary outcome of the study was 30-day moderate or major complications and mortality. This was present in 36.6% of the intervention group as compared to 43.4% in the usual care group with a relative risk (RR) of 0.84 (95% CI 0.71–1.01; p = 0.07). The primary outcome as well as all secondary outcomes including morbidity on day 7, infection, critical care-free days, all-cause mortality at 30/180 days, and length of stay were not significantly different between the groups. Thus, this study did not confirm previous data suggesting that GDT has an outcome benefit.

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that GDT was associated with a shorter ICU stay and time to discharge and faster return of GI function [8]. These findings suggest GDT to be safe when considering the potential cardiac effects of introducing boluses of intravenous fluid and increased cardiac demand with inotropes.

Most studies on GDT focus on initial complications and mortality as primary and secondary endpoints. This data may one day direct and change the standard of clinical care on patients, but there are limited studies investigating patient-centered outcomes such as disability or cognitive deficits 1 year after surgery. Long term survival may be improved in these patients as evidenced by a follow-up study conducted 15 years after the initial randomized control trial on GDT [9]. In that study, median survival was 3 years longer in the treatment group. With the aging population and government focus on cutting health-care costs, patient-centered outcomes are becoming an important and worthwhile measure of clinical care.

Conclusion
The question of whether or not GDT is truly beneficial still remains unanswered. Assuming there is a benefit, another question which needs to be addressed is the type of fluid to administer and if the addition of an inotrope, as well as which one, is necessary for GDT to succeed. The algorithm varies between studies making it difficult to interpret the results of meta-analyses including their data. And what is the best hemodynamic goal to direct therapy? Some studies assess cardiac output or stroke volume while others use mixed venous oxygen saturation or another parameter. No single hemodynamic goal or monitoring method has been accepted across the literature [10]. To mention, OPTIMISE 2 is in the works with plans to address fluid choice with or without an inotropic agent as well as which monitor is the best option. The outcomes may need to be broadened, and studies which include disability-free survival at 1 year as well as other patient-centered outcomes should be completed. Additional studies are warranted before conclusions on GDT can be made, and a single algorithm with which clinicians should direct care may be difficult to universalize.

Abbreviations
GDT: Goal-directed therapy; ICU: Intensive care unit; GI: Gastrointestinal; RR: Relative risk.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
JBO and ADS were both involved in the preparation of the article. Both authors read and approved the final manuscript.

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References


