Less Fluids and a More Physiological Approach

Marc Licker[1], Frédéric Triponez[2],
Christoph Ellenberger[1], Wolfram Karenovics[2]

[1]Department of Anesthesiology, Pharmacology and Intensive Care, University Hospital of Geneva, Switzerland

[2]Department of Thoracic and Endocrine Surgery, University Hospital of Geneva, Switzerland

The goals to achieve a "zero fluid balance" and to minimize the early weight gain over the perioperative period are fully shared with our Italian colleagues. Indeed, based on convincing clinical and experimental data, we all agree that weight gain exceeding 10% is associated with increased mortality and that positive fluid balance is an independent risk factor of postoperative morbidity (1).

Despite the growing body of knowledge regarding perioperative hemodynamic optimization, we remain dubious and critical about the clinical applicability of the goal-directed therapy (GDT) and its real impact on postoperative outcome. Our Italian colleagues suggest that the aim of the GDT approach should be to optimize cardiac output (CO) or stroke volume (SV) intraoperatively and in the early 8-12 hours after surgery, particularly in high-risk patients and high-risk surgery.

The term "optimization" is extensively used to express the investigator and clinician's wishes to deliver the best interventions that will not harm and provide beneficial effects to the patient. As clinicians, we must admit having difficulties to grasp the real difference (if any) between *hemodynamic optimization* and *hemodynamic maximization* (2). To our understanding, "*optimization*" should encompass, - not only intravenous fluid titration-, but also the administration of cardiovascular drugs (e.g., vasodilators, vasopressors, inotropes, beta-blockers, alpha-2 agonists) with the aims to control the determinants of cardiac output (preload, cardiac contractility/relaxation, afterload and heart rate) and to match flow/oxygen delivery (DO_2) to the changing metabolic needs and oxygen consumption (VO_2). From our point of view, hemodynamic *maximization* is an appropriate strategy in patients with shock-like situation who need resuscitative interventions (Figure 1a) whereas it may lead to deleterious effects in patients undergoing major elective surgery (Figure 1b).

Assuming that some patients may experience an oxygen debt during the pre-intra- and postoperative period, preemptive GDT has been advocated as a promising approach for reducing mortality-morbidity after major surgery. The GDT strategy with optimization/maximization of CO/SV was believed to correct the oxygen debt and, -by maintaining oxygen delivery well above the critical anaerobic threshold-, to prevent postoperative organ dysfunction and enhance wound healing (3, 4).

In the eighties, landmark papers from Dr Shoemaker's group clearly demonstrated a link between the presence of a perioperative oxygen debt (calculated by subtracting the measured VO_2 from the estimated VO_2 requirements corrected for temperature and anesthesia) and the development of postoperative organ

Address for Correspondence:
Dr. Marc Licker
E-mail: marc-joseph.licker@hcuge.ch

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dysfunction and death (5). Subsequently, the concept of deliberate perioperative supra-normal DO_2 has been tested in several RCTs that demonstrated its effectiveness in improving clinical outcome when applied preoperatively and in patients with a very high-risk of mortality-morbidity, presuming an ongoing oxygen debt (6, 7). In a high risk group of hypovolemic or septic patients who required emergent surgery, we recently applied GDT algorithms based either on conventional hemodynamic parameters with pressure pulse variation or on cardiac index, global end-diastolic volume index and stroke volume variation as derived from the PiCCO monitoring system (8). Interestingly, both GDT treatment arms resulted in a marked reduction in postoperative mortality-morbidity endpoints when compared with expected outcomes based on POSSUM. Although similar amounts of fluids were given in both groups, postoperative clinical outcome was significantly improved when conventional parameters and PPV were applied whereas the more invasive PiCCO-derived approach failed to provide any clinical advantage. These data emphasize the importance of designing simple algorithms, regardless of hemodynamic monitors, that can be implemented by all members of the perioperative medical and nursing team.

Regarding *elective* major surgery, surgical outcomes have dramatically improved over the last three decades, along with preoperative risk stratification and patient preparation, better control of pain as well as implementation of various protective strategies that are focused on a more standardized and targeted-approach of anesthesia/analgesia, mechanical ventilation and hemodynamics. For instance, in the modern area of the Enhanced Recovery After Surgery (ERAS), as alluded by Della Rocca and Vetrugno, the rate of postoperative complications has declined steadily and all ERAS protocols entail recommendations to avoid bowel preparation and to keep oral hydration with clear fluid until 2 hours before surgery whereas during the intraoperative period, the vascular compartment and cardiac preload are kept within a normal range (9). Moreover, the risk for developing an intraoperative oxygen debt is further minimized since anesthetic agents and neuromuscular blocking drugs reduce VO_2 by 10 to 15% while DO_2 remains unchanged or undergo minimal changes, the critical anaerobic threshold being shifted leftwards when examining the VO_2/DO_2 relationship (Figure 1b).

The restrictive "zero-fluid balance" combined with a simple goal-directed strategy (targeting arterial pressure, hemoglobin levels, central venous saturation or SVV/PPV) has been successfully applied in major surgery such as liver resection and radical cystectomy (10, 11). We agree that the utilization of CO monitors should be encouraged in the operating rooms in high-risk patients and/or complex and lengthy operation. Whenever possible, clinicians should apply the lesser invasive techniques (e.g., ultrasounds, finger cuff continuous arterial pressure, thoracic bioimpedance or bioreactance, pulse contour analysis of direct arterial pressure, thermodilution) while considering the cost-effectiveness and the adhesion of all heath care professionals involved in the perioperative care processes. In teaching and academic institutions, physiologic monitors are certainly justified for educational and scientific purposes and for training nurses, medical students and junior medical staff.

In conclusion, we believe that perioperative hemodynamic optimization should adopt the 'restrictive' principles and target a zero-fluid balance as the first step (1-3 mL/kg/h balanced solutions). An individualized approach guided by dedicated algorithms targeting SVV/PPV, direct SV/CO measurements as well as tissue oximetry and/or central venous oxygen saturation should be considered as the second important step. In that regard, optimization of cardiovascular parameters may require fluid titration (crystalloids, colloids) and/or the administration of vasoactive drugs or inotropes (Figure 1c).

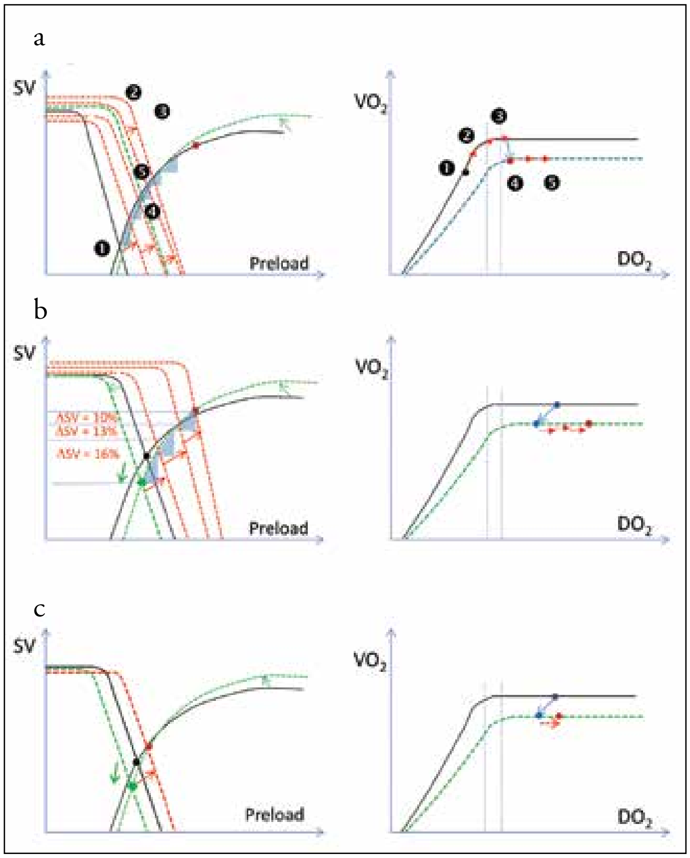

Figure 1. a-c. Hemodynamic optimization based on the Frank-Starling cardiac output relationship and Guyton's venous return curves. (a) The oxygen debt associated with any shock state can be corrected preoperatively by increasing oxygen delivery (DO_2) to match oxygen consumption (VO_2). The black curves indicate the basal condition, the red curves indicate hemodynamic optimization and the green curves indicate the effect of anesthesia. (1) Baseline, hypovolemic shock; (2) & (3) following fluid resuscitation; (4) after anesthesia induction; (5) after goal-directed therapy aimed to maximize oxygen delivery (DO_2). (b) The goal-directed therapy is illustrated by stepwise infusion of 250 mL intravenous fluids, until the gain in stroke volume is less than 10%. (c) The restrictive approach can be combined with the administration of cardiovascular drugs taking into account the effects of anesthetic agents, to achieve a "zero-fluid balance " target

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