Effect of Intraoperative Fluid Management on Outcome after Intraabdominal Surgery

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Background: The debate over the correct perioperative fluid management is unresolved.

Methods: The impact of two intraoperative fluid regimes on postoperative outcome was prospectively evaluated in 152 patients with an American Society of Anesthesiologists physical status of I–III who were undergoing elective intraabdominal surgery. Patients were randomly assigned to receive intraoperatively either liberal (liberal protocol group [LPG], n = 75; bolus of 10 ml/kg followed by 12 ml · kg^{-1} · h^{-1}) or restrictive (restrictive protocol group [RPG], n = 77; 4 ml · kg^{-1} · h^{-1}) amounts of lactated Ringer's solution. The primary endpoint was the number of patients who died or experienced complications. The secondary endpoints included time to initial passage of flatus and feces, duration of hospital stay, and changes in body weight, hematocrit, and albumin serum concentration in the first 3 postoperative days.

Results: The number of patients with complications was lower in the RPG ($P = 0.046$). Patients in the LPG passed flatus and feces significantly later (flatus, median [range]: 4 [3–7] days in the LPG *vs.* 3 [2–7] days in the RPG; $P < 0.001$; feces: 6 [4–9] days in the LPG *vs.* 4 [3–9] days in the RPG; $P < 0.001$), and their postoperative hospital stay was significantly longer (9 [7–24] days in the LPG *vs.* 8 [6–21] days in the RPG; $P = 0.01$). Significantly larger increases in body weight were observed in the LPG compared with the RPG ($P < 0.01$). In the first 3 postoperative days, hematocrit and albumin concentrations were significantly higher in the RPG compared with the LPG.

Conclusions: In patients undergoing elective intraabdominal surgery, intraoperative use of restrictive fluid management may be advantageous because it reduces postoperative morbidity and shortens hospital stay.

PERIOPERATIVE fluid management continues to be a daily challenge in anesthesia practice. Abdominal surgical procedures in particular are associated with dehydration from preoperative fasting, bowel preparation, underlying illness, and intraoperative and postoperative fluid and electrolyte loss.[1] The exact quantity of this fluid loss is difficult to ascertain, and estimates for replacement with balanced salt solutions range from 0 to 67 ml · kg^{-1} · h^{-1} of surgery.[2]

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The widespread use of "dry" fluid regimen in pulmonary surgery with resulting decrease in pulmonary morbidity supports the safety of this regimen in high-risk patients undergoing major surgical procedures.[1,3,4] Nevertheless, no widely accepted recommendations are currently available for the optimal perioperative fluid regimen to be used in nonthoracic surgery. According to textbook recommendations, intraoperative fluid administration in patients undergoing intraabdominal procedures should be in the range of 10–15 ml · kg^{-1} · h^{-1}.[5–7] This regimen, however, is not evidence based. Recent studies that investigated the effects of different amounts of perioperative fluids on outcome reported conflicting results depending on the patient population, the type of surgery, and the regimen. Holte *et al.*[8] tried to mimic the perioperative course of minor to moderately sized surgery in healthy volunteers and found that infusion of 40 ml/kg lactated Ringer's (RL) solution over 3 h caused significant increases in body weight and reductions in pulmonary function compared with infusions of 5 ml/kg. In a subsequent study,[9] the same investigators reported that the intraoperative administration of 40 ml/kg rather than 15 ml/kg RL solution to patients with an American Society of Anesthesiologists (ASA) physical status of I or II who were undergoing laparoscopic cholecystectomy led to improved pulmonary function, exercise capacity, and general well-being and shortened hospital stay. The benefit of administering a "high" volume of fluids (20 ml/kg) has also been demonstrated in patients undergoing general anesthesia for short ambulatory procedures.[10] Recently, the effect of different fluid regimens on outcome was evaluated in patients undergoing more extensive operations. Two studies in patients undergoing colectomy[11,12] or colorectal resection[12] found that restricted postoperative[11] and perioperative[12] fluid administration resulted in reduced hospital stays, faster return of gastrointestinal function,[11] and reduced postoperative complications.[12] The objective of the current study was to evaluate whether the postulated benefits of fluid restriction can be demonstrated in a more diverse population of surgical patients, *i.e.*, patients with an ASA physical status of I–III who are undergoing a variety of extensive intraabdominal surgery. Because the use of liberal fluid regimens has, as reported before,[1] deleterious effects on recovery of gastrointestinal motility, wound/anastomotic healing, coagulation, and cardiac and pulmonary function, we tested the hypothesis that restrictive fluid administration for patients undergoing intraabdominal surgery is associated with a lower incidence of adverse outcomes.

Materials and Methods

Patients

After institutional review board (Hadassah University Medical Center, Jerusalem, Israel) approval and written, informed patient consent, 156 adult patients with an ASA physical status of I–III who were presenting for major elective intraabdominal surgery were prospectively studied. Surgical procedures included all types of colon/rectum procedures, small bowel resections, gastric resections, and pancreaticoduodenectomy/partial pancreas resections. Patients undergoing hepatectomy were not included in the study because relative fluid restriction and low central venous pressures during certain stages of the operation have been shown to be beneficial.[13,14] Also excluded from the study were patients aged younger than 18 yr; pregnant patients; and those with coagulopathy, significant hepatic (liver enzymes > 50% upper limit of normal value) or renal (creatinine > 50% upper limit of normal value) dysfunction, and congestive heart failure.

Intraoperative Management

Patients were randomized into one of two groups, a liberal protocol group (LPG) or a restricted protocol group (RPG), by using a random number generator in sealed envelopes. Study investigators and research personnel were not directly involved in the care of these patients and hence were blinded to the treatment assignments. Diuretics were discontinued the day before surgery. All patients received identical bowel preparation, which consisted of 3 l Precolonoscopic Solution (polyethylene glycol). One liter of 5% dextrose–0.45% NaCl was administered during the night intravenously. All patients fasted after midnight and received 10 mg diazepam orally as premedication 1 h before surgery. Anesthesia was induced using thiopental (4–5 mg/kg), fentanyl (2 μg/kg), and vecuronium (0.1 mg/kg) and was maintained with a balanced technique involving isoflurane, nitrous oxide, and oxygen. Neuromuscular blockade was performed with intravenous vecuronium. Additional doses of 1.5 μg/kg intravenous fentanyl were given when the mean arterial blood pressure or heart rate increased 25% above baseline value. Ventilation was adjusted to maintain an arterial carbon dioxide tension of 35–40 mmHg, and temperature was maintained at greater than 35.5°C throughout surgery. Patients received epidural analgesia for postoperative pain relief. No drugs (local anesthetic or narcotic) were administered *via* the epidural catheter during surgery. Postoperatively, all patients received continuous epidural administration of bupivacaine (0.5%) and methadone (0.2%) (9 ml bupivacaine and 7 ml methadone at a rate of 60–80 mm/24 h) until postoperative day 3. Thereafter, patients' pain treatment consisted of nonsteroidal anti-inflammatory drugs.
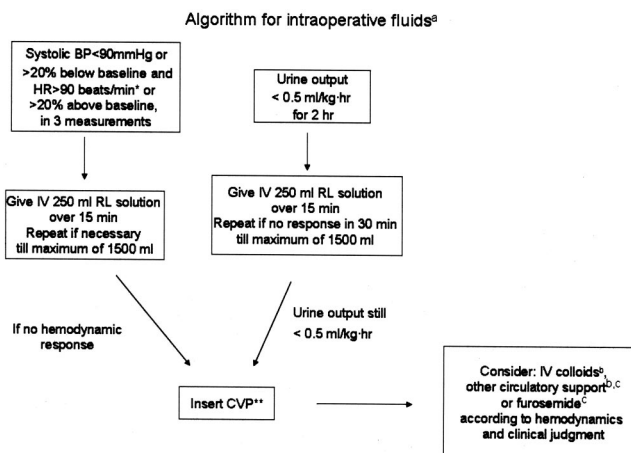

Algorithm for intraoperative fluids[a]

Fig. 1. Algorithm for intraoperative fluid administration. [a] Indications for blood transfusion were acute massive hemorrhage, when the hematocrit was less than 24% in patients with no history of coronary artery disease or no evidence of myocardial ischemia, when the hematocrit was less than 30% in patients with a history of coronary artery disease or evidence of myocardial ischemia, and when the hematocrit was less than 30% and greater than 24% but with ongoing bleeding. [b] Central venous pressure (CVP) less than 15 mmHg. [c] CVP greater than 15 mmHg. [*] Fluid bolus may also be administered in patients with systolic blood pressure (BP) less than 90 mmHg and heart rate (HR) less than 90 beats/min when the patient's HR cannot be increased (β-blocker treatments, pacemaker). [**] CVP may be introduced earlier; however, bolus administration of fluid before this stage should be based on hemodynamic parameters and urine output. IV = intravenous; RL = lactated Ringer's solution.

Patients in the RPG received 4 ml · kg^{-1} · h^{-1} RL solution throughout the intraoperative period, whereas patients in the LPG received an initial bolus of 10 ml/kg RL solution before skin incision followed by 12 ml · kg^{-1} · h^{-1}. No additional boluses of fluid were administered before skin incision, and all hemodynamic changes during this period were treated pharmacologically. Intraoperative treatment of tachycardia (heart rate > 90 beats/min or > 20% above baseline) accompanied by low blood pressure (< 90 mmHg or > 20% below baseline) was guided by a fluid algorithm (fig. 1). Fluid boluses (250 ml RL solution) were also provided if urine output decreased below 0.5 ml · kg^{-1} · h^{-1} for 2 h. Patients were reassessed after each fluid challenge to determine whether the target hemodynamic/urine output goals were achieved. If hemodynamics or urine output were not improved with the first bolus of fluid, additional boluses of RL solution were administered in accordance with the fluid algorithm to a maximum of 1,500 ml. A central venous catheter was introduced thereafter if no response was observed in urine output or hemodynamics. In a hemodynamically unstable patient, a central venous pressure of less than 15 mmHg could trigger one of two treatment options: intravenous administration of colloid (6% hydroxyethyl starch) or pharmacologic circulatory support. A central venous pressure of greater than 15 mmHg could trigger the intravenous administration of furosemide or pharmacologic circula-

tory support, depending on the patient's hemodynamics. Further insertion of a pulmonary artery catheterization was left to the discretion of the attending anesthesiologist. The fluid regimen was continued until admission to the recovery room, where departmental routines ensued. For management of surgical hemorrhage, in both groups, lost blood was replaced with RL solution in a 3:1 volume replacement. Blood was transfused during acute massive hemorrhage, when the hematocrit was less than 24% in patients with no history of coronary artery disease or no evidence of myocardial ischemia, when the hematocrit was less than 30% in patients with a history of coronary artery disease or evidence of myocardial ischemia, and when the hematocrit was less than 30% and greater than 24% but with ongoing bleeding. To ensure uniformity, transfusion guidelines were also established for administration of fresh frozen plasma (prothrombin time, activated partial thromboplastin time $>$ 1.5 times normal), cryoprecipitate (fibrinogen concentrations < 100 mg/dl), and platelets ($< 50 \times 10^3$/mm^3) in the presence of continuous uncontrolled bleeding with no evidence of clot formation.[15] Blood loss (estimated by assessment of the suction bottles, sponges, and the surgical drapes and gowns), urine output, and doses of drugs (fentanyl, furosemide) given during the surgical procedure or the need to start vasoactive infusion were recorded.

Postoperative Management and Monitoring

In the postoperative period, the surgical staff, who were unaware of the patient's group assignment and were not part of the investigator team, guided fluid therapy. The routine in our General Surgery department is not to feed patients during the early postoperative period. The volumes of crystalloids administered in the first 3 postoperative days were recorded. The "standard" fluid treatment of the surgical department consists of 5% dextrose–0.45% NaCl at 1–1.5 ml · kg^{-1} · h^{-1}. In addition, the number of units of blood and blood products administered until hospital discharge was also recorded. Postoperative follow-up included measurements of body weight (with standardized hospital uniforms), oxygen saturation, hematocrit, potassium, sodium, albumin, and creatinine concentrations in the first 3 postoperative days and before discharge. All measurements were made in the morning (between 8:00 AM and 10:00 AM). Additional blood tests, electrocardiography, and measurements of cardiac enzymes were performed when clinically indicated. Time to first passage of flatus and feces was also recorded. Postoperatively, all patients were examined and interviewed daily. Complications that were detected by the examining physician were validated by two investigators who were not aware of the patient's group assignment. Postoperative day 1 was defined as starting from patient admittance to the recovery room and ending 24 h later than postoperative day 2 would start.

Endpoints

The primary endpoint of the study combined the number of patients who died or experienced complications. The secondary endpoints included time to initial passage of flatus and feces; duration of hospital stay; differences in body weight, hematocrit, creatinine, and albumin serum concentrations in the first 3 postoperative days; changes in oxygen saturation in the first 3 postoperative days; and number of patients receiving transfusion of blood and blood products.

Definition of Complications

Wounds were considered infected when pus could be expressed from the incision or aspirated from a loculated mass within the wound and when bacteria were cultured from the pus. Wound dehiscence was diagnosed clinically and was treated by secondary suturing. Peritonitis, gastrointestinal bleeding, anastomotic leak, and intestinal obstruction would not be considered complications unless they necessitated surgery. Intraabdominal abscess required diagnosis by an ultrasound or computerized tomography scan. Diagnosis of pneumonia required new infiltrate on chest x-ray combined with two of the following: temperature greater than 38°C, leukocytosis, and positive sputum culture. Urinary tract infection was diagnosed when symptoms consistent with the diagnosis, such as dysuria, frequency, fever, or an increased peripheral leukocyte count, prompted urinary analysis that showed bacterial counts greater than 100,000 and positive culture. Diagnosis of sepsis required bacterial infection and at least two of the following clinical signs: abnormalities of body temperature (hypothermia or hyperthermia), heart rate (tachycardia), respiratory rate (tachypnea), and leukocyte count (leukocytopenia or leukocytosis). Diagnosis of myocardial infarction required an increase of the creatine kinase MB isoenzyme or troponin T concentration above the hospital laboratory's myocardial infarction threshold and either new Q waves (duration ≥ 0.03 s) or persistent changes (4 days) in ST-T segment. Congestive heart failure and pulmonary edema were defined by clinical (shortness of breath, rales, jugular venous distention, peripheral edema, third heart sound) and radiologic (cardiomegaly, interstitial edema, alveolar edema) signs that required a change in medication involving at least treatment with diuretic drugs. Arrhythmias required 12-lead electrocardiographic confirmation. Cerebrovascular accident was diagnosed when a new focal neurologic deficit of presumed vascular etiology persisted more than 24 h with a neurologic imaging study that did not indicate a different etiology. A diagnosis of acute respiratory distress syndrome was established when there was an acute onset of respiratory distress, evidence on chest

radiographs of airspace changes in all four quadrants, a ratio of partial pressure of oxygen to inspired fraction of oxygen of less than 200, and pulmonary artery wedge pressure less than 18 mmHg or no clinical evidence of left atrial hypertension. Pulmonary embolism was diagnosed only after evidenced by spiral computerized tomography scanning. Renal dysfunction was defined by creatinine greater than 50% upper limit of normal value.

Statistical Analysis

Categorical data were analyzed using the chi-square test or Fisher exact test. Differences between the means of the two groups and the median units of blood transfused were compared using the Student t test and the Mann–Whitney test, respectively. Data within each group were analyzed using analysis of variance for repeated measurements. When appropriate, *post hoc* analyses were performed with the Newman-Keuls test. Exact confidence intervals were computed for the overall rate of complications. Analysis was performed using Statistical Analysis System software (version 6.12; SAS Institute, Cary, NC). $P < 0.05$ was considered to represent statistical significance. Results are expressed as mean $\pm$ SD. Analysis was by intention to treat. A power analysis for postoperative complication rate as an outcome, with 80% power to detect a 20% reduction in this outcome and significance of 0.05 or greater, indicated that 75 patients were required in each group.

Results

Demographic and Surgical Data

A total of 156 patients who fulfilled the entry criteria were enrolled in the study, 78 in each group; among them, 4 (3 from the LPG) were excluded because surgery was not extensive. Demographic and surgical data are listed in tables 1 and 2. Randomization was successful in achieving comparable groups for all characteristics listed, including sex, age, weight, height, ASA physical status, and percentage of patients with concomitant diseases. The same was true for the type and duration of surgery and estimated blood loss. Significantly more patients in the RPG received, in accordance with the fluid algorithm (fig. 1), fluid boluses. Despite the administration of fluid boluses in a third of the patients in the RPG, the intraoperative volumes of fluid administered were significantly lower in the RPG compared with the LPG. Also, in the first 3 postoperative days, the mean amounts of fluid infused were similar among the groups (table 3). Compared with the LPG, significantly more patients in the RPG experienced episodes of hypotension. Hypotension that required the administration of a fluid bolus occurred in 21 patients, 1 from the LPG (1 episode of hypotension) compared with 20 from the RPG (who experienced a total of 36 episodes of hypotension). A

Table 1. Patient Characteristics

	Liberal Protocol Group (n = 75)	Restrictive Protocol Group (n = 77)
Sex, M/F	40/35	38/39
Age, yr	59.4 ± 12.1	62.8 ± 13.4
Weight, kg	68.2 ± 13.5	71.5 ± 14.6
Height, cm	164 ± 8	166 ± 7
ASA physical status, I/II/III	19/37/19	15/42/20
Ischemic heart disease	14 (19%)	16 (21%)
Hypertension	24 (32%)	29 (38%)
Cholesterol ≥ 240 mg/dl	11 (15%)	7 (9%)
Diabetes mellitus*	10 (13%)	13 (17%)
Smoking	18 (24%)	15 (19%)
Pulmonary disease	4 (5%)	5 (6%)
Cardiac medications		
β-Adrenergic blockers	18 (24%)	22 (29%)
Calcium channel blockers	1 (1%)	3 (4%)
Diuretics	7 (9%)	5 (6%)
Nitrates	11 (15%)	15 (19%)
ACE inhibitors	15 (20%)	13 (17%)

Values are presented as mean ± SD. There were no significant differences between the groups.

* All patients had type II diabetes mellitus.

ASA = American Society of Anesthesiologists; ACE = angiotensin-converting enzyme.

subgroup of patients who received daily cardiac medication was evaluated separately for parameters that could reflect hemodynamic instability. There was no significant difference between patients receiving cardiac medications in the LPG *versus* the RPG in the need for pharmacologic support after induction of anesthesia and before skin incision. In this subgroup of patients, significantly more patients in the RPG compared with the LPG needed intraoperative bolus fluid administration: 11 *versus* 0, respectively.

Endpoints

None of the patients died during the perioperative period. The number of patients with complications was smaller in the RPG compared with the LPG ($P = 0.046$; table 4). Significantly greater increases in body weight were observed in patients in the LPG compared with patients in the RPG in the early postoperative period (1.93 ± 0.52 and 1.85 ± 0.62 kg on the first and third postoperative days, respectively, in the LPG *vs.* 0.51 ± 0.67 and 0.24 ± 0.61 kg in the RPG; $P < 0.01$). Patients in the LPG passed flatus and feces significantly later than RPG patients (flatus, median [range]: 4 [3–7] days in the LPG *vs.* 3 [2–7] days in the RPG; $P < 0.001$; feces: 6 [4–9] days in the LPG *vs.* 4 [3–9] days in the RPG; $P < 0.001$). The duration of hospital stay was 9 days (7–24) in the LPG compared with 8 days (6–21) in the RPG ($P = 0.01$). There were no significant differences between the groups in the number of patients receiving blood or blood product transfusion or in the median number of units of blood transfused.

Table 2. Surgical Data

	Liberal Protocol Group (n = 75)	Restrictive Protocol Group (n = 77)
Type of surgery, %		
Colon resection	30 (40)	26 (34)
Resections including the rectum	22 (29)	25 (32)
Small bowel resection	2 (3)	0
Gastric resection	8 (11)	10 (13)
Pancreaticoduodenectomy	12 (16)	14 (18)
Pancreas resection	1 (1.3)	2 (3)
Duration of surgery, min, mean ± SD	251 ± 91	268 ± 112
Total volume of fluid administered, ml, median (range)	3,670 (1,880–8,800)	1,230 (490–7,810)*
Estimated blood loss, ml, median (range)	440 (50–1,800)	400 (50–2,100)
Patients receiving bolus of fluids (as indicated by fluid algorithm),	1 (1.3)	26 (33)*
Number of patients receiving 6% hydroxyethyl starch	0	3
Patients receiving blood transfusion, %	19 (25)	12 (15.5)
Patients receiving blood products, %	3 (4)	2 (3)
Number of units of blood transfused, median (range)	0 (0–3)	0 (0–4)
Dose of fentanyl administered, g, mean ± SD	345 ± 135	368 ± 124
Patients receiving furosemide	0	2
Patients receiving vasoactive infusion	0	0

* $P < 0.001$.

Preoperative hematocrit, creatinine, albumin, and arterial oxygen saturation were similar in both groups. In the immediate postoperative period (first 3 postoperative days), hematocrit and serum albumin concentration were significantly higher in the RPG compared with the LPG; however, at discharge there were no significant differences between the groups (fig. 2). Mean creatinine serum concentrations were within the normal range and were not significantly different between the groups at all

Table 3. Total Volume of Fluid Administered

	Liberal Protocol Group (n = 75)	Restrictive Protocol Group (n = 77)
Intraoperative	3,878 ± 1,170	1,408 ± 946*
Postoperative day 1†	2,012 ± 475	2,170 ± 476
Postoperative day 2	1,985 ± 534	2,052 ± 492
Postoperative day 3	1,870 ± 475	1,955 ± 542

Values are presented as mean ± SD (ml).

* $P < 0.001$.   † Postoperative day 1: starting from patient admittance to the recovery room and ending 24 h later than postoperative day 2 would start.

Table 4. Perioperative Complications

Complications	Liberal Protocol Group (n = 75)	Restrictive Protocol Group (n = 77)
Infectious		
Wound dehiscence/infection	11	7
Peritonitis/anastomotic leak/ intraabdominal abscess	3	2
Pneumonia	5	3
Urinary tract infection	2	3
Sepsis	1	0
Cardiovascular		
Myocardial infarction	1	1
Congestive heart failure/pulmonary edema	2	0
Arrhythmias (need to start new treatment)	3	1
Cerebrovascular accident	0	0
Gastrointestinal		
Bleeding	0	0
Bowel obstruction	2	0
Pulmonary		
Acute respiratory distress syndrome	2	0
Pulmonary emboli	0	0
Renal		
Renal dysfunction	0	0
Death	0	0
Total number of complications	32	17
Total number of patients with complications	23	13*

* $P < 0.05$ vs. liberal protocol group.

times. Postoperative oxygen saturation decreased significantly in the first 3 postoperative days in both groups; however, values were not different between groups. Baseline and postoperative values for sodium and potassium were comparable among the groups (data not shown). Hemodynamic data at baseline, before skin incision, at skin closure, and 8 and 24 h after the operation were not significantly different between the groups (table 5).

Discussion

The major finding of the current study is that relative intraoperative fluid restriction in patients with an ASA physical status of I–III who are undergoing major intraabdominal surgery reduces the number of patients who experience complications and shortens the time to recovery of gastrointestinal function and to hospital discharge. Our study extends previous work of Lobo *et al.* and Brandstrup *et al.*, who demonstrated the efficacy of using postoperative[9] and perioperative[12] fluid restriction in patients undergoing intraabdominal operations. In contrast to our study, however, these studies were performed in relatively homogenous groups of healthy patients (mainly with an ASA physical status of I or II) undergoing either colectomy or colorectal resection, whereas the current study included patients undergoing
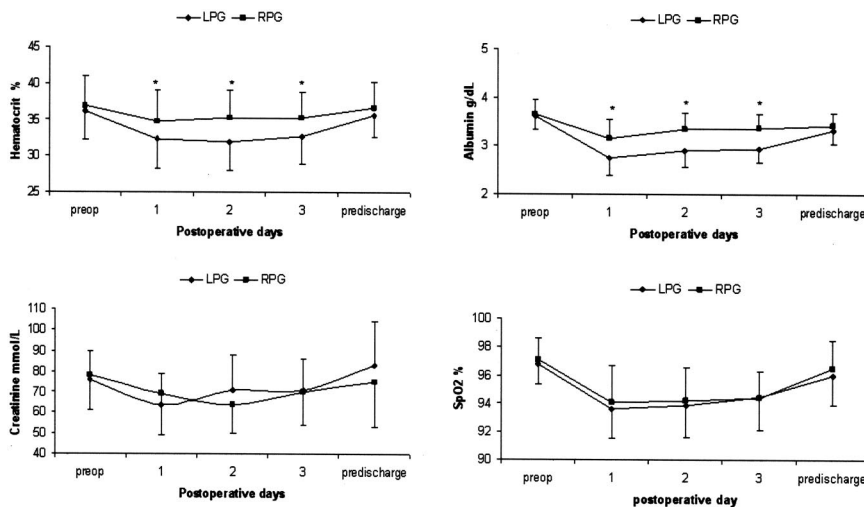
Fig. 2. Hematocrit, serum concentrations of creatinine and albumin, and oxygen saturation in the preoperative period (preop = day before surgery); postoperative days 1, 2, and 3; and the day of hospital discharge. Values are presented as mean ± SD. * *P* < 0.01 compared with liberal protocol group (LPG). RPG = restrictive protocol group.

a variety of major intraabdominal surgeries, a quarter of whom had an ASA physical status of III. In addition, unlike the study by Brandstrup *et al.*,[12] in which oral intake was started on the first postoperative day, in the current study, patients were treated in the first few postoperative days with intravenous fluid only, as in the study by Lobo *et al.*[11] Other major differences between the study of Brandstrup *et al.*[12] and the current study include the higher percentage of alcohol consumers (approximately two third of patients *vs.* none in our study) and the use of a different type of fluids, mostly normal saline in the standard group, as well as 5% glucose, all of which could have affected outcome.[9,16] In the current study, RL and 5% dextrose–0.45% NaCl were used.

Fluid Regimen

The volumes of intraoperative and postoperative fluid administered in the LPG seem high. However, these

volumes are consistent with previous studies, recommendations, and hospital routines described in previous articles. In a recent study[8] designed to mimic minor to moderate operations, healthy volunteers in the "liberal group" received 40 ml/kg lactated Ringer's solution over 3 h (*i.e.*, approximately 13 ml · kg^{-1} · h^{-1}). In laparoscopic cholecystectomy,[9] patients received either 40 or 15 ml/kg lactated Ringer's solution infused over 1.5 h (*i.e.*, 26.7 *vs.* 10 ml · kg^{-1} · h^{-1}). In yet another study[8] of ambulatory surgery lasting approximately 30 min, patients received preoperatively either 20- or 2-ml/kg infusions of isotonic solution. According to textbook recommendations, intraoperative fluid administration in patients undergoing intraabdominal procedures should range from 10 to 15 ml · kg^{-1} · h^{-1}.[5–7] In this patient population, Jenkins *et al.*[17] suggested that the fluid regimen should consist of 12–15 ml/kg for the first hour and 6–10 ml/kg for the next 2 h. Similarly, Campbell *et al.*[18] observed that cardiovascular stability during major operations is much better preserved when intraoperative crystalloids are given at the rate of 10–15 ml · kg^{-1} · h^{-1}. The amount of intraoperative fluid used in the LPG in the current study is therefore consistent with these recommendations. Two recent prospective studies used different fluid regimens in patients undergoing colectomy. In one study in which surgery lasted less than 2 h and involved minimal bleeding,[11] the authors compared postoperative administration of 3 l fluid/day (liberal group) with 1.5–2 l/day. Intraoperatively, all patients received 2.5–2.8 l fluid. In the second study,[12] the median amounts of fluid administered on the day of surgery were 2,740 and 5,388 ml in the restrictive and standard groups, respectively. Postoperatively, the total amount of fluid administered (intravenous plus oral) was in the range of 2.5 l (restrictive group) *versus* 3.5 l. In the current study, the volume of fluid administered in the postoperative period in both groups (1.5–2.5 l) was similar to the restrictive groups in both previous studies.[11,12]

Table 5. Hemodynamic Measurements and Oxygen Saturation in the Two Groups

	Mean Arterial Blood Pressure, mmHg	Heart Rate, beats/min	Oxygen Saturation, %
LPG baseline*	76 ± 14	75 ± 10	98.1 ± 1.5
RPG baseline*	73 ± 11	71 ± 14	98.0 ± 1.4
LPG before skin incision	75 ± 12	68 ± 12	98.2 ± 0.8
RPG before skin incision	68 ± 10	73 ± 11	98.3 ± 0.9
LPG before skin closure	81 ± 14	79 ± 13	97.7 ± 1.0
RPG before skin closure	80 ± 12	83 ± 14	97.5 ± 1.6
LPG 8 h after surgery	86 ± 17	82 ± 12	97 ± 1.5
RPG 8 h after surgery	82 ± 15	87 ± 11	97.2 ± 1.6
LPG 24 h after surgery	73 ± 16	78 ± 13	97.3 ± 1.2
RPG 24 h after surgery	75 ± 12	83 ± 12	97.0 ± 1.6

Values are presented as mean ± SD. No significant differences were noted between the groups at the specified time points.

* Baseline (before induction of anesthesia).

LPG = liberal protocol group; RPG = restrictive protocol group.

Effect on Outcome

Studies in minor/ambulatory surgery suggest that high-dose fluid regimens may improve early recovery measures such as dizziness, drowsiness,[9,19] nausea, and thirst; improve pulmonary function and exercise capacity; and shorten hospital stay.[9] The results of these studies, however, cannot be extrapolated to major intraabdominal surgical procedures in which substantially larger third space loss, larger stress response, and altered capillary permeability occur. The decreases in hemoglobin and albumin concentrations that were observed only in patients from the LPG in the current study are in accord with previous studies[11,12] and probably reflect the dilutional effect of the larger fluid volumes. Also, the increase in body weight is most probably the result of fluid overload as changes in weight have been shown to reflect fluid balance.[20,21] The current study also found that the median time to flatus and feces passage was significantly longer in the LPG compared with the RPG. Positive postoperative fluid balance can result in gut edema, which may contribute to intestinal dysfunction.[1,22] In the 1930s, Mecray et al.[23] found that modest positive salt and water balance caused weight gain after elective colectomy and was associated with delayed recovery of gastrointestinal function, increased complication rates, and extended hospital stays. Similar findings were demonstrated later in human studies.[11,24–26] Hypoproteinemia has been associated with extended gastric emptying, delayed small bowel transit, and postoperative ileus.[11,23–26] Whether the effect is due to hypoalbuminemia per se or the result of positive fluid balance is unknown because it is difficult to separate these two conditions.[20] Others have challenged these findings and reported that increased perioperative fluid administration was associated with improved indices of gut perfusion and reduced intestinal dysfunction.[27,28] These studies, however, were unblinded and involved a different patient population (cardiac[28] and mostly urologic and gynecologic patients[27]). In the study by Gan et al.,[27] both groups received "liberal" fluid administration (approximately 4.5 l clear crystalloids for surgeries with a mean duration of 4 h), with no significant difference in the amount of crystalloids administered between the groups. Moreover, in both studies, the differences in outcome could have been attributed to the type of fluid, because patients in the protocol group received more colloids. The finding that more patients in the high-volume group had complications is consistent with previous reports in similar patient populations.[12] Larger fluid volumes may exert harmful effects on cardiac and pulmonary function, tissue oxygenation, coagulation, wound healing, and gastrointestinal function.[1] The exact mechanism by which liberal intraoperative fluid administration increases morbidity was not evaluated in this study, but possible mechanisms have been recently reviewed.[1]

There are several limitations to this study. The possibility that the observed differences were due to factors other than the amount of resuscitation fluid cannot be excluded. However, this is a prospective study with an intent-to-treat design and with well-defined endpoints. In addition, the study was not conducted in a totally blinded fashion. Although the anesthesiologist treating the patient in the intraoperative period was not blinded to the patient's group assignment, the indications for additional fluid administration were standardized. During the postoperative period, adverse outcomes were detected by the examining physician, who was not aware of the patient's assignment. Late complications could have been missed because we followed patients only until hospital discharge. In addition, the design of this study does not enable us to compare its results with studies that used algorithms focused on achieving endpoints directed by invasive monitoring. In those studies, however, patients did not receive overly large volumes of fluid but were adequately resuscitated to optimize oxygen delivery. Finally, the postoperative management of patients undergoing intraabdominal surgery is frequently institution and department specific. Some surgical centers start oral intake of fluid early in the postoperative period. Nevertheless, this may add up to a significant amount as shown in a recent study,[12] and the results may therefore be applicable to these patients as well. Further studies are needed to address this point.

Significant healthcare resources are used to provide care to patients with prolonged postoperative hospitalization. Clinicians, hospitals, and healthcare payers are increasingly focusing on reducing "unnecessary" days of hospitalization after surgery. Gastrointestinal dysfunction has a substantial effect on resource utilization.[29] In two large studies that included patients undergoing major noncardiac surgeries, Bennett-Guerrero et al.[30,31] demonstrated that gastrointestinal dysfunction was the most common morbid event that was associated with prolongation of hospital stay. The current study found that intraoperative use of "restrictive" fluid regimen shortens return of gastrointestinal function and reduces the number of patients experiencing postoperative complications with subsequent shortening of hospital stay. The results from this trial demonstrate that some morbidity observed in surgical patients may be preventable by using this fluid strategy. As this study evaluated only two volumes of fluid and focused only on intraoperative management; it is possible to speculate that a different dose regimen might have further improved outcome. Therefore, additional studies are needed to establish the optimal volume of fluid to be infused during and after intraabdominal surgery and other major procedures.

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