Conservative vs Restrictive Individualized Goal-Directed Fluid Replacement Strategy in Major Abdominal Surgery

A Prospective Randomized Trial

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Objectives: To compare the influence of 2 volumes of fluid, integrated with goal-directed fluid therapy, on hypovolemia (a key trigger of tissue hypoperfusion) and central venous oxygen saturation (ScvO₂) and to assess their relationships with postoperative morbidity.


Interventions: Patients were randomly assigned to 6 mL/kg/h of crystalloid (a restrictive fluid strategy) or 12 mL/kg/h of crystalloid (a more conservative fluid strategy). In both groups, a fluid bolus was administered when respiratory variation in peak aortic flow velocity (ΔPV) was greater than 13%. Data on hypovolemia (ΔPV ≥ 13%), ScvO₂, and postoperative complications were recorded for all patients.

Main Outcome Measures: Overall incidence of postoperative complications, especially anastomotic leak and sepsis.

Results: Overall incidence of complications, including postoperative anastomotic leak and sepsis, was higher in the restrictive group than in the conservative group (all P ≤ .05). The number of patients with hypovolemia increased significantly in the restrictive group compared with the conservative group (P < .001). The perioperative mean ScvO₂ (P = .02) and mean minimum ScvO₂ (P = .04) were significantly lower in the restrictive group than in the conservative group. Multivariate analysis showed that both hypovolemia and mean minimum ScvO₂ were independently associated with anastomotic leak and sepsis.

Conclusions: Excessive fluid restriction increased the level of hypovolemia, leading to reduced ScvO₂ and thereby increased incidence of postoperative complications. Excessive fluid restriction should be applied cautiously in surgical patients.

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Postoperative organ failure severely affects the prognosis of surgical patients. Adequate tissue perfusion is an essential component of oxygenation and can improve postoperative outcomes. Optimal perioperative fluid management continues to be highly challenging, especially in patients undergoing major abdominal surgery.

There are 2 main, partially overlapping strategies in perioperative fluid management: (1) fluid substitution using unmonitored fixed regimens and estimations of fluid losses (and suggesting high or low volumes of fluids) and (2) goal-directed fluid therapy (GDT) based on the maximization of flow-related parameters. Although perioperative fluid restriction has been found to reduce postoperative morbidity and to promote faster recovery compared with more liberal approaches, a recent animal study suggested that, compared with a restricted fluid strategy, goal-directed fluid optimization markedly increased tissue oxygen tension and microcirculatory perfusion in both healthy and perianastomotic tissues. To our knowledge, these strategies have not been compared in humans. Fluid overload may expose a patient’s tissue to edema, impairing oxygenation and predisposing to anastomotic breakdown. Conversely, excessive fluid restriction, especially using unmonitored and fixed volumes, may expose a patient’s tissue to hypovolemia and hypoperfusion, which are key triggers of organ dysfunction. Nevertheless, maintenance of the volume of intravascular fluid is essential to ensure adequate organ perfusion.
fusion. Surgical trauma is associated with endothelial damage arising from mechanical stress, endotoxin exposure, ischemia-reperfusion injury, or inflammation, all of which can lead to increased endothelial permeability and unpredictable extravascular fluid shifts.

Individualized GDT, especially esophageal Doppler-guided fluid optimization, has been shown to improve patient outcomes and to reduce in-hospital stays compared with conventional fluid replacement. With such an individualized approach, based on the maximization of flow-related parameters, hypovolemia and fluid overload could be prevented at least in theory because fluid administration is terminated when the applied parameter is maximized.

Recent data suggest that targeting indicators of early tissue hypoxia such as central venous oxygen saturation (ScvO₂), which reflects the oxygen delivery-consumption relationship, may be important in the management of surgical patients. However, the effects of different fluid strategies on perioperative ScvO₂ modifications remain unknown.

We therefore investigated the effects of restrictive and conservative approaches to fluid substitution, using an intraoperative GDT approach, on both hypovolemia and ScvO₂ modifications and assessed relationships between these parameters and postoperative complications in patients undergoing major abdominal surgery. We hypothesized that, compared with a higher-volume regimen, fluid restriction would increase the incidence of hypovolemia, leading to impaired tissue oxygenation and a higher rate of postoperative complications.

**METHODS**

**PATIENTS**

Patients with an American Society of Anesthesiology (ASA) score of 1 to 3 who presented for major abdominal surgery (with an expected duration of ≥60 minutes) were prospectively studied. All procedures were performed by senior surgeons and included colon and/or rectal resections, gastric resections, duodenopancreatectomy, and hepatectomy. Exclusion criteria included an age younger than 18 years, a body mass index (calculated as weight in kilograms divided by height in meters squared) greater than 35, pregnancy, chronic obstructive pulmonary disease with a forced expiratory volume in the first second of expiration of less than 50%, emergency surgery, coagulopathy, sepsis or systemic inflammatory response syndrome, significant hepatic failure (prothrombin ratio <30% and factor V level <30%) or renal failure (creatinine level >50% the upper limit of the normal value), and a contraindication for epidural analgesia.

**RANDOMIZATION AND INTERVENTION**

All consecutive patients were enrolled from May 1, 2008, to December 30, 2008. The study protocol was approved by our institutional review board, and all patients provided written informed consent.

Patients were randomly assigned to restrictive GDT (R-GDT) (ie, 6 mL/kg/h of crystalloid [lactated Ringer solution]) or conservative GDT (C-GDT) (ie, 12 mL/kg/h of crystalloid [lactated Ringer solution]) on the basis of a concealed allocation approach (computer-generated codes) using opaque sealed envelopes containing the randomization schedule. These envelopes were opened immediately before anesthesia induction. The therapies of R-GDT and C-GDT are recognized clinical practices for restricted and more conservative fluid administration, respectively. There were no restrictions on randomization. Study investigators, but not anesthesiologists, were blinded to treatment assignments. Preoperatively, no patients fasted or received bowel preparation. Fluid perfusion, maintained until resumption of normal food intake, consisted of 5% dextrose at 1 to 1.5 mL/kg/h as previously performed. Postoperative parenteral nutrition was administered in cases of preoperative denutrition. Anesthesia was induced using propofol (2 mg/kg), remifentanil hydrochloride (0.25 µg/kg/min), and cisatracurium besylate (0.15 µg/kg) and was maintained to a target bispectral index of 40 to 50 with a balanced technique involving desflurane, nitrous oxide and oxygen, and continuous infusion of remifentanil. Normothermia was maintained using a convective air warming system (WarmTouch; Tyco Healthcare, Pleasanton, California).

Patients were ventilated with a tidal volume of 8 mL/kg ideal body weight, a respiratory rate adjusted to maintain PaCO₂ of 35 to 40 mm Hg, an inspired oxygen fraction adjusted to maintain arterial oxygen saturation of 95% or more, and a positive end-expiratory pressure of 5 cm H₂O. Prophylactic antibiotics were administered as recommended. Before surgery, an epidural catheter was inserted for postoperative pain relief. About 30 minutes before the end of surgery, all patients were given continuous epidural analgesia with ropivacaine hydrochloride, 0.2%, and sufentanil citrate (0.25 mg/mL). Oral paracetamol (1 g every 6 hours) and ketoprofen (50 mg every 6 hours) were given after surgery. Antiemetic drugs (8 mg of dexamethasone sodium phosphate and 1 mg of droperidol) were administered if necessary. Oxygen was given, if required, to maintain an oxygen saturation greater than 95% as measured by pulse oximetry. Bladder catheters were removed after 24 hours, and epidural catheters after 48 hours. All patients were subjected to enforced mobilization and postoperative physiotherapy, in line with fast-track methods. In all patients, perioperative management was similar, except for intraoperative fluid administration.

**INTRAOPERATIVE GDT**

Preoperatively, all patients were equipped with central venous and arterial catheters. Standard monitoring included continuous recording of electrocardiographic data, heart rate, body temperature, pulse oximetry, end-tidal carbon dioxide level, urinary output, and arterial pressure. Immediately after anesthesia induction, an esophageal Doppler probe (HemoSonic 100; Arrow International, Everett, Massachusetts) was inserted and adjusted to obtain the highest Doppler velocity signal from the descending aorta. This monitoring device enabled continuous measurements of descending thoracic aortic blood velocity and aortic diameter. All anesthesiologists were trained in this technique and performed all measurements. In both groups, respiratory variations in peak aortic flow velocity (ΔPV) as previously described, were used to define hypovolemia, was corrected with a 250-mL colloid bolus (6% hydroxyethyl starch 130/0.4). The fluid challenge was repeated (≤50 mL/kg) if necessary until APV was corrected and there was no further increase in stroke volume. In other cases (ΔPV >13% and hemodynamic instability), a vasoreactive or inotropic support (norepinephrine bitartrate, epinephrine hydrochloride, or dobutamine hydrochloride) could be added. Colloids were preferred to crystalloids, in line with recent data. Blood was transfused when the hemoglobin level was less than 8 g/dL, or less than 10 g/dL in patients with a history of coronary artery disease (to convert hemoglobin to grams per liter, multiply by 10).0
OUTCOME MEASURES AND DATA COLLECTION

The primary outcome was the incidence of overall postoperative complications. Secondary end points included incidence of intraoperative hypovolemia, infused volumes of hydroxyethyl starch, and changes in the oxygen delivery index, ScvO₂, and lactate, albumin, C-reactive protein, procalcitonin, and creatinine levels.

Preoperative and postoperative data and data on postoperative complications were recorded by nonresearch staff (physicians not involved in the intraoperative management) blinded to the patient’s allocation group. Before surgery, data were recorded on sex, age, body mass index, ASA score, Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity, routine biological variables (including serum creatinine, lactate, C-reactive protein, procalcitonin, albumin, and prealbumin levels), and history of renal, cardiac, and respiratory dysfunction. During surgery, data were recorded on the infused volumes of crystalloids, hydroxyethyl starch, and blood products and on any need for vasoactive support. Arterial blood gas and ScvO₂ were measured by intermittent sampling and co-oximetry (IL Synthesis1720 Blood Gas Analyzer; Instrumentation Laboratory, Paris, France) before anesthesia induction and hourly until discharge from the postanesthesia care unit. During surgery, anesthesiologists were blinded to ScvO₂ and oxygen delivery index measurements. Venous lactate, hemoglobin, hematocrit, creatinine, C-reactive protein, procalcitonin, and albumin levels were measured at admission to the postanesthesia care unit and during the 48 hours following surgery.

Postoperative complications were assessed according to previously defined criteria. A wound infection was defined as pus expressed from the incision and a positive bacterial culture result. Anastomotic leak and intra-abdominal perianastomotic abscess were diagnosed by computed tomography. Reinterventions were systematically recorded. Diagnosis of urinary tract infection required a bacterial count of greater than 10⁵/mL and a positive culture result. Diagnosis of pneumonia required a new infiltrate seen on a chest radiograph and 2 of the following: fever, leukocytosis, or a positive sputum culture result. Diagnoses of sepsis, acute lung injury, or acute respiratory distress syndrome were based on international consensus guidelines. Data on cardiac failure (myocardial infarction, congestive heart failure, and arrhythmias), pulmonary embolism, pneumothorax, neurological complications (confusion and cerebrovascular accident), pulmonary embolism, and renal dysfunction (urine output <500 mL/d, an increase in the creatinine level of >30% from the preoperative level, or need for dialysis for acute renal failure) were also recorded. As was status (survived or died) at hospital discharge.

STATISTICAL ANALYSIS

To calculate sample size, we used available data from previous studies on postoperative complications. A 30% absolute reduction in overall postoperative complications was considered clinically relevant, requiring approximately 66 patients, with a type I error of .05 and a power of 80%. Results were expressed as means (SDs) in Tables 1, 2, 3, and 4. The χ² test was used to compare qualitative data. Qualitative and quantitative data were correlated using the t test or analysis of variance when normally distributed (and variances were equivalent) and the Mann-Whitney U test or the Kruskal-Wallis H test when not normally distributed. A multivariate analysis of variance was used to explore longitudinal data. Multiple logistic regression was used to identify independent risk factors for postoperative complications. The results of logistic regression are reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Receiver operator characteristic curves were constructed to identify optimal cutoff values for outcome associations. An optimal cutoff was defined as the value associated with the highest sum of sensitivity and specificity (the Youden index). Analysis was performed using SEM software version 2.0 (Centre Jean Perrin, Clermont-Ferrand, France), and P < .05 was considered statistically significant.

RESULTS

Eighty consecutive patients fulfilling the entry criteria were assessed for eligibility between May 1, 2008, and December 30, 2008. Ten patients were excluded, 6 of whom refused to participate and 4 whose duration of surgery was expected to be shorter than 1 hour. Complete follow-up

| Table 1. Characteristics of Patients Who Received Restrictive Goal-Directed Fluid Therapy and Patients Who Received Conservative Goal-Directed Therapy |
|-----------------|-----------------|-----------------|
| Characteristic   | R-GDT Group (n=36) | C-GDT Group (n=34) |
| Age, mean (SD), y | 61.9 (12) | 60.4 (14) |
| Sex, % | .58 | .98 |
| Male | 55 | 56 |
| Female | 45 | 44 |
| BMI, mean (SD) | 25.5 (5) | 24.3 (4) |
| P-POSSUM, mean (SD) | 34.3 (6) | 32.8 (6) |
| ASA score, % | .56 | .61 |
| 1 | 54 | 60 |
| 2 | 25 | 18 |
| 3 | 21 | 22 |
| Comorbidities, % of patients |
| Hypertension | 42 | 44 |
| Cardiac failure | 6 | 12 |
| Ischemic heart disease | 14 | 9 |
| Diabetes mellitus | 14 | 18 |
| Dyslipidemia | 17 | 18 |
| COPD | 19 | 9 |
| Chronic renal insufficiency | 22 | 12 |
| Neoplasia, % | 91 | 82 |
| Duration of surgery, mean (SD), min | 257 (66) | 224 (72) |
| Levels of preoperative biological analytes, mean (SD) |
| Hemoglobin, g/dL | 13 (2) | 13 (1) |
| Hematocrit, % | 38 (5) | 38 (6) |
| Albumin, g/dL | 3.6 (0.3) | 3.5 (0.4) |
| Prealbumin, mg/dL | 24 (6) | 24 (7) |
| Creatinine, mg/dL | 0.89 (0.32) | 0.89 (0.26) |
| Lactate, mg/dL | 10.8 (0.9) | 13.5 (4.5) |
| Procalcitonin, mg/dL | 0.06 (0.3) | 0.09 (0.13) |
| C-reactive protein, mg/L | 6.8 (16.9) | 9.9 (18.5) |

Abbreviations: ASA, American Society of Anesthesiology; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); C-GDT, conservative goal-directed fluid therapy; COPD, chronic obstructive pulmonary disease; P-POSSUM, Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity; R-GDT, restrictive goal-directed fluid therapy.

Statistical factors: To convert hemoglobin to grams per liter, multiply by 10; to convert hematocrit to proportion of 1.0, multiply by 10; to convert albumin to grams per liter, multiply by 10; to convert prealbumin to milligrams per liter, multiply by 10; to convert creatinine to micromoles per liter, multiply by 88.4; to convert lactate to millimoles per liter, multiply by 0.111; and to convert C-reactive protein to nanomoles per liter, multiply by 9.524.
The number of patients with complications was significantly greater in the R-GDT group compared with the C-GDT group (21 [58%] vs 9 [36%], respectively; P < .007). The R-GDT group as compared with the C-GDT group had significantly more incidences of anastomotic leak and/or perianastomotic abscess (12 [33%] vs 4 [12%], respectively; P = .03) and postoperative sepsis (16 [44%] vs 5 [15%], respectively; P = .007). The 2 groups did not differ, however, in rates of reintervention (P = .12), wound abscess (P = .14), pneumonia (P = .13), or urinary tract infection (P = .35) (Table 5). Postoperative parenteral nutrition was similar in the 2 groups (P = .93). Incidence of postoperative acute lung injury or acute respiratory distress syndrome was significantly higher in the R-GDT group than in the C-GDT group (6 [17%] vs 0, respectively; P = .04). Intraoperative hypovolemia was significantly associated with anastomotic leak and/or perianastomotic abscess (P = .04) and sepsis (P = .003). Despite the significant decrease in postoperative urine output observed in the R-GDT group (Table 2), the rate of renal dysfunction was similar in the 2 groups (P = .14) (Table 5).

MODIFICATIONS IN ScvO2 AND ASSOCIATION WITH ORGAN DYSFUNCTION

Despite comparable baseline values, at the end of surgery, the mean and mean minimum values of ScvO2 were significantly higher in the C-GDT group than in the R-GDT group (P = .03) (Table 3). The C-GDT group as compared with the R-GDT group had significantly higher perioperative mean (SD) ScvO2 (81.1% [4.2%] vs 78.9% P < .007). The R-GDT group as compared with the C-GDT group had significantly more incidences of anastomotic leak and/or perianastomotic abscess (12 [33%] vs 4 [12%], respectively; P = .03) and postoperative sepsis (16 [44%] vs 5 [15%], respectively; P = .007). The 2 groups did not differ, however, in rates of reintervention (P = .12), wound abscess (P = .14), pneumonia (P = .13), or urinary tract infection (P = .35) (Table 5). Postoperative parenteral nutrition was similar in the 2 groups (P = .93). Incidence of postoperative acute lung injury or acute respiratory distress syndrome was significantly higher in the R-GDT group than in the C-GDT group (6 [17%] vs 0, respectively; P = .04). Intraoperative hypovolemia was significantly associated with anastomotic leak and/or perianastomotic abscess (P = .04) and sepsis (P = .003). Despite the significant decrease in postoperative urine output observed in the R-GDT group (Table 2), the rate of renal dysfunction was similar in the 2 groups (P = .14) (Table 5).
Table 4. Postoperative Biological Data on Patients Who Received Restrictive Goal-Directed Fluid Therapy and Patients Who Received Conservative Goal-Directed Fluid Therapy

<table>
<thead>
<tr>
<th>Measure</th>
<th>R-GDT Group (n=36)</th>
<th>C-GDT Group (n=34)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At admission to PACU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>1.1 (0.2)</td>
<td>1.1 (0.2)</td>
<td>.53</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.85 (0.32)</td>
<td>0.72 (0.21)</td>
<td>.06</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>4.3 (3.2)</td>
<td>5.9 (11.3)</td>
<td>.16</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>32 (4)</td>
<td>32 (4)</td>
<td>.47</td>
</tr>
<tr>
<td>Lactate, mg/dL</td>
<td>24.3 (18.0)</td>
<td>21.6 (18.0)</td>
<td>.38</td>
</tr>
<tr>
<td>1 d after surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>1.1 (0.2)</td>
<td>1.0 (0.1)</td>
<td>.29</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>71 (34)</td>
<td>63 (23)</td>
<td>.12</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>2.7 (0.4)</td>
<td>2.6 (0.4)</td>
<td>.21</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>76 (41)</td>
<td>81 (43)</td>
<td>.62</td>
</tr>
<tr>
<td>Procalcitonin, mg/L</td>
<td>1.2 (2.5)</td>
<td>1.6 (3.2)</td>
<td>.92</td>
</tr>
<tr>
<td>Lactate, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 7 h</td>
<td>15.3 (5.4)</td>
<td>14.4 (6.3)</td>
<td>.87</td>
</tr>
<tr>
<td>At 18 h</td>
<td>14.4 (5.4)</td>
<td>13.5 (4.5)</td>
<td>.81</td>
</tr>
<tr>
<td>2 d after surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>1.0 (0.2)</td>
<td>1.0 (0.1)</td>
<td>.75</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.72 (0.32)</td>
<td>0.66 (0.24)</td>
<td>.21</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>2.6 (0.4)</td>
<td>2.5 (0.4)</td>
<td>.33</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>113 (63)</td>
<td>110 (70)</td>
<td>.73</td>
</tr>
<tr>
<td>Procalcitonin, mg/L</td>
<td>0.9 (1.8)</td>
<td>1.2 (2.2)</td>
<td>.90</td>
</tr>
<tr>
<td>Lactate, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 7 h</td>
<td>10.8 (3.6)</td>
<td>9.9 (4.5)</td>
<td>.10</td>
</tr>
<tr>
<td>At 18 h</td>
<td>10.8 (3.6)</td>
<td>12.6 (4.5)</td>
<td>.20</td>
</tr>
</tbody>
</table>

Abbreviations: C-GDT, conservative goal-directed fluid therapy; PACU, postanesthesia care unit; R-GDT, restrictive goal-directed fluid therapy.

SI conversion factors: To convert hemoglobin to grams per liter, multiply by 10; to convert creatinine to micromoles per liter, multiply by 88.4; to convert C-reactive protein to nanomoles per liter, multiply by 9.524; to convert lactate to millimoles per liter, multiply by 10; to convert creatinine to micromoles per liter, multiply by 88.4; to convert albumin to grams per liter, multiply by 0.111; to convert hematocrit to proportion of 1.0, multiply by 0.01; to convert lactate to millimoles per liter, multiply by 0.111; and to convert albumin to grams per liter, multiply by 10.

The main finding of this study is that intraoperative fluid restriction, even using a goal-directed fluid strategy, increases the incidence of hypovolemia and markedly impairs postoperative organ function after major abdominal surgery. Fluid restriction was associated with an increased incidence of postoperative complications such as an anastomotic leak and/or perianastomotic abscess (33%) and sepsis (44%).

In a recent animal study, Kimberger et al14 showed that intraoperative fluid restriction, as proposed for humans in a recent article,12 may be associated with altered tissue perfusion and microcirculation. To our knowledge, prior to our study, no report integrated GDT with existing knowledge on intraoperative fluid management.13 Although fluid restriction has been found to reduce the incidence of postoperative morbidity,9,11,12 optimal fluid substitution strategies remain controversial.13 Moreover, recent randomized trials did not confirm the supposed benefits of fluid restriction on recovery after elective surgery.7,8 In a recent experimental study, Marjanovic et al18 demonstrated the negative effect of fluid excess on the functional and structural stability of intestinal anastomoses. However, no significant differences were found between restrictive and conventional fluid administration in terms of the tissue wet-dry ratio and histological evaluation.16 We found that fluid restriction was associated with increased intraoperative hypovolemia. Although study designs and the fluid algo-

[4.1%], respectively; P = .02) and mean (SD) minimum ScvO2 (72% [6%] vs 69% [6%], respectively; P = .04). Postoperative mean minimum ScvO2 correlated with the mean minimum ScvO2 recorded during surgery (r = 0.43; P < .001). In patients with complications as compared with patients without complications, both the mean (SD) ScvO2 (80.8% [4.2%] vs 78.2% [3.9%], respectively; P = .02) and the mean (SD) minimum ScvO2 (72.4% [6.4%] vs 67.3% [6.4%], respectively; P = .002) were significantly reduced.

Univariate analysis identified 4 variables associated with anastomotic leak and/or perianastomotic abscess and sepsis: intraoperative hypovolemia (P = .004), group (P = .007), mean minimum ScvO2 (P = .003), and body mass index (P = .02). Multivariate analysis showed that intraoperative hypovolemia (OR, 1.33 [95% CI, 1.01-1.95]; P = .04) and a mean minimum ScvO2 less than 70% (OR, 4.2 [95% CI, 1.1-14.3]; P = .02) were independently associated with anastomotic leak and/or perianastomotic abscess. Hypovolemia (OR, 1.46 [95% CI, 1.12-2.20]; P = .005) and a mean minimum ScvO2 less than 70% (OR, 4.2 [95% CI, 1.2-12.5]; P = .02) were also independently associated with postoperative sepsis. The area under the receiver operating characteristic curve was 0.707 (95% CI, 0.551-0.863) for anastomotic leak and/or perianastomotic abscess and 0.731 (95% CI, 0.602-0.864) for sepsis. The optimal mean minimum ScvO2 was 67.6% (sensitivity, 75.9%; specificity, 66.7%) for discriminating between patients who did and patients who did not develop anastomotic leak and/or perianastomotic abscess and 70.6% (sensitivity, 72.9%; specificity, 71.4%) for discriminating between patients with and patients without sepsis.
rhythm were not comparable, the significant increase in additional fluid boluses in the fluid restriction group in the study by Nisanevich et al\textsuperscript{12} also suggested frequent episodes of intraoperative hypovolemia. The expected volume of fluid administered in the study by Nisanevich et al (4 mL/kg) was lower than the volume of fluid administered in our restrictive group. Surgical trauma is associated with an increase in endothelial permeability,\textsuperscript{51} leading to unpredictable extravascular fluid shifts, which cannot currently be monitored.\textsuperscript{7} In this context, it may be difficult to generalize unmonitored fluid restriction, as reported previously,\textsuperscript{9,11,12} to the general surgical population, especially to those undergoing major abdominal surgery.

Recent reports suggest that the timing of fluid challenge may be more important than the absolute quantities of fluid delivered.\textsuperscript{2,5,52} Several randomized trials showed improved patient outcome when esophageal Doppler-guided fluid optimization was performed.\textsuperscript{24,25,28,52,53} Esophageal Doppler monitoring has been demonstrated to be valuable for detecting hypovolemia and predicting volume responsiveness.\textsuperscript{41,42} We found that hypovolemia was an independent predictor of anastomotic leak and postoperative sepsis. Hypovolemia, which leads to poor organ perfusion, is thought to be a major determinant of organ dysfunction.\textsuperscript{28,50} Because of the high incidence of tissue hypoperfusion during major abdominal surgery,\textsuperscript{3,4} early detection and correction of occult hypovolemia are important and facilitate the use of early-warning tissue hypoperfusion signals.\textsuperscript{2}

Although our study was not designed to assess tissue perfusion, we hypothesized that postoperative complications might be related to hypovolemia-induced tissue hypoxia. A recent study found that fluid restriction was associated with decreased intestinal microcirculatory blood flow and tissue oxygen tension.\textsuperscript{14} We found that fluid restriction, even when using GDT to correct hypovolemia, was associated with reduced perioperative ScvO\textsubscript{2}. We also observed associations between reduced ScvO\textsubscript{2}, hypovolemia, and postoperative complications. Experimental studies have shown that changes in ScvO\textsubscript{2} closely reflect circulatory disturbances during periods of tissue hypoxia.\textsuperscript{55}

Our results confirm previous findings\textsuperscript{30,31} and suggest that reductions in ScvO\textsubscript{2} are associated with postoperative complications. In patients who developed complications, both the mean and mean minimum ScvO\textsubscript{2} were reduced, by 72.4% and 67.3%, respectively; these findings were in good agreement with previous results in surgical patients.\textsuperscript{30,31} By closely monitoring oxygen extraction calculated from ScvO\textsubscript{2}, Donati et al\textsuperscript{2} found that early correction of altered tissue oxygenation reduced postoperative morbidity.

The generalization of our findings may be restricted because our study had limitations. The number of included patients was relatively small. However, the strength of our study lies in the inclusion of all consecutive patients. Moreover, the sample size was sufficient to allow us to detect differences in postoperative outcomes. All patients were subjected to evidence-based postoperative practices. Nevertheless, some aspects of our patient-care algorithm that have not been uniformly adopted (such as the omission of mechanical bowel preparation and the use of relatively low volumes of fluid postoperatively) may have influenced our results. Our study included a variety of intra-abdominal procedures. Nevertheless, postoperative morbidity has been assumed to be directly related not to the type of surgical procedure but rather to a surgical stress response of combined metabolic and inflammatory origin.\textsuperscript{56} Our study was performed in a relatively homogeneous group of patients (mainly with ASA scores of 1 or 2). Nevertheless, our patients’ characteristics were not unusual for patients scheduled for abdominal surgery.\textsuperscript{29,27,28} Moreover, the Portsmouth Physiological and Operative Severity Scores for enUmeration of Morality and Morbidity were similar in both groups, indicating an even overall distribution of operative risk.\textsuperscript{37} Although not statistically different, there was a trend toward greater blood loss and higher operating time in the R-GDT group, and therefore these variables were considered in the multivariate analysis. These variables were not associated with an increased incidence of postoperative complications. Our study was not designed to assess differences in hospital lengths of stay. Although this is important and has economic implications, confounding factors may affect interpretation. The anesthesiologists who treated patients in the operating room were not blinded to patient group assignment. Nevertheless, our goal-directed fluid replacement strategy was standardized, and physicians who were unaware of patient group assignment recorded all postoperative organ failures.

### Table 5. Modified Postoperative Organ Dysfunction and Outcomes of Patients Who Received Restrictive Goal-Directed Fluid Therapy and Patients Who Received Conservative Goal-Directed Fluid Therapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>R-GDT Group (n=36)</th>
<th>C-GDT Group (n=34)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>12 (33)</td>
<td>4 (12)</td>
<td>.03</td>
</tr>
<tr>
<td>Anastomotic leak and/or perianastomotic abscess</td>
<td>4 (11)</td>
<td>0</td>
<td>.14</td>
</tr>
<tr>
<td>Wound abscess</td>
<td>7 (19)</td>
<td>3 (9)</td>
<td>.35</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>6 (17)</td>
<td>1 (3)</td>
<td>.13</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>16 (44)</td>
<td>5 (15)</td>
<td>.007</td>
</tr>
<tr>
<td>Sepsis and/or septic shock</td>
<td>8 (23)</td>
<td>3 (9)</td>
<td>.12</td>
</tr>
<tr>
<td>Reintervention</td>
<td>3 (9)</td>
<td>0</td>
<td>.26</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>5 (14)</td>
<td>0</td>
<td>.07</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>0</td>
<td>.50</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>3 (9)</td>
<td>0</td>
<td>.26</td>
</tr>
<tr>
<td>Postoperative hemorrhage</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>.50</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1 (3)</td>
<td>0</td>
<td>.26</td>
</tr>
<tr>
<td>Neurological event</td>
<td>5 (14)</td>
<td>0</td>
<td>.7</td>
</tr>
<tr>
<td>Postoperative confusion</td>
<td>5 (14)</td>
<td>0</td>
<td>.07</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>0</td>
<td>0</td>
<td>.50</td>
</tr>
<tr>
<td>Death</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>.50</td>
</tr>
<tr>
<td>Patients with complications</td>
<td>21 (58)</td>
<td>9 (36)</td>
<td>.007</td>
</tr>
<tr>
<td>&gt;1</td>
<td>15 (42)</td>
<td>5 (15)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; C-GDT, conservative goal-directed fluid therapy; NR, not rated; R-GDT, restrictive goal-directed fluid therapy.

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In conclusion, although we used GDT, we found that intraoperative fluid restriction increased the incidence of hypovolemia (leading to reduced $\text{ScvO}_2$) and increased the incidence of postoperative complications. Early detection and correction of potential tissue hypoxia triggers such as hypovolemia are fundamentally important. Although individualized fluid substitution and fluid challenge timing may be more important than the absolute quantities of fluid delivered, excessively restrictive strategies, particularly if unmonitored fixed regimens are used, should be applied cautiously to surgical patients.

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