REVIEWS

Perioperative goal directed therapy using automated closed-loop fluid management: the future?

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Abstract

Although surgery has become much safer, it has also becoming increasingly more complex and perioperative complications continue to impact millions of patients worldwide each year. Perioperative hemodynamic optimization utilizing Goal Directed Therapy (GDT) has attracted considerable interest within the last decade due to its ability to improve postoperative short and long-term outcomes in patients undergoing higher risk surgeries. The concept of GDT in this context can be loosely defined as collecting data from minimally invasive hemodynamic monitors with the intention of using such data (flow-related parameters and/or dynamic parameters of fluid responsiveness) to titrate therapeutic interventions (intravenous fluids and/or inotropic therapy administration) with the ultimate aim of optimizing end organ tissue perfusion. Recently, the increasing amount of evidence supporting the implementation of GDT strategies has been considered so robust as to allow for the creation of national recommendations in the United Kingdom (UK), France, and Europe. These recommendations from such influential scientific societies and the potential clinical and economic benefits of GDT protocols need to also be examined within the current shift from a "pay for service" to a "pay for performance" health care system. This shift is strongly encouraged within emerging systems such as the Perioperative Surgical Home (PSH) paradigm from the United States. As a result, hospitals and clinicians around the world have become increasingly incentivized to implement perioperative hemodynamic optimization using GDT strategies within their departments. Unfortunately, its adoption continues to be quite limited and a lack of standardized criteria for perioperative fluid administrations has resulted in significant clinical variability among practitioners. This current review will provide a brief up-to-date overview of GDT, discuss current clinical practice, analyze why implementation has been limited and finally, describe the newer closed-loop GDT concept along with its potential risks and benefits.

Key words: goal directed therapy; hemodynamic optimization; closed-loop; cardiac output

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It has been estimated that approximately 240 million anaesthesia procedures are completed worldwide every year [1]. Of these, approximately 10%, or 24 million, are conducted on "high risk" surgical patients. However, this subset disproportionally accounts for more than 80% of perioperative mortality [2]. Moderate risk surgery is much more common as it represents approximately 40% of annual procedures, or 96 million patients. Thankfully, most of these patients continue on to have an uncomplicated postopera-tive course. However, it is estimated that approximately 30% of these moderate risk surgeries, or 29 million patients a year, end up having a "minor" postoperative complication (most commonly a gut injury inducing delayed enteral feeding, abdominal distension, nausea, vomiting or wound complica-tions) [3]. Even if these complications are said to be "minor", they still lead to increased postoperative treatment, length of stay in the hospital and overall costs related to the perio-perative management. A recent international trial ("EUSOS"

study) in non-cardiac surgical patients demonstrated that the mortality rate was high (4%) and varied substantially across European countries, suggesting the need for national and international guidelines to improve postoperative outcomes [4]. We currently know that most of this documented post-operative morbidity is related to tissue hypoperfusion [3, 5]. As such, one of the most critical goals of the physician in the operating room (OR) or intensive care unit (ICU) is to correct hypovolemia and maintain adequate tissue perfusion via the optimization of fluid management. To achieve this goal, as stated by Arthur Guyton in his Textbook of Medical Physiology, one needs "an adequate perfusion pressure in order to force blood into the capillaries of all organs and an adequate cardiac output to deliver oxygen and substrates, and to remove carbon dioxide and other metabolic products" [6, 7]. However, while blood pressure monitoring is part of the American Society of Anesthesiologists (ASA) guidelines for basic monitoring [8], a recent international survey has demonstrated that cardiac output and other relevant hemodynamic parameters are rarely monitored, even during high-risk surgery [9].

FLUID ADMINISTRATION: WHERE ARE WE COMING FROM?

Throughout the developed and developing world most anaesthesiologists commonly use their clinical experience in conjunction with formulas of fixed-volume calculations such as the "4–2–1" rule [10], alongside other basic traditional static variables (e.g. heart rate, blood pressure, central venous pressure and urine output), to guide their perioperative fluid administration [11]. Unfortunately, although these variables are considered important components of a global patient assessment, they have consistently been shown to be poor predictors of fluid responsiveness (defined as the percent change in stroke volume induced by volume expansion) [11]. This is because such static signs of hypovolemia (tachycardia, hypotension, and oliguria) may be present in normovolemia and absent in hypovolemia. Resulting con-

fusion and poor management can lead to adverse clinical outcomes related to either hypovolemia or hypervolemia (Table 1). Both of these sets of complications can potentially cause a decrease in oxygen delivery to the tissues which can then lead to an increase in postoperative morbidity (Fig. 1) [12]. In addition, Le Manach et al. recently demonstrated that blood pressure changes could not be used to track stroke volume changes induced by volume loading [13]. They also revealed that the relationship between arterial pressure, ventricular stroke volume, and venous return is not simple and certainly not linear. Consequently, cardiac output optimization in the operating room (which relies heavily on the idea that fluid administration increases venous return) cannot be optimally performed with standard basic monitoring parameters, such as arterial pressure and heart rate**.**

FLUID RESPONSIVENESS AND GDT: WHERE ARE WE?

Moving beyond such static indices, newer dynamic parameters relying on cardiopulmonary interactions in mechanically ventilated patients under general anaesthesia have been developed since the year 2000 [14, 15]. They are increasingly being used to evaluate volume status as they have consistently been shown to be superior to static parameters for the prediction of fluid responsiveness [16]. These dynamic variables can be obtained using a variety of modern cardiac output (CO) monitoring technologies which have rapidly evolved from being very invasive to minimally invasive [12, 17, 18]. Such devices are beginning to allow for the widespread practice of accurate perioperative hemodynamic optimization. However, as with many novel technologies, clinicians are still unsure about how and which of them to use in their daily practice. Moreover, these dynamic parameters of fluid responsiveness have several limitations that need to be known and understood before such variables can be adequately utilized in a clinical setting. Firstly, these variables have to be used in mechanically ventilated patients undergoing general anaesthesia as studies performed in spontaneously breathing patients

Table 1. Comparison between complications associated with hypervolemia and hypovolemia

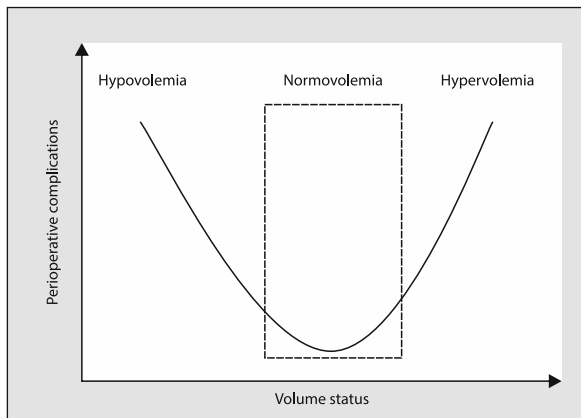| Complications of hypervolemia	Complications of hypovolemia
Increases venous pressure resulting in loss of fluid from the intravascular to interstitial space which can lead to pulmonary and peripheral edema impairing tissue oxygenation	Reduces effective blood circulatory volume resulting in diversion of blood flow from non vital organs (skin, gut, kidneys) to vital organs (heart and brain)
Increases demand on cardiac function	Activates the sympathetic nervous and renin angiotensin system
Decreases tissue oxygenation with delayed wound healing	Increases inflammatory response
May cause coagulation disturbances through hemodilution	May also lead to vasopressor agent administration which may increase hypo perfusion and ischemia [102]
Is associated with increased daily fluid balance and mortality [103]. Chappell et al. also demonstrates a relationship between weight gain related to excessive fluid administration and mortality [104]	

Figure 1. The classic relationship between perioperative volume status and perioperative complications. The relationship describes a U shape with an increased risk of complication for both perioperative hypovolemia and perioperative hypervolemia, emphasizing the importance of perioperative fluid optimization

failed to demonstrate that pulse pressure variation (PPV) can predict fluid responsiveness [19]. Moreover, tidal volume has an impact on the predictive value of PPV and a tidal volume of 8 mL kg^{-1} of body weight is generally required [20], although adjustments in the cut off value for PPV can be made in patients with smaller tidal volumes. Additionally, patients have to be in sinus rhythm with their chest closed (open chest, as well as open pericardium strongly modify the cardiopulmonary interactions), while intra-abdominal pressure has to be within normal ranges [21]. One should also keep in mind that around 40 % of all patients undergoing surgical procedures in the operating room met the strict criteria for the monitoring of fluid responsiveness using PPV [22] and that, despite its strong predictive value, PPV may be in the inconclusive "gray zone" (between 9% and 13%) in approximately 25% of patients during general anaesthesia. [23]. Its utility may be even worse with regard to intensive care units. Mahjoub *et al.* demonstrated that a very low percentage (only 2%) of patients satisfied the validity criteria for using PPV [24] in this setting.

Finally, we should keep in mind that such hemodynamic monitoring systems are simply measurement tools and, to quote Dr. Michael Pinsky: "no monitoring device, no matter how simple or sophisticated, will improve patients' outcome unless coupled to a treatment which itself improves outcome" [25]. Thus, all of these minimally invasive CO monitoring devices only have the ability to improve postoperative patients' outcome if they are integrated into protocols that guide appropriate therapeutic interventions.

Perioperative Goal directed therapy is a general concept of managing fluids and/or vasopressor agents using these minimally invasive technologies, coupled with predefined treatment algorithms, in order to achieve physiological targets with the ultimate goal of optimizing tissue oxygen delivery [26]. This concept, based on the optimization of flow parameters and/or preload responsiveness indices, has consistently been shown to be useful in decreasing postoperative morbidity, reducing hospital length of stay [27–32] and hospital costs [33] in patients undergoing high risk surgery. As noted above, the large amount of evidence supporting GDT is currently so robust that clinical societies in the United Kingdom [34], France [35] and Europe [36] have established relevant national guidelines. These professional societies strongly consider GDT as the best practice for perioperative hemodynamic optimization in high risk surgical patients. The most significant progress, however, has been made in the United Kingdom where the National Institute of Health and Clinical Excellence has recommended the specific use of oesophageal Doppler or similar fluid responsiveness monitoring devices to titrate fluid administration during the perioperative period in high risk surgery [37]. Additionally, many UK health care trusts currently receive payment to incentivize the implementation of this strategy as standard of care for at least 80% of eligible patients [37]. Hopefully, similar national guidelines will be created in the future by other countries looking for decreased perioperative morbidity.

GDT WITHIN ERAS AND PSH MODELS: WHERE WE SHOULD GO?

Progress towards a more standardized approach for optimal perioperative fluid managements has already been made. Moreover, such GDT approaches can be applied alone or as a part of the newer comprehensive practices, such as the Enhanced Recovery After Surgery [38] programs (ERAS) in Europe and the Perioperative Surgical Home model (PSH) [39–41] in the United States, both of which emphasize the importance of "precise fluid management" during surgery [42, 43]. The Enhanced Recovery After Surgery (ERAS) program initiated in Europe has evolved considerably over the past few years and is gaining traction throughout the world [44]. The aim of this program is to apply best practices to high-risk surgical patients, which requires the participation of all clinicians involved in relevant patient care. In the United States, the perioperative surgical home (PSH) model has recently been gaining momentum. It is defined as a "patient-centered and team-based approach that guides the patient throughout the entire surgical experience by developing protocols and guidelines to improve perioperative management that also incorporates the anesthesiologist into a central management role." This philosophy is aimed at reducing variability and mistakes through better coordination of care and increased evidence-based standardization. This PSH design may soon become the standard of care in the US as it has been shown to result in improved clinical outcomes [45, 46].

IMPLEMENTATION OF A GDT PROTOCOL IN DAILY CLINICAL PRACTICE: WHAT'S THE PROBLEM?

Unfortunately, despite strong published data highlighting the clinical and economic benefits of GDT [28], translating this evidence to the bedside remains a challenge and is further complicated as it is inconsistently applied [9, 47]. Unfortunately, it has been estimated that only around 50% of participating patients receive recommended therapies [48, 49]. Specific to fluid management, there remains significant variability within fluid administration practices among clinicians which likely contributes to observed variability in surgical outcomes [50]. One possible reason for low utilization is that protocols are intrinsically both time and attention intensive; even under optimal study conditions, clinicians' compliance to similar protocols is inconsistent and often not greater than 50% [51–53]. Another explanation for slow adoption may be the moderate learning curve which accompanies such protocols when implemented correctly in practice. The "OPTIMISE" trial recently demonstrated that such a learning curve, combined with the inherent difficulty adhering to a new protocol, are both significant weakness of our current approach to the larger utilization of GDT [54]. This is the largest multicenter trial to date reporting the results of high-risk patients undergoing gastrointestinal surgery who were randomized to receive either standard care or GDT. Although the results of this study showed no difference in the primary outcome between the two groups, the results became significant when they were adjusted for protocol adherence, with GDT leading to fewer postoperative complications than the control group. As the first 10 patients of each centre were excluded after this adjustment, one can likely presume that a large learning curve exists and that the protocols are not necessarily easy to follow in an operating room already saturated with monitors, tasks, and frequent distractions. A final potential reason for minimal compliance may be explained by the fact that GDT strategies have never been well standardized and today no single consensus on the use of GDT has been widely accepted across the published literature [55] . Furthermore, studies of GDT have utilized a plethora of different techniques, algorithms and minimally invasive devices making it difficult for clinicians to choose an approach and leading to confusion about how and when to use each technique correctly.

AUTOMATION AND CLOSED-LOOP TECHNOLOGY: WHERE ARE WE GOING IN THE NEAR FUTURE?

With the above understanding of the current state of GDT, the natural next questions becomes whether we can create a link between such evidence-based recommendations and consistent clinical adoption at the bedside. Anaesthesiologists are well-known to be routinely confronted with computer based-systems in their daily management and, as a result, are increasingly comfortably with relevant computational advancements [56]. As increasingly sophisticated monitoring devices are developed, however, anaesthesiologist may feel overwhelmed by the constantly growing quantity of displayed hemodynamics, especially if the minutia of a GDT protocol has to be followed very closely. A natural extension, using an engineering paradigm, would be to automate the aspects of fluid administration and integrate pre-defined algorithms into applicable computer hardware [57]. Indeed, a closed-loop hemodynamic system offers one an elegant and suitable way to integrate these different data streams in order to decrease clinical distractions and increase compliance.

Very briefly, a closed-loop system is a system wherein a controller monitors one or multiple variables and adjusts one or more interventions using a feedback process [57]. A simple example would be a thermostat adjusting heating and cooling functions based on real time measurements of temperature. A clinical example would be the completely automated closed-loop fluid administration system recently developed by Dr. Cannesson and Dr. Rinehart at UC Irvine, which is designed to assist anaesthesiologists by automating goal directed fluid therapy protocols. Such automation would decrease unnecessary distractions and optimize fluid delivery using well establish protocols. This closed-loop system uses flow-based parameters (stroke volume, cardiac output) and/or dynamic parameters of fluid responsiveness (pulse pressure variation, stroke volume variation) collected from a minimally invasive CO monitoring device (EV-1000, Edwards Lifesciences, Irvine, USA) to automatically control fluid boluses in order to apply GDT protocols consistently with minimal provider workload (Fig. 2). The closed-loop software and hardware can easily track each bolus that has been given and, using patient specific accumulated data, can project the anticipated benefit of an additional bolus. This approach has been extensively tested in simulation [58, 59], engineering [60], and animal [61] studies before being tested in clinical practice.

After accounting for expected risks, what increased benefits could this system bring for anaesthesiologists in the operating room?

Firstly, the automated closed-loop system has been shown to be more precise in monitoring clinical variables than human practitioners, as well as maintaining such hemodynamic parameters more steadily and consistently than trained anaesthesiologists [58, 59] in simulated and animal haemorrhage models [61]. This difference has been explained by an earlier onset of fluid administration. Indeed, the closed-loop software and hardware was more adept at responding to multiple variables indicating a need for fluid therapy. This automated administration more quickly
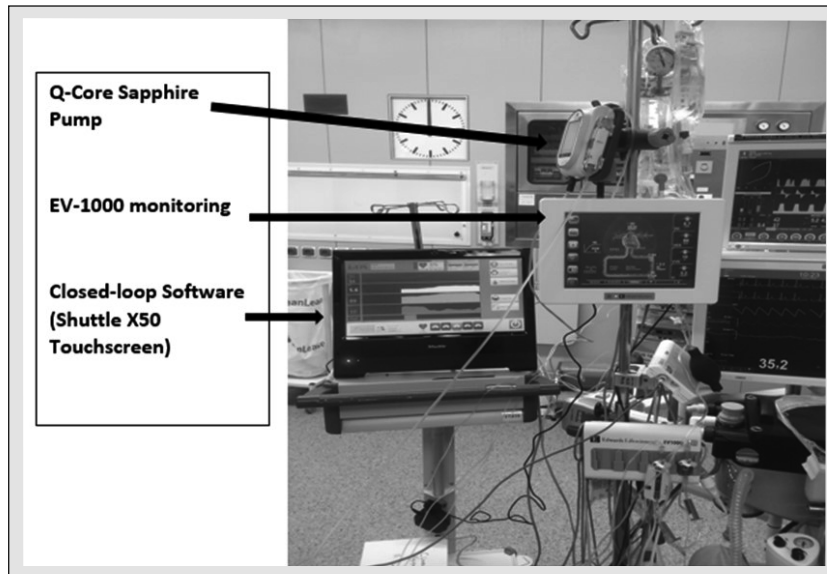
Figure 2. Closed-loop set-up in Irvine and Brussels. The closed-loop is connected to EV-1000 monitoring devices with a USB-to serial adapter connected to the device's serial output port. The closed-loop software runs on a Shuttle X50 touchscreen PC. A Q-Core Sapphire Multi-Therapy Pump (Q-Core, Netanya, Israël) is used to deliver the fluid boluses

optimizes intraoperative stroke volume in order to bring the patient onto the plateau of the Frank-Starling curve when compared to anaesthesiologists acting alone.

Secondly, the closed-loop algorithm can decrease individual operator variability in managing fluid titration and thus help standardize goal directed fluid therapy delivery across clinicians and institutions. Reducing variability has been shown to be a key factor in improving medical quality and patient safety [62]. Concordantly, the automated system can facilitate the implementation of high-quality, standardized, goal directed fluid therapy protocols with a high adherence when compared to standard practice. By optimizing patients' fluid status using a very mundane and repetitive task (titration of fluid), especially during long surgery cases, such a system will systemically reduce overall provider workload, thus allowing more time for the anaesthesiologist to focus his or her attention on other, more pertinent, medical decisions.

Lastly, along with reducing variability and allowing for increased provider focus, such a system will likely decrease medical errors, which have been shown to be a source of preventable morbidity in anaesthesiology and critical care [51, 63].

Two clinical studies have shown the feasibility of a closed-loop system for providing high-compliance goal directed fluid therapy while using a minimally invasive, and even a completely non-invasive CO monitoring system in patients undergoing high-risk [64] and moderate-risk [65] surgeries, respectively. The automated fluid administration systems were deemed successful if the patient spent more than 85% of intraoperative time in a preload-independent state (defined as a pulse pressure variation < 13 % and/or a cardiac index > 2.5 L min^{-1} m^{-2}). A more recent study [66], comparing closed loop assisted versus manual goal directed fluid therapy management during major abdominal surgery, showed that closed-loop assistance also resulted in a greater portion of case time spent in a preload independent state when compared to manual delivery of goal directed fluid therapy, without any difference in total fluid volumes administered to patients. Further trials are still needed to examine the benefits of this closed-loop system on clinical outcomes.

Recent advances in clinical technology have likely disproportionately benefitted the practice of anaesthesia when compared to other specialties. The time for bridging long-standing automated engineering practices with such improvements in clinical monitoring is fast approaching. One common question posed when providers hear about this technology has been, "Will this automation eventually replace me in the operating room?" As we have seen with most emergent automated processes, a more appropriate question should be, "What benefit can automation have on my daily clinical practice and how can this system improve patient care while also mastering mundane clinical tasks?" Although this question has not yet been fully answered, it is now being worked on at an unprecedented rate. While this field will continue to train experts in physiology, it will also shift to create anaesthesiologists who are increasingly adept at guiding patients throughout the entire perioperative process. Closed-loop technology, alongside the knowledge and expertise of a well-trained physician, will help ensure that a higher level of standardization, safer individualized

fluid administration and the highest quality of care are all being employed consistently and effectively.

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References:

1. *Weiser TG, Regenbogen SE, Thompson KD et al.:* An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet 2008; 372: 139–144. doi: 10.1016/S0140-6736(08)60878-8.
2. *Pearse RM, Harrison DA, James P et al.:* Identification and characterisation of the high-risk surgical population in the United Kingdom. Crit Care (London, England) 2006; 10: R81.
3. *Bennett-Guerrero E, Welsby I, Dunn TJ et al.:* The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. Anesth Analg 1999; 89: 514–519.
4. *Pearse RM, Moreno RP, Bauer P et al.:* Mortality after surgery in Europe: a 7 day cohort study. Lancet 2012; 380: 1059–1065. doi: 10.1016/S0140-6736(12)61148-9.
5. *Gan TJ, Mythen MG:* Does peroperative gut-mucosa hypoperfusion cause postoperative nausea and vomiting? Lancet 1995; 345: 1123–1124.
6. *Guyton AH, Hall JE:* Heart muscle: the heart as a pump and function of the heart valves. In: *Guyton AH, Hall JE (ed.):* Textbook of medical physiology, 11th edition. Philadelphia: Elsevier, Inc 2006: 103–115.
7. Guyton AH, Hall JE: Overview of the circulation: medical physics of pressure, flow, and resistance. In: *Guyton AH, Hall JE (ed.):* Textbook of medical physiology, 11th edition. Philadelphia: Elsevier, Inc 2006: 161–170.
8. American Society of Anesthesiologists, Standards of the American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring, http: //www.asahq.org/For-Members/~/media/For%20Members/documents/Standards%20Guidelines%20Stmts/Basic%20Anesthetic%20 Monitoring%202011.ashx; 12.01.2012.
9. *Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A:* Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. Crit Care (London, England) 2011; 15: R197. doi: 10.1186/cc10364.
10. *Bailey AG, McNaull PP, Jooste E, Tuchman JB:* Perioperative crystalloid and colloid fluid management in children: where are we and how did we get here? Anesth Analg 2010; 110: 375–390. doi: 10.1213/ANE .0b013e3181b6b3b5.
11. *Marik PE, Cavallazzi R:* Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Crit Care Med 2013; 41: 1774–1781. doi: 10.1097/CCM.0b013e-31828a25fd.
12. *Cannesson M:* Arterial pressure variation and goal-directed fluid therapy. J Cardiothorac Vasc Anesth 2010; 24: 487–497. doi: 10.1053/j. jvca.2009.10.008.
13. *Le Manach Y, Hofer CK, Lehot JJ et al.:* Can changes in arterial pressure be used to detect changes in cardiac output during volume expansion in the perioperative period? Anesthesiology 2012; 117: 1165–1174. doi: 10.1097/ALN.0b013e318275561d.
14. *Michard F, Boussat S, Chemla D et al.:* Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. Am J Respir Crit Care Med 2000; 162: 134–138.
15. *Feissel M, Michard F, Mangin I, Ruyer O, Faller JP, Teboul JL:* Respiratory changes in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic shock. Chest 2001; 119: 867–873.
16. *Marik PE, Cavallazzi R, Vasu T, Hirani A:* Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. Crit Care Med 2009; 37: 2642–2647. doi: 10.1097/CCM.0b013e3181a 590da.
17. *Michard F:* Changes in arterial pressure during mechanical ventilation. Anesthesiology 2005; 103: 419–428; quiz 449–415.
18. *Lansdorp B, Ouweneel D, de Keijzer A, van der Hoeven JG, Lemson J, Pickkers P:* Non-invasive measurement of pulse pressure variation and systolic pressure variation using a finger cuff corresponds with intra-arterial measurement. Br J Anaesth 2011; 107: 540–545. doi: 10.1093/bja/aer187.
19. *De Backer D, Pinsky MR:* Can one predict fluid responsiveness in spontaneously breathing patients? Intensive Care Med 2007; 33: 1111––1113.
20. *De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL:* Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. Intensive Care Med 2005; 31: 517–523.
21. *Duperret S, Lhuillier F, Piriou V et al.:* Increased intra-abdominal pressure affects respiratory variations in arterial pressure in normovolaemice and hypovolaemic mechanically ventilated pigs. Intensive Care Med 2007; 33: 163–171.
22. *Maguire S, Rinehart J, Vakharia S, Cannesson M:* Technical communication: respiratory variation in pulse pressure and plethysmographic waveforms: intraoperative applicability in a North American academic center. Anesth Analg 2011; 112: 94–96. doi: 10.1213/ANE .0b013e318200366b.
23. *Cannesson M, Le Manach Y, Hofer CK et al.:* Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a "gray zone" approach. Anesthesiology 2011; 115: 231–241. doi: 10.1097/ALN.0b013e318225b80a.
24. *Mahjoub Y, Lejeune V, Muller L et al.:* Evaluation of pulse pressure variation validity criteria in critically ill patients: a prospective observational multicentre point-prevalence study. Br J Anaesth 2014; 112: 681–685. doi: 10.1093/bja/aet442.
25. *Pinsky MR, Payen D:* Functional hemodynamic monitoring. Crit Care (London, England) 2005; 9: 566–572.
26. *Cecconi M, Corredor C, Arulkumaran N et al.:* Clinical review: goal-directed therapy-what is the evidence in surgical patients? The effect on different risk groups. Crit Care (London, England) 2013; 17: 209. doi: 10.1186/cc11823.
27. *Benes J, Giglio M, Brienza N, Michard F:* The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: a meta-analysis of randomized controlled trials. Crit Care (London, England) 2014; 18: 584. doi: 10.1186/s13054-014-0584-z.
28. *Ebm C, Cecconi M, Sutton L, Rhodes A:* A cost-effectiveness analysis of postoperative goal-directed therapy for high-risk surgical patients. Crit Care Med 2014; 42: 1194–1203. doi: 10.1097/CCM.0000000000000164.
29. *Corcoran T, Rhodes JE, Clarke S, Myles PS, Ho KM:* Perioperative fluid management strategies in major surgery: a stratified meta-analysis. Anesth Analg 2012; 114: 640–651. doi: 10.1213/ANE.0b013e318240d6eb.
30. *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: 1392–1402. doi: 10.1213/ANE .0b013e3181eeaae5.
31. *Pearse RM, Harrison DA, MacDonald N 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: 2181–2190. doi: 10.1001/jama.2014.5305.
32. *Giglio MT, Marucci M, Testini M, Brienza N:* Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: a meta--analysis of randomized controlled trials. Br J Anaesth 2009; 103: 637–646. doi: 10.1093/bja/aep279.
33. *Manecke GR, Asemota A, Michard F:* Tackling the economic burden of postsurgical complications: would perioperative goal-directed fluid therapy help? Crit Care (London, England) 2014; 18: 566. doi: 10.1186/s13054-014-0566-1.
34. NICE draft guidance on cardiac output monitoring device published for consultation, http://www.nice.org.uk/newsroom/pressreleases/Draft-GuidanceOnCardiacOutputMonitoringDevice.jsp; 29.09.215.
35. *Vallet B, Blanloeil Y, Cholley B, Orliaguet G, Pierre S, Tavernier B:* Guidelines for perioperative haemodynamic optimization. Ann Fr Anesth Reanim 2013; 32: e151–158. doi: 10.1016/j.annfar.2013.09.010.
36. Gustafsson UO, Scott MJ, Schwenk W et al.: Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery

(ERAS(®)) Society recommendations. World J Surg 2013; 37: 259–284. doi: 10.1007/s00268-012-1772-0.

37. National Institute for Health and Clinical Excellence. Medical techno-logies guidance MTG3: CardioQ ODM oesophageal doppler monitor. March 2011, http: //www.nice. org.uk/MTG3; accessed 3.10.2011.

38. *Lassen K, Soop M, Nygren J et al:* Consensus review of optimal perio-perative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. Arch Surgery 2009; 144: 961–969. doi: 10.1001/archsurg.2009.170.

39. *Cannesson M, Kain Z:* Enhanced recovery after surgery versus perio-perative surgical home: is it all in the name? Anesth Analg 2014; 118: 901–902. doi: 10.1213/ANE.0000000000000177.

40. *Cannesson M, Kain ZN:* The role of perioperative goal-directed therapy in the era of enhanced recovery after surgery and perioperative surgical home. J Cardiothorac Vasc Anesth 2014; 28: 1633–1634. doi: 10.1053/j.jvca.2014.09.015.

41. *Kain ZN, Vakharia S, Garson L et al.:* The perioperative surgical home as a future perioperative practice model. Anesth Analg 2014; 118: 1126–1130. doi: 10.1213/ANE.0000000000000190.

42. *Garson L, Schwarzkopf R, Vakharia S et al.:* Implementation of a total joint replacement-focused perioperative surgical home: a management case report. Anesth Analg 2014; 118: 1081–1089. doi: 10.1213/ANE.0000000000000191.

43. *Kain ZN, Vakharia S, Garson L et al.:* The perioperative surgical home as a future perioperative practice model. Anesth Analg 2014; 118: 1126–1130. doi: 10.1213/ANE.0000000000000190.

44. *Kehlet H:* Enhanced Recovery After Surgery (ERAS): good for now, but what about the future? Can J Anaesth 2015; 62: 99–104. doi: 10.1007/s12630-014-0261-3.

45. *Garson L, Schwartzkopf R, Vakharia S et al.:* Implementation of a total joint replacement-focused perioperative surgical home: a management case report. Anesth Analg 2014; 118: 1081–1089. doi: 10.1213/ANE.0000000000000191.

46. *Kain ZN, Vakharia S, Garson L et al.:* The Perioperative Surgical Home as a Future Perioperative Practice Model. Anesth Analg 2014; 118: 1081–1089. doi: 10.1213/ANE.0000000000000191.

47. *Miller TE, Roche AM, Gan TJ:* Poor adoption of hemodynamic optimiza-tion during major surgery: are we practicing substandard care? Anesth Analg 2011; 112: 1274–1276. doi: 10.1213/ANE.0b013e318218cc4f.

48. *McGlynn EA, Asch SM, Adams J et al.:* The quality of health care delivered to adults in the United States. New Engl J Med 2003; 348: 2635–2645.

49. *Baker R, Camosso-Stefinovic J, Gillies C et al.:* Tailored interventions to overcome identified barriers to change: effects on professional prac-tice and health care outcomes. Cochrane Database Syst Rev 2010(3): Cd005470. doi: 10.1002/14651858.CD005470.pub2.

50. *Lilot M, Ehrenfeld JM, Lee C, Harrington B, Cannesson M, Rinehart J:* Varia-bility in practice and factors predictive of total crystalloid administra-tion during abdominal surgery: retrospective two-centre analysis. Br J Anaesth 2015; 114: 767–76. doi: 10.1093/bja/aeu452.

51. *Gill F, Corkish V, Robertson J, Samson J, Simmons B, Stewart D:* An explo-ration of pediatric nurses' compliance with a medication checking and administration protocol. J Spec Pediatr Nurs 2012; 17: 136–146. doi: 10.1111/j.1744-6155.2012.00331.x.

52. *Lipton JA, Barendse RJ, Schinkel AF, Akkerhuis KM, Simoons ML, Sijbrands EJ:* Impact of an alerting clinical decision support system for glucose control on protocol compliance and glycemic control in the inten-sive cardiac care unit. Diabetes Technol Ther 2011; 13: 343–349. doi: 10.1089/dia.2010.0100.

53. *Spanjersberg WR, Bergs EA, Mushkudiani N, Klimek M, Schipper IB:* Proto-col compliance and time management in blunt trauma resuscitation. Emerg Med J 2009; 26: 23–27. doi: 10.1136/emj.2008.058073.

54. *Pearse RM, Harrison DA, MacDonald N et al.:* Effect of a periopera-tive, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014; 311: 2181–2190. doi: 10.1001/jama.2014.5305.

55. *Wilms H, Mittal A, Haydock MD, van den Heever M, Devaud M, Windsor JA:* A systematic review of goal directed fluid therapy: rating of evidence for goals and monitoring methods. J Crit Care 2014; 29: 204–209. doi: 10.1016/j.jcrc.2013.10.019.

56. *Cannesson M, Rinehart J:* Innovative technologies applied to anesthesia: how will they impact the way clinicians practice? J Cardiothorac Vasc Anesth 2012; 26: 711–720. doi: 10.1053/j.jvca.2012.02.012.

57. *Rinehart J, Liu N, Alexander B, Cannesson M:* Review article: closed-loop systems in anesthesia: is there a potential for closed-loop fluid mana-gement and hemodynamic optimization? Anesth Analg 2012; 114: 130–143. doi: 10.1213/ANE.0b013e318230e9e0.

58. *Rinehart J, Chung E, Canales C, Cannesson M:* Intraoperative stroke volume optimization using stroke volume, arterial pressure, and heart rate: closed-loop (learning intravenous resuscitator) versus anesthe-siologists. J Cardiothor Vasc Anesth 2012; 26: 933–939. doi: 10.1053/j.jvca.2012.05.015.

59. *Rinehart J, Alexander B, Le Manach Y, Hofer C, Tavernier B, Kain ZN, Cannesson M:* Evaluation of a novel closed-loop fluid-administration system based on dynamic predictors of fluid responsiveness: an in silico simulation study. Crit Care (London, England) 2011; 15(6): R278. doi: 10.1186/cc10562.

60. *Rinehart J, Lee C, Cannesson M, Dumont G:* Closed-loop fluid resuscitation: robustness against weight and cardiac contractility variations. Anesth Analg 2013; 117: 1110–1118. doi: 10.1213/ANE.0b013e3182930050.

61. *Rinehart J, Lee C, Canales C, Kong A, Kain Z, Cannesson M:* Closed-loop fluid administration compared to anesthesiologist management for hemodynamic optimization and resuscitation during surgery: an in vivo study. Anesth Analg 2013; 117: 1119–1129. doi: 10.1213/ANE.0b013e3182937d61.

62. *Mackey DC:* Can we finally conquer the problem of medical quality? The systems-based opportunities of data registries and medical team-work. Anesthesiology 2012; 117: 225–226. doi: 10.1097/ALN.0b013e-318259aa06.

63. *Franklin BD, Taxis K, Barber N:* Parenteral drug errors. Reported error rates are likely to be underestimation. BMJ 2009; 338: b1814. doi: 10.1136/bmj.b1814.

64. *Rinehart J, Le Manach Y, Douiri H et al.:* First closed-loop goal directed fluid therapy during surgery: a pilot study. Ann Fr Anesth Reanim 2014; 33: e35–41. doi: 10.1016/j.annfar.2013.11.016.

65. *Joosten A, Suehiro K, Canales C, Cannesson M, Rinehart J:* Goal-Directed Fluid Therapy with Closed-loop Assistance during Moderate Risk Sur-gery Using Noninvasive Cardiac Output Monitoring: A Pilot Study. Br J Anaesth 2015; 114: 886–892. doi: 10.1093/bja/aev002.

66. *Rinehart J, Lee C, Joosten A et al.:* Closed Loop Assisted vs. Manual Goal--Directed Fluid Therapy During High-Risk Abdominal Surgery: A Case Control Study with Propensity Matching. Crit Care 2015; 19: 94. doi: 10.1186/s13054-015-0827-7.

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