# What is the Goal of Fluid Management “Optimization”?

*"Fluid management" (FM) is a complicated, unsolved riddle. I think we should first find the "good questions"; or rather, we have to formulate the questions in an appropriate way. Otherwise, it may the case that you compare "liberal" (?) vs "restrictive" (?) strategies; and find at the end that you have given even more fluid in the restrictive group because of the "rescue". Not to mention is that what you call "liberal" in some studies is defined in some other studies as "restrictive".*

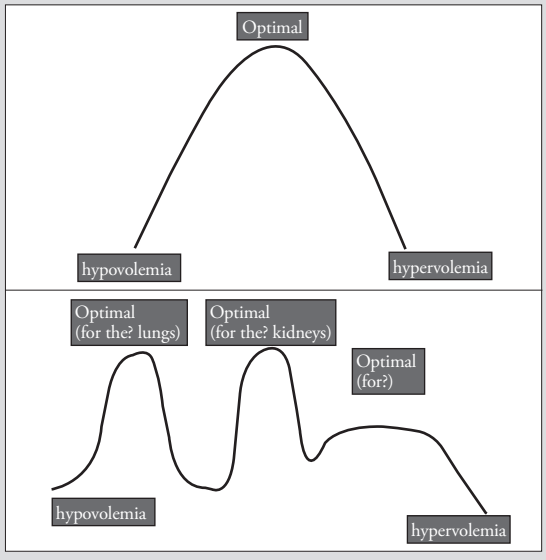
*Now we have a third way: "optimised FM". It sounds and seems to be rational, but are there also some limitations or drawbacks of this approach? Or rather: "Can optimal FM be really optimal?".*

*Let me expand my question with further questions: Some authors advocate that being restrictive is optimal to avoid edema, whereas others defend that FM should not cost AKI (acute kidney injury). Is "optimal FM" indeed a peak between "hypovolemia" and "hypervolemia" (curve A); or is the FM curve maybe an irregular, fluctuant curve with several peaks, maybe "u"-shaped instead of "v"? (curve B).*

*In those terms, I want you to remind the keyword "glycocalyx". With increasing information about glycocalyx, we recognize that we have to revise all the knowledge we have, such as Frank-Starling Curve.*

*My last question is a stupid one: what is actually the "3rd space"? Does it really exist somewhere in the body?*

**Mert Şentürk**
**Editor**




# What is the Goal of Fluid Management "Optimization"?

**Giorgio Della Rocca, Luigi Vetrugno**
*University of Udine, Department of Medical and Biological Sciences, Udine, Italy*

The debate about fluid management in the operating room is still far from reaching a unanimous conclusion (1-3). However, the concept that fluid administration holds the potential to worsen or improve patient outcome is generally accepted as true and in the last decade the concept that "zero-balance" has overtaken other classical approaches, including the liberal fluid strategy or Goal-Directed-Therapy (GDT) (4, 5).

The origins of this peaceful 'revolution' can be traced back to the work of Brandstrup et al. (6), which raised questions about the standard clinical practices in use at the time. They showed that fluid administration during major colon-rectal surgery was associated with perioperative weight gain and an increased risk of complications. In other words, because of excessive fluid administration during surgery, patients were gaining too much weight: Perioperative weight gain indicates that the fluids given exceeded fluid losses.

Even after prolonged pre-operative fasting, healthy patients remain euvolemic (7). In addition, insensible perspiration during the perioperative period has been re-evaluated, as reported in the study by Lamke et al., (8) since baseline evaporation during large abdominal surgery was shown to be approximately 0.5 to 1 mL/kg/h. Finally, definitive evidence has come to light indicating that the 'third space' does not exist and therefore does not need to be replaced (9).

Fluid retention is a normal neuro-hormonal response to surgery and permissive oliguria less than 0.5 mL/kg/h for up 2-4 hours should be accepted (10-12). The link between maintaning body weight and perioperative intravenous fluid administration is currently associated with a lower risk of complications following abdominal surgery (13).

The fluid regimen illustrated by Brandstrup et al. (6) aimed to achieve zero-balance, i.e. zero gain in body weight; this non-restricted, non-liberal fluid approach was mainly performed in American Society of Anesthesiology (ASA) 1, 2 patients. Brandstrup's results are also supported by the Enhanced Recovery After Surgery (ERAS) programme in which, of the 20 variables evaluated by multiple regression analysis, fluid management represents the major independent predictive factor of postoperative outcome, together with preoperative carbohydrate administration (14).

It has also been shown that for each additional litre of fluids given in the operating room, there is a 16% increase in the risk of postoperative symptoms and a 32% increase in the probability of postoperative complications (14). In the United States, where the ERAS principles are not widely accepted or implemented, high fluid volume given on the day of surgery has also been associated with increased length of stay (LOS) and increased costs (15): Anesthesiologist practices can make the difference.

**Address for Correspondence:**
Dr. Giorgio Della Rocca
E-mail: giorgio.dellarocca@uniud.it

Turk J Anaesthesiol Reanim 2016; 44: 224-6
DOI: 10.5152/TJAR.2016.005

Available online at www.jtaics.org

On the other hand, assessing "normovolemia" is quite difficult; the problem is that not only hypovolemia but also hypervolemia has been associated with a 'restrictive' approach.

However, there are no clear indications to what a "liberal approach" actually means compared with a "restricted" one in terms of mL/kg/h and the type of fluid that should be given (5, 16). Fluids can be administered in the form of fluid maintenance or a fluid challenge (FC); except in the case that a patient continues to lose blood, when the volume of fluids administered are deemed to be sufficient, current research indicates that fluid administration should be suspended and vasopressor infusion commenced until an "acceptable systemic blood pressure" is reached. As stated before, one of the most important recent changes in clinical practice has been in the management of "fluid maintenance". The concept of FC remains the same (17): a FC constitutes a test that allows the clinician to understand whether the patient is on the Franc-Starling curve and whether he has a preload reserve that can be used to increase the stoke volume (SV) and cardiac output (CO). In the case of a positive response, additional FC can be given if required. In the case of a negative response, further FC should be avoided and the only extra fluid given to the patient should be that administered if the patient fails to respond; this volume is usually equal to or no more than 200 mL or 3 mL/kg (17). This approach forms the basis of most GDT algorithms that aim to optimize tissue perfusion by maximizing oxygen delivery (DO2).

Esophageal Doppler (ED) monitoring and its related flow algorithm is the most common tool cited in the literature used to perform GDT. ED has been recommended as a routine monitoring system for abdominal surgery in the UK (18) and France (19) and endorsed by Medicare and the Medicaid Service in the USA (20).

**Compared with the liberal fluid approach, GDT is superior in terms of risk of postoperative complication, in selected population**

Hamilton et al. (21) reported that over the last 10 years the mortality rate of patients not receiving GDT (compared with those who did receive GDT) was significantly lower (7% compared with 13.5%, respectively), probably due to improvements made in surgical and anesthetic practices.

In order to demonstrate a 2% difference in mortality rate between patients receiving GDT and control patients (no GDT), a study would need to be conducted involving at least 2312 patients per group. No such study has been published to date.

A meta-analysis study by Cochrane (22) concluded: *"The balance of current evidence does not support widespread implementation of this approach to reduce mortality but does suggest that complications and duration of hospital stay are reduced"*. The study considered 24 studies with a combined total of 2677 patients and revealed a $p<0.02$ for mortality in elective surgery. Moreover, it suggests that the use of GDT reduced the rate of three morbidities: renal failure, respiratory failure and wound infection.

**GDT decreases risk of complications during the first 30 postoperative days and may improve long term outcome, in selected population**

A study known as the OPTIMIZE study (23) enrolled the largest population of high-risk patients ever achieved to date and compared the GDT with usual care. This study showed a strong trend for patients receiving GDT to experience fewer complications in the first 30 postoperative days (36.6%) than control patients (43.4%), although the difference did not quite achieve statistical significance ($p=0.07$). However, more than 50% of the patients in this study were ASA 1-2 undergoing elective surgery. The calculated sample size was based on a much higher expected incidence of postoperative complications (50% higher), leaving the study without the power to show potential differences (24).

How can we interpret this evidence into a take home message? The majority of the available studies in literature published before 2006 compared GDT with a liberal approach to fluid administration in patients who were mainly ASA 1 or 2, and generated results in favour of GDT (25). Later studies that compared GDT with a restricted approach or ERAS programme showed no differences, and again mainly concerned ASA 1 or ASA 2 patients (26, 27).

We know that the risk of adverse events during and after surgery is increased in patients with limited cardiovascular and/or respiratory reserve. From the ethical standpoint, research into invasive hemodynamic monitoring and fluid management cannot be performed in healthy patients, as such techniques can only be justified in sicker and higher risk patients (28). We also know that the type of surgery (low-intermediate versus high risk) can make the difference (29). Considering these facts, we can conclude that:

1) The best patients to study should comprise high risk surgical patients ASA 3 and 4;
2) Cardiac output monitoring should also be applied to the appropriate types of surgery;
3) Maintenance fluid administration should be no more than 1-3 mL/kg/h;
4) A GDT approach should be an "active" approach, the aim of which is not to "maximize" but to "optimize" the goal only in patients classified as fluid responders;
5) …. goals should be maintained for up to 6-8 postoperative hours.

## References

1. Doherty M, Buggy DJ. Intraoperative fluids: how much is too much? Br J Anaesth 2012; 109: 69-79.
2. Hahn RG. Fluid therapy might be more difficult than you think. Anesth Analg 2007; 105: 304-5. [CrossRef]
3. Minto G, Mythen GM. Perioperative fluid management: science, art or random chaos? Br J Anaesth 2015; 114: 717-21.
4. Miller TE, Raghunathan K, Gan TJ. State-of-the-art fluid management in the operating room. Best Pract Res Clin Anaesthesiol 2014; 28: 261-73. [CrossRef]

5. Frost EAM. Perioperative Fluids: An Evidence-Based Review. Anesthesiology News 2014; download at: http://www.anesthesiology-news.com/download/FluidManagement_ANSE14_WM.pdf
6. Brandstrup B, Tønnesen H, Beier-Holgersen R, Hjortsø E, Ørding H, Lindorff-Larsen K, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens randomized assessor-blinded multicenter trial. Ann Surg 2003; 238: 641-8. [CrossRef]
7. Jacob M, Chappell D, Conzen P, Finsterer U, Rehm M. Blood volume is normal after pre-operative overnight fasting. Acta Anaesthesiol Scand 2008; 52: 522-9. [CrossRef]
8. Lamke LO, Nilsson GE, Reithner HL. Water loss by evaporation from the abdominal cavity during surgery. Acta Chir Scand 1977; 143: 279-84.
9. Jacob M, Chappell D, Rehm M. The 'third space fact or fiction? Best Pract Res Clin Anaesthesiol 2009; 23: 145-57.
10. Desborough JP. The stress response to the trauma and surgery. Br J Anaesth 2000; 85: 109-17. [CrossRef]
11. Gupta R, Gan TJ. Peri-operative fluid management to enhance recovery. Anaesthesia 2016; 71: 40-5. [CrossRef]
12. Kheterpal S, Tremper KK, Englesbe MJ, O'Reilly M, Shanks AM, Fetterman DM, et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. Anesthesiology 2007; 107: 892-902. [CrossRef]
13. Miller TE, Roche AM, Mythen M. Fluid management and goal-directed therapy as an adjunct to Enhanced Recovery After Surgery (ERAS). Can J Anaesth 2015; 62: 158-68. [CrossRef]
14. Gustafsson UO, Hausel J, Thorell A, Ljungqvist O, Soop M, Nygren J. Enhanced Recovery After Surgery Study Group. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. Arch Surg 2011; 146: 571-7. [CrossRef]
15. Lilot M, Ehrenfeld JM, Lee C, Harrington B, Cannesson M, Rinehart J. Variability in practice and factors predictive of total crystalloid administration during abdominal surgery: retrospective two-centre analysis. Br J Anaesth 2015; 114: 767-76. [CrossRef]
16. Della Rocca G, Vetrugno L, Tripi G, Deana C, Barbariol F, Pompei L. Liberal of restricted fluid administration: are we ready for a proposal of a restricted intraoperative approach? BMC Anesthesiology 2014; 14: 62.
17. Cecconi M, Parson AK, Rhodes A. What is fluid challenge? Curr Opin Crit Care 2011; 17: 290-5.
18. National Institute for Health and Clinical Excellence: CardioQ-ODM oesophageal Doppler monitor. Medical Technology Guide 3. 2011, Available at: http://www.nice.org.uk/nicemedia/live/13312/52624/52624.pdf
19. Vallet B, Blanloeil Y, Cholley B, Orliaguet G, Pierre S. Guidelines for perioperative haemodynamic optimization. Société FranÇaise d'anesthésie et de réanimation. Ann Fr Anesth Reanim 2013; 32: 454-62. [CrossRef]
20. Agency for Healthcare Research and Quality. Esophageal Doppler ultrasound-based cardiac output monitoring for real-time therapeutic management of hospitalized patients: a review http://www.cms.gov/Medicare/Coverage/DeterminationProcess/ downloads/id45TA.pdf
21. Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. Anesth Analg 2011; 112: 1392-402. [CrossRef]
22. Grocott MP, Dushianthan A, Hamilton MA, Mythen MG, Harrison D, Rowan K. Optimisation Systematic Review Steering Group. Perioperative increase in global blood flow to explicit defined goals and outcomes after surgery: a Cochrane Systematic Review. Br J Anaesth 2013; 111: 535-48. [CrossRef]
23. Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, et al. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014; 311: 2181-90. [CrossRef]
24. Cannesson M, Gan TJ. PRO: Perioperative Goal-Directed Fluid Therapy Is an Essential Element of an Enhanced Recovery Protocol. Anesth Analg 2016; 122: 1258-260. [CrossRef]
25. Bundgaard-Nielsen M, Holte K, Secher NH, Kehlet H. Monitoring of peri-operative fluid administration by individualized goal-directed therapy. Acta Anaesthesiol Scand 2007; 51: 331-40. [CrossRef]
26. Srinivasa S, Taylor MH, Singh PP, Yu TC, Soop M, Hill AG. Randomized clinical trial of goal-directed fluid therapy within an enhanced recovery protocol for elective colectomy. Br J Surg 2013; 100: 66-74. [CrossRef]
27. Phan TD, D'Souza B, Rattray MJ, Johnston MJ, Cowie BS. A randomised controlled trial of fluid restriction compared to oesophageal Doppler-guided goal-directed fluid therapy in elective major colorectal surgery within an Enhanced Recovery After Surgery program. Anaesth Intensive Care 2014; 42: 752-60.
28. De Hert S, Imberger G, Carlisle J, Diemunsch P, Fritsch G, Moppett I, et al. Task Force on Preoperative Evaluation of the Adult Noncardiac Surgery Patient of the European Society of Anaesthesiology. Preoperative evaluation of the adult patient undergoing non-cardiac surgery: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol 2011; 28: 684-722. [CrossRef]
29. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, Hert SD, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: Cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: Cardio- vascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 2014; 14: 2383-431. [CrossRef]