

to fluid responders as long as they respond should not become the iatrogenic syndrome of the decade.”<sup>9</sup> Bearing this sentiment in mind, and considering these two criteria for fluid administration, it is not surprising that the results of this trial are negative. Gómez-Izquierdo *et al.*’s important work critically underscores the notion that intraoperative fluid administration based solely on fluid responsiveness is neither physiologically sound nor should it be expected to improve surgical outcomes.

## Competing Interests

Dr. Bloomstone is on the speaker’s bureau of the Edwards Lifesciences’s (Irvine, California) Critical Care Division and is on the steering committee of the American Society for Enhanced Recovery (ASER; Milwaukee, Wisconsin). Dr. Kramer has ownership positions in Arcos, Inc. (Missouri City, Texas), and Resuscitation Solutions, Inc. (Galveston, Texas). Dr. Navarro e Lima declares no competing interests.

**Joshua A. Bloomstone, M.D., C.S.S.G.B., C.L.S., Lais Helena Navarro e Lima, M.D., Ph.D., George Kramer, Ph.D.** University of Arizona, Phoenix, Arizona (J.A.B.). [jbloomstone@cox.net](mailto:jbloomstone@cox.net)

## References

- Gómez-Izquierdo JC, Trainito A, Mirzakandov D, Stein BL, Liberman S, Charlebois P, Pecorelli N, Feldman LS, Carli F, Baldini G: Goal-directed fluid therapy does not reduce primary postoperative ileus after elective laparoscopic colorectal surgery: A randomized controlled trial. *ANESTHESIOLOGY* 2017; 127:36–49
- Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, Grocott MP, Ahern A, Griggs K, Scott R, Hinds C, Rowan K; OPTIMISE Study Group: 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
- Rollins KE, Lobo DN: Intraoperative goal-directed fluid therapy in elective major abdominal surgery: A meta-analysis of randomized controlled trials. *Ann Surg* 2016; 263:465–76
- Gupta R, Gan TJ: Peri-operative fluid management to enhance recovery. *Anaesthesia* 2016; 71 Suppl 1:40–5
- 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
- Bloomstone JA, Loftus T, Hutchison R: ERAS: Enhancing recovery one evidence-based step at a time. *Anesth Analg* 2015; 120:256
- Nicholson A, Lowe MC, Parker J, Lewis SR, Alderson P, Smith AF: Systematic review and meta-analysis of enhanced recovery programmes in surgical patients. *Br J Surg* 2014; 101:172–88
- Navarro LH, Bloomstone JA, Auler JO Jr, Cannesson M, Rocca GD, Gan TJ, Kinsky M, Magder S, Miller TE, Mythen M, Perel A, Reuter DA, Pinsky MR, Kramer GC: Perioperative fluid therapy: A statement from the International Fluid Optimization Group. *Perioper Med (Lond)* 2015; 4:3
- Takala J: Volume responsive, but does the patient need volume? *Intensive Care Med* 2016; 42:1461–3

(Accepted for publication November 27, 2017.)

## Goal-directed Hemodynamic Therapy: Neither for Anyone, Neither the Same for Everyone

*To the Editor:*

Gómez-Izquierdo *et al.* report the results of a randomized, methodologically flawless clinical trial to analyze the influence of goal-directed hemodynamic therapy in the postoperative ileus within a well-established enhanced recovery protocol.<sup>1</sup> This strategy eliminates all the confounding factors that could alter the results of a single intervention. Taking into account that fluid therapy in the control group was based on traditional principles, the conclusion about the goal-directed hemodynamic therapy obtained from this study should be generalizable. Nevertheless, there are certain aspects to consider:

There is scientific interest in removing the goal-directed hemodynamic therapy from the enhanced recovery protocols and questioning the value of its individual components, especially the value of the stroke volume optimization.<sup>2</sup> However, intraoperative fluid management outside clinical trials is extremely variable,<sup>3</sup> and both an excessively restrictive and an excessively liberal approach lead to an increase in postoperative ileus.<sup>4</sup> Moreover, observational studies performed within enhanced recovery protocols repeatedly showed that inadequate fluid therapy was independently associated with postoperative complications.<sup>5,6</sup> Although it has been suggested that goal-directed hemodynamic therapy, and especially the stroke volume optimization,<sup>2</sup> lead to excessive fluid administration, the systematic review recently published by Michard *et al.* confirmed otherwise.<sup>7</sup> The same outcome has been corroborated by a Gómez-Izquierdo *et al.* study, in which similar amounts of fluids were given on the day of surgery.<sup>1</sup> The administration of vasopressors and inotropics were also similar in both groups. Interestingly, these drugs were administered to both groups without a clinical protocol. Additionally, although the goal-directed hemodynamic therapy group had higher cardiac output, stroke volume, and mean arterial pressure values throughout the surgery, these were not significantly higher compared with the control arm.<sup>1</sup> Consequently, using an equivalent amount of fluids and vasopressors, both groups reached the same hemodynamic goals, which could explain the lack of efficacy of the goal-directed hemodynamic therapy in this trial, even with a significantly higher weight balance gain on the first day in the control group. As in previous trials,<sup>8</sup> it would have been interesting to analyze which (risk) patients and which hemodynamic values were associated with postoperative complications.

Certain subsets of patients rather than all patients undergoing colorectal surgery with enhanced recovery protocols seem to benefit the most from goal-directed hemodynamic therapy. Meta-analysis demonstrated the futility of the goal-directed hemodynamic therapy in low-risk surgical patients.<sup>2,9</sup> Gómez-Izquierdo *et al.* conducted their study in

relatively healthy (mainly American Society of Anesthesiologists status II) and young patients, and the incidence of postoperative ileus was lower than expected. This subgroup of patients probably has a higher risk of volume overload than tissue hypoperfusion, so a balanced fluid therapy generally should be sufficient to achieve outcomes. Recently, Tengberg *et al.* showed a statistically significant reduction in postoperative mortality in acute high-risk abdominal surgery by implementing enhanced recovery protocols with goal-directed hemodynamic therapy, based mainly on stroke volume optimization with colloids (15 vs. 22%;  $P = 0.005$ ).<sup>10</sup> This is consistent with a previous meta-analysis that showed a reduction in complications only in high-risk patients (relative risk 0.57; 95% CI, 0.41 to 0.78;  $P = 0.0005$ ).<sup>2</sup> In conclusion, future goal-directed hemodynamic therapy research should focus specifically on high-risk surgical patients, both within and outside enhanced recovery pathways.

### Competing Interests

Dr. Ripollés-Melchor received travel funding from Deltex Medical (Chichester, United Kingdom) and honoraria for lectures from Fresenius Kabi (Bad Homburg, Germany), Edwards Lifesciences (Irvine, California), Deltex Medical, and Merck Sharp & Dohme (Kenilworth, New Jersey). He is currently the Chief of Fluid Management section of Grupo Español de Rehabilitación Multimodal (GERM/ ERAS Spain Chapter; Zaragoza, Spain). Dr. Aldecoa declares no competing interests.

**Javier Ripollés-Melchor, M.D., César Aldecoa, Ph.D.**  
Infanta Leonor University Hospital, Madrid, Spain (J.R.-M.).  
ripo542@gmail.com

### References

- Gómez-Izquierdo JC, Trainito A, Mirzakandov D, Stein BL, Liberman S, Charlebois P, Pecorelli N, Feldman LS, Carli F, Baldini G: Goal-directed fluid therapy does not reduce primary postoperative ileus after elective laparoscopic colorectal surgery: A randomized controlled trial. *ANESTHESIOLOGY* 2017; 127:36–49
- Ripollés-Melchor J, Casans-Francés R, Espinosa A, Abad-Gurumeta A, Feldheiser A, López-Timoneda F, Calvo-Vecino JM; EAR Group, Evidence Anesthesia Review Group: Goal directed hemodynamic therapy based in esophageal Doppler flow parameters: A systematic review, meta-analysis and trial sequential analysis. *Rev Esp Anestesiología Reanim* 2016; 63:384–405
- 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
- Thacker JK, Mountford WK, Ernst FR, Krukas MR, Mythen MM: Perioperative fluid utilization variability and association with outcomes: Considerations for enhanced recovery efforts in sample US surgical populations. *Ann Surg* 2016; 263:502–10
- ERAS Compliance Group: The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: Results from an international registry. *Ann Surg* 2015; 261(6):1153–9
- Askild D, Segelman J, Gedda C, Hjærn F, Pekkarinen K, Gustafsson UO: The impact of perioperative fluid therapy on short-term outcomes and 5-year survival among patients undergoing colorectal cancer surgery—A prospective cohort study within an ERAS protocol. *Eur J Surg Oncol* 2017; 17:30445–6
- Michard F, Giglio MT, Brienza N: Perioperative goal-directed therapy with uncalibrated pulse contour methods: Impact on fluid management and postoperative outcome. *Br J Anaesth* 2017; 119:541–3
- Schmid S, Kapfer B, Heim M, Bogdanski R, Anetsberger A, Blobner M, Jungwirth B: Algorithm-guided goal-directed haemodynamic therapy does not improve renal function after major abdominal surgery compared to good standard clinical care: A prospective randomised trial. *Crit Care* 2016; 20:50
- 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
- Tengberg LT, Bay-Nielsen M, Bisgaard T, Cihoric M, Lauritsen ML, Foss NB; AHA study group: Multidisciplinary perioperative protocol in patients undergoing acute high-risk abdominal surgery. *Br J Surg* 2017; 104:463–71

(Accepted for publication November 27, 2017.)

### In Reply:

We would like to thank Bloomstone *et al.* for their important comments on our study.<sup>1</sup> We certainly agree with Bloomstone *et al.* that fluid responsiveness should not be confused with hypovolemia. Being a fluid responder does not necessarily mean requiring additional intravenous fluids. *Vice versa*, fluid responsiveness should be determined before volume expansion, when clinical signs of hypovolemia suggest that patients might require additional intravenous fluids. Identifying hypovolemic patients might be challenging, however, given that standard hemodynamic parameters or biologic markers used during surgery may not be specific enough, or may fail to identify hypovolemic patients in a timely fashion. Furthermore, the majority of studies evaluating the effectiveness of goal-directed fluid therapy on postoperative outcomes, including ours, include protocols that preemptively maximize stroke volume by administering bolus of fluids based on dynamic indices or on the stroke volume response to a fluid challenge, independent of the presence of clinical signs of hypovolemia. As Bloomstone *et al.* also reported in their referenced and important consensus statement, stroke volume maximization has been considered “the cornerstone of most goal-directed therapy protocols.”<sup>2</sup>

Although consensus statements and recommendations on perioperative fluid therapy (that we fully support) properly advocate to first determine whether “the patient requires hemodynamic support or augmentation of cardiovascular function”<sup>2</sup> or to contextualize the presence of fluid responsiveness (*i.e.*, is there a problem justifying additional fluid administration?),<sup>3</sup> and second, to establish the presence of fluid responsiveness,<sup>2,3</sup> it must be acknowledged that these recommendations are based on studies mainly adopting maximal stroke volume optimization protocols,<sup>4–7</sup> rather than protocols based on stroke volume optimization when ascertained clinically.