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# Closed-Loop Hemodynamic Management

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**Abstract:** As the operating room and intensive care settings become increasingly complex the required vigilance practitioners must dedicate to a wide array of clinical systems has increased concordantly. The resulting shortage of available attention to these various clinical tasks creates a vacuum for the introduction of systems that can administer well established goal-directed therapies without significant provider feedback. Recently there has been an explosion of academic exploration into creating such automated systems, with a strong specific focus on hemodynamic control. Within this field, the largest focus has been on goal directed fluid therapy as systems automating vasopressor administration have only recently become viable options. Our goal in this review article is to summarize the validity of the relevant goal directed hemodynamic systems and explore the expanding role of automation within these systems.

**Key Words:** Automation, Vasoconstrictor agents, Fluid Therapy, Intraoperative monitoring

**Practice Points:**

- Closed loop hemodynamic systems are evolving at an unprecedented pace and increase compliance to goal directed strategies while having the potential to improve outcomes when compared to manually controlled systems.
- Closed-loop systems should be seen as an aid to the clinicians. The authors and developers of these systems strive to provide solutions to make the perioperative setting ever safer and more consistent for our patients.

**Research Agenda:**

- The major research priorities moving forward would be to increase understanding and acceptance of closed loop systems while also testing their safety and efficacy in a wider variety of hemodynamic (and other) clinical settings.

-The interaction between multiple closed-loop systems will also be an important hurdle for the growth of various automated systems.

- Regulatory pathways, acceptance by clinicians are going to be the next challenge

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## **Introduction:**

One of the fastest changing aspects of perioperative medicine is the relationship anesthesia providers have with the increasingly complex devices that surround them in the operating room. While our field once consisted of a medical practitioner providing ventilation, sedation, and monitoring through a simple face mask artfully dribbled with ether, it has now evolved into an environment where we are surrounded by a wide array of increasingly complex and sophisticated physiologic technologies. As a result, many perioperative physicians and practitioners do not *completely* understand the devices they rely so heavily upon.[1, 2] The theoretical long-term conclusion of this evolution is perioperative systems that are largely independent of practitioner intervention for frequent, repetitive actions (relying instead on practitioner input for more high-level goal selection and navigation of the anesthetic). In theory, the standardization and vigilance gained from such an arrangement could – just as it has in the airline industry – lead to lower complication rates, reduced patient morbidity and mortality, and lower costs. Although it is an interesting concept to discuss, such elaborate systems will likely not exist for many decades.

That being said, steps towards automating individual aspects of perioperative patient care are underway and one category receiving large amounts of interest is hemodynamic optimization. The reasons for this particular expansion are plentiful but largely consist of advancements in computing, development of a plethora of perioperative monitoring devices, evidence-based data-driven protocols, reduced physician workload and improved affordability. Automation of hemodynamic control has mainly been focused on two areas: fluid delivery and vasopressor administration. Significantly more literature addressing the automation of fluid therapy has been disseminated as various goal directed fluid therapy (GDFT) protocols known to

decrease perioperative morbidity have become widely accepted. Additionally, vasopressor automation is also gaining traction and will likely continue to expand in the upcoming years. Our goal here is to provide an overview of the recent evidence addressing various closed-loop systems designed to optimize perioperative hemodynamics.

## **The Rationale for Hemodynamic Targets and Protocols**

Before discussing the merits of automation, it is important to first ask if we have something worth automating. Do the protocols at the backbone of closed-loop systems actually improve our patients' outcome? The general theory behind these protocols are that a large proportion of perioperative complications are related to the imbalance of oxygen supply and demand, which is affected significantly by tissue hypo and hyper perfusion [3]. In order to avoid such perfusion abnormalities, which are very difficult to directly quantify, perioperative physicians have subsequently aimed to optimize the best available hemodynamic surrogates. These include arterial pressure, cardiac function, fluid status, end organ function, oxygenation and many other clinical variables known to affect oxygen delivery. Using these targets, the overarching strategy of goal directed hemodynamic therapy (GDHT) is to decrease suspected malperfusion via the clinical optimization of fluid status, vasopressors, and inotropes [4]. As stated above, the majority of recent hemodynamic optimization literature has been focused on GDFT and its ability to decrease patient morbidity. While there has been increased focus on goal directed vasopressor and inotrope administration, it will likely still require future academic investigations to completely rationalize its widespread implementation.

What does the data show regarding both GDFT and GDHT? Fortunately and unfortunately, the technologic and physiologic end points used in most studies is being updated at an incredible rate. When examined individually, older literature contains protocols, devices and/or statistical approaches that are significantly outdated or irrelevant to modern hemodynamic therapy. When examining modern data, the overall picture is also slightly blurry. Currently, there is a strong trend towards improved morbidity, although it may be potentially less-so than

previously thought. A large, randomized, prospective trial in 2014 (“OPTIMISE”) indicated that the clinical benefits of GDHT may have been previously overstated [5]. Interestingly, the same trial, when integrated into a large meta-analysis of 38 previous trials, demonstrated decreased perioperative morbidity, decreased length of stay (LOS), and even a strong trend towards a statistically significant decrease in mortality for patients cared for with GDHT [5]. Two studies published around the same time also concluded that GDHT may be less clinically advantageous than previously believed [6, 7], although advances in control groups “baseline” fluid therapy may have reduced the impact of protocolization. Additionally, it is worth clarifying that the strongest data supporting the use of GDHT has largely been in high-risk surgical patients [8, 9], as low to moderate risk surgeries require significantly larger sample sizes to demonstrate meaningful clinical benefit.

Beyond the above mentioned large meta-analysis in 2014, additional recent evidence has also emerged in *support* of establishing GDHT protocols. The most significant of these being a randomized, multicenter, prospective trial that found a 50% decrease in moderate to severe complications (acute kidney disease, pulmonary edema, respiratory distress syndrome, wound infections, etc.) and a decreased length of hospital stay in the GDHT group [10]. The reduction in complications was isolated to patients undergoing gastrointestinal procedures, although that was 75% of the patient population included in the study. Other, smaller studies have also been recently completed that are worth discussing. One group from University of California, Irvine demonstrated decreased LOS and morbidity with GDHT implementation via a historical, prospective, quality improvement (QI) study [11]. In another recent QI study, Jin et al found decreased morbidity but no decreased 30-day mortality, LOS, or cost associated with the implementation of a GDFT program using a pre and post implementation comparison [12]. In

another match-controlled study, Russo et al found decreased fluid administration, increased intraoperative diuresis, lower post-operative lactate levels, shorter times to bowel recovery, and decreased length of stay for surgical gynecologic patients maintained with goal directed hemodynamic managements, which included both fluid and vasopressor/inotrope support [13]. Finally, Lima et al demonstrated that the implementation of a hemodynamic protocol resulted in a significant decrease in postoperative complications compared to standard of care therapy [14].

When solely examining vasopressor administration independent of a fluid therapy protocol, the evidence is less robust. Importantly, in order to justify the potential automation of vasopressor administration systems, it is important to examine the efficacy of manually titrated vasopressor administration. While there are multiple previous studies indicating that keeping a patient within a target range is difficult, quantifying the actual discrepancies has proven to be quite challenging [15-19]. Fortunately, one group has recently completed such a study at two large international academic centers examining patients in both the ICU and OR under vasopressor therapy. This study demonstrated that patients only remained in the desired blood pressure target range for 48% of their vasopressor administration period, with most patients being kept above the target range (likely allow for a buffer if provider vigilance diminished).[20]

Moving beyond this unacceptable efficacy of manually titrated vasopressor infusions, there have been multiple studies highlighting the importance of perioperative blood pressure control in the operating room [18, 21-25] and intensive care unit [17, 26-29]. The combination of both a demonstrated benefit and poor provider control is alarming and clearly justifies the need for further research into the development of novel systems that can improve vasopressor administration.

When looking at all of this data cohesively, it appears that GDHT protocols do consistently decrease perioperative morbidity in moderate and high-risk surgical patients although conclusive effects on LOS and mortality still require additional clinical research. Furthermore, there is sufficient evidence that automating vasopressor administration in the OR and ICU would provide significant improvements in blood pressure management and potentially patient outcome.

### **The Benefits of Automation: Increased Protocol Adherence and Decreased Variability**

Due to the strong evidence of decreased morbidity and moderate evidence for decreased LOS and mortality, implementation of these GDHT protocols should already be widely accepted in the anesthesia community. Unfortunately, the amount of moderate to high-risk anesthetics administered around the world that have successfully employed and reported their GDHT results is remarkably limited. This can be due to many issues, including: increased initial workload, cost, clinician acceptance, fear of computer-physician replacement, and/or internal results not being reported.

What options do we have for improving adherence to these clinically beneficial GDHT protocols? Additional education is always an option, but this approach is time consuming and the concepts behind GDHT are relatively straightforward and should already be understood by most practicing clinicians. The necessary technology is already standard in most first-world operating rooms and ICUs. It is important to also note that many trials have demonstrated extremely large variability in fluid administration in the operating room and ICU with extremes of fluid therapy being associated with increased morbidity [30-32]. This variability is the nemesis of protocolized treatment and has been found to be largely due to provider specific preferences, and is further

complicated by a lack of vigilance and evidence-based knowledge [33]. Such variability was at the heart of implementing and maintaining GDHT protocols within various institutions and governments around the world. Unfortunately, as anyone who works in a large hospital system can undoubtedly understand, the adherence to these protocols themselves has large variability and an overall poor compliance [11, 34-36]. This is consistently true even with data associating improved compliance of enhance recovery after surgery (ERAS) protocols with decreased length of stay, 30 day mortality, and readmission rates [37, 38]. It now appears obvious that this problem of poor adherence to GDHT protocols must be addressed by a more fundamental change in the perioperative physician's tool belt.

Luckily, as computing has advanced, a novel and efficient approach to this problem has emerged: "automation". The definition of automation in this context includes any system that uses real time information to partially or completely guide therapeutic interventions, which includes both closed and open loop technology. Closed-loop systems are completely automated and use input variables (physiologic variables in this context) to change output variables (fluid, vasopressors and inotropes in this context) without the required input of clinicians. Open loop systems do the same task but require a minimal amount of clinician input prior to therapies being automatically initiated or adjusted (e.g. final approval before actually administering the fluid bolus or adjusting the vasopressor infusion rate). Removing all or most aspects of repetitive provider workload, combined with the incredible ability for computer systems to never lose vigilance and make thousands of observations and adjustments every second, has allowed for vastly improved compliance, decreased variability and is even starting to independently demonstrate improved outcomes for patients treated with GDHT systems.

Additionally, closed-loop systems have recently been shown to better maintain a hemodynamic target within a desired range, via a decrease in overshooting and undershooting of physiologic end points, all while decreasing physician workload and increasing compliance to GDHT protocols [39, 40]. Additionally, closed-loop GDFT systems have been shown to increase cardiac output when compared to manually adjusted hemodynamic therapy [41].

What do these GDHT systems look like? Typically, there is a computer with input connections to a patient's hemodynamic data and output connections to one or more protocolized interventions (fluid therapy, vasopressors, and/or inotropes). As the case progresses, the computer has software that is constantly (usually many times per second) analyzing the collected data and using well established GDHT protocols to adjust the output interventions. In its simplest form, these systems are perfectly positioned to increase adherence to established GDHT protocols, while also decreasing provider workload. **Figure 1** represents an operating room in Erasme Hospital, Brussels, Belgium where the entire anesthetic was managed using several closed-loop systems operating in parallel.

One particularly frequent question perioperative clinicians propose regarding closed-loop technology is: "Will this automation eventually replace me in the operating room?" In other words, due to the recent development of extremely sophisticated 21<sup>st</sup>- century perioperative monitoring devices, could closed-loop systems expose the specialty of anesthesiology to substitution by robots coupled or not with artificial intelligence? As stated elsewhere, our research group feels that a more appropriate question would be: "What benefit could automation have on my daily clinical practice and how could this system improve patient care while also mastering mundane clinical tasks?" We do not yet have a finalized answer to this question but research on the subject is being reported at an unprecedented rate. Closed-loop hemodynamic

systems that utilize a validated decision support system, implemented alongside the knowledge and expertise of a well-trained perioperative clinician, will help to ensure that the highest quality of care is being employed consistently and effectively for all patients. Lastly, it is important to keep in mind that the patient, not the computer, must always come first.

## **Specific Potential and Realized Closed-Loop Hemodynamic Management Systems**

### *Fluid Therapy*

Fluid therapy was actually one of the earliest interventions to be automated by researchers. In the 1970's, a group in Utah linked a fluid pump to an electronic measurement of urine output [42, 43]. Since then, a variety of measures have been used to guide fluid therapy including blood pressure [44, 45], near-infrared spectroscopy [46], dynamic predictors of fluid responsiveness [47], or a combination of hemodynamic variables [48].

The algorithmic approach used by many goal-directed fluid therapy (GDFT) protocols [49-51] lends itself quite naturally to computer implementation. Authors of the present review have performed multiple clinical studies using such a closed-loop GDFT algorithm and have shown increased protocol compliance [52-54], decreased length of hospital stay [53], and decreased postoperative complications [55] in a variety of clinical settings. **Table 1** summarizes studies performed with our recent closed-loop system for fluid administration.

Many groups are currently working on closed-loop fluid resuscitation algorithms and this is a space that is likely to grow rapidly in the coming years [41, 56-58]. Other groups are also exploring the co-application of anesthesia closed-loop systems with fluid management systems [59, 60]. These systems do not yet coordinate actions to work cooperatively but have been shown to function without interference, an important safety step [59, 60]. Finally, closed-loop

fluid delivery systems have also been used as unbiased interventionalists in studies examining the effects of different resuscitation fluids [61, 62]. **Tables 1** summarizes all the studies performed with our closed-loop fluid administration system over the past 8 years.

### *Vasopressor*

Vasopressor administration, having a single “controlled” physiologic variable readily measured with arterial blood pressure, is another intervention that saw early efforts in automation [63-65]. As stated above, there is a substantial amount of evidence indicating the importance of blood pressure control in the operating room and ICU, while there is also limited evidence that the manual titration of vasopressors is inefficient and inaccurate [20]. This combination indicates that development of a clinical solution may be particularly impactful and be the future for blood pressure management in both surgical and ICU patients [66, 67].

There was a slowdown where the medical community lost interest in these systems, but as of the last 5-8 years a number of research groups have shown renewed interest. Modern systems are currently being developed for operating and ICU use [68-70], obstetrics and spinal-induced hypotension [71-73], and septic shock [74]. Moreover, one group in Paris is beginning to explore the natural combination of vasopressor plus fluid administration systems with promising results [75].

### *Cardiac Function*

Cardiac function has not been as prolifically studied a topic for closed-loop pharmacologic interventions. This may be a natural result of the types of effects most often sought in cardiac medication (slowing the rate and increasing inotropy), as many drugs have

non-linear effects and ceiling effects are common and often occur at low rates. The obvious exception to this is implantable cardiac pacemakers, which are obviously quite advanced and contain many layers of control algorithms governing their operation [76].

That being said, there are groups that have explored pharmacologic rate control via closed-loop algorithms [77], particularly in the setting of cardiac stress tests where isoproterenol is often used, though other drugs have been trialed [78]. Studies have also been performed in inotropes [79, 80].

### *Vasodilator*

Vasodilators, like vasopressors, have a natural and easily-monitored control variable in arterial pressure and was another very early system prototyped [81]. Despite this, relatively few studies have explored vasodilator titration, possibly due to the relative rarity of need for vasodilation drips and the risk of overtreatment. Two studies did explore automatic titration via closed-loop for intracranial surgery [82] and following open-heart surgery [83].

## **From Closed-Loop Therapy to Predictive Therapy**

While computers are adept at automatically and quickly reacting to abrupt hemodynamic changes, they have the potential for even more advantageous functions when paired with predictive analytics. As computational power continues to expand, recent research has demonstrated that complex algorithms validated with large clinical data sets have the ability to predict periods of hemodynamic compromise before they happen. One significant approach is a recent study by *Hatib et al* demonstrating that high resolution analysis of arterial line tracings can be analyzed to produce a variable known as a “hypotension predictive index”. This index

was shown to predict hypotension 15 minutes prior to any hypotension occurring in 84% of hypotensive episodes [84]. Another group also demonstrated the ability of machine learning to predict post induction hypotension with similar efficacy [85]. This technique is very exciting and has the potential to revolutionize the influence that computational systems have on patient care and outcomes. Outside of the healthcare industry, predictive algorithms work together with autonomous systems to adjust titration of an output. In the future, it is likely that personalized titration of drugs will be based on intelligent systems which would compare the patients they are currently taking care of to data from prior patient with similar demographics. These systems would be able to more accurately predict the response of a given patient to specific drugs and use these predictive models within their treatment protocols. This would allow for true *precision medicine*. Finally, artificial intelligence and advanced analytics will be used to better understand the interactions between various closed-loop systems working together and will help refine the way these systems work.

## **Summary**

In summary, the clinical benefits for establishing and ensuring proper adherence to GDHT protocols are well established and automation (closed and open loop systems) increases adherence to such protocols while also decreasing hemodynamic variability. Closed loop hemodynamic systems have focused on fluid and vasopressor management, although other interventions have been explored. Finally, novel research systems combining multiple automated systems together and others using predictive analytics are strong areas of future exploration, although all aspects of automated hemodynamic systems have a dire need for additional research.

| <b>Author</b>       | <b>Pub Date</b> | <b>Institution(s)</b>                                   | <b># of Participants</b> | <b>Main Findings</b>   |
|---------------------|-----------------|---|--------------------------|--|
| Joosten et al [52]  | Sept 2018       | Erasme University Hospital, Brussels, Belgium           | 208                      | Closed-loop GDFT protocol was superior in complications and LOS when compared with no GDFT protocol  |
| Joosten et al [86]  | Jun 2018        | Erasme University Hospital, Brussels, Belgium           | 40                       | Closed-loop GDFT had similar cardiovascular endpoints to protocolized fluid therapy  |
| Joosten et al [59]  | May 2018        | Erasme University Hospital, Brussels, Belgium           | 13                       | Combining Closed-loop GDFT with Closed-loop Hypnosis/ Analgesia is feasible  |
| Joosten et al [61]  | Jan 2018        | Erasme University Hospital, Brussels, Belgium           | 160                      | Closed-loop GDFT systems were used to compare colloid and crystalloid, with colloid having less morbidity  |
| Lilot et al [41]    | Jan 2018        | Lyon University Hospital, Lyon, France                  | 46                       | Cardiac index increased more in closed-loop group versus manual control, otherwise no differences noted  |
| Joosten et al [87]  | Dec 2016        | Erasme University Hospital, Brussels, Belgium           | 1<br>(case report)       | Dual closed loop systems (Hypnosis and GDFT control) are possible  |
| Joosten et al [54]  | Jun 2015        | University of California, Irvine, USA                   | 13                       | Intraoperative closed-loop GDFT control using a non-invasive advanced hemodynamic monitoring device is feasible  |
| Rinehart et al [53] | Mar 2015        | University of California, Irvine, USA                   | 50                       | Closed-loop GDFT control group spent more time in a preload independent state compared to manual GDFT group  |
| Rinehart et al [88] | Mar 2014        | CHU Pitié Salpêtrière, Paris, France and UC Irvine, USA | 12                       | Closed-loop GDFT control is possible and reproducible  |
| Rinehart et al [89] | Nov 2013        | University of California, Irvine, USA                   | 16<br>(Porcine)          | Closed-loop GDFT control during hemorrhage can be effective with low variability   |
| Rinehart et al [90] | Oct 2012        | University of California, Irvine, USA                   | NA<br>(Simulation)       | Closed loop GDFT control of simulated patient hemorrhages outperforms manual control   |
| Rinehart et al [47] | Nov 2011        | University of California, Irvine, USA                   | NA<br>(Simulation)       | Closed loop system is an effective volumetric resuscitator in simulated hemorrhage scenarios and improved physician management of the simulated hemorrhages. |

**Table 1:** Studies performed with our closed-loop fluid administration system.

Legend: Pub Date: publication date; NA: Non applicable; GDFT: Goal directed fluid therapy

**Figure legend:**

Figure 1 represents our operating room in Erasme Hospital, Brussels, Belgium where the entire anesthetic was managed using several closed-loop systems operating in parallel.

## References:

1. Squara P, Bennett D, Perret C: **Pulmonary artery catheter: does the problem lie in the users?** *Chest* 2002, **121**(6):2009-2015.
2. Joosten A, Desebbe O, Suehiro K, Essiet M, Alexander B, Ricks C, Rinehart J, Faraoni D, Cecconi M, Van der Linden P *et al*: **Impact of advanced monitoring variables on intraoperative clinical decision-making: an international survey.** *Journal of clinical monitoring and computing* 2017, **31**(1):205-212.
3. Lugo G, Arizpe D, Domínguez G, Ramírez M, Tamariz O: **Relationship between oxygen consumption and oxygen delivery during anesthesia in high-risk surgical patients.** *Crit Care Med* 1993, **21**(1):64-69.
4. Lobo S: **Effects of "Restrictive" and "Liberal" strategies of intra-operative fluid management during optimisation of oxygen delivery in high-risk surgical patients.** <http://isrctn.org/> 2013.
5. Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, Grocott MPW, Ahern A, Griggs K, Scott R *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**(21):2181-2190.
6. Pestaña D, Espinosa E, Eden A, Nájera D, Collar L, Aldecoa C, Higuera E, Escribano S, Bystritski D, Pascual J *et al*: **Perioperative goal-directed hemodynamic optimization using noninvasive cardiac output monitoring in major abdominal surgery: a prospective, randomized, multicenter, pragmatic trial: POEMAS Study (PeriOperative goal-directed thERapy in Major Abdominal Surgery).** *Anesth Analg* 2014, **119**(3):579-587.
7. Brandstrup B, Svendsen PE, Rasmussen M, Belhage B, Rodt SÅ, Hansen B, Møller DR, Lundbech LB, Andersen N, Berg V *et al*: **Which goal for fluid therapy during colorectal surgery is followed by the best outcome: near-maximal stroke volume or zero fluid balance?** *Br J Anaesth* 2012, **109**(2):191-199.
8. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED: **Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445].** *Crit Care* 2005, **9**(6):R687-693.
9. Rhodes A, Cecconi M, Hamilton M, Poloniecki J, Woods J, Boyd O, Bennett D, Grounds RM: **Goal-directed therapy in high-risk surgical patients: a 15-year follow-up study.** *Intensive Care Med* 2010, **36**(8):1327-1332.
10. Calvo-Vecino JM, Ripollés-Melchor J, Mythen MG, Casans-Francés R, Balik A, Artacho JP, Martínez-Hurtado E, Serrano Romero A, Fernández Pérez C, Asuero de Lis S *et al*: **Effect of goal-directed haemodynamic therapy on postoperative complications in low-moderate risk surgical patients: a multicentre randomised controlled trial (FEDORA trial).** *Br J Anaesth* 2018, **120**(4):734-744.
11. Cannesson M, Ramsingh D, Rinehart J, Demirjian A, Vu T, Vakharia S, Imagawa D, Yu Z, Greenfield S, Kain Z: **Perioperative goal-directed therapy and postoperative outcomes in patients undergoing high-risk abdominal surgery: a historical-prospective, comparative effectiveness study.** *Crit Care* 2015, **19**:261.
12. Jin J, Min S, Liu D, Liu L, Lv B: **Clinical and economic impact of goal-directed fluid therapy during elective gastrointestinal surgery.** *Perioper Med (Lond)* 2018, **7**:22.

13. Russo A, Aceto P, Grieco DL, Anzellotti GM, Perilli V, Costantini B, Romanò B, Scambia G, Sollazzi L, Antonelli M: **Goal-directed hemodynamic management in patients undergoing primary debulking gynaecological surgery: A matched-controlled precision medicine study.** *Gynecol Oncol* 2018, **151**(2):299-305.
14. Lima MF, Mondadori LA, Chibana AY, Gilio DB, Giroud Joaquim EH, Michard F: **Outcome impact of hemodynamic and depth of anesthesia monitoring during major cancer surgery: a before-after study.** *Journal of clinical monitoring and computing* 2018.
15. Asfar P, Meziani F, Hamel J-F, Grelon F, Megarbane B, Anguel N, Mira J-P, Dequin P-F, Gergaud S, Weiss N *et al*: **High versus low blood-pressure target in patients with septic shock.** *N Engl J Med* 2014, **370**(17):1583-1593.
16. Lamontagne F, Cook DJ, Meade MO, Seely A, Day AG, Charbonney E, Serri K, Skrobik Y, Hebert P, St-Arnaud C *et al*: **Vasopressor Use for Severe Hypotension—A Multicentre Prospective Observational Study.** *PLoS One* 2017, **12**(1):e0167840.
17. Maheshwari K, Nathanson BH, Munson SH, Khangulov V, Stevens M, Badani H, Khanna AK, Sessler DI: **The relationship between ICU hypotension and in-hospital mortality and morbidity in septic patients.** *Intensive Care Med* 2018.
18. Jinadasa SP, Mueller A, Prasad V, Subramaniam K, Heldt T, Novack V, Subramaniam B: **Blood Pressure Coefficient of Variation and Its Association With Cardiac Surgical Outcomes.** *Anesth Analg* 2018.
19. Sessler DI, Turan A, Stapelfeldt WH, Mascha EJ, Yang D, Farag E, Cywinski J, Vlah C, Kopyeva T, Keebler AL *et al*: **Triple-low Alerts Do Not Reduce Mortality: A Real-time Randomized Trial.** *Anesthesiology* 2018.
20. Rinehart J, Ma M, Calderon MD, Bardaji A, Hafiane R, Van der Linden P, Joosten A: **Blood pressure variability in surgical and intensive care patients: Is there a potential for closed-loop vasopressor administration?** *Anaesthesia, critical care & pain medicine* 2019, **38**(1):69-71.
21. Stapelfeldt WH, Yuan H, Dryden JK, Strehl KE, Cywinski JB, Ehrenfeld JM, Bromley P: **The SLUScore: A Novel Method for Detecting Hazardous Hypotension in Adult Patients Undergoing Noncardiac Surgical Procedures.** *Anesth Analg* 2017.
22. Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, Kurz A: **Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery: A Retrospective Cohort Analysis.** *Anesthesiology* 2017, **126**(1):47-65.
23. Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, Bertran S, Leone M, Pastene B, Piriou V *et al*: **Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery: A Randomized Clinical Trial.** *JAMA* 2017, **318**(14):1346-1357.
24. van Waes JA, van Klei WA, Wijesundera DN, van Wolfswinkel L, Lindsay TF, Beattie WS: **Association between Intraoperative Hypotension and Myocardial Injury after Vascular Surgery.** *Anesthesiology* 2016, **124**(1):35-44.
25. Sessler DI, Meyhoff CS, Zimmerman NM, Mao G, Leslie K, Vasquez SM, Balaji P, Alvarez-Garcia J, Cavalcanti AB, Parlow JL *et al*: **Period-dependent Associations between Hypotension during and for Four Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death: A Substudy of the POISE-2 Trial.** *Anesthesiology* 2018, **128**(2):317-327.
26. Townsend SR, Tefera L, Rivers EP: **Evidence Underpinning the Centers for Medicare & Medicaid Services' Severe Sepsis and Septic Shock Management Bundle (SEP-1).** *Ann Intern Med* 2018.

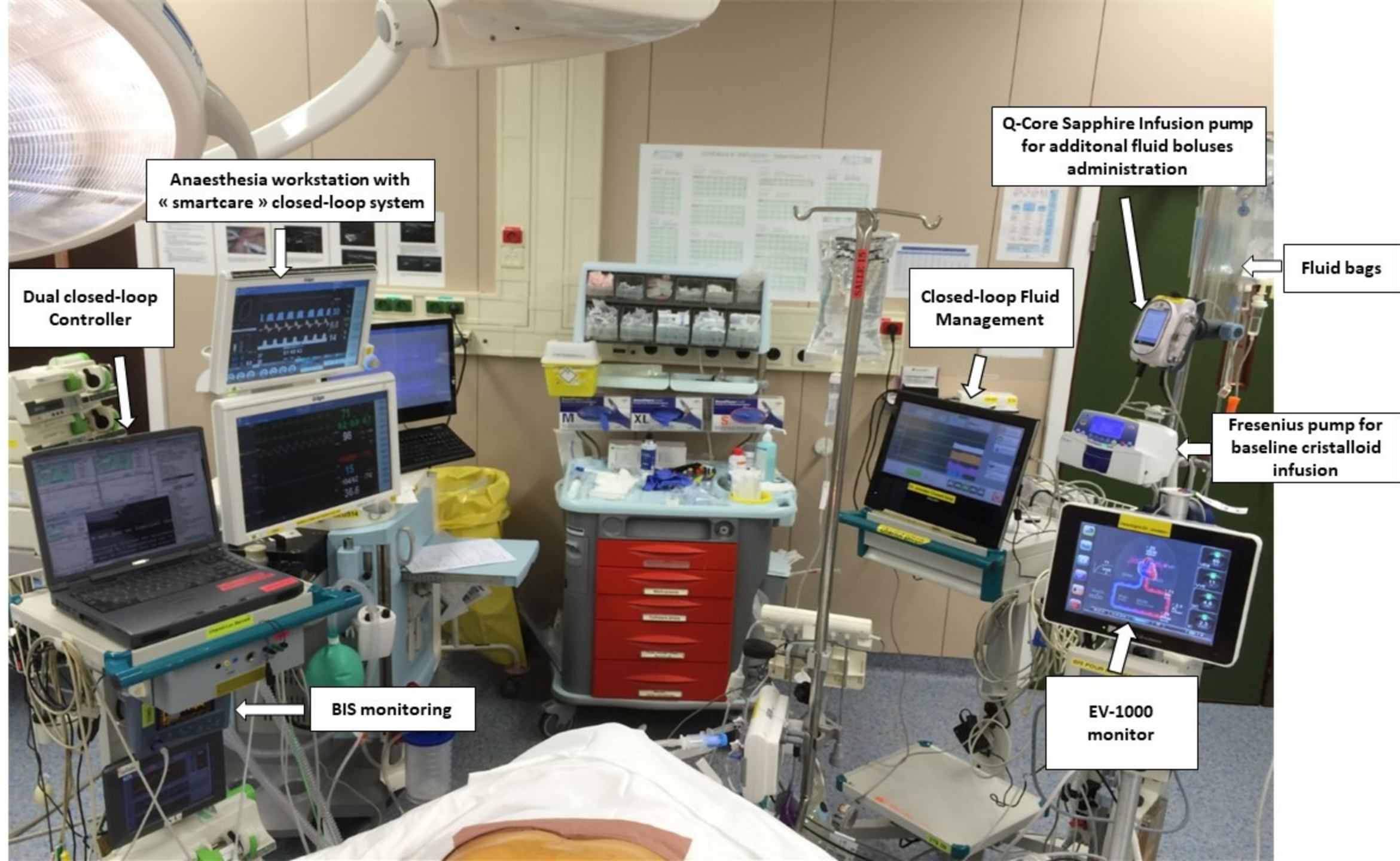
27. Yapps B, Shin S, Bighamian R, Thorsen J, Arsenault C, Quraishi SA, Hahn JO, Reisner AT: **Hypotension in ICU Patients Receiving Vasopressor Therapy.** *Sci Rep* 2017, **7**(1):8551.
28. Vincent JL, Nielsen ND, Shapiro NI, Gerbasi ME, Grossman A, Doroff R, Zeng F, Young PJ, Russell JA: **Mean arterial pressure and mortality in patients with distributive shock: a retrospective analysis of the MIMIC-III database.** *Annals of intensive care* 2018, **8**(1):107.
29. Nguyen DN, Huyghens L, Parra J, Schiettecatte J, Smits J, Vincent JL: **Hypotension and a positive fluid balance are associated with delirium in patients with shock.** *PLoS one* 2018, **13**(8):e0200495.
30. 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.** *Annals of surgery* 2016, **263**(3):502-510.
31. 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.** *British journal of anaesthesia* 2015, **114**(5):767-776.
32. Shin CH, Long DR, McLean D, Grabitz SD, Ladha K, Timm FP, Thevathasan T, Pieretti A, Ferrone C, Hoefft A *et al*: **Effects of Intraoperative Fluid Management on Postoperative Outcomes: A Hospital Registry Study.** *Annals of surgery* 2018, **267**(6):1084-1092.
33. Minto G, Mythen MG: **Perioperative fluid management: science, art or random chaos?** *Br J Anaesth* 2015, **114**(5):717-721.
34. Spanjersberg WR, Bergs EA, Mushkudiani N, Klimek M, Schipper IB: **Protocol compliance and time management in blunt trauma resuscitation.** *Emerg Med J* 2009, **26**(1):23-27.
35. Godier A, Bacus M, Kipnis E, Tavernier B, Guidat A, Rauch A, Drumez E, Susen S, Garrigue-Huet D: **Compliance with evidence-based clinical management guidelines in bleeding trauma patients.** *Br J Anaesth* 2016, **117**(5):592-600.
36. Lipton JA, Barendse RJ, Schinkel AFL, Akkerhuis KM, Simoons ML, Sijbrands EJG: **Impact of an alerting clinical decision support system for glucose control on protocol compliance and glycemic control in the intensive cardiac care unit.** *Diabetes Technol Ther* 2011, **13**(3):343-349.
37. Gustafsson UO: **Adherence to the Enhanced Recovery After Surgery Protocol and Outcomes After Colorectal Cancer Surgery.** *Arch Surg* 2011, **146**(5):571.
38. Bakker N, Cakir H, Doodeman HJ, Houdijk APJ: **Eight years of experience with Enhanced Recovery After Surgery in patients with colon cancer: Impact of measures to improve adherence.** *Surgery* 2015, **157**(6):1130-1136.
39. Pasin L, Nardelli P, Pintaudi M, Greco M, Zambon M, Cabrini L, Zangrillo A: **Closed-Loop Delivery Systems Versus Manually Controlled Administration of Total IV Anesthesia: A Meta-analysis of Randomized Clinical Trials.** *Anesth Analg* 2017, **124**(2):456-464.
40. Brogi E, Cyr S, Kazan R, Giunta F, Hemmerling TM: **Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials.** *Anesth Analg* 2017, **124**(2):446-455.
41. Lilot M, Bellon A, Gueugnon M, Laplace MC, Baffleuf B, Hacquard P, Barthomeuf F, Parent C, Tran T, Soubirou JL *et al*: **Comparison of cardiac output optimization with an automated closed-loop goal-directed fluid therapy versus non standardized manual fluid administration during elective abdominal surgery: first prospective**

- randomized controlled trial.** *Journal of clinical monitoring and computing* 2018, **32**(6):993-1003.
42. Bowman RJ, Westenskow DR: **A microcomputer-based fluid infusion system for the resuscitation of burn patients.** *IEEE Trans Biomed Eng* 1981, **28**(6):475-479.
  43. DeBey RK, Westenskow DR, Jordan WS, McJames SW: **A urine based control system for fluid infusion.** *Biomed Sci Instrum* 1987, **23**:195-198.
  44. Blankenship HB, Wallace FD, Pacifico AD: **Clinical application of closed-loop postoperative autotransfusion.** *Med Prog Technol* 1990, **16**(1-2):89-93.
  45. Hoskins SL, Elgjo GI, Lu J, Ying H, Grady JJ, Herndon DN, Kramer GC: **Closed-loop resuscitation of burn shock.** *Journal of burn care & research : official publication of the American Burn Association* 2006, **27**(3):377-385.
  46. Chaisson NF, Kirschner RA, Deyo DJ, Lopez JA, Prough DS, Kramer GC: **Near-infrared spectroscopy-guided closed-loop resuscitation of hemorrhage.** *J Trauma* 2003, **54**(5 Suppl):S183-192.
  47. 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.** *Critical care (London, England)* 2011, **15**(6):R278.
  48. 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 Anesthesiologists.** *J Cardiothorac Vasc Anesth* 2012.
  49. Rollins KE, Lobo DN: **Intraoperative Goal-directed Fluid Therapy in Elective Major Abdominal Surgery: A Meta-analysis of Randomized Controlled Trials.** *Annals of surgery* 2016, **263**(3):465-476.
  50. Ripolles-Melchor J, Espinosa A, Martinez-Hurtado E, Abad-Gurumeta A, Casans-Frances R, Fernandez-Perez C, Lopez-Timoneda F, Calvo-Vecino JM: **Perioperative goal-directed hemodynamic therapy in noncardiac surgery: a systematic review and meta-analysis.** *Journal of clinical anesthesia* 2016, **28**:105-115.
  51. Ramsingh DS, Sanghvi C, Gamboa J, Cannesson M, Applegate RL, 2nd: **Outcome impact of goal directed fluid therapy during high risk abdominal surgery in low to moderate risk patients: a randomized controlled trial.** *Journal of clinical monitoring and computing* 2013, **27**(3):249-257.
  52. Joosten A, Coeckelenbergh S, Delaporte A, Ickx B, Closset J, Roumeguere T, Barvais L, Van Obbergh L, Cannesson M, Rinehart J *et al*: **Implementation of closed-loop-assisted intra-operative goal-directed fluid therapy during major abdominal surgery: A case-control study with propensity matching.** *Eur J Anaesthesiol* 2018, **35**(9):650-658.
  53. Rinehart J, Lilot M, Lee C, Joosten A, Huynh T, Canales C, Imagawa D, Demirjian A, Cannesson M: **Closed-loop assisted versus manual goal-directed fluid therapy during high-risk abdominal surgery: a case-control study with propensity matching.** *Critical care (London, England)* 2015, **19**:94.
  54. Joosten A, Huynh T, Suehiro K, Canales C, Cannesson M, Rinehart J: **Goal-Directed fluid therapy with closed-loop assistance during moderate risk surgery using noninvasive cardiac output monitoring: A pilot study.** *British journal of anaesthesia* 2015, **114**(6):886-892.
  55. Joosten A, Hafiane R, Pustetto M, Van Obbergh L, Quackels T, Buggenhout A, Vincent JL, Ickx B, Rinehart J: **Practical impact of a decision support for goal-directed fluid therapy on protocol adherence: a clinical implementation study in patients undergoing major abdominal surgery.** *Journal of clinical monitoring and computing* 2018.

56. Jin X, Bighamian R, Hahn JO: **Development and In Silico Evaluation of a Model-Based Closed-Loop Fluid Resuscitation Control Algorithm.** *IEEE transactions on bio-medical engineering* 2018.
57. Gholami B, Haddad WM, Bailey JM, Geist B, Ueyama Y, Muir WW: **A pilot study evaluating adaptive closed-loop fluid resuscitation during states of absolute and relative hypovolemia in dogs.** *J Vet Emerg Crit Care (San Antonio)* 2018, **28**(5):436-446.
58. Hundeshagen G, Kramer GC, Ribeiro Marques N, Salter MG, Koutrouvelis AK, Li H, Solanki DR, Indrikovs A, Seeton R, Henkel SN *et al*: **Closed-Loop- and Decision-Assist-Guided Fluid Therapy of Human Hemorrhage.** *Crit Care Med* 2017, **45**(10):e1068-e1074.
59. Joosten A, Jame V, Alexander B, Chazot T, Liu N, Cannesson M, Rinehart J, Barvais L: **Feasibility of Fully Automated Hypnosis, Analgesia, and Fluid Management Using 2 Independent Closed-Loop Systems During Major Vascular Surgery: A Pilot Study.** *Anesthesia and analgesia* 2018.
60. Joosten A, Delaporte A, Cannesson M, Rinehart J, Dewilde JP, Van Obbergh L, Barvais L: **Fully Automated Anesthesia and Fluid Management Using Multiple Physiologic Closed-Loop Systems in a Patient Undergoing High-Risk Surgery.** *A A Case Rep* 2016.
61. Joosten A, Delaporte A, Ickx B, Touihri K, Stany I, Barvais L, Van Obbergh L, Loi P, Rinehart J, Cannesson M *et al*: **Crystalloid versus Colloid for Intraoperative Goal-directed Fluid Therapy Using a Closed-loop System: A Randomized, Double-blinded, Controlled Trial in Major Abdominal Surgery.** *Anesthesiology* 2018, **128**(1):55-66.
62. Joosten A, Delaporte A, Mortier J, Ickx B, Van Obbergh L, Vincent JL, Cannesson M, Rinehart J, Van der Linden P: **Long-term Impact of Crystalloid versus Colloid Solutions on Renal Function and Disability-free Survival after Major Abdominal Surgery.** *Anesthesiology* 2019, **130**(2):227-236.
63. Packer JS, Mason DG, Cade JF, McKinley SM: **An adaptive controller for closed-loop management of blood pressure in seriously ill patients.** *IEEE Trans Biomed Eng* 1987, **34**(8):612-616.
64. Mason DG, Packer JS, Cade JF, McDonald RD: **Closed-loop management of blood pressure in critically ill patients.** *Australas Phys Eng Sci Med* 1985, **8**(4):164-167.
65. Potter DR, Moyle JT, Lester RJ, Ware RJ: **Closed loop control of vasoactive drug infusion. A preliminary report.** *Anaesthesia* 1984, **39**(7):670-677.
66. Michard F, Liu N, Kurz A: **The future of intraoperative blood pressure management.** *Journal of clinical monitoring and computing* 2018, **32**(1):1-4.
67. Joosten A, Rinehart J: **Part of the Steamroller and Not Part of the Road: Better Blood Pressure Management Through Automation.** *Anesthesia and analgesia* 2017, **125**(1):20-22.
68. Rinehart J, Joosten A, Ma M, Calderon MD, Cannesson M: **Closed-loop vasopressor control: in-silico study of robustness against pharmacodynamic variability.** *Journal of clinical monitoring and computing* 2018.
69. Rinehart J, Ma M, Calderon MD, Cannesson M: **Feasibility of automated titration of vasopressor infusions using a novel closed-loop controller.** *J Clin Monit Comput* 2017.
70. Joosten A, Delaporte A, Alexander B, Su F, Creteur J, Vincent JL, Cannesson M, Rinehart J: **Automated Titration of Vasopressor Infusion Using a Closed-loop Controller: In Vivo Feasibility Study Using a Swine Model.** *Anesthesiology* 2018.
71. Ngan Kee WD, Tam YH, Khaw KS, Ng FF, Lee SW: **Closed-Loop Feedback Computer-Controlled Phenylephrine for Maintenance of Blood Pressure During**

- Spinal Anesthesia for Cesarean Delivery: A Randomized Trial Comparing Automated Boluses Versus Infusion.** *Anesth Analg* 2017.
72. Ngan Kee WD, Khaw KS, Tam YH, Ng FF, Lee SW: **Performance of a closed-loop feedback computer-controlled infusion system for maintaining blood pressure during spinal anaesthesia for caesarean section: a randomized controlled comparison of norepinephrine versus phenylephrine.** *Journal of clinical monitoring and computing* 2017, **31**(3):617-623.
  73. Ngan Kee WD, Tam YH, Khaw KS, Ng FF, Critchley LA, Karmakar MK: **Closed-loop feedback computer-controlled infusion of phenylephrine for maintaining blood pressure during spinal anaesthesia for caesarean section: a preliminary descriptive study.** *Anaesthesia* 2007, **62**(12):1251-1256.
  74. Merouani M, Guignard B, Vincent F, Borron SW, Karoubi P, Fosse JP, Cohen Y, Clec'h C, Vicaut E, Marbeuf-Gueye C *et al*: **Norepinephrine weaning in septic shock patients by closed loop control based on fuzzy logic.** *Crit Care* 2008, **12**(6):R155.
  75. Libert N, Chenegros G, Harrois A, Baudry N, Cordurie G, Benosman R, Vicaut E, Duranteau J: **Performance of closed-loop resuscitation of haemorrhagic shock with fluid alone or in combination with norepinephrine: an experimental study.** 2018, **8**(1):89.
  76. Tjong FV, Reddy VY: **Permanent Leadless Cardiac Pacemaker Therapy: A Comprehensive Review.** *Circulation* 2017, **135**(15):1458-1470.
  77. Sarabadani Tafreshi A, Klamroth-Marganska V, Nussbaumer S, Riener R: **Real-time closed-loop control of human heart rate and blood pressure.** *IEEE Trans Biomed Eng* 2015, **62**(5):1434-1442.
  78. Valcke CP, Chizeck HJ: **Closed-loop drug infusion for control of heart-rate trajectory in pharmacological stress tests.** *IEEE Trans Biomed Eng* 1997, **44**(3):185-195.
  79. Uemura K, Kawada T, Zheng C, Sugimachi M: **Less Invasive and Inotrope-Reduction Approach to Automated Closed-Loop Control of Hemodynamics in Decompensated Heart Failure.** *IEEE Trans Biomed Eng* 2016, **63**(8):1699-1708.
  80. Osswald S, Cron T, Gradel C, Hilti P, Lippert M, Strobel J, Schaldach M, Buser P, Pfisterer M: **Closed-loop stimulation using intracardiac impedance as a sensor principle: correlation of right ventricular dP/dtmax and intracardiac impedance during dobutamine stress test.** *Pacing Clin Electrophysiol* 2000, **23**(10 Pt 1):1502-1508.
  81. Hammond JJ, Kirkendall WM, Calfee RV: **Hypertensive crisis managed by computer controlled infusion of sodium nitroprusside: a model for the closed loop administration of short acting vasoactive agents.** *Comput Biomed Res* 1979, **12**(2):97-108.
  82. Mackenzie AF, Colvin JR, Kenny GN, Bisset WI: **Closed loop control of arterial hypertension following intracranial surgery using sodium nitroprusside. A comparison of intra-operative halothane or isoflurane.** *Anaesthesia* 1993, **48**(3):202-204.
  83. Bednarski P, Siclari F, Voigt A, Demertzis S, Lau G: **Use of a computerized closed-loop sodium nitroprusside titration system for antihypertensive treatment after open heart surgery.** *Crit Care Med* 1990, **18**(10):1061-1065.
  84. Hatib F, Jian Z, Buddi S, Lee C, Settels J, Sibert K, Rinehart J, Cannesson M: **Machine-learning Algorithm to Predict Hypotension Based on High-fidelity Arterial Pressure Waveform Analysis.** *Anesthesiology* 2018, **129**(4):663-674.
  85. Kendale S, Kulkarni P, Rosenberg AD, Wang J: **Supervised Machine-learning Predictive Analytics for Prediction of Postinduction Hypotension.** *Anesthesiology* 2018, **129**(4):675-688.

86. Joosten A, Raj Lawrence S, Colesnicenco A, Coeckelenbergh S, Vincent JL, Van der Linden P, Cannesson M, Rinehart J: **Personalized Versus Protocolized Fluid Management Using Noninvasive Hemodynamic Monitoring (Clearsight System) in Patients Undergoing Moderate-Risk Abdominal Surgery.** *Anesthesia and analgesia* 2018.
87. Joosten A, Delaporte A, Cannesson M, Rinehart J, Dewilde JP, Van Obbergh L, Barvais L: **Fully Automated Anesthesia and Fluid Management Using Multiple Physiologic Closed-Loop Systems in a Patient Undergoing High-Risk Surgery. A & A case reports** 2016, **7**(12):260-265.
88. Rinehart J, Le Manach Y, Douiri H, Lee C, Lilot M, Le K, Canales C, Cannesson M: **First closed-loop goal directed fluid therapy during surgery: a pilot study.** *Annales francaises d'anesthesie et de reanimation* 2014, **33**(3):e35-41.
89. 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.** *Anesthesia and analgesia* 2013, **117**(5):1119-1129.
90. 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 anesthesiologists.** *Journal of cardiothoracic and vascular anesthesia* 2012, **26**(5):933-939.



Anaesthesia workstation with « smartcare » closed-loop system

Q-Core Sapphire Infusion pump for additional fluid boluses administration

Dual closed-loop Controller

Closed-loop Fluid Management

Fluid bags

Fresenius pump for baseline crystalloid infusion

BIS monitoring

EV-1000 monitor