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Management of perioperative volume therapy –
monitoring and pitfalls

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Abstract

Over 300 million surgical processes were performed every year worldwide and anesthesiologists play an important role in the perioperative process to assess the overall risk of surgery for the patient. The goal is to improve complications after surgery and one piece in the puzzle of improving outcomes in perioperative patients is certainly perioperative hemodynamic and volume management. There is ongoing discussion about goal directed therapy, however there is consensus that fluid overload and severe fluid depletion in the perioperative period is harmful and leads to unfavorable outcomes. This article should give an overview about how to evaluate the fluid responsiveness of the patients and what parameters could be used and what limitations should be noted.

Keywords: Cardiac output monitoring; Crystalloids; Hypotension; Hemodynamic monitoring; colloids; Volume therapy.
Introduction

Anesthesiologists play an important role in the perioperative process to assess the overall risk of surgery, including risk factors of the surgical procedure and risk factors of the patient. Regarding the risk of anesthesia, there has been a substantial development over the last decades. In the early days of anesthesia the risk of the anesthetic procedure itself has been high and anesthesia itself led in a number of cases to fatal outcome (1,2). This has changed dramatically and nowadays death related to anesthesia is extremely low. This is a development our specialty can be proud of and is probably related to better drugs, better understanding of physiology, and better monitoring and management. However, death after surgery, including the whole perioperative process has not declined substantially over the last decades. In fact, compared to the immediate risk of surgery and anesthesia the risk of death within the next 30 days after surgery is 1000 times more likely (3). According to recent data, death within 30 days after surgery is the third leading cause of death in the United States only topped by cardiac diseases and malignancy(4).

Some recent studies assessed this risk in greater detail. According to the group of Weiser et al., it is estimated that worldwide more than 310 million surgical procedures are performed and the exact rate of complications and the risk of death after these procedures are largely unknown(5). However, it is estimated that – depending on type of surgery and comorbidities - about 30-40% of the patients develop complications and in up to 20% of these are severe and possibly life threatening(6-8). The mortality risk of surgery is also not exactly understood. It can be estimated that 3-12 million patients die worldwide after surgery. The European Surgical Outcome study evaluated this question in greater detail and recruited in this seven days cohort study 46,539 patients of 498 European centers. Patients were followed up to 60 days after the surgical procedure. The most important result was that 1,855 patients died during the hospital treatment giving an in-hospital mortality rate of 4.7%. Another, probably the most important finding of this study was that there was substantial
variation of risk adjusted mortality between European centers giving the opportunity to find strategies that might have led to better outcome in some of those centers(9).

One piece in the puzzle of improving outcomes in perioperative patients is certainly perioperative hemodynamic and volume management. There is ongoing discussion what fluid at what rate should be administered to which patient, however there is also great consensus that fluid overload and severe fluid depletion in the perioperative period is harmful and leads to unfavorable outcomes(10). Unfortunately, adequate management of volume therapy is difficult and needs additional testing and monitoring that is seldom used in clinical practice, even in high risk patients (11,12).
Physiology of volume replacement

Certainly an important piece in this puzzle of improving perioperative outcomes is adequate fluid and volume therapy during and after anesthesia. Without doubt the most common intervention done by anesthesiologists is prescription of fluids. This is certainly important as normovolemia is an essential factor of hemodynamic stability and homeostasis between intravascular fluid and extravascular space. However, the traditional concept to give fluids in any case where hemodynamic compromise is recognized (e.g., hypotension) following the principle “in doubt give volume” has been proven wrong (13). Especially, in abdominal surgery the concept of “restrictive” fluid therapy that was introduced at the beginning of this century was quite successful and lead to better outcome compared to the traditional liberal volume therapy used historically (14). In particular, complications that were associated with fluid overload like pulmonary edema, anastomotic leakage, anemia, coagulopathy, and cardiovascular compromise were dramatically reduced leading to an overall better outcome. The only problem was that in further studies “restrictive” and “liberal” was not really well defined and what was restrictive in one study was considered liberal by other authors (15). Another problem displayed that in some studies a too restrictive approach led to severe hemodynamic compromise with decreased perfusion, decreased oxygen delivery, and complications like acute kidney injury (16).

Fluid overload has been recognized to be harmful. Unfortunately, fluid overload is common, silent, and deadly. Bellamy et al. put together in a theoretical frame work their concept that there is a U-shape relationship between fluid therapy and outcome (17). Both sides, excess fluids overload and severe fluid restriction can lead to unfavorable outcome, and it is one of the most important tasks of the anesthesiologist to find the “sweet spot” of ideal volume status of the individual patients that we could call normovolemia (Fig. 1). This theoretical idea was recently proven by two retrospective
studies that showed in the real world that fluid overload and hypovolemia is indeed associated with unfavorable outcome as acute kidney injury (AKI), pulmonary complications, and even mortality (10,13). Therefore, it is important to recognize on one side the need for fluid in our patients, however also the need for deresucitation in other cases. Thus, we need to clearly define the aim of giving fluids to our patients. Do we want to expand the extracellular space to compensate for losses or do we want to increase the intravascular space to achieve an improvement of filling pressures and potentially cardiac output (CO)? In this review only volume therapy – giving additional fluids to improve hemodynamic parameters - will be discussed. Fluid therapy, mostly necessary in internal medicine patients to compensate mainly extravascular losses and regain fluid homeostasis is beyond the scope of this article and will not be discussed.

The first question before getting additional fluid to our patient that we need to answer is whether there is a problem with our patient that we think can be solved by increasing stroke volume and thereby cardiac output. However, we have to keep in mind that we usually do not really want to increase only cardiac output. In most cases, if not all, our aim is to increase oxygen delivery to the tissues. To achieve this aim, however, the first step is to increase global oxygen delivery. Nevertheless, we have to admit that with present technology we cannot be certain that this will also lead to increased oxygen delivery to individual tissues as monitoring of the microcirculation is certainly possible, however have not gained general acceptance in clinical practice (18). In a very nice review article, Monnet et al. pointed out all necessary circumstances that a volume bolus will lead to increased tissue perfusion and function (19). The first step is to increase mean systemic filling pressure which can be counteracted by capillary leakage and venodilatation. The role of artificial and natural colloids to be more effective to increase mean systemic filling pressure has been discussed extensively and no final conclusion has been reached. Nevertheless, it seems that
colloids are more suitable to achieve this with lesser amount of fluid and longer intravascular half-life. Therefore it is only moderately surprising that colloids including starches were overall used in 86% of studies included in a review of fluid boluses (20). What is however somewhat surprising, is that this was done in spite that several studies showed, in critically ill patients, the use of colloids and especially starches being associated with an increased risk of renal failure and death (21-23). Of interest is, however, that recent meta-analysis do not confirm these caveats in surgical patients (24,25). Obviously, given the aim is to increase global oxygen delivery, of paramount importance is that the patient is fluid responsive and can increase stroke volume by additional fluid loading. As stated above not all patients that increase stroke volume and cardiac index after fluid loading will also increase oxygen consumption and show better microcirculatory flow. Further research is certainly needed to identify mechanisms for uncoupling of global perfusion indices from regional indexes and the identification of suitable treatment algorithms to amend this uncoupling. However, as optimized global perfusion is a necessary prerequisite to also optimize micro perfusion in the following section methods to assess the need for intravascular volume therapy to increase stroke volume will be critically discussed.

**How to assess fluid responsiveness**

The concept to assess treatment effects of therapies applied to patients is not really new. When we administer vasopressors and would not measure arterial blood pressure before and after the intervention, certainly our colleagues would accuse us of malpractice. However, when we administer fluids during surgery, the verification of a positive drug effect seems not to be indicated as in the majority of our patients the decision to give fluids are based in uncertain grounds if any testing or indication is taking place at all. Almost a hundred years ago, Prof. Jarisch complained that
“it was fatal for the development of our understanding of circulation, that blood flow is relatively
difficult to measure, whereas blood pressure is easily measured: This is the reason why the blood
pressure meter has gained such a fascinating influence, although most organs do not need pressure,
but blood flow (26).” However, if we do not measure blood flow, how can we then be sure that
additional volume given to our patient is actually increasing blood flow? A recent study by Cecconi
et al. tried to elucidate what drives the decision to give additional volume to ICU patients (27). The
inconvenient truth was that in 42.7% of the patients no testing of fluid responsiveness took place at
and the decision was only based on clinical experience, which is certainly not a good parameter and
in another 35.5% the decision was based on static parameters like central venous pressure (CVP) or
atrial blood pressure that we will discuss below. The second most interesting finding of this
excellent study was that despite the result of testing, positive, uncertain or negative, about 50% in
all groups of patients received additional fluids. Certainly, a result which can be improved in the
future.

Pressure based volume therapy – arterial blood pressure, CVP

In recent years it was general practice to give huge amount of fluids to patients undergoing surgery,
especially when there was some sort of hemodynamic deterioration like hypotension. The idea
behind this concept was that a “liberal” policy of fluid management in surgical patients is required.
This concept is based on ideas and studies from Tom Shires, Chief of Surgery at the University of
Texas Southwestern, Dallas, Texas (28). His work led him to conclude that an extracellular fluid
deficit in surgical patients and the consequent and appropriate elevations of aldosterone and
antidiuretic hormone is caused by extravasations of fluid from the extracellular compartment to the
third space along with evaporative losses (29,30). A strategy of aggressive fluid replacement
emerged as the mainstay of perioperative care to compensate for these losses was advised (31,32).
However, hypotension can occur quite often during surgical procedures and in many cases hypotension is not linked with hypovolemia. Intraoperative hypotension has been studied since many years. Therefore, it is surprising that still not specific definition for intraoperative hypotension exists. In a study of Bijker et al. in 130 studies 140 different definitions of hypotension were described. Risk factors for hypotension are besides hypovolemia also increased age, higher American Society of Anesthesiologists (ASA) score, induction medication that might lead to vasodilatation, and neuro-axial anesthesia (33). Also, during different time frames of anesthesia different risk factors have been published, describing post-induction hypotension, early intraoperative hypotension, and late intraoperative hypotension (34,35). Obviously, hypovolemia is only one out of many possibilities that can cause hypotension. Therefore, any given value of an arterial blood pressure cannot be used to make the decision to give fluid to a patient to increase cardiac output. Nevertheless, hypotension in context with a clinical picture can certainly help to find the indication to give fluids. In a given example of a polytraumatized patient with ongoing bleeding certainly one first step is to give fluids. However, during the procedure, just by measuring arterial blood pressure it will not be possible to tell when resuscitation is complete and the status of normovolemia is reached.

Another option might be to measure venous filling pressures like CVP or pulmonary artery occlusion pressure (PCWP). Measurement of filling pressures were advocated for a long time in many guidelines like the surviving sepsis campaign guideline (36). In this guideline it was formerly recommended that patients should receive additional fluids to optimize perfusion until their CVP was 8–12 or 12–15 cm H₂O, if mechanically ventilated. Unfortunately, this has proven wrong. Filling pressures like the CVP and the PCWP are influenced by many other factors that are not related to the fluid status nor fluid responsiveness such as cardiac compliance, intra-abdominal
pressure, airway pressure and positive end expiratory pressure (PEEP), pulmonary vascular resistance, and cardiac pathologies such as mitral/tricuspid regurgitation and congestive heart failure. It is therefore not possible to estimate from a single value of the CVP or PCWP, neither from a change in these parameters during a preload modifying maneuver whether a patient is fluid responsive or nor any better than by change. Extensive research has been performed to come to this conclusion. Several meta-analyses have been performed and also many recent guideline confirm: You shall not use the CVP or PCWP to make the decision to give addition fluids or not (37,38).

Nevertheless, there is some value in measuring the CVP curve. Recent work focused on different waves of the CVP curve and found some association with preload dependence versus no preload dependence (39,40). However, this work still has to be seen as preliminary, also given the fact that no study has been performed that tested this in a relevant number of patients using a multicenter approach and its effect on relevant outcome measures. Yet, the absolute number of the CVP might also play an important role. Even when an absolute number of the CVP does not precluded fluid-responsiveness, it can be used for risk assessment for unfavorable outcome. As the CVP is somehow the “zero-mark” of the cardiovascular system, it plays an important role for the venous return and the microcirculation. Therefore, severely elevated values for the CVP can be used as a stop sign for further fluid challenges, even when patients might remain fluid responsive (41). It has been shown that CVP values over 15 mmHg are associated with an increased rate of unfavorable outcome like AKI (42).

Therefore, in these patients the CVP can be used as a marker when to stratify increased risk versus benefit of further fluid loading.

*Stroke volume based volume therapy*
One easy method to test whether the patient is able to increase stroke volume by fluid loading is to actually give a defined volume bolus and measure before and after the intervention. This concept is based on the physiological framework of Frank and Starling. Until a certain cut-off regarding the preload of the left ventricle it can increase its stroke volume. Therefore, only patients that are below this cut-off should receive additional fluids and this is best estimated by taking advantage of the steep part of the Frank–Starling curve. Here small increases in preload will lead to relatively large increases in stroke volume. Unfortunately, this cut-off varies from person to person and can also change during different loading conditions. This is especially troublesome as therefore all static parameters like filling pressures (CVP and PCWP) as well as volumetric measures such as global end-diastolic volume can for a very physiological reason provide no magic number as a cut-off for fluid responsiveness.

A fluid challenge is a maneuver in which a defined bolus of fluid, most cases an artificial colloid, is given within a short time frame. In a recent review, it was pointed out that the bolus is relatively standardized within the goal-directed hemodynamic therapy (GDT) literature, usually consisting of 250 mL (20). In 86% of the studies a colloid was used. It is important that the fluid bolus is given relatively rapidly so that it can stretch first the right ventricle to detect an increase in stroke volume in responders. Therefore, most authors apply the bolus within 5-10 minutes or shorter. If the bolus is too small or given too slowly so that an acute increase of the right ventricular end-diastolic volume is not reached, then there is no way that stroke volume will be able to increase with the risk of a false negative test. Most authors recommend to measure stroke volume before and after the fluid challenge. An increase in stroke volume of at least 10 – 15% is considered a positive response (43). Theoretically any device that is able to measure stroke volume could be used. However, as we like to see the immediate effect of this fluid challenge in most studies uncalibrated pulse wave analysis technology was preferred to estimate the effect of the fluid challenge.
Within many algorithms used to optimize hemodynamics, also called hemodynamic GDT, a fluid challenge is used (44). One of the simplest algorithms is just to measure stroke volume, give a fluid challenge and repeat this until the stroke volume does no longer increase by more than 10%. The charm of these simple algorithms is that they are easy to follow with potentially high implementation rates. However, an important pitfall might be that repeated negative fluid challenges, especially in the ICU, if the trigger might also be hypotension can lead to a substantial positive fluid balance. One has to remember, an unsuccessful fluid challenge does not increase significantly stroke volume and therefore might actually decrease oxygen delivery due to inherent hemodilution if not blood is used for the fluid challenge.

**Volume therapy based on dynamic parameters**

Another way to optimize the fluid status of the patient is using dynamic parameters like stroke volume variation (SVV), pulse pressure variation (PPV), or pleth variability index (PVI). The dynamic preload parameters SVV and PPV are based on changes in the arterial pressure waveform due to changes in stroke volume in relation to positive pressure ventilation. The PVI is an algorithm that allows continuous and automatic estimation of respiratory variations in the pulse oximeter waveform amplitude to assess fluid responsiveness. To use these parameters for GDT it is mandatory to continuously measure the blood pressure or the pulse oximeter waveform amplitude. Today there are different technologies available, where this can be measured invasively or non-invasively. Different studies have shown that SVV and PPV are better predictors of fluid responsiveness than the static parameters CVP, PCWP and mean arterial pressure (MAP). SVV (area under the curve [AUC] 0.84) and PPV (AUC 0.94) are good predictors of fluid responsiveness with clinically acceptable levels of sensitivity (0.82 and 0.89) and specificity (0.86 and 0.88) (45).
The cut-off for SVV has been published between 10% and 12%(46). Benes et al. investigated hemodynamic goal directed protocol based on SVV in high risk surgery patients undergoing elective abdominal operation. The results show that the GDT-group had a better intraoperative hemodynamic stability, decrease in serum lactate at the end of surgery, and lower incidence of postoperative organ complications in comparison with the control group (47).

Scheeren et al. investigated a combination of SVV and stroke volume optimization in 64 high risk surgery patients, which were divided into two groups. Primary outcome measures were the number of postoperative complications. The authors could show that a SVV and stroke volume optimization protocol is feasible and can decrease postoperative wound infections. The number of patients with at least one complication (46 vs. 62%) and the number of postoperative complications per patients tended to be lower in the study group (48).

Other studies investigated the PPV as a goal for GDT. The best cut-off for prediction of fluid responsiveness is published with 10-15% (49). Salzwedel and colleagues performed a multi-center study in 160 patients undergoing major abdominal surgery and could show that hemodynamic GDT using PPV, cardiac index trending, and MAP leads to a significant decrease in postoperative complications (50).

Even though the dynamic parameters have shown to have the best prediction for fluid responsiveness, they have some important limitations the user has to know. First of all, the patient needs to be mechanically ventilated without spontaneous breathing. The published cutoffs in fluid responsiveness for SVV and PVV were validated in patients with a tidal volume > 8mL/kg. So, if the patient is ventilated with a lower tidal volume the patient may be false negative for volume responsiveness. Another limitation displays a low heart rate/respiratory ratio. In patients with extreme bradycardia or high respiratory rate (e.g., high frequency ventilation) the results may be false negative for predicting fluid responsiveness. Another special situation are patients under open
chest condition. In these situation the PPV (AUC 0.55) and SVV (AUC 0.49) show a low predictive power and should also be used with caution, because the results may be false negative either (51). In spontaneous breathing patients and in patients with arrhythmia, dynamic parameters cannot be used as either ventricular filling is depending on the variation of diastolic filling in severe arrhythmia or there is no controlled stimulus in spontaneous breathing patients.

**Volume therapy based on physiologic testing**

**Passive leg raising (PLR)**

Widely known for the treatment of acute circulatory failure, passive leg raising (PLR) has gained increasing interest for the perioperative prediction of fluid responsiveness. PLR displays a safe method for reversible and rapid autotransfusion of approximately 300 mL blood without the need for further fluid bolus (52,53). Since the accuracy of PLR is not dependent from a sinus rhythm or high tidal volume ventilation, it offers also an application when dynamic preload parameters are not viable. On the other hand, surgical procedures which are not compatible with the movement of legs or the Trendelenburg position (e.g., neurosurgery, orthopedic surgery of the lower limbs) represent relative contraindications for PLR.

Even though most studies investigating the PLR derive from critically ill patients, the predictive value can also be assumed for perioperative patients. A meta-analysis summarized 23 studies investigating the diagnostic accuracy of PLR (measured by flow-based hemodynamic monitoring tools). The pooled sensitivity of PLR was calculated to 86% (95% CI: 79 %– 92%) while its specificity displayed 92% (95% CI: 88% – 96%) proofing its high diagnostic performance for predicting fluid responsiveness (54). A second systematic review of 991 patients was able to confirm these findings but emphasizes the need for CO measurement as target parameter in order to
achieve reliable results (55). It has to be highlighted that not only the need but also the lack of necessity for fluid therapy can be detected with PLR. However, even though the practical implementation seems not very challenging, some pitfalls have to be considered thoroughly in order to increase the predictive accuracy. Monnet and Teboul summarized these pitfalls (53): The measurement starts from the semi-recumbent and not from supine position and should rather target CO or its indices than blood pressure. CO can be assessed with different devices (e.g., echocardiography, pulse contour analysis) but it is of high importance that the measurements are able to detect rapid changes (<1 min). Furthermore, the procedure does not end by the patient’s reposition but with a postinterventional observation period until the hemodynamic situation has been normalized. The depth of anesthesia should be appropriate in order to avoid sympathetic activation and adrenergic stimulation blurring the effect of PLR. If these rules are taken in concern, PLR displays a powerful diagnostic tool for predicting perioperative fluid responsiveness and is recommended by several international guidelines (56-58).

**End-expiratory occlusion test (EEOT)**

A decade ago, Monnet et al. introduced the EEOT (59). The underlying principle uses the influence of deep inspiration on cardiac preload. By carrying out a short (15-30 seconds) end-expiratory occlusion in mechanically ventilated patients, CO is impaired while atrial filling is simultaneously facilitated leading to an increase of ventricular stroke volume. In order to receive reliable prediction of fluid responsiveness continuous CO measurement is necessary during EEOT (60). Furthermore, an EEOT-induced change of 5% of CO is generally accepted as a proof of fluid responsiveness (60). Pulse contour analysis performs superior to echocardiography in terms of precise detection of changes of CO during EOOT (61). However, also other devices such as echocardiography, non-
invasive CO measurements and Doppler-based methods are feasible but still need more confirmative studies (20,62,63).

EEOT imitates a fluid challenge without the need for fluid application. In contrast to the PLR test, no movement of the patient is necessary making it to an attractive solution for the surgery room. Its predictive value was confirmed in several studies for patients ventilated with tidal volumes ≥8 mL/kg, while its accuracy in patients ventilated with smaller tidal volumes is still under discussion (20,59,60,64-66). Most studies investigating EEOT under low-tidal volume ventilation derive from an intensive care setting and are cannot directly transmitted to the surgery room (65,67). Only one study of neurosurgical patients directly compared the effect of low- to regular-tidal volume ventilation on the accuracy of EEOT and showed a very low predictive value of EEOT under low-tidal volume ventilation (AUC of the change of cardiac index 0.53 [95% CI: 0.35 to 0.71]) (68). Guinot et al. published the only study showing a low predictive value of EEOT for fluid responsiveness under sufficient tidal volumes (of 8.2 mL/kg) in a heterogenous study collective of surgical patients (66). The reason for these findings remains unclear but differences between the perioperative and intensive care ventilation strategies might offer an explanation. However, it has been shown that the level of PEEP does not affect the reliability of the EEOT (69).

**Novel physiological tests for the prediction of fluid responsiveness**

End-tidal carbon dioxide concentration (P\textsubscript{ETCO}2) displays a surrogate for CO and is well-known for the detection of successful cardiopulmonary resuscitation. It has not only been shown that P\textsubscript{ETCO}2 directly correlates to CO but also that it offers sufficient prediction for fluid responsiveness when combined with PLR testing (70,71). Tusman et al. introduced a further method based on volumetric CO\textsubscript{2} measurement by quantifying the amount instead of the concentration of exhaled CO\textsubscript{2} (72). In order to detect a lack of intravascular fluids, patient’s fluid responsiveness was provoked with an
elevation of PEEP from 5 to 10 cmH₂O for one minute while simultaneously monitored with volumetric capnography and pulse contour analysis. Afterwards patients received 500 ml of crystalloids and measurements were repeated. A decrease of exhaled CO₂ volume during the PEEP challenge was predictive for fluid responsiveness. Furthermore, ROC-analysis revealed a high predictive performance which was superior to change of end-tidal CO₂ concentration and PPV. Even though this method is only available in ventilated patients, it offers also a non-invasive and accurate approach for predicting fluid responsiveness, worth of further validation (72,73).

Already in 2005, the respiratory systolic variation test (RSVT) has been introduced for the prediction of fluid responsiveness in surgical patients (74). The RSVT is performed by the application of three consecutive inspiratory breaths with increasing peak inspiratory pressures (of 10, 20, and 30 cmH₂O) and simultaneously detection of the three lowest systolic arterial pressures. Next, this blood pressure is correlated to the peak pressure of the inspiratory breath resulting in a RSVT slope. The slope corresponds to the Frank-Starling curve enhancing a physiologic comprehension of the fluid challenge and offers comparable prediction to fluid responsiveness as PPV and SVV analysis (74,75).

**De-resuscitation strategies using monitoring of volume status**

Originally de-resuscitation describes a strategy aiming to treat fluid overload following the resuscitation and stabilization of critically ill patients. Fluid therapy is used to restore the intravascular volume homeostasis with the goal of achieving a sufficient tissue oxygenation and can be characterized by the Resuscitation, Optimization, Stabilization, and Evacuation (ROSE) concept (76,77). First, patients have to be resuscitated from circulatory shock (resuscitation). In order to avoid adverse outcome associated to fluid overload, fluid responsiveness
should be guided by validated tests such as PLR and EEOT (optimization and stabilization). After stabilization of the patient’s hemodynamic status, de-escalation should be considered early and just like in stabilization phase monitored with tests for fluid responsiveness (Evacuation) (76). The goal of the evacuation, respectively de-resuscitation phase, is to restore the patient’s physiologic homeostatic intravascular balance and to eliminate superfluous fluids. In the intensive care setting this can be performed with restrictive volume therapy, diuretics and/or renal replacement therapy. It has been shown that a negative fluid balance over three days predicts independently an improved ICU survival (76-78). However, two questions arise: First, what is the best approach to guide de-resuscitation and second, should we consider de-resuscitation strategies in the perioperative setting? In order to treat fluid overload, it has first to be diagnosed properly. In the assumption that fluid non-responders reflect patients with balanced or overloaded fluid status, a possible approach poses their identification by using fluid responsiveness tests. Since these patients do not benefit from a volume challenge, it can be assumed that CO does not decrease through fluid removal. On the other hand, fluid removal can be performed until the tests for fluid responsiveness return again to positive results. Next to PLR and EEOT, also dynamic preload parameters, body weight quantification, bioimpedance measurements, and respiratory variations of the diameter of the inferior caval vein have already been evaluated as treatment goals for de-resuscitation (73,76,79-83). In order to reduce adverse outcome after acute lung injury, Cordemans et al. used the extra vascular lung water index and intra-abdominal pressure to guide the treatment protocol consisting of high PEEP levels, small volume resuscitation with albumin, and fluid removal (PAL, [PEEP, albumin, and Lasix®]) (84). However, the role of albumin application in critically ill patients has to be further investigated because two prospective studies failed to show a beneficial effect of albumin therapy(85,86). While the Furosemide and Albumin for Diuresis of Edema (FADE) study failed to proof feasibility (86), the Albumin Italian Outcome Sepsis (ALBIOS) study showed not improved 28- respectively 90-
days survival after targeting an albumin plasma level $\geq 30$ g/L over 28 days after septic shock (85).

Since the phases of ROSE do not generally apply to surgical patients, it cannot directly be adopted to the perioperative setting. However, it is well-known that perioperative fluid overload is associated to adverse outcome and should therefore be avoided (87-89). Hence, smart perioperative volume therapy should prevent fluid overload and the need for a perioperative “de-resuscitation”.

Over the last decade, several GDT protocols have been introduced and evaluated. A recent meta-analysis summarized 95 randomized-controlled trials and was able to show a GDT-induced reduction of mortality, morbidity, and length of hospital stay (90). Contrary, the Optimisation of Cardiovascular Management to Improve Surgical Outcome (OPTIMISE) study was not able to proof a benefit of GDT (88). The OPTIMISE study protocol aimed for a maximized CO by optimizing it individually with fluids (until no increase of stroke volume was detectable anymore) with further support using dopexamine. Since no reduction of mortality or morbidity was detected, it can be questioned if a maximized CO target is reasonable. This does not only include the use of dopexamine but since fluid responsiveness displays a physiological condition also the question whether patients should receive fluids until their preload capacity is completely exploited (73,91).

Hence, modern GDT protocols do not aim for a maximized CO but rather utilize a personalized hemodynamic GDT management using multiple parameters for the assessment of blood flow and fluid responsiveness (91). Even though the beneficial effect of personalized GDT is indisputable, only a small degree of patients receive this hemodynamic management highlighting the need for improved implementation in the daily anesthetic routine (12).

Summarizing, fluid overload remains a common problem after the stabilization of critically ill patients. De-resuscitation strategies using tests for fluid responsiveness as well as hyperoncotic infusion combined with diuretics, respectively renal replacement therapy, might help to remove the
superfluous fluids and increase survival. However, further high-quality studies are necessary to confirm these encouraging findings. Furthermore, the role of de-resuscitation has to be discussed in terms of intensifying actions for the prevention of perioperative fluid overload. To achieve this, personalized hemodynamic treatment goals combined with GDT protocols represent an effective approach.

Conclusions

Unfavorable outcome after surgery is still common leading to the fact that surgery is considered as one of the leading causes of death comparable to cancer and cardiovascular diseases. Many prospective and retrospective studies have shown that volume management and the dark side of it – fluid overload – can have detrimental effect on postoperative outcome. Therefore, strategies to prevent fluid overload and help to assess the individual need of volume during and after surgery should be implemented to increase patient safety. Still today, in many of our patients no monitoring of volume therapy is used or inadequate static parameters like arterial blood pressure, venous filling pressures or volumetric parameters that cannot assess fluid responsiveness. As a gold standard to assess whether a patients can benefit by an increase of stroke volume and therefore potentially by an increase in oxygen delivery dynamic testing should be used. This can be done by either dynamic parameters like SVV or PPV, or by forced manipulation of the preload e.g. by a volume challenge, PLR or other physiological testing.

In combination with a goal directed hemodynamic monitoring protocol also applying vasopressors and inotrope medication a reduction of mortality with a number needed to treat of 58 has been shown in a recent meta-analysis (90). Whether goal directed volume therapy alone can reduce perioperative mortality still need to be demonstrated in larger multicenter studies. The new concept
to use suitable parameters for goal directed de-resuscitation can reduce complication rates and potentially mortality in the perioperative setting still awaits confirmation by larger trials. Nevertheless, this concept seems promising.
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Fig. 1. Relationship between morbidity, hypo- normo- and hypervolemia.

Bellamy et al. [17] put together in a theoretical frame work their concept that there is a U-shape relationship between fluid therapy and outcome. Therefore, prevention of hypo- and hypervolemia by goal directed fluid management is essential.