Monitoring of peri-operative fluid administration by individualized goal-directed therapy

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Background: In order to avoid peri-operative hypovolaemia or fluid overload, goal-directed therapy with individual maximization of flow-related haemodynamic parameters has been introduced. The objectives of this review are to update research in the area, evaluate the effects on outcome and assess the use of strategies, parameters and monitors for goal-directed therapy.

Methods: A MEDLINE search (1966 to 2 October 2006) was performed to identify studies in which a goal-directed therapeutic strategy was used to maximize flow-related haemodynamic parameters in surgical patients, as well as studies referenced from these papers. Furthermore, methods applied in these studies and other monitors with a potential for goal-directed therapy are described.

Results: Nine studies were identified pertaining to fluid optimization during the intra- and post-operative period with goal-directed therapy. Seven studies (n = 725) found a reduced hospital stay. Post-operative nausea and vomiting (PONV) and ileus were reduced in three studies and complications were reduced in four studies. Of the monitors that may be applied for goal-directed therapy, only oesophageal Doppler has been tested adequately; however, several other options exist.

Conclusion: Goal-directed therapy with the maximization of flow-related haemodynamic variables reduces hospital stay, PONV and complications, and facilitates faster gastrointestinal functional recovery. So far, oesophageal Doppler is recommended, but other monitors are available and call for evaluation.

Accepted for publication 15 October 2006

Key words: algorithms; fluid therapy; monitoring; treatment outcome.

Research on peri-operative fluid therapy has recently focused on two strategies, fixed high- vs. low-volume regimens and individualized optimization strategies, so-called goal-directed therapy (1), as supplements to routine cardiovascular monitoring.

The fixed volume strategy is based on several randomized studies which have shown that a fluid amount of more than 1.5 l facilitates recovery following minor surgery (2–4), whereas excessive amounts (> 5–6 l) impair outcome following major surgical procedures (5, 6). At the same time, it is agreed that hypo- and hypervolaemia are deleterious for peri-operative organ function, and adversely affect outcome (7, 8). Fixed volume strategies, however, do not take the considerable individual differences, including gender, age, complicating illnesses, body composition and, notably, hydration, into account. We consider that a fixed volume strategy is insufficient for peri-operative fluid therapy.

Routine cardiovascular monitoring of the surgical patient includes the recording of blood pressure (BP) and heart rate (HR). Yet, BP is influenced not only by the central blood volume (CBV) but also by anaesthetics and surgical stress, complicating the diagnosis of hypovolaemia. Although widely used to guide fluid therapy, BP and HR are poor parameters of CBV (9). Thus, the assessment of BP and HR is not sufficient to detect mild hypovolaemia which can lead to compromised tissue oxygenation, especially in the splanchnic circulation (10). In addition, diuresis and a calculated fluid balance are used to estimate the intravascular volume. Peri-operative diuresis, however, is affected not only by hypovolaemia, but also by the surgical stress response, causing fluid retention. We therefore consider BP and HR to be inadequate monitors of CBV, and a low diuresis to be a late and imprecise monitor of hypovolaemia.

The goal-directed strategy is based on the hypothesis that peri-operative fluid management should contribute to the maximization of oxygen delivery through well-defined goals for therapy, based on flow-related parameters. Furthermore, an individualized
approach has been introduced with the maximization of flow-related variables, such as the stroke volume (SV) of the heart, by fluid challenges (1, 11). This individual approach is considered to be essential, and it is emphasized that the strategy seeks to maximize flow-related parameters rather than to obtain pre-defined absolute values. With this strategy, both hypovolaemia and fluid overload are prevented because fluid administration is terminated when the applied flow-related parameter is maximized. Although some goal-directed therapy studies have been evaluated in a recent meta-analysis (12), the subject has not been addressed specifically. As goal-directed therapy is rational and supported by randomized studies, the purpose of this review was two-fold: to review the literature pertaining to the influence of goal-directed therapy on post-operative outcome and to discuss the recommendation of strategies, parameters and monitors.

Methods
To identify trials using an individualized peri-operative goal-directed therapy strategy, a MEDLINE search (1966 to 2 October 2006) was performed. Only randomized studies published in English-language journals were selected. The search terms ‘fluid therapy’ and ‘surgery’ were combined. The search term ‘goal-directed therapy’ was also included. Additional studies were found in the cited references of the identified studies. Only studies comparing standard peri-operative fluid administration with fluid administration guided by a goal-directed strategy, as defined, were included. Studies with a pre-defined absolute value of a chosen goal were therefore excluded. Papers in which additional medical therapy was administered were included only if the fluid therapy fulfilled the described criteria and the studies were required to evaluate therapy in the context of outcome. Trials in which only pre- and intra-operative outcomes were evaluated and trials in paediatric surgery were not included. In this search, 3047 studies were identified, nine of which met the inclusion criteria (Table 1). To identify monitors that could be recommended for goal-directed therapy, we first describe the monitors used in the identified studies. Secondly, we describe monitors with a potential for goal-directed therapy. The criteria for consideration were as follows: (i) historic importance for fluid optimization; (ii) modalities for the evaluation of cardiac performance that are or could be applicable for goal-directed therapy; and (iii) methods that evaluate either global or peripheral oxygenation.

Results
Nine studies were identified: seven focused on the intra-operative period (13–19) and two assessed the early post-operative period (20, 21).

Monitor
Oesophageal Doppler (OD) was dominant; the lithium dilution cardiac output method (LiDCO™) was used in only one study (Table 1). In all studies, supplemental boluses of colloid, in addition to background infusions, were guided by the fluid challenge strategy (SV maximization).

Amount and type of fluid
In eight studies, patients received more fluid and relatively more colloid than in control groups. In one study, patients received less fluid but relatively more colloid (19). In the two studies pertaining to the post-operative period, supplemental medical therapy (inotropes and vasodilators) was used to reach pre-defined absolute goals related to mean arterial pressure or an oxygen delivery index.

Outcome
Seven studies showed a reduced hospital stay and two studies found a reduced stay in an acute hospital bed or intensive care unit (15, 17) (Table 1). In addition, Venn et al. (18) showed that patients achieved discharge criteria earlier, but that social confounding factors in this population (hip fracture) kept the patients in hospital. Conway et al. (13) did not find a reduced hospital stay, but found reduced critical care admissions. Three studies demonstrated positive effects on recovery of gastrointestinal function (ileus) or post-operative nausea and vomiting (PONV) (14, 16, 19). Complications were reduced in four studies (15, 16, 19, 21), whereas two studies showed only a trend for a reduction (13, 20).

Conclusion
Individualized goal-directed therapy in the intra- and post-operative period may improve outcome by augmenting gut function (ileus and PONV) and reducing morbidity and hospital stay.

Discussion
Peri-operative individualized fluid treatment guided by goal-directed therapy improves outcome in several procedures (Table 1). This is in contrast with the inconsistent results obtained with the use of the pulmonary artery catheter (PAC), probably reflecting
<table>
<thead>
<tr>
<th>Author and Year</th>
<th>No of Patients / Procedure</th>
<th>Timing</th>
<th>Infusion Strategies and Additional Therapy</th>
<th>Used Fluid Type</th>
<th>Volumes Infused</th>
<th>Endpoints</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mythen 1995 (15)</td>
<td>60 / Cardiac surgery</td>
<td>Intra-</td>
<td>Control: “routine administration” GDT: additional colloid boluses guided by OD and CVP</td>
<td>All: crystalloid, colloid (HES) and blood.</td>
<td>Control vs. GDT: Cryst: ≈1100 vs. ≈867 ml Coll: ≈734 vs. ≈1367 ml Blood: both ≈234 ml</td>
<td>Gut mucosal perfusion</td>
<td>↓ Gut mucosal perfusion ↓ Hospital stay ↓ ICU stay ↓ Complications</td>
</tr>
<tr>
<td>Sinclair 1997 (17)</td>
<td>40 / Femoral fracture</td>
<td>Intra-</td>
<td>Control: fluid loss, maintain BP and HR. GDT: Additional colloid boluses guided by OD</td>
<td>All: crystalloid and colloid (HES)</td>
<td>Control vs. GDT: Cryst: 1000 vs. 725 ml Coll: 0 vs. 750 ml</td>
<td>Fitness to discharge Hospital stay (in acute bed; in acute plus long stay bed), Mortality</td>
<td>Faster medically fit ↓ hospital stay ↓ mortality ↓ SV and CO</td>
</tr>
<tr>
<td>Conway 2002 (13)</td>
<td>55 / Major bowel surgery</td>
<td>Intra-</td>
<td>Control: “anaesthetist choice” GDT: additional colloid boluses guided by OD</td>
<td>Control: “anaesthetist choice” GDT: Additional colloid (HES)</td>
<td>Control vs. GDT Total: 55,2 vs. 64,6 ml/kg Coll: 19,4 vs. 28,0 ml/kg</td>
<td>Haemodynamic performance Hospital stay Postoperative complications</td>
<td>↑ SV and CO ↓ Hospital stay ↓ Postoperative complications ↓ Critical care admissions</td>
</tr>
<tr>
<td>Gan 2002 (14)</td>
<td>98 / General, urological, gynological</td>
<td>Intra-</td>
<td>Control: urinary output, HR, MAP, CVP and when “clinically indicated” GDT: estimated blood loss and additional fluid boluses guided by OD</td>
<td>All: crystalloid (Ringer), colloid (HES up to 20 ml/kg) and blood</td>
<td>Control vs. GDT: Coll: 282 vs. 847 ml Cryst.: 4375 vs. 4405 ml Blood: 118 vs. 168 ml</td>
<td>Hospital stay Gastrointestinal and renal function</td>
<td>Hospital stay PONV Tolerated oral solid regimen earlier</td>
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<tr>
<td>Venn 2002 (18)</td>
<td>90 / Hip fracture</td>
<td>Intra-</td>
<td>Control: “clinician choice” GDT 1: additional colloid boluses guided by CVP GDT 2: additional colloid boluses guided by OD</td>
<td>All: crystalloid (Hartmann), colloid (gelofusine) and blood</td>
<td>Control vs. GDT 1 vs. GDT 2: Cryst: 1286 vs. 1156 vs. 1120 ml Colloid: 448 vs. 1123 vs. 1207 ml Total minus blood loss: 1392 vs. 1850 vs. 2051 ml</td>
<td>Fitness to discharge Hospital stay Postoperative morbidity</td>
<td>Faster fit for discharge Hospital stay ↓ Postoperative morbidity</td>
</tr>
<tr>
<td>Mckendry 2004 (20)</td>
<td>174 / Cardiac surgery</td>
<td>Post-</td>
<td>Control: “conventional management” GDT: blood or colloid boluses guided by OD, Glyceryl trinitrate or adrenaline guided by MAP.</td>
<td>All: crystalloid, colloid and blood.</td>
<td>Control vs. GDT: Cryst: 328 vs. 353 ml Coll: 1042 vs. 1667 ml</td>
<td>Hospital stay ICU stay Complications</td>
<td>Hospital stay ↓ ICU stay ↓ Major complications and death</td>
</tr>
<tr>
<td>Wakeling 2005 (16)</td>
<td>128 / Major bowel surgery</td>
<td>Intra-</td>
<td>Control: CVP (12-15 mmHg) GDT: “routine fluid management” and additional colloid boluses guided by OD and CVP</td>
<td>All: crystalloid and colloid (Haemacel)</td>
<td>Control vs. GDT: Cryst: Same (3000 ml) Coll: 1500 vs. 2000 ml</td>
<td>Hospital stay Gut function</td>
<td>Hospital stay ↑ Gut function recovery Gastrointestinal and overall morbidity</td>
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</table>
several differences in the set-up. Firstly, in the studies identified, goal-directed therapy is individualized to meet the patient’s functional capacity, and no stress is applied to reach a pre-defined goal that may be outside the potential of the patient. For example, goal-directed therapy may be carried out with SV maximization, where fluid administration is terminated when the individual maximized SV is reached. Secondly, timing is essential, as prompt therapy prevents the development of undesirable pathophysiological processes. Studies in which goal-directed therapy is used within the peri-operative period have evaluated the maximization of flow-related haemodynamic variables in response to fluid boluses in addition to standard fluid therapy. The tendency to provide more colloids when individualized goal-directed therapy is applied cannot be interpreted as a general recommendation, but rather a consequence of meeting the patient’s physiological needs as they appear. In addition, the use of crystalloids vs. colloids remains debatable and calls for comparative randomized studies within the concept of individualized goal-directed therapy. It can be stated, however, that when the choice is crystalloids, physiological solutions are preferable to isotonic saline when using large volumes, thereby minimizing the risk of hyperchloremic metabolic acidosis (22).

It is a problem that the most frequently used outcome variable for goal-directed therapy is the duration of hospital stay. Hospital stay is influenced by multiple factors, and interventions should ideally be assessed in a standardized regimen, such as the fast-track concept (23). A better approach is to evaluate organ function, as applied in some goal-directed studies in which PONV and gastrointestinal function have been assessed. However, a further application of physiological organ function parameters in the evaluation of goal-directed fluid therapy is needed (24). Furthermore, goal-directed therapy studies have focused on pre- and intra-operative optimization. In major procedures with significant fluid shifts, it seems rational to combine pre-, intra- and post-operative optimization and monitoring of fluid requirements in order to avoid unnecessary and detrimental fluid excess or hypovolaemia. It is emphasized that the available goal-directed therapy outcome studies have been carried out in the context of moderate to major surgery. As fluid therapy is likely to influence factors such as PONV and orthostatic dysfunction, which may prolong hospital stay after ambulatory surgery (7, 23), goal-directed therapy should also be evaluated in ambulatory and semi-ambulatory surgical settings. The OD technique

<table>
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<tr>
<td><strong>Author and year</strong></td>
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<td><strong>Volumes infused</strong></td>
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<td>Control vs. GDT: Cryst: 900 vs. 930 ml. Coll: 600 vs. 625 ml. Blood: 0 vs. 25 ml.</td>
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<td><strong>Complications Hospital stay</strong></td>
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<td><strong>Infusion strategy and timing</strong></td>
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<td>Control vs. GDT: Cryst: 2625 vs. 2298 ml. Coll: 1209 vs. 1340 ml.</td>
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<td><strong>Endpoints</strong></td>
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<td><strong>Result</strong></td>
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<td>Complications</td>
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<tr>
<td>Hospital stay</td>
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<tr>
<td>Tolerated solid oral regimen earlier</td>
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is the predominant method used in randomized goal-directed therapeutic trials, but other modalities may be applied. The cost–benefit differences between monitors cannot be evaluated because of the limited number of outcome studies using methods other than OD. There is a need for comparative and, ultimately, procedure-specific randomized trials to evaluate monitors with the potential for goal-directed therapy. In the following sections, we describe the strategies, parameters and monitors relevant for goal-directed therapy. This discussion is summarized in Table 2.

**Strategies and parameters in goal-directed therapy**

The fluid challenge strategy is based on the assumption that normovolaemia, in a supine individual, may be defined as the pre-load that is required to establish a maximal SV or cardiac output (CO) in accordance with Starling’s law of the heart (25). Subsequent fluid challenges until SV no longer increases indicate that the ‘flat part’ of the Starling curve has been reached, and this individual goal is used as a set point for therapy. In most algorithms, a 10% increase in SV is required to justify a further fluid challenge of 200–250 ml of colloid, thereby minimizing the risk of fluid overload. The demand for a 10% increase in SV is also a safety against the bias that normovolaemic haemodilution increases CO *per se* (26). A method of reversible volume loading in the context of SV changes has been described using passive leg raising to mimic a fluid challenge (27). Although not evaluated perioperatively, this method may have the potential to minimize the risk of fluid overload.

The prediction of fluid responsiveness is a strategy that aims to predict the response of a fluid challenge before it is administered (28, 29) and, ideally, avoids the administration of unnecessary fluid boluses. Parameters can be divided into static and functional. As functional parameters appear to be superior in their ability to predict the response to fluid administration (28), we evaluate the parameters and monitors in this context. In the context of goal-directed therapy, these functional parameters of fluid responsiveness cover several variables that change with the intra-thoracic pressure during mechanical ventilation and influence the pre-load to the heart. By analysing, for example, the variation in pulse pressure (PP) or continuous SV during manipulation of ventilation (29), this method estimates the reaction to a fluid load. Although variations in SV-related variables are appreciated, the method requires that the patient’s lungs are mechanically ventilated, and it is therefore not applicable to the awake patient. Functional parameters of fluid responsiveness in the perioperative period have not been evaluated in relation to clinical outcome.

<table>
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<tr>
<th>Strategy</th>
<th>PAC</th>
<th>OD</th>
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<th>PICCO</th>
<th>LiDCO</th>
<th>CVC (SO₂)</th>
<th>NIRS</th>
<th>GT</th>
<th>MD</th>
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a., arterial line; Challenge, fluid challenge strategy; CVC, central venous catheter; fem.a., femoral arterial line; GT, gastric tonometer; Imp, thoracic impedance; Intra-op., intra-operative; LiDCO, lithium dilution cardiac output method; MD, microdialysis; MF, Modelflow; min, minimally invasive; NIRS, near-infrared spectroscopy; OD, oesophageal Doppler; PAC, pulmonary artery catheter; PICCO, pulse contour cardiac output method; Post-op, post-operative; Pre-op, pre-operative; rec/s.c., placement of probe in rectal lumen or subcutaneous cannula; Responsiveness, fluid responsiveness strategy; SO₂, venous oxygen saturation; TOE, trans-oesophageal echocardiography; ✓, suitable; (✓), practicable with limitations; X, unsuitable; ?, evidence missing.
Monitors to guide fluid administration in goal-directed therapy

In addition to being associated with an improved outcome, the ideal monitor to guide fluid treatment in goal-directed therapy should be safe, easy (require minimal skills, quick to install and to interpret), non-invasive, precise and prompt to allow early intervention and applicable throughout the entire peri-operative period.

Pulmonary artery catheter

PAC has been used widely in the peri-operative setting for the determination of cardiopulmonary variables, and Shoemaker et al. (30) introduced the concept of ‘supraphysiological haemodynamic values’. The use of PAC in the evaluation of survivors of shock provided absolute values for oxygen delivery (Do2), cardiac index and oxygen consumption to guide therapy. Although initial studies to optimize the surgical patient were promising, later research using PAC has been disappointing, with inconsistent results ranging from improved outcome (31) to no significant effect (32), and even adverse effects (33). Randomized studies without individual goals for therapy have not shown a positive effect of PAC (34), and are bewildering and misleading in the discussion of goal-directed therapy. The timing of monitoring and intervention in the era of PAC may also explain the inconsistency of the results. In the critically ill patient with multi-organ failure, intervention is not as efficacious as in earlier stages of illness (31), probably because of more advanced pathophysiological processes. The use of PAC is also complicated by the invasiveness of the procedure and potential complications. In addition, PAC requires training and experience, and its popularity has declined because of the introduction of less invasive modalities with comparable precision. With a specially built PAC, it is possible to obtain a beat-to-beat estimation of variables that guide fluid therapy, including venous oxygen saturation (SvO2). In relation to PAC, the important issue of venous oxygenation is discussed below (see ‘Venous oxygenation’ section). Therefore, although continuous measurements of flow-related variables are possible, the strategy used previously has evaluated PAC in the context of the achievement of pre-defined absolute values. No identified study has used individualized strategies, such as SV maximization, and only observational studies have maximized SvO2 (35). Although feasible, no studies have evaluated variables such as PP, SV or other functional parameters of fluid responsiveness to predict fluid requirements using continuous PAC measurements. In summary, PAC is not recommended when performing goal-directed therapy in the routine peri-operative setting.

Oesophageal Doppler

For more than 20 years, the estimation of blood velocities in the aorta has been possible (36). By introducing a Doppler probe through the mouth or nose to the mid-oesophagus, it is possible to measure the velocity of blood in the descending aorta. This velocity can be transformed to a corresponding SV by a nomogram derived from correlation studies with PAC measurements, or by measurement of the cross-sectional area, depending on the chosen device (37). Consequently, an OD-derived CO shows a high correlation with a PAC estimate (38, 39). In addition to SV and CO, OD produces a corrected value of the systolic flow time, which may indicate systemic vascular resistance. The normal range of the systolic flow time is 330–360 ms and, with lower values, hypovolaemia should be suspected. Importantly, OD has been used in goal-directed therapy settings with improved outcome (13–18, 20). OD does not require calibration and relatively little training is needed to provide a reproducible result (40). The position of the probe, however, must be accurate and adjustments are required frequently. Values for SV and CO must therefore be interpreted with attention to the probe position. It is recommended that patients are anaesthetized or sedated before placement of the probe, because of the sensitivity to movement and inconvenience of the probe, but softer probes for use in the awake patient are under evaluation. The fluid challenge strategy is the most frequently used technique with this monitor, but the fluid responsiveness strategy is also feasible, although not an option with the present devices. Although proven to be valuable for intra-operative goal-directed therapy, OD is not, currently, optimal in the awake patient, and therefore not applicable for the entire peri-operative period. In summary, although associated with problems in the awake patient, OD is validated in a clinical goal-directed therapy setting and can therefore be recommended.

Pulse contour and pulse power analysis

By analysing arterial pulse waveforms supported by computer analysis, continuous real-time SV and CO, together with other cardiopulmonary variables, can be estimated, making the techniques suitable for the fluid challenge strategy. In addition, PP and SV variations are provided, and therefore the fluid responsiveness strategy is practicable.
The pulse contour cardiac output method (PiCCO) is the most validated system in pulse contour analysis and shows acceptable correlation with PAC thermodilution measurements (41–45). PiCCO is calibrated by transpulmonary thermodilution and is therefore invasive, as, in addition to a central venous catheter, it requires a femoral or axillary artery line. Recently, it has been questioned whether PiCCO is a less invasive procedure than PAC (46). Although the installation of PiCCO may be considered to be easier than that of PAC, the use of PiCCO in the pre-operative period is complicated by its invasiveness. In addition, results in patients with arrhythmia may be unreliable because of the irregular arterial waveforms. The invasive procedure of PiCCO makes it unsuitable for goal-directed therapy in routine surgery.

LiDCO™ is an alternative monitor that uses pulse power analysis. It requires initial calibration, either by a small lithium bolus or a value of CO attained with another monitor. Measurements with LiDCO™ suggest a comparable accuracy to PiCCO (47), and reports propose comparable precision to CO determined by thermodilution (48, 49). LiDCO™ requires venous and arterial lines (radial artery). As the administration of an arterial line is safe and not associated with major inconvenience under local anaesthesia, this monitor is applicable for the entire peri-operative period. The amount of lithium used to calibrate the system has not been associated with any reported side-effects. However, there is interference with non-depolarizing neuromuscular blockers, i.e. calibration with lithium must take place before or 15–30 min after their administration. Like PiCCO, LiDCO™ is not recommended in patients with arrhythmias. LiDCO™ has been reported to be contraindicated in patients weighing less than 40 kg, in the first trimester of pregnancy and in patients on lithium therapy. Reports on the clinical application of LiDCO™ are limited, but it has been evaluated in a goal-directed therapy setting by post-operative SV maximization with a positive effect on outcome (21). In summary, LiDCO™ may be an option in moderate to major surgery where an arterial line is often required.

Modelflow (MF)
MF estimates beat-to-beat SV and CO by an arterial line or a non-invasive finger pressure (50) using a non-linear three-component model of arterial impedance. MF is easy to install and requires minimal technical skills. Absolute values of SV and CO can be obtained in a clinical setting by calibrating against a monitor that provides an absolute value for SV (51, 52). Changes in SV measured with MF have been validated against other modalities (50, 51, 53, 54). However, the absolute value of SV is of importance as it determines the increase in SV demanded for the administration of further challenges. However, with calibration, the fluid challenge strategy may be possible. The fluid responsiveness strategy is also possible, but not a feature with available devices. The cuff used to measure finger pressure is unreliable under circumstances in which the patient develops peripheral vasoconstriction, and hence an estimate by an arterial line is more robust. In summary, MF may be a useful modality for goal-directed therapy, but it has not been applied for outcome studies.

Venous oxygenation
By definition, the acquisition of the mixed venous oxygenation (Svo2) and central venous oxygenation (Scvo2) is invasive, requiring PAC and a central venous catheter, respectively. Because placement of such catheters most often takes place after the induction of anaesthesia in elective surgery, the use of Svo2 is not advantageous in the pre-operative period. Scvo2 has been proposed as a marker of CBV (55, 56), but has received only limited testing for peri-operative goal-directed therapy with a pre-defined Svo2 value of more than 70% (57). The use of Scvo2 rather than Svo2 is argued by studies showing consistently higher values of Scvo2 than Svo2 of approximately 5% (58), but with parallel changes in response to a volume load (26). A pre-defined Svo2 value of more than 70% is widely used in the treatment of sepsis in intensive care, where it is part of a regimen of so-called ‘early goal-directed therapy’ (59). It has been suggested that normovolaemia in the supine person is reached when fluid boluses result in a maximum Scvo2 value that, most likely, is higher than 70% (55, 56), and the fluid challenge strategy may be applicable. The use of Scvo2 rather than SV is of interest, especially when loading a patient with fluids other than blood. In this case, CO increases with haemodilution (26), an effect also known in anaemia in which CO is elevated (60). Thus, during normovolaemic haemodilution, CO increases, whereas Scvo2 remains stable until the haemoglobin level is reduced by approximately 50% (26). When the patient gains consciousness after anaesthesia, Svo2 is also influenced by an increase in oxygen consumption, posture and possibly cardiac function (61–63), leading to interpretation problems. In summary, Svo2 and Scvo2 may represent potential parameters for
intra-operative goal-directed therapy, but comparative studies with other modalities of goal-directed therapy are needed, as well as outcome studies, before recommendations can be made.

Estimating tissue oxygenation
The essence of fluid therapy monitoring is to evaluate whether organs and tissues are adequately perfused and supplied with a sufficient amount of oxygen. Rather than analysing global oxygenation, as is the case for $S_o_2$, the maximization of peripherally derived values of flow or oxygenation may be used as end-points for goal-directed therapy.

Near-infrared spectroscopy (NIRS) facilitates the estimation of oxygenation within tissue. By the use of an optode placed on the skin, near-infrared light is sent through the tissue and the reflected light is used to estimate oxygenation. Using this method, the oxygenation of the brain and other organs, including skeletal muscles and the kidney, may be estimated (64). As changes in muscle perfusion, and thereby oxygenation, are affected early in hypovolaemia, NIRS may be applicable in goal-directed therapy. Because NIRS is non-invasive, it is safe; it is also easy to install and to interpret. However, NIRS has not been evaluated in goal-directed therapy, and a comparative study with monitors proven to be effective in goal-directed therapy has not been encouraging (65). Therefore, NIRS cannot be recommended as a main monitor in goal-directed therapy.

The gastric tonometer is used for the evaluation of perfusion to the splanchnic bed. Reduced perfusion and resulting ischaemia are registered by changes in the pH of the gastric mucosa using a probe. A decreased pH of the gastric mucosa is associated with a poorer outcome (8). Gastric tonometry is a valuable tool in understanding detrimental circulatory changes, but its use in fluid therapy in a surgical setting has been questioned (66). It may be more rational to prevent hypovolaemia-induced gastric hypoperfusion, for example, with the use of SV maximization as demonstrated by Mythen and Webb (15), and gastric tonometry is unlikely to become the monitor of choice for goal-directed therapy.

Microdialysis and equilibrium dialysis can also be used to estimate regional tissue oxygenation. No outcome or comparative studies have been carried out in which these monitors have been used to guide fluid therapy. Although microdialysis and equilibrium dialysis are intriguing concepts, and are useful in the perception of pathophysiological mechanisms (67, 68), these monitors are unsuitable for clinical use as they require either subcutaneous placement of a cannula or placement of a probe in the rectal lumen. Moreover, the time required for the detection of deviations, as shown in CBV manipulation on a tilt table (69), limits the ability for immediate intervention. In summary, the dialysis techniques are not feasible for goal-directed therapy.

Other monitors
Thoracic impedance and trans-oesophageal echocardiography are other monitors used to estimate the pre-load to the heart. Although development in impedance technology is encouraging (70), no individualized goal-directed outcome studies are available. Trans-oesophageal echocardiography visualizes the real-time anatomy and physiology of the heart, which is useful in a variety of circumstances and notably for cardiac surgery. As SV can be estimated by echocardiography, both the fluid challenge and fluid responsiveness strategies can be applied. The visualized changes in pre-load detect even minor volume deficits (71). However, echocardiography requires expert personnel and training, and the calculations to derive SV, and thereby the variation in SV, are most often made off-line. Moreover, the inconvenience of the probe makes it unsuitable in the awake patient. Fluid therapy guided by echocardiography has not been evaluated in an outcome study.

Conclusion
Individualized goal-directed therapy in the perioperative period improves gut function and reduces PONV, morbidity and hospital stay. SV maximization with OD has been used most commonly to guide goal-directed therapy, but other less invasive and potentially more feasible modalities and strategies are available and require evaluation. Such studies should include the entire peri-operative period to reduce the risk of hypovolaemia and fluid excess. Future research on goal-directed therapy should be procedure specific, including its role in optimizing functional recovery in minor (ambulatory) surgery.

References
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